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Changes in Cis(Z)-Flupentixol-induced Dopamine Blockade Produce Contrast Effects in Rats

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Two groups of rats were trained under a 45-sec variable-interval schedule. The magnitude of reinforcement used in each test session alternated daily between one and four 45-mg food pellets, the magnitude of reinforcement available at any time being signalled by lights in the operant chamber. Testing took place over two consecutive 11-day phases. During the first phase one group of rats was injected with 0.06 mg/kg of cis(Z)-flupentixol prior to testing; the other group received vehicle injections. In the second phase drug conditions were reversed. The change in drug conditions between phases produced both positive and negative successive contrast effects, consistent with the hypothesis that dopamine blockade attenuated the hedonic impact of reinforcement. Embedded within each session were two short signalled probe periods during which the reinforcement magnitude was switched to that used on the alternate days. No contrast effects were found during these brief daily probe periods.

A major difficulty in assessing the role of dopamine in reinforcement processing stems from its confounding action on motor processes. For example, any simple effect that dopamine blockade may have in reducing an animal's response to reinforcers can be attributed to a disruption of motor control systems rather than to a reduction in responsiveness to reinforcement. Methods that have been used to circumvent this problem include measuring the effects of dopamine blockade on the distribution of responses between concurrent schedules for food (Heyman, Kinzie, & Seiden, 1986; Heyman, Monaghan, & Clody, 1987; Heyman & Seiden, 1985; Morley, Bradshaw, & Szabadi, 1984) or between amounts of food in a conditional discrimination task (Martin-Iverson, Wilkie, & Fibiger, 1987). Another approach has been to examine the effects of dopaminergic manipulations on intracranial self-stimulation current resetting points selected by the animal (Zarevics

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& Setler, 1979) or on the relationship between response rate and pulse frequency in self-stimulation (Gallistel & Freyd, 1987; Miliaressis, Malette, & Coulombe, 1986). Experiments in which the effect of dopamine blockade can subsequently be measured under drug-free conditions (Ettenberg, 1990; Ettenberg & Horowitz, 1990) can avoid the problems associated with motor effects but may be confounded by state dependence. In spite of the many ingenious experiments that have been undertaken, confounding motor- or state-dependent effects continue to limit our understanding of the role of dopamine in reinforcement mechanisms.

In the present study successive contrast effects (Crespi, 1942) were used in an attempt to dissociate the behavioural actions of dopaminergic drugs. An assumption underlying this study is that contrast effects can be used as markers for sudden changes in the perceived value of rewards. That is, both negative contrast (the excessive decrease in responding following a downshift in reinforcement) and positive contrast (the excessive increase in responding following an upshift in reinforcement) are a consequence of changes in the hedonic impact of rewards.

Successive contrast effects (Figure 1) may be used to investigate the role of dopamine in reinforcement in two ways. (1) Contrast effects produced by manipulating the magnitude of reinforcement (e.g. by changes in the number of food pellets) can be used to assess the action of dopaminergic drugs. If, for example, dopamine blockade does reduce sensitivity to reinforcers, then it might be expected to attenuate both positive and negative

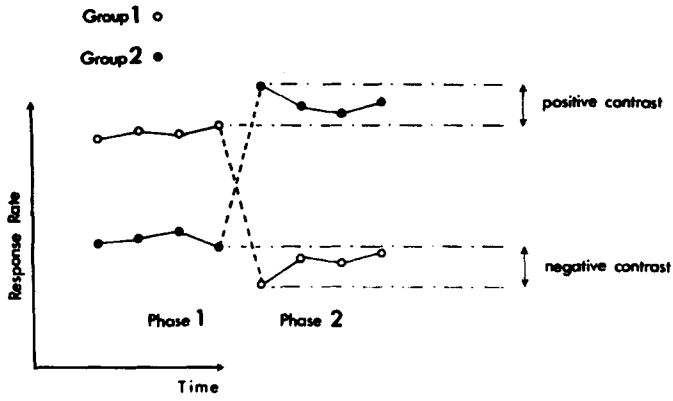

FIG. 1. The response rate comparisons required for testing the presence of successive contrast effects (hypothetical data after Zeaman, 1949). Group 1 receives a high-value reinforcer during Phase 1 and switches to a low-value reinforcer during Phase 2. These conditions are reversed for Group 2. Potential contrast effects are assessed by comparing the response rates of one group at the end of Phase 1 with that of the other group at the beginning of Phase 2.

