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Research report

Excessive lever pressing following post-training signal attenuation in rats: A possible animal model of obsessive compulsive disorder?

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Abstract

This study aimed at developing a rat model of obsessive compulsive disorder based on the hypothesis that a deficient response feedback mechanism underlies obsessions and compulsions. Rats were trained to lever press for food, whose delivery was signaled by the presentation of a compound stimulus (light + tone). Subsequently, the classical contingency between the stimulus and food was extinguished (signal attenuation). Experiment 1 showed that this manipulation resulted in increased lever pressing during a subsequent extinction test, which was highly correlated with an increase in the number of trials on which the rat did not attempt to collect the food reward. This behavioral pattern was not evident in an extinction test not preceded by signal attenuation (Experiment 2), suggesting that the latter is a crucial factor in the development of this behavioral pattern. Excessive lever pressing was attenuated by the selective serotonin re-uptake inhibitor, fluoxetine (10 mg/kg; Experiment 3), but not by the anxiolytic drug, diazepam (2 mg/kg; Experiment 4). Based on these results we propose that post-training signal attenuation may provide a rat model of obsessive compulsive disorder.

Keywords: Animal model; Diazepam; Fluoxetine; OCD (obsessive compulsive disorder); Post-training signal attenuation; Rat

1. Introduction

Obsessive compulsive disorder (OCD) is a psychiatric affliction with a lifetime prevalence of 1–3% [24,29]. DSM-IV classifies OCD as an anxiety disorder characterized by obsessive thinking and compulsive behavior. A major characteristic of obsessions and compulsions is that they are excessive and unreasonable [3]. However, both obsessions and compulsions (e.g., doubting, checking, washing) may be viewed as an exaggeration of normal thoughts and behaviors [21,25,27].

Most current animal models of OCD can be divided into two classes, ethological and pharmacological. The former include naturally occurring repetitive or stereotypic behaviors, such as tail chasing, fur chewing, weaving, etc. (for review see Refs. [32,36]); innate motor behaviors that occur during periods of conflict or stress (displacement behaviors) such as grooming, cleaning and pecking (for review see Ref. [22,28,36]); and natural behaviors that occur following some behavioral manipulations, such as schedule-induced polydipsia [37] and food restriction-induced hyperactivity [2]. Pharmacological models are based on drug-induced behavioral alterations which bear a similarity to some specific characteristics of the behavior of humans diagnosed with OCD, such as perseveration and indecision [39], or compulsive checking [6,33].

It has been suggested that obsessions and compulsions result from a deficient response feedback mechanism or deficient signaling that the conditions have changed following the organism's response. As a result, the successful completion of an action does not lead to the cessation of that action, as would normally occur (e.g., [10,14,22,26], for review see Refs. [19,20]). The aim of the present study was to test, in rats, whether attenuation of an external feedback for operant behavior will lead to an excessive emission of this behavior.

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The procedure included four stages. In the first stage (magazine training) rats underwent classical conditioning to a compound stimulus (light + tone) and food, thus establishing the stimulus as a signal for the delivery of food. In the second stage (lever press training) rats were trained to lever press for food in a discrete-trial procedure (i.e., the levers were introduced into the operant box at the beginning of each trial and retracted from the box after the rat inserted its head into the food magazine to collect the food reward). Food delivery was signaled by the stimulus. In the third stage (signal attenuation) rats underwent extinction of the classical contingency between the stimulus and food. We hypothesized that the extinction of the stimulus–food contingency in this stage would attenuate the feedback provided by the stimulus on the effectiveness of the lever press response. At the last stage (test), rats' lever press behavior was assessed under extinction conditions, i.e., pressing the lever resulted in the presentation of the stimulus, but no food was delivered. As in stage 2, the levers were retracted from the operant box only after the rat inserted its head into the food magazine, thus allowing the rat to make more than one lever press response per trial.

Since Experiment 1 showed that the procedure was effective in producing excessive lever pressing, and that this behavior was highly correlated with trials on which the rat did not attempt to collect a reward, three additional experiments were conducted to further establish this procedure as a rat model of OCD. Experiment 2 tested whether the same behavioral pattern was also induced by regular extinction of the lever press behavior (i.e., not preceded by the signal attenuation stage), and Experiments 3 and 4 tested whether this pattern would be selectively blocked by the serotonin re-uptake inhibitor (SSRI), fluoxetine, but not by the anxiolytic drug, diazepam, in accord with the differential efficacy of these drugs in treating OCD patients [5,23,40].

2. Materials and methods

2.1. Subjects

Male Wistar rats (Tel-Aviv University Medical School, Israel), approximately 3 months old, weighing 300–420 g, were housed 4 to a cage under reversed cycle lighting (lights on 19:00–07:00 h). They were maintained on a 22 h food restriction schedule with freely available water, and weighed twice a week to ensure that their body weight was not reduced below 90%.

2.2. Apparatus

Behavioral testing was conducted in four operant chambers (Campden Instruments, UK) fitted with a food magazine and two retractable levers (4 cm wide, positioned 2.8 cm from the side walls, 7.5 cm on each side of the food magazine and 5 cm from the grid floor). The chambers could be illuminated by a house light located on the ceiling. Access to the food magazine was through a hinged perspex panel, the opening of which activated a micro-switch. The food magazine could be illuminated by a 3 w light. A 80 dB, 2.8 kHz tone was produced by a Sonalert module (model SC 628). A food dispenser delivered 45 mg 'dustfree' sucrose pellets (Noyes). The operant chambers were housed in sound-attenuated boxes with ventilating fans mounted on the side of each box. Equipment programming and data recording were computer controlled.

