ELSEVIER

European Journal of Pharmacology 426 (2001) 55–63

ejp

www.elsevier.com/locate/ejphar

Differential patterns of performance impairment result from changed reinforcer efficacy or distracting stimulation in a two-choice rodent spatial signal detection task

Jian-Bin Mao [a,b], Gregory Kanhai [a], Diana Moglia [a], John K. Robinson [a,*]

[a] *Department of Psychology, State University of New York at Stony Brook, Stony Brook, NY 11994-2500, USA*
[b] *Department of Neurobiology and Behavior, State University of New York at Stony Brook, Stony Brook, NY 11994-2500, USA*

Received 3 July 2001; accepted 13 July 2001

Abstract

Measures of the discriminabililty of stimuli in signal detection tasks can be influenced by alterations of motivational state. In the present study, rats performed an operant signal detection procedure that required the completion of a fixed number of responses before a stimulus was presented at one of two front cue lamps to separately measure the motivation to respond from the ability to respond accurately. One manipulation, presession water access, affected the speed and frequency that trials were initiated, but did not affect response accuracy. In contrast, a flashing houselight during the session, and i.p. ((5*R*,10*S*)-(+)-5-methyl-10,11-dihydro-5*H*-dibenzo[*a*,*d*,]cyclohepten-5,10-imine (dizocilpine or MK-801), a glutamate *N*-methyl-D-aspartate receptor antagonist, impaired response accuracy in a stimulus duration-dependent manner. These results suggest that it is possible to procedurally isolate the motivation to respond to stimuli from accuracy of detection, and thereby protect attending from side effects of drugs that influence the motivation to respond. © 2001 Published by Elsevier Science B.V.

Keywords: Attention, sustained; MK-801; Motivation; Signal detection

1. Introduction

Variations of the signal-detection paradigm have been used to measure sustained attention in rats (e.g. Bushnell et al., 1997; Moore et al., 1992; Muir et al., 1992; Robbins et al., 1989a,b; Sahgal, 1987). All require that the subject respond either by following the presentation of a stimulus against a masking background ("noise") or based upon the presentation of a stimulus at one of two or more possible spatial locations. Both methods require the application of effort over time, whether detecting a signal against noise, or among presentation places. This conceptualization of attention as effort is especially appropriate for thinking about sustained attention in non-human animals. This is because attention is operationally defined in terms of observable behavior rather than in terms of covert attentional processes only inferred from behavior. This conceptualization points to the importance of the outcome of attending to the animal, and highlights that correct responding to stimuli would not just be based on the physical properties of the stimuli, but also on the relationship between attending and reward.

Signal detection is usually thought of as having to do more with perception than behavior. Non-stimulus factors are conceived of only producing a response bias (β) that is readily dissociated from stimulus detectability (d'; Green and Swets, 1974). Therefore, using this analysis, accuracy measures corrected for bias such as d' would offer the apparent advantage of removing the influence of motivational factors because even an incorrect response is presumably predicated by the same "expectation of reward" as a correct response. However, studies conducted with pigeons (e.g. Davison and McCarthy, 1980; Nevin, 1982) and humans (e.g. Tomporowski and Tinsley, 1996) have demonstrated that measures of the discriminabililty of stimuli can be influenced by alterations of reinforcement contingencies.

For psychopharmacologists, this appears to threaten the construct validity of animal signal-detection tasks. Measures of attention with high construct validity should only measure attention, and not be influenced by reinforcement

* Corresponding author. Tel.: +1-631-632-7832; fax: +1-631-632-7876.
E-mail address: jrobinson@ms.cc.sunysb.edu (J.K. Robinson).