"reinforcer-induced" contrast effects. The value of studying contrast effects in this way lies in the premise that the same drug cannot attenuate both an upswing and a downswing in responding if its effects are motorific. (2) If dopaminergic drugs affect the perceived values of reinforcers then they may themselves be used to produce "drug-induced" contrast effects. In this way negative contrast would be induced by the introduction of a dopamine antagonist after prolonged training under drug-free conditions. Conversely, positive contrast would be induced by the introduction of a dopamine agonist.

In the present experiment an automated operant task was used to examine both drug-induced and reinforcer-induced contrast effects within a single experimental design. The aim of this design was both to examine the effects of a drug on reinforcer-induced contrast effects and to assess whether the drug could produce drug-induced contrast effects independently of the embedded reinforcer-induced contrast design. The selective dopamine antagonist cis(Z)-flupentixol (Møller-Neilsen et al., 1973), which is almost equally effective in blocking D-1 and D-2 dopamine receptors (O'Boyle & Waddington, 1984), was used as the drug in this study. In order to use the same drug for both positive and negative drug-induced contrast effects, one group of rats was trained under drug-free (saline) conditions and then switched to flupentixol ("negative contrast"), and the other group was trained under flupentixol and then switched to saline ("positive contrast"). The animals received high and low levels of reinforcement on alternate days, the value of reinforcement on a particular day being signalled by a discriminative stimulus. This design exposes animals to differing reinforcer values and so may enhance contrast effects (Benefield, Ocós, & Ehrenfreud, 1974). It does, however, mean that the effects of the change in drug regime must be assessed over two days.

At the same time, the animals were also tested on a reinforcer-induced contrast task that was embedded within the main drug-induced contrast

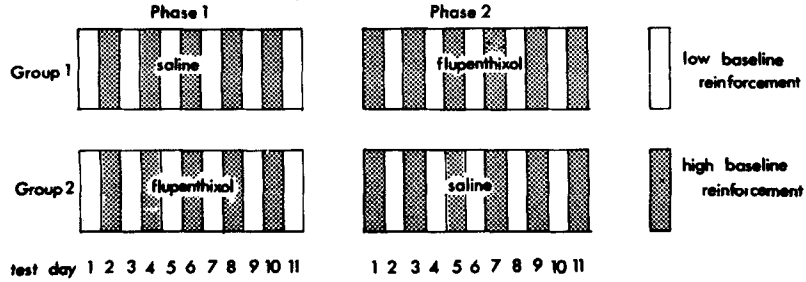

FIG. 2. Diagrammatic representation of the experimental design showing the baseline level of reinforcement and drug condition of each group on every day of the experimental period. Each drug condition lasted throughout a given phase.

experiment (Figure 2). For this embedded task, two short periods were included in each test session where the reinforcement normally obtained on the other day, together with its associated discriminative stimulus, replaced the baseline reinforcement value. This design was used as it has proved possible to measure contrast effects on every day and to look at both positive and negative contrast in the same animals (Baltzer, Hubert, & Weiskrantz, 1979; Baltzer & Weiskrantz, 1970).

The dose of flupentixol used in this experiment was chosen so as to minimize any effects on motor systems. Although doses of between 0.1 and 0.4 mg/kg have typically been used in rats (e.g. Corbett, Stellar, Stinus, Kelly, & Fouriezos, 1983; Ettenberg & Carlisle, 1985; Ettenberg, Koob, & Bloom, 1981), much lower doses can have behavioural effects (e.g. 0.03 mg/kg used by Robbins & Watson, 1981). In the present experiment a dose of 0.06 mg/kg was used, as other studies in this laboratory had shown it to be the lowest dose that reliably affected responses to appetitive reinforcers.

Method

Subjects. The subjects were 23 male rats of the DA strain (Bantin & Kingman, Hull, U.K.), which were caged individually. The animals were housed in a single room with a 14:10 hour light/dark photoperiod, all testing taking place during the light period. At the start of the study the animals were aged about 4 months and weighed approximately 200 g each. The animals were weighed daily and fed an amount of laboratory diet ("Beekay rat and mouse", Bantin & Kingman, Hull) which was individually adjusted to maintain their body weights at 90% (±2%) of their normal body weights.