2.3. Procedure

2.3.1. Handling

Prior to the beginning of the experimental procedure, rats were handled for about 2 min daily for 5 days. A 22 h food restriction schedule was initiated simultaneously with handling and continued throughout the experiment. Food in the home cage was given between 14:00–16:00 h, and at least half an hour after the end of the behavioral session. On the last 2 days, following handling, 20–30 food pellets used as reinforcement for operant training were introduced into the home cages on a tray. The tray was removed from the cage only after each rat was observed to consume at least two pellets.

The experimental procedure consisted of four stages as follows

2.3.2. Magazine training

On days 1–3, rats were trained to collect food pellets from the food magazine in the operant chamber, with the levers retracted. On the 1st day of magazine training, six food pellets were placed in the food magazine, and training began only after each of the four rats had collected its food pellets. At the start of each trial, the house light was turned on. Following a 5 s variable delay, a single food pellet was dropped into the food magazine, simultaneously with the onset of a compound stimulus consisting of the magazine light and a tone. The compound stimulus and house light were turned off after the rat's head entered the food magazine or after 15 s. Each trial was followed by a 30 s inter-trial interval. Each rat was trained until it collected 30 food pellets or until 40 trials were attained.

2.3.3. Lever press training

On days 4–6 rats were trained to lever-press using a discrete-trial procedure. The start of each trial was signaled by the onset of the house light. Five seconds later, both levers were introduced into the chamber.

Responding on one of them (reinforced lever, RL) resulted in the delivery of a single food pellet into the magazine, accompanied by the presentation of the compound stimulus. The levers were retracted and the compound stimulus and house light turned off after the rat's head entered the food magazine or after 15 s had elapsed. Responding on the other lever (NRL) had no programmed consequences. The lever designated as RL remained the same for each rat over the entire experimental procedure but was counterbalanced across subjects. Each trial was followed by a 30 s inter-trial interval. On day 4, each rat was trained until it collected 24 food pellets or until 60 trials were attained. Rats which failed to collect at least 20 pellets, were returned to the test chamber at the end of the day for an additional session. Rats which did not collect at least 20 pellets in the second session were excluded from the experiment. On days 5 and 6, all rats were trained as on day 4, except that the compound stimulus was turned off after 10 s instead of 15 s, and training ended when the rat collected 40 food pellets or when 60 trials were attained. The following measures were recorded: (1) the number of unrewarded lever presses on each trial, i.e., the number of presses following the first response on the RL (extra lever-presses) and the number of lever presses on the NRL; and (2) the number of trials, in ten-trial blocks, in which the rat did not press the lever (un-pressed trials), pressed the lever and inserted its head into the food magazine (completed trials) and pressed the lever without inserting its head into the food magazine (uncompleted trials).

2.3.4. Signal attenuation

On days 7–9, with the levers retracted, rats were exposed to the presentation of the compound stimulus as on days 1–3, but no food was delivered to the food magazine (i.e., pressing the lever resulted in the presentation of the stimulus only). Rats received 40 such trials on each day.

2.3.5. Test

On day 10, rats were trained as on days 5–6 but no food was delivered to the food magazine (i.e., pressing the lever resulted in the presentation of the stimulus only), and training lasted for 50 trials.

2.4. Drugs

Drugs were administered IP in a volume of 1 ml/kg 30 min prior to the beginning of the test session. Fluoxetine (Sigma) was dissolved in distilled water and administered at a dose of 10 mg/kg. Diazepam (Sigma) was diluted with saline and administered at a dose of 2 mg/kg. These doses were selected based on previous studies testing the behavioral effects of acute administration of these drugs (fluoxetine: [2,11,17,30,37,39], diazepam: [8,31,34]). In addition, in a preliminary study we found that 4 mg/kg diazepam abolished responding in the test stage. No-drug controls received an equivalent volume of the corresponding vehicle.

2.5. Experimental design

2.5.1. Experiment 1

Twenty four rats were tested in the post-training signal attenuation procedure described above.

2.5.2. Experiment 2

Twenty four rats were randomly assigned to two groups, one of which underwent regular extinction of the lever press behavior (i.e., stages 1, 2 and 4) and the other underwent extinction preceded by signal attenuation (i.e., stages 1–4). During stage 3, rats in the regular extinction group were brought to the laboratory and left in their home cages for the duration of time of the signal attenuation stage in the other group.

2.5.3. Experiment 3

Sixteen rats were randomly assigned to two drug conditions, fluoxetine and vehicle, and trained in the post-training signal attenuation procedure (stages 1–4).

2.5.4. Experiment 4

Thirty two rats were randomly assigned to two drug conditions, diazepam and vehicle, and trained in the post-training signal attenuation procedure (stages 1–4).

3. Results

3.1. Experiment 1: post-training signal attenuation

Of the 24 rats tested, seven needed a second training session on day 4. One of these rats did not attain the criterion of 20 completed trials and was excluded from the experiment. Thus, the final analysis included 23 rats.

From the second day of lever press training, rats rarely pressed the NRL, and on the last day of lever press training all rats attained 40 completed trials with no more than 2 un-pressed trials and no uncompleted trials.

There was an increase in lever presses on the RL in the test (mean extra lever-presses per trial = 1.109, SE = 0.183) compared with the last training session (mean = 0.482, SE = 0.062), without a comparable increase on the NRL (none of the rats pressed the NRL

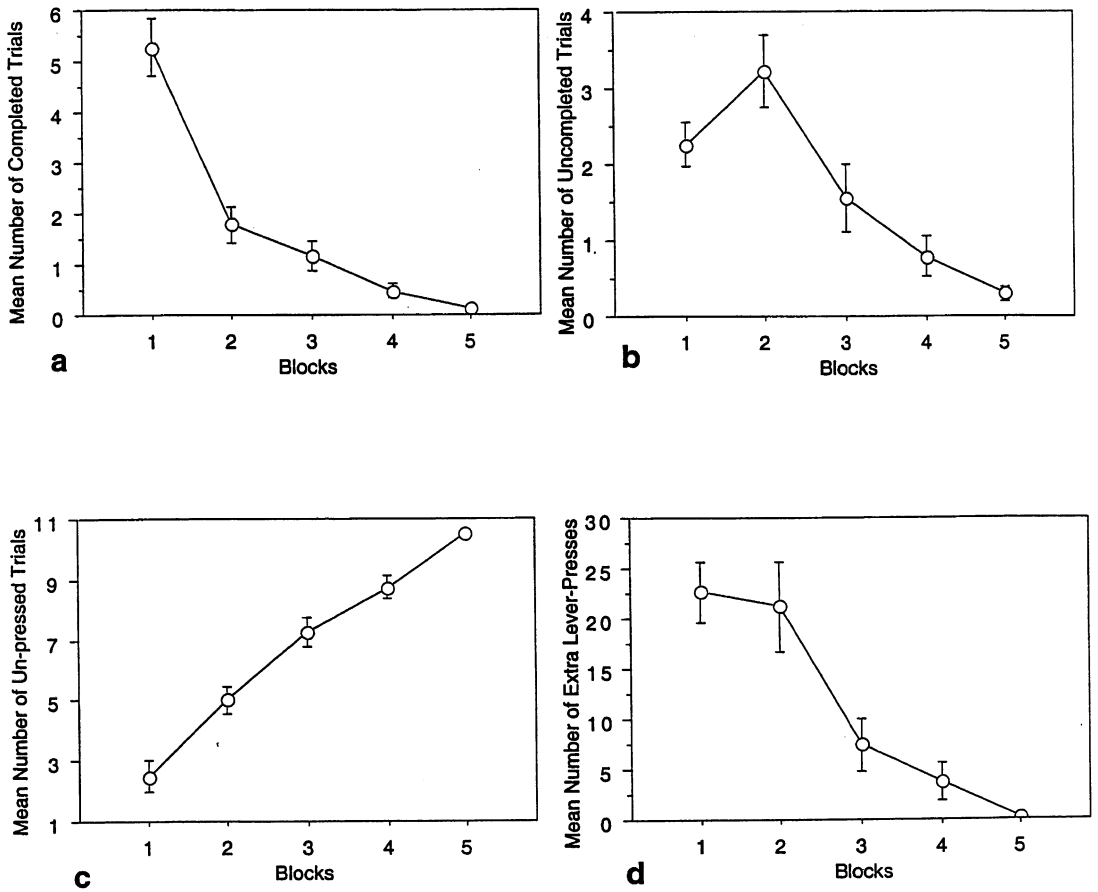

Fig. 1. Mean number of (a) completed, (b) uncompleted, and (c) un-pressed trials and (d) mean number of extra lever-presses, in ten trial blocks, on the test day.

on the last training session and only two of the 23 rats pressed it on the test, mean extra lever-presses per trial = 0.348, SE = 0.248). ANOVA with two repeated measurements factors of lever (RL, NRL) and day (last training day, test) yielded significant effects of lever and day, as well as a significant lever × day interaction, $F(1,22) = 60.66$, $P < 0.0001$, $F(1,22) = 12.20$, $P < 0.01$, and $F(1,22) = 12.53$, $P < 0.01$, respectively.

Fig. 1a-d presents the number of completed, uncompleted, and un-pressed trials and the number of extra lever-presses, respectively, in ten trial blocks, on the test day. As can be seen, as the session progressed the number of completed trials gradually decreased while that of un-pressed trials increased, as can be expected in extinction. In addition, in the first two blocks rats exhibited two behaviors which were rarely seen on regular training trials, namely, pressing the lever without attempting to collect food from the food magazine (uncompleted trials; mean on last training session was 0) and pressing the lever more than once per trial (extra lever-presses). Both behaviors gradually decreased after the first two blocks. ANOVAs with a repeated measurements factor of blocks performed on the number of completed, uncompleted, and un-pressed trials and extra lever-presses yielded significant effect of blocks (all $P < 0.0001$).

In order to assess whether extra lever-presses were specifically related to either completed or uncompleted trials, the correlations between the number of extra lever-presses and the number of completed trials as well as between the number of extra lever-presses and the number of uncompleted trials were calculated for each of the five test (ten trials) blocks. Table 1 presents these correlations. As can be seen, whereas in each of the

Table 1
The correlations between the number of extra lever-presses and the number of completed trials as well as between the number of extra lever-presses and the number of uncompleted trials for each of the five test (ten trials) blocks

Block number	Completed × extra lever-presses	Uncompleted × extra lever-presses
1	0.091	0.487*
2	−0.04	0.697*
3	0.06	0.822*
4	0.694*	0.841*
5	0.013	0.537*

* Correlation is significantly ($P < 0.05$) different from 0.