Apparatus. The apparatus consisted of four standard two-lever Skinner boxes (Campden Instruments Ltd., Loughborough) controlled by a BBC Model B microcomputer (Acorn Computers Ltd., Cambridge) connected to two 16-channel optically isolated laboratory interfaces (Control Universal Ltd., Cambridge). The left lever in each box was kept retracted throughout the experiment.

The operant response levers, which were located 6 cm above the floor, required a response force of 0.1 N for operation. Each box was fitted with a house light in the centre of the ceiling, a white stimulus light 3 cm above the extended right response lever, a red (less intense) stimulus light the same height above the retracted left lever, and a light inside the food hopper.

Procedure. The experiment consisted of 10 days of pre-training and two consectutive 11-day test phases (Figure 2). Animals were maintained at 90% of their ad lib body weights throughout the experimental and pre-training periods.

Animals were magazine trained and gradually introduced to a pseudo-random variable-interval 45-sec (VI 45) reinforcement schedule over 10 days. Schedule operation was signalled by the stimulus light above the extended response lever. Once a reinforced response had been made, this light was turned off for an 8-sec reinforcement period, and two food pellets (45-mg food pellets, Campden Instruments Ltd., Loughborough) were dispensed into the food hopper. The first pellet was dispensed immediately after the reinforced response, the second followed 4 sec later. The food hopper light was turned on during the 8 sec of the reinforcement period. The solenoid-operated food dispenser made a clearly audible click each time a pellet was dispensed.

In the experimental period the low and high magnitudes of reinforcement were one and four pellets, respectively. When a reinforced response was made, pellets were dispensed at 4-sec intervals, making a reinforcement period of 16 sec for the high-reward condition and 4 sec for the low-reward condition. Differential stimuli were associated with each reward magnitude. For half of the animals the house light signalled the high reward, and the red stimulus light above the second retracted lever signalled the low reward (with the house light extinguished), whereas for the other animals these stimuli were reversed. In both conditions the light above the extended lever served as the discriminative stimulus signalling schedule operation. Each animal's daily test session lasted 45 min.

Animals were divided into two groups in order to assess drug-induced contrast effects. One group of 12 animals received cis(Z)-flupentixol (Lundbeck, Copenhagen), dissolved in 0.9% saline at a dose of 0.06 mg/kg body weight and injected intra-peritoneally in a volume of 1.0 ml/kg body weight, for the first 11 test days and then switched to an equal volume of saline for the remaining 11 test days (Figure 2). Conversely, the other group of 11 animals received saline in the first test phase and flupentixol in the second test phase. These injections were made 2½ hours before each daily session. Both groups received the same value of reinforcer on any day, with high- and low-reinforcement days alternating (Figure 2).

The design of the embedded reinforcer-induced contrast experiment was based on that of Baltzer and Weiskrantz (1970). During any session, one level of reward (1 or 4 pellets) was available during most of the session, and the contrasting level of reward (4 or 1 pellets) and its associated stimulus was available during two short probe periods. These probe periods started immediately after a reinforcement period and lasted 4 min. The

onset of the probe periods was quasi-random, with the constraints that the first probe period started no earlier than 11 min into the session and the second probe followed between 6 and 23 min later.

Analysis

Drug-Induced Contrast Effects. Any change in response rate between phases of the experiment must be attributable to the change in drug conditions between phases, and not simply to the drug conditions themselves, if it is to be considered a drug-induced contrast effect. The appropriate comparison for assessing drug-induced contrast is therefore between the response rates produced by animals that have been repeatedly exposed to a given drug condition and those that have just been switched to that condition. This means that positive contrast was assessed by comparing the "saline" response rates of Group 1 (saline, then flupentixol) on the last day of Phase 1 with those of Group 2 (flupentixol, then saline) on the first day of Phase 2. Conversely, negative contrast was assessed by comparing the "flupentixol" response rates of Group 2 on the last day of Phase 1 with those of Group 2 on the first day of Phase 2. As there are clear predictions as to the expected direction of any effects, these analyses were performed as one-tailed tests.

The rate of responding within a session was taken from the period between the first reinforcement and the first 4-min probe period. This period was used as subsequent behaviour in a session might be affected by the change in reinforcement during the 4-min probe period. Response rates were therefore taken during the 4 min preceding the first probe period. Reinforcement periods were excluded from the calculation of these response rates.