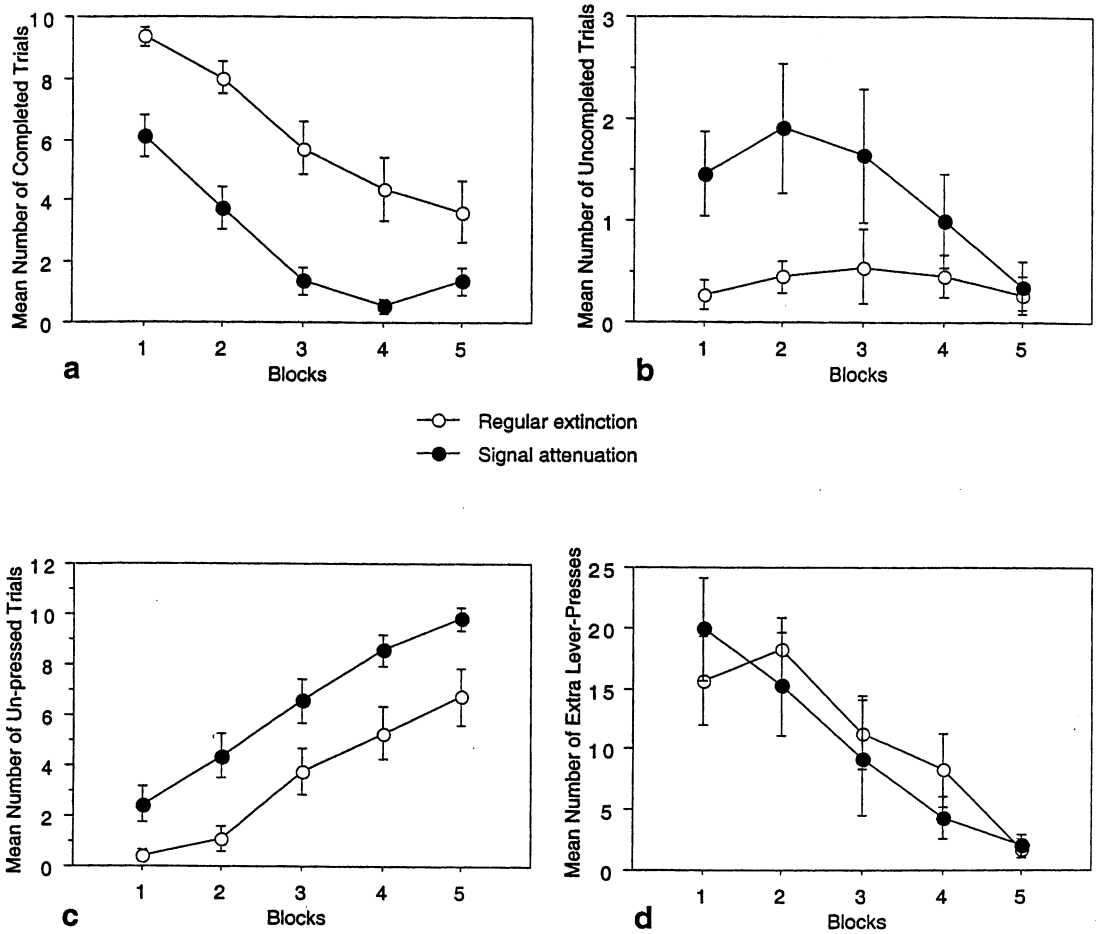

Fig. 2. Mean number of (a) completed, (b) uncompleted, and (c) un-pressed trials and (d) mean number of extra lever-presses, in ten trial blocks, on the test day, of rats in the signal attenuation and regular extinction groups.

blocks the correlation between extra lever-presses and uncompleted trials was significant, the correlation between extra lever-presses and completed trials was significant only in the fourth block.

3.2. Experiment 2: post-training signal attenuation versus regular extinction

Of the 24 rats tested, six needed a second training session on day 4. Two of these rats did not attain the criterion of 20 completed trials and were excluded from the experiment. Thus, the final analysis included 11 rats in each group.

There were no differences between the two groups in the magazine and lever press training stages. From the second day of lever press training rats rarely pressed the NRL, and on the last day of lever press training all rats attained 40 completed trials with no more than one un-pressed trial and no uncompleted trials. In both groups there was no increase in lever presses on the NRL in the test stage.

Fig. 2a-d presents the number of completed, uncompleted, and un-pressed trials, and the number of extra lever-presses, respectively, of the two groups in ten trial blocks, on the test day. As can be seen, both groups had a similar number of extra lever-presses. However, rats in the signal attenuation group had less completed and more un-pressed trials, reflecting faster extinction, and more uncompleted trials than rats in the regular extinction group. One way ANOVAs with a main factor of condition (signal attenuation, regular extinction) and a repeated measurements factor of blocks performed on the number of completed, uncompleted, and un-pressed trials yielded a significant effect of condition $F(1,80) = 40.974$, $P < 0.0001$, $F(1,80) = 5.229$, $P < 0.05$, and $F(1,80) = 14.862$, $P < 0.001$, respectively, whereas the effect of condition on the number of extra lever-presses was not significant ($F < 1$). Similarly, comparison of the mean number of extra lever-presses per trial on the last training session (day 6) and on the test (day 10; Fig. 3) yielded only a significant effect of day $F(1,20) = 24.840$, $P < 0.0001$.

The correlations between the number of extra lever-presses and the number of completed trials, as well as between the number of extra lever-presses and the number of uncompleted trials, for each group in each

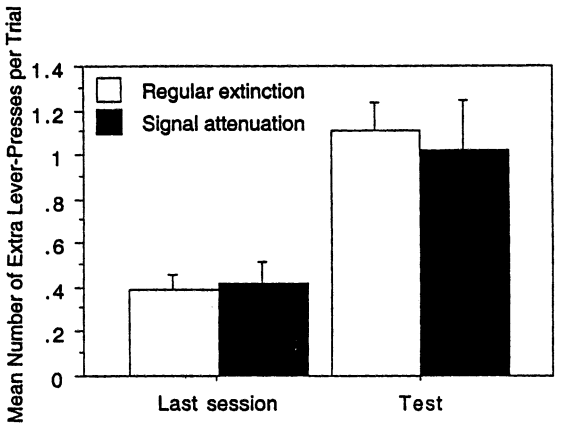

Fig. 3. Mean number of extra lever-presses per trial on the last training session and on the test of rats in the signal attenuation and regular extinction groups.

of the five test blocks are presented in Table 2. As can be seen, in the signal attenuation group, in each of the blocks except for the first one, the correlation between extra lever-presses and uncompleted trials was significant, whereas none of the correlations between extra lever-presses and completed trials was significant. In contrast, in the regular extinction group, the correlation between extra lever-presses and uncompleted trials was significant only in the third and fourth blocks and the correlation between extra lever-presses and completed trials was significant in the fourth block.

3.3. Experiment 3: the effects of fluoxetine in the post-training signal attenuation procedure

Of the 16 rats tested, two needed a second training session on day 4. The final analysis included eight rats in each drug condition.

There were no differences between the two groups in stages 1–3. As in previous experiments, in both groups there was no increase in the number of lever presses on the NRL in the test compared to the last training session.

Fig. 4a-d presents the number of completed, uncompleted, and un-pressed trials and the number of extra lever-presses, respectively, of the two groups in ten trial blocks, on the test day. As can be seen, fluoxetine did not affect the number of completed, uncompleted, and un-pressed trials, but significantly reduced the number of extra lever-presses. One way ANOVAs with a main factor of drug and a repeated measurements factor of blocks performed on the number of completed, uncompleted, and un-pressed trials yielded only a significant effect of blocks (all $P < 0.0001$), whereas an ANOVA performed on the number of extra lever-presses yielded significant effects of drug $F(1,52) = 4.642$, $P = 0.0505$ and blocks $F(4,52) = 10.707$, $P < 0.0001$. Similarly, comparison of the mean number of extra lever-presses per trial on the last training session and on the test (Fig. 5) yielded a significant effect of day $F(1,13) = 7.938$, $P < 0.05$ as well as a nearly significant drug × day interaction $F(1,13) = 3.540$, $P = 0.0825$.

In addition to reducing the number of extra-lever-presses, the administration of fluoxetine abolished the correlation between extra lever-presses and uncompleted trials seen in the vehicle group (Table 3). Thus, whereas in the vehicle group the correlation between extra lever-presses and uncompleted trials was significant in four out of the five blocks, while the correlation between extra lever-presses and completed trials was significant in none of the blocks, in fluoxetine-treated rats the correlation between extra lever-presses and uncompleted trials was significant only in the first block, and the correlation between extra lever-presses and completed trials was significant in two blocks.

3.4. Experiment 4: the effects of diazepam in the post-training signal attenuation procedure

Of the 32 rats tested, four needed a second training

Table 2
The correlations between the number of extra lever-presses and the number of completed trials as well as between the number of extra lever-presses and the number of uncompleted trials for each of the five test (ten trials) blocks for the signal attenuation and the regular extinction groups

Condition	Block number	Completed × extra lever-presses	Uncompleted × extra lever-presses
Signal attenuation	1	0.043	0.597
	2	0.409	0.681*
	3	0.258	0.950*
	4	0.345	0.938*
	5	−0.071	0.927*
Regular Extinction	1	0.215	0.073
	2	0.180	0.367
	3	0.375	0.646*
	4	0.674*	0.670*
	5	0.334	−0.028

* Correlation is significantly ($P < 0.05$) different from 0.