Finally, split-plot analysis of variance with the factors day and group were carried out on the response rates produced on all days of Phase 1 in order to assess whether flupentixol significantly affected baseline response rates.

Reinforcer-Induced Contrast Effects. These effects were evaluated by comparing response rates during the probe period of one day with baseline rates of the previous day, the baseline rate coming from the 4-min period immediately prior to the probe. During these periods the animals received the same magnitude of reward, but during the baseline period this was the expected level of reward, whereas during the next day's probe this differed from the baseline level of reward. Separate analyses on the effects of flupentixol on positive and negative contrast were carried out.

Contrast scores were calculated by dividing the difference between these response rates by their sum. That is, the contrast score (C_n) on Day n is given by:

$$C_n = \frac{P_n - Q_{n-1}}{P_n + Q_{n-1}}$$

where P_n is the response rate during the probe period on Day n, and Q_{n-1} is the response rate during the 4 min prior to the probe period on Day $n - 1$.

This analysis produced five negative and five positive contrast scores for each animal during each phase of the experiment. These were then combined to give a mean negative and positive contrast score for each animal in each phase, and these scores were examined in separate 2-way split-plot analyses of variances for negative and positive contrast, each with the between-subject factor group and the within-subject factor phase. As the drug treatment of the two groups is reversed between phases, any effects of flupentixol on contrast will be reflected in the Group × Phase interaction factor in the analysis.

Results

An initial analysis was carried out to confirm that the animals could behaviourally differentiate between the high (4 pellets) and low (1 pellet) magnitudes of reinforcement used in this study. This was achieved by comparing the Phase 1 response rates on alternate days for the 4 min immediately preceding the first probe period of each session (Figure 3; Phase 1, S4 and F4 versus S1 and F1). This comparison showed a large effect of reinforcement size $F(1, 21) = 97.52$, $p < 0.0001$, but no effect of drug ($F < 1$), and no Drug × Reinforcement interaction ($F < 1$). There was a significant day-to-day variation in response rate over Phase 1, $F(1, 21) = 3.21$, $p < 0.05$, but linear trend analysis (Keppel, 1973) indicated that this did not reflect a systematic change in response rate across the 11 sessions ($F < 1$). A Greenhouse–Geisser correction for sphericity (Huynh & Feldt, 1970) in the day factor did not alter the significance of these results.

Drug-Induced Contrast Effects

Negative contrast effects were predicted when Group 1 was shifted from saline to flupentixol, the appropriate comparison being between baseline response rates from the first day of Group 1 with flupentixol and those from the last day of Group 2 with flupentixol (Figure 3). In the high-reward condition (Figure 3, left) this comparison revealed a significant negative contrast effect, $t(21) = 6.31$, $p < 0.0001$. Although evidence of a similar negative contrast effect was found for the low-reward condition (Figure 3, right), the difference between the response rates of Group 2 on the final day of Phase 1 and those of Group 1 on the first day of Phase 2 was not significant.

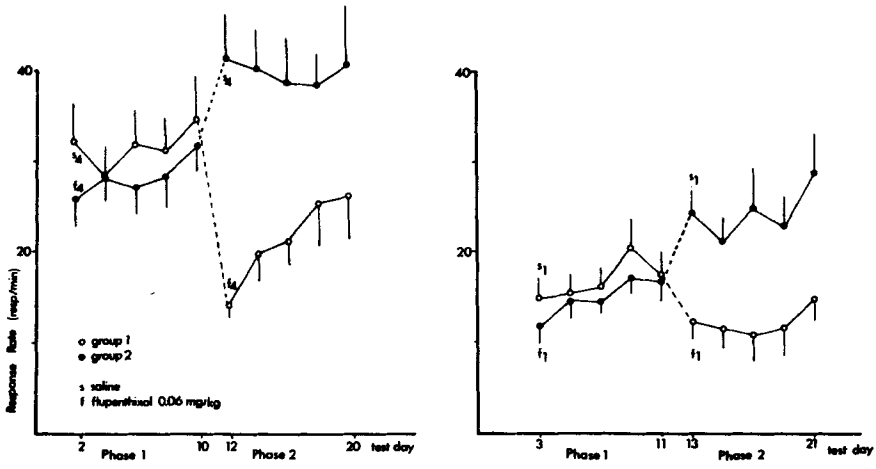

FIG. 3. Mean response rates (and standard errors) during the 4 min preceding the first probe period for the five test days before and after the shift in drug conditions for high-reward days (left) and low-reward days (right). Note that high- and low-reward days alternate, so successive data points in each portion of the figure are drawn from every second day of testing.