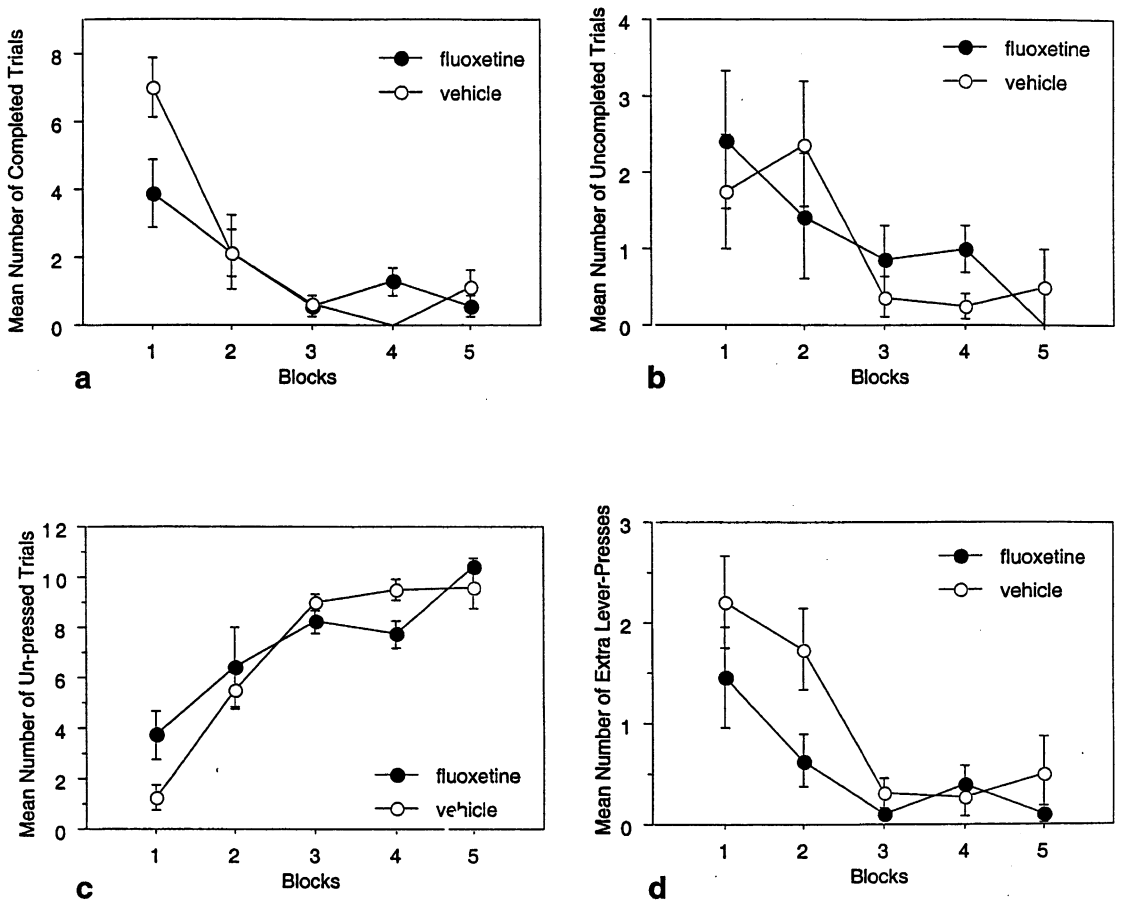

Fig. 4. Mean number of (a) completed, (b) uncompleted, and (c) un-pressed trials and (d) mean number of extra lever-presses, in ten trial blocks, on the test day, of rats in the vehicle and fluoxetine groups.

session on day 4. Two of these rats did not attain the criterion of 20 completed trials and were excluded from the experiment. Thus, the final analysis included 14 rats in the vehicle group and 16 in the diazepam group.

There were no differences between the two groups in stages 1–3, and in both groups there was no increase in lever presses on the NRL in the test.

Fig. 6a-d presents the number of completed, uncompleted, and un-pressed trials and the number of extra lever-presses, respectively, of the two groups in ten trial blocks, on the test day. As can be seen, there were no differences between the two groups in any of the measures. One way ANOVAs with a main factor of drug and a repeated measurements factor of blocks performed on the number of completed, uncompleted, and un-pressed trials, and the number of extra lever-presses yielded only a significant effect of blocks (all $P < 0.0001$, except for the number of uncompleted trials in which $P = 0.06$). Similarly, comparison of the mean number of extra lever-presses per trial on the last training session and on the test (Fig. 7) yielded only a significant effect of day $F(1,28) = 20.054$, $P < 0.0001$.

The administration of diazepam did not affect the correlation between extra lever-presses and uncompleted trials (Table 4). Thus, in vehicle-treated rats the correlation between extra lever-presses and uncompleted trials was significant in four blocks, whereas the correlation between extra lever-presses and completed trials was significant in one block. Similarly, in diazepam-treated rats the correlation between extra lever-presses and

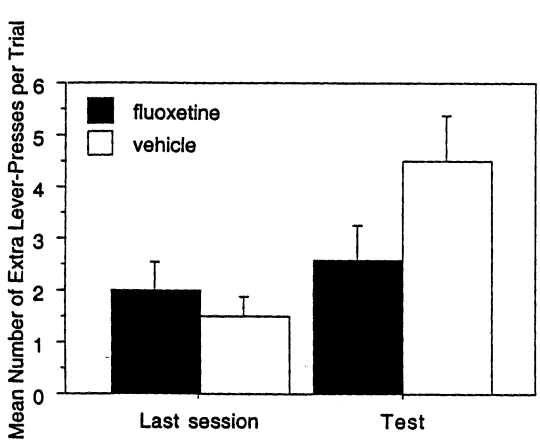

Fig. 5. Mean number of extra lever-presses per trial on the last training session and on the test of rats in the vehicle and fluoxetine groups.

Table 3
The correlations between the number of extra lever-presses and the number of completed trials as well as between the number of extra lever-presses and the number of uncompleted trials for each of the five test (ten trials) blocks for the vehicle and fluoxetine groups

Drug	Block number	Completed × extra lever-presses	Uncompleted × extra lever-presses
Vehicle	1	0.105	0.290
	2	−0.122	0.822*
	3	0.017	0.953*
	4		0.987*
	5	0.682	0.986*
Fluoxetine	1	0.384	0.806*
	2	0.919*	0.489
	3	0.423	0.694
	4	0.344	0.511
	5	0.853*	

* Correlation is significantly ($P<0.05$) different from 0.

uncompleted trials was significant in four blocks, whereas the correlation between extra lever-presses and completed trials was not significant in any of the blocks.

4. Discussion

The present study showed that extinction of a classical contingency between a stimulus signaling the availability of reward following a lever press response and the reward, led, in a subsequent test stage in which lever pressing resulted in the presentation of the signal only (i.e., extinction of operant behavior), to increased emission of the lever press response which was associated with an increased number of trials in which the rat did not attempt to collect a food pellet from the food magazine. This behavioral pattern was not seen in regular extinction, i.e., not preceded by signal attenuation (Experiment 2). Excessive lever-pressing and its association with uncompleted trials was abolished by acute administration of the SSRI, fluoxetine, but not of the anxiolytic drug, diazepam (Experiments 3 and 4). These results suggest that attenuation of an external feedback of an operant behavior may provide an animal analogue to a deficient response feedback mechanism, which has been suggested to underlie obsessions and compulsions in OCD patients.

Increased emission of the lever-press response in the test stage is consistent with other reports of increased response rate at the initial stages of extinction, as well as following an encounter of non-reward in other situations (e.g., faster rates of lever-press responding after non-rewarded compared with rewarded responses [15,38], increased running speed in the double runway procedure [4,9]). However, although an increase in lever-press behavior occurred in both conventional extinction and in extinction preceded by signal attenuation, its association with an increased number of trials in which the rat did not attempt to collect a reward was unique to the latter condition.

In addition to regular extinction, our experimental procedure bears some similarities to two other procedures, namely, conditioned reinforcement and post-training reinforcement devaluation. Similarly to conditioned reinforcement procedures, the present procedure includes an early stage of classical conditioning between a neutral stimulus and an unconditioned stimulus. However, the conditioned stimulus in the present procedure does not subsequently serve as a conditioned reinforcer, i.e., it does not serve as a reinforcer for the acquisition of a new operant response in the absence of a primary reinforcer, or used to maintain operant responding in extinction [13]. In fact, in the present procedure the conditioned stimulus is presented without a primary reinforcer (in the test stage) only after its conditioned reinforcer properties have been extinguished (in the signal attenuation stage).

In post-training reinforcement devaluation procedures (e.g., [1]) animals are first trained to perform an operant response to obtain a reward, then the value of the reward is reduced without the rat emitting the response (e.g., by sickness-induced conditioned aversion to the reinforcer), and this is followed by assessment of the operant behavior under extinction conditions. Typically, animals which underwent reinforcement devaluation exhibit faster extinction of the operant response compared to animals which have not received this manipulation. While post-training reinforcement devaluation procedures and the present procedure intersperse between operant training and test a stage in which response outcome is manipulated without the rat emitting the operant response, and both yield faster extinction compared to rats which undergo 'regular extinction', the former attenuates the value of the primary reinforcer (i.e., food) rather than the signal of reward, and does not induce excessive emission of the operant response in the test stage.

The behavioral phenomenon produced by post-training signal attenuation does not lend itself easily to interpretation in terms of its underlying cognitive mech-

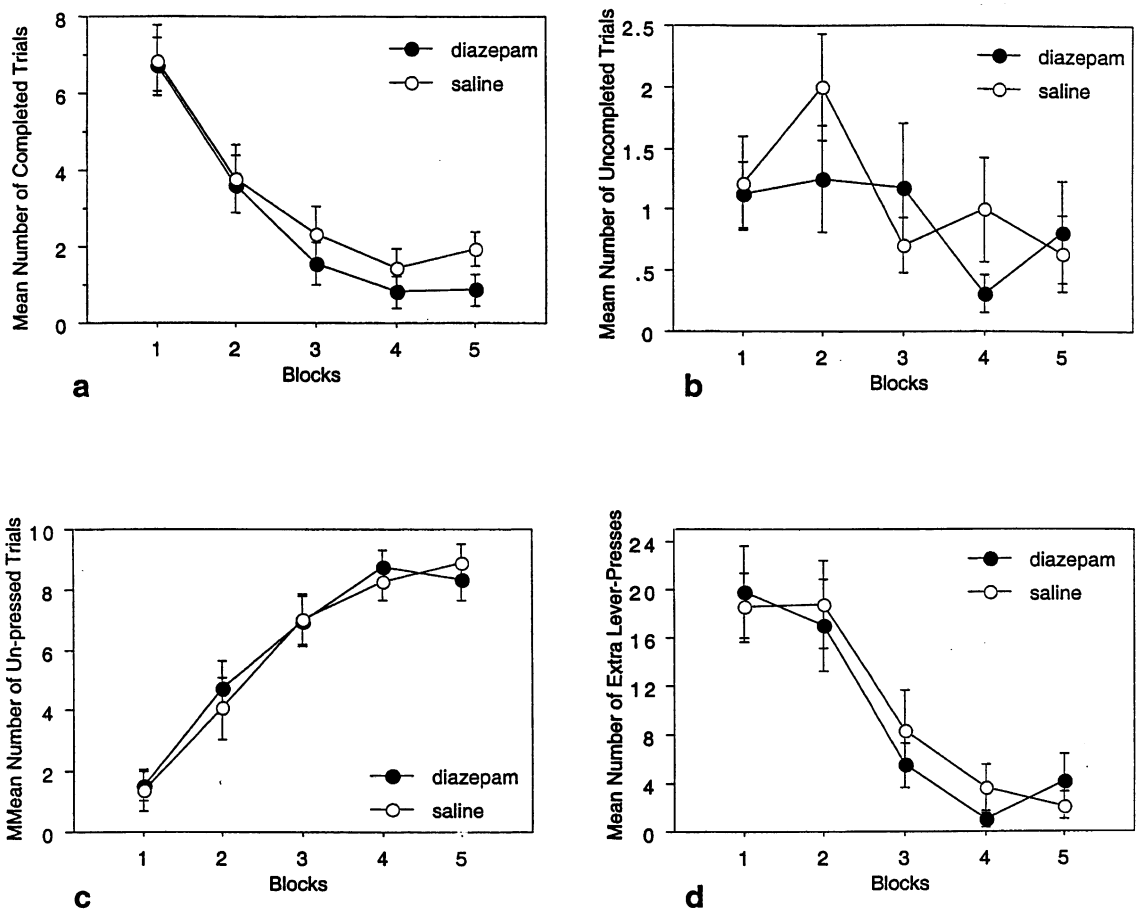

Fig. 6. Mean number of (a) completed, (b) uncompleted, and (c) un-pressed trials and (d) mean number of extra lever-presses, in ten trial blocks, on the test day, of rats in the vehicle and diazepam groups.