Positive contrast effects were predicted when Group 2 was shifted from flupentixol to saline, the appropriate comparison being between the first day of Group 2 with saline and the last day of Group 1 with saline (Figure 3). In the low-reward condition (Figure 3, right) this comparison revealed a significant positive contrast effect, $t(21) = 1.91$, $p < 0.05$. Once again, although there was a similar elevation of response rate in the high-reward condition, the difference in response rates between Groups 1 and 2 were not found to be significant ($t < 1$).

Further evidence that switching the drug condition brought about contrast effects is provided by the within-group changes in response rate between the first two comparable post-shift sessions (presumably reflecting a transient overshoot or undershoot followed by a return towards baseline). The transient nature of the negative contrast effect (Figure 3, left, Group 1) is highlighted by the difference in response rates between the immediate post-shift session and the next comparable session, $t(10) = 2.21$, $p < 0.05$. Similarly, the transience of the positive contrast effect (Figure 3, right, Group 2) is reflected by a significant decrease in response rates from the first to the next comparable session after the change in drug condition, $t(11) = 2.62$, $p < 0.025$. Apart from these two comparisons, none of the other pairs of consecutive sessions in Phase 2 of the experiment produced differences in response rates that approached significance at the 5% level.

Reinforcer-Induced Contrast Effects

The results of the embedded experiment did not show any contrast effects in the probe periods. Although response rates during probe periods increased during high-reinforcement probes, $F(1, 21) = 68.84, p < 0.001$, and decreased during low-reinforcement probes, $F(1, 21) = 37.03, p < 0.001$, these rates did not overshoot the baseline rates for high and low reinforcement as determined from the previous test day. This was found to be the case for both drugged and non-drugged groups. As a consequence, analyses of drug effects on contrast induced by changes of actual reinforcement during the probe periods could not be justified. It should be added that the same pattern of results was obtained when the second probe period within each session was considered. Similarly, removal of the first five sessions from each 11-day phase, to exclude any effect of drug-induced contrast, left the findings unaltered.

DISCUSSION

If dopamine is involved in mediating the magnitude of reinforcement, then negative contrast effects should be expected when dopamine blockade is suddenly initiated. Conversely, positive contrast effects should accompany the cessation of dopamine blockade. The present study obtained just such a pattern of results (Figure 3), showing that both transient negative and transient positive contrast effects can be produced by switches to and from flupentixol. Although clear-cut negative contrast effects were only found when animals were working for the high reward level (Figure 3, left), and clear-cut postitive contrast effects were only found when animals were working for the low reward (Figure 3, right), these findings are consistent with ceiling (Figure 3, left) and floor (Figure 3, right) effects on the levels of responding after the shift. This susceptibility of contrast to ceiling and floor effects has been found in earlier studies, e.g. Panksepp and Trowill (1971); such an effect may often contribute to the elusive nature of positive contrast.

The possibility that the contrast effects observed in the present study reflect either motor or tolerance effects can be rejected. First, the low dose of flupentixol meant that there was no marked fall in baseline response rate during Phase 1 of the experiment (Figure 3), so ruling out any severe motor effects. In addition, a trend analysis of response rates in Phase 1 failed to reveal a signficant increase in response rate across sessions, and this, coupled with the lack of any interaction in Phase 1 with the saline condition, helps rule out any marked tolerance to the drug. As a consequence there is no support for the notion that the negative contrast effect (Figure 3, left) could be the result of a motor effect coupled with a sub-

sequent adjustment or tolerance to the drug. More importantly, this same explanation cannot account for the appearance of a positive contrast effect, where both comparison groups are receiving saline (Figure 3, right). For similar reasons a state-dependency mechanism could not account for *both* increases and decreases of response rates after changes in drug conditions.