anisms. Thus, it cannot be easily described as reflecting increased or decreased resistance to extinction, because different measures of the rats' performance present different pictures, i.e., rats that underwent signal attenuation stopped pressing the lever sooner than rats that underwent regular extinction, but the two groups did not differ in the number of lever press responses (Experiment 2). Likewise, although excessive lever pressing can be seen as reflecting a preseveration of the operant response in spite of changed environmental contingencies, the faster cessation of the attempts to collect a food pellet from the food magazine is suggestive of an enhanced response to changed environmental contingencies. The latter indicates that the observed behavioral pattern does not reflect general insensitivity to response outcomes. Rather, the change in contingencies seems to have exerted different effects on responses which precede the presentation of the conditioned stimulus and those succeeding it. Thus, the emission of the operant response (lever press), for which the stimulus serves as a feedback, was enhanced, whereas the emission of responses elicited by the stimulus, i.e., approaching the food magazine and collecting a food pellet, was decreased. Although these two components seem inconsistent in the sense that the rat increases the emission of a behavior in spite of detecting the change in its consequences, both may result from the weakened association between the stimulus and food. Such a weakening should result, on the one hand, in reduced inhibition of responses for which the stimulus

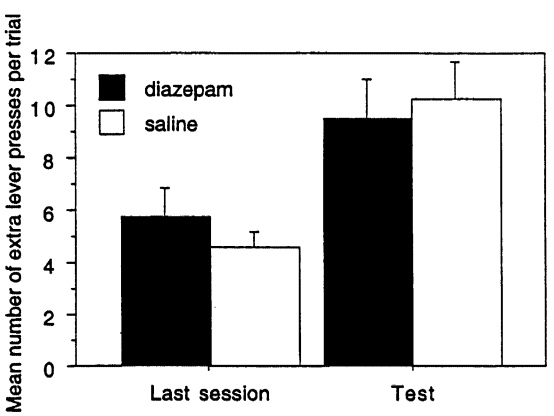

Fig. 7. Mean number of extra lever-presses per trial on the last training session and on the test of rats in the vehicle and diazepam groups.

Table 4
The correlations between the number of extra lever-presses and the number of completed trials as well as between the number of extra lever-presses and the number of uncompleted trials for each of the five test (ten trials) blocks for the vehicle and diazepam groups

Drug	Block number	Completed × extra lever-presses	Uncompleted × extra lever-presses
Vehicle	1	0.517	0.728*
	2	0.159	0.727*
	3	0.300	0.596*
	4	0.684*	0.903*
	5	0.435	0.312
Diazepam	1	0.302	0.577*
	2	0.307	0.668*
	3	0.244	0.847*
	4	−0.165	0.409
	5	0.478	0.724*

* Correlation is significantly ($P<0.05$) different from 0.

provides feedback, leading to their increased emission, and on the other hand, in reduced activation of the responses which the stimulus elicits, leading to their decreased emission.

The apparent inconsistency of the responses to signal attenuation may be particularly relevant to the suitability of the present procedure to serve as an animal model of OCD. It has been often stressed that the mere observation that a specific behavior is repetitive, stereotyped or exaggerated does not suffice to define it as compulsive. Rather, the definition of compulsions relies on the fact that such behaviors are experienced as inappropriate and unreasonable [3,23,27]. An evident limitation of animal models of OCD is that it is not possible to assess the experience associated with the observed behavior. While this applies also to the present model, we suggest that the cessation of the attempts to collect a reward, which indicates that the rat detected the change in response consequences, combined with the increased emission of the lever press behavior, makes the excessive operant behavior 'inappropriate' or 'unreasonable'. Moreover, the present results suggest that such 'unreasonable' behavior may be the consequence of attenuation of a response feedback, as suggested for obsessions and compulsions.

The suggestion that the behavioral pattern induced by signal attenuation may provide an animal model of OCD was further supported by the finding that it was abolished by fluoxetine, but not by diazepam, in line with the differential efficacy of these drugs in treating OCD patients [5,23,40].

The lack of diazepam effect in the test stage may seem surprising given that anxiolytic drugs, including diazepam at the dose used here, have been shown to affect extinction (e.g. Refs. [7,12,16,31,34], but see [8]). The inefficacy of diazepam in the present study may be specifically related to the inclusion of the signal attenuation stage prior to extinction. Alternatively, it may be due to the fact that the present procedure employed a discrete-trial lever press procedure, whereas previous studies employed free-operant procedures [16,34].

To the best of our knowledge, the effects of SSRI's on extinction have not been tested, but these drugs have been shown to reduce excessive behavior in several behavioral paradigms considered to model OCD [2,18,24,33,37]. These studies have typically used chronic administration of SSRIs, because these drugs require several weeks of treatment to produce beneficial effects in humans. The present model detected the effect of an SSRI on excessive behavior, as well as discriminated between an SSRI and an anxiolytic drug, with acute administration of both drugs. As pointed out by Willner [35], the demonstration of drug effects in the model after a period of chronic administration is important for establishing its face validity, but differences in treatment regime (acute vs. chronic) between the animal model and the modeled disease do not undermine the model's predictive validity and its ability to serve as a screening test for treatments for this disease. Clearly, further studies testing the effects of additional doses and drugs in the model are needed to establish whether the present procedure can serve as a screening test for anti-obsessional/anti-compulsive drugs, but the present results provide preliminary evidence for such a capacity.

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