A more complex argument for "response–cost"-induced contrast can also be rejected. It could be argued that the net value of a reinforcer to an animal is the hedonic value of the reinforcer less the cost of obtaining the reinforcer. If dopamine blockade increases the cost of obtaining the reinforcer because of a motor effect, then a change in net reinforcement value leading to contrast effects could be produced without any direct effect on hedonia. This argument depends critically on the ability of a change in response cost alone to induce a contrast effect. Studies by Chung (1965) and by Hunter and Davison (1982) examined just this possibility. Neither study reported any evidence for simultaneous contrast following changes in the operant response force requirement. Chung (1965) did report evidence for transient changes in response rates following changes in the force required to make the response but could not measure responses made below the new force requirements as he did not use force-transducing levers. As a consequence, the transient effects upon measured response rate could not be distinguished from those expected in any animal mastering a new response force requirement (see e.g. Notterman & Mintz, 1965, p. 76). This latter account, suggesting that the animals were merely adapting to the new appropriate response force, is also more consistent with the fact that the elevations in response rate following decreases in the force requirement were larger than the depressions in rate following increases in the force requirement—a pattern of results opposite to that typically found with contrast effects (Flaherty, 1982). It is therefore unlikely that response–cost changes could produce the clear-cut contrast effects found here. Of course, response–cost explanations of these results could also be addressed by the use of a positive partially paralytic control treatment; however, in the light of the argument above, this seems unnecessary. The use of a positive sedative control could also resolve any suggestion that apparent contrast effects may be produced by the sedative effects of flupentixol. It is, however, unclear how sedative effects that are not motorific and do not differentially affect the perception of reinforcement through some reinforcement-specific attentional deficit could produce apparent contrast effects.

Previous experiments have examined the actions of dopaminergic drugs on contrast effects, but the findings have been weakened by either the design of the experiment or the choice of drugs. In a study of drug-induced contrast effects Royall and Klemm (1981) reported apparent negative and positive contrast following administration of a dopamine blocker (haloperidol) and a dopamine agonist (apomorphine), respectively. These drugs

were given to rats that had been trained in a food-reinforced runway task under drug-free conditions. Unfortunately, their experiment did not include conditions with animals running under drug treatment from the start of the experiment, and, as a consequence, there were no adequate control groups with which contrast performance could be assessed.

In a very different type of study, Baltzer et al. (1979) studied "reinforcer-induced" contrast effects in rats working on a schedule for food reward. This design, on which the present experiment was based, made it possible to measure drug effects on both positive and negative contrast in the same animals. Unfortunately the only dopaminergic drugs they assessed were chlorpromazine and d-amphetamine, both of which have additional noradrenergic actions. Amphetamine had no effect on contrast, and chlorpromazine produced small attenuation in negative, but not positive, contrast (Baltzer et al., 1979).

The failure of the embedded reinforcer-induced study to produce contrast effects in the present experiment may be attributed to the comparatively short duration of the experiment. The study of Baltzer et al. (1979), which used a comparable design, lasted from 88 to 110 days and included at least 24 days of drug-free training on the full contrast schedule (i.e. alternating high- and low-reward magnitude days with contrast probes) before drug testing began. It is therefore quite possible that reinforcer-induced contrast effects would have been found had a much more extended testing period been used in the present study.

A key feature of the present study was the use of the same drug at the same dose level to produce both positive and negative contrast effects and appropriate controls with which they can be compared. In comparison, previous experiments into the effects of dopamine agonists or antagonists on contrast effects have employed different drugs to mimic positive or negative contrast effects (Royall & Klemm, 1981) or to disrupt positive and negative contrast effects (Baltzer et al., 1979). The demonstration of symmetrical effects of agonists and antagonists of a particular neurotransmitter on a behaviour provides extremely convincing evidence for the mediation of that behaviour by that transmitter; however, our approach of using introduction and cessation of the same drug to produce symmetrical effects also has its advantages. In particular, one does not need to equate doses between different drugs or to address the issue of whether direct or indirect agonists are more appropriate models of the opposite effects of antagonists. By using the same drug throughout, the present experiment has excluded these potential problems, so considerably strengthening this paradigm as a means of investigating the selective actions of dopaminergic systems on reinforcement processing.

Although the embedded reinforcement-induced contrast experiment failed to produce contrast effects, it may have served to accentuate any action of flupentixol on incentive stimuli. It is therefore possible that a

simpler experimental design, which did not include the embedded experiment, may not have produced such convincing drug-induced contrast results. In the embedded experiment animals were exposed to two different values of reinforcement, signalled by different discriminative stimuli. The fact that these stimuli did not control behaviour sufficiently strongly to cause the response rates produced during the probe periods to overshoot the previous day's baseline response rates has two possible causes. (1) The associations of reinforcement values to the discriminative stimuli may have been too weak for the stimuli to control response rates without animals experiencing the associated value of reinforcement directly. (2) The animals may not have been attending sufficiently to the discriminative stimuli for the change in discriminative stimulus during the probe to control response rate. An action of flupentixol that further weakened the associations of reinforcement values with the discriminative stimuli and hence decreased their incentive value is consistent with the results obtained. If, however, flupentixol decreased discriminability between the two incentive stimuli without devaluing the absolute levels of reinforcement associated with them (perhaps through an attentional deficit), then the net effect predicted is that the incentive value of the high-reward discriminative stimulus should be decreased under flupentixol, and that signalling the low reward should increase in perceived value. If these shifts in perceived value were large enough, then the expected effects of the introduction of flupentixol treatment would be negative contrast in the high-reward condition but positive contrast in the low-reward condition. The opposite pattern would be predicted when flupentixol treatment ceased. There was no suggestion of these mixed patterns of contrast effects when flupentixol treatment was introduced or withdrawn in the present experiment.

In conclusion it has been shown that the introduction and cessation of flupentixol treatment produced transient changes in operant response rates, which can be explained most parsimoniously as contrast effects produced by drug-induced changes in the processing of reinforcement-related stimuli. The experimental design makes the explanation of these results in terms of dopamine's involvement in motor control quite implausible. The precise nature of flupentixol's effect on reinforcement processing is not, however, addressed in the current experiment. The results obtained are consistent with two actions that have been attributed to dopamine antagonists. The simplest of these is flupentixol-induced devaluation of primary reinforcement (anhedonia, Wise, 1982); however, effects weakening the incentive value of secondary reinforcers (e.g. Beninger, 1983) would also produce contrast effects in the present design.

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Modifications dans le blocage de dopamine induit par le Cis(Z)-Flupentixol et effets de contraste chez le rat

Deux groupes de rats ont été entraînés avec une protocole d'intervalle de variable de 45 secondes. Le renforcement utilisé lors de chaque session-test était alternativement, chaque jour, une ou quatre croquettes de nourriture de 45 mg. La quantité de renforcement disponible était toujours signalée par des lumières dans le dispositif opérant. L'expérience s'est déroulée en deux phases consécutives de 11 jours. Pendant la première phase, un groupe de rats était injecté avec 0.06 mg/kg de Cis(Z)-Flupentixol avant le test alors que l'autre groupe recevait des injections d'excipient. Lors de la seconde phase, les conditions d'injection étaient inversées. Le changement des conditions d'injection d'une phase à l'autre produit des effets de contraste successifs, positifs et négatifs, en accord avec l'hypothèse selon laquelle le blocage dopaminergique atténue l'impact hédonique du renforcement. A l'intérieur de chaque session, on soumettait les sujets à deux brèves périodes de contrôle pendant lesquelles la quantité de renforcement était celle du jour précédent. On ne trouve pas d'effet de contraste pendant ces brèves phases quotidiennes de contrôle.

Cambios en Bloqueo Dopaminérgico y efectos de contrastes inducidos por Cis(Z)-Flupentixol en ratas

Dos grupos de ratas fueron entrenados en un programa de reforzamiento de intervalo variable de 45 segundos. La magnitud del refuerzo usada en cada prueba alternó diariamente entre uno y cuatro pellets de 45 mg, siendo señalizada en cada caso por luces en la cámara operante. Los ensayos tuvieron lugar en dos fases consecutivas de 11 días cada una. Durante la primera fase un grupo de ratas fue inyectado con 0.06 mg/kg de Cis(Z)-Flupentixol antes de los ensayos mientras que el otro grupo recibió inyecciones control del vehículo solamente. En la segunda fase los tratamientos fueron invertidos. Los cambios en tratamiento entre las fases produjeron efectos de contraste positivos y negativos, consistentes con la hipótesis de que el bloqueo dopaminérgico atenuó el impacto hedónico del refuerzo. En cada sesión se insertaron dos cortos períodos señalizados de prueba durante los que la magnitud del refuerzo se cambió a aquélla usada en los días alternados. No se encontraron efectos de contraste en estos cortos períodos diarios de prueba.