0014-2999/01/$ - see front matter © 2001 Published by Elsevier Science B.V.
PII: S0014-2999(01)01212-2

or motivational factors. One way to isolate response tendency from choice accuracy is to use two spatially distinct choices in a discrimination task where stimulus duration is varied. By presenting the subject with stimulus durations that vary from 100 ms to 2.0 s, one assesses a simple light–dark discrimination along a continuum requiring varying degrees of vigilance. An operant task used previously in our lab and others in which a panel with two cue-lamps with corresponding response levels underneath has been shown to differentiate the effects of drugs known to alter perception and attention in humans (Presburger and Robinson, 1999; also see for example Givens, 1997). In this task, the duration of the cue presented at one or the other cue lamp was varied from 100 ms to 1.0 s. Evidence for the validity of this task was established by observing that choice accuracy diminished as a function of decreased stimulus duration. Presburger and Robinson (1999) also showed that cannabinoid receptor agonist (−)-Δ^9-tetrahydrocannabinol produced an additional reduction in choice accuracy only when the stimulus duration was shortest (called "duration-dependent"), without effects on the rate of response omissions. In contrast, cholinergic muscarinic receptor antagonist (−)-scopolamine hydrobromide and glutamate *N*-methyl-D-aspartate receptor antagonist ((5*R*,10*S*)-(+)-5-methyl-10,11-dihydro-5*H*-dibenzo[*a*,*d*,]cyclohepten-5,10-imine (Dizocilpine or MK-801) produced impairments of choice accuracy at all stimulus durations (a "duration-independent effect"), and a concomitant and substantial decrease in the tendency to respond on either response lever following a stimulus presentation (a response omission). One interpretation of the duration-independent effects is that they resulted from alteration of reward or motivational factors. However, the specific cause of these changes could not be determined as the response omissions measure in this procedure was unable to clearly distinguish effects resulting from a loss of reinforcer efficacy from those resulting from enhanced distractibility to irrelevant contextual stimuli.

To better isolate these potential influences, the present experiments modified the procedures used in Presburger and Robinson (1999) in two ways. The first was to require the subjects to satisfy a fixed ratio of responses to initiate the stimulus presentation, as a way of separating the motivation to respond from the ability to respond accurately to the stimulus. We also decreased the predictability of the stimulus presentation in time to make them more sensitive to mild increases in distractibility. We then performed two manipulations designed (1) to decrease the motivation to initiate a trial, and (2) to enhance distractibility by altering the environmental context. Potentially, both of these manipulations could produce either a failure to initiate trials, an impairment in choice accuracy, or both. Finally, we re-examined the effects of MK-801, to determine if these procedural modifications resulted in a different pattern of impairment than observed previously (Presburger and Robinson, 1999).

2. Methods

2.1. Subjects

The subjects were 30 male Sprague–Dawley rats, maintained on a 23.5-h daily water-restriction regimen on weekdays, and were given unlimited water access on weekends. All subjects were housed individually in plastic tub cages in a temperature- and humidity-controlled room with a 12-h light–dark cycle. All subjects were handled in accordance with the policies of the N.I.H. Guide for the Care and Use of Laboratory Animals (U.S. Department of Health and Human Services, 1985) and the SUNY at Stony Brook Institutional Animal Care and Use Committee.

2.2. Apparatus

All behavioral training and testing were conducted in six identical operant chambers enclosed in sound-attenuating boxes with fans for ventilation and masking extraneous noises (Med Associates, East Fairfield, VT). The dimensions for each chamber were 28 cm in length × 22 cm in width × 28 cm in height. Droplets of water (0.1 ml each) were delivered into a centered aperture of 5 × 5 cm on the front panel as reinforcers. Above the aperture, two response levers were mounted 4 cm above the floor of the chamber, 1.3 cm away from the side-wall and 11.5 cm apart from each other. An identical response lever was mounted centrally on the real panel. A white cue lamp was mounted 6 cm over each lever. A 28-V houselight was mounted above the rear cue lamp. All experimental events and data collecting were controlled by a Micron PC using MEDstate Notation (MED Associates, Hatfield, VT) programming language.

2.3. Behavioral training and testing procedures

All training and testing were conducted between 12:30 p.m. and 5 p.m. on weekdays. In the first two 20-min sessions, an approximately 0.1 ml water droplet was delivered every 15 s, and a press on either front lever led to the immediate delivery of the reward. In the next four sessions, a single press (fixed-ratio 1) at the lever under the illuminated lamp was rewarded, with randomized onset of either left or right lamp to prevent development of a position bias.

In the next three sessions, after a 15-s intertrial interval, the rear lamp was illuminated for 30 s, during which a press at the rear lever extinguished the rear-cue lamp and illuminated one front cue lamp. The illumination time of the front lamp was 10 s, during which a press at the cued lever was rewarded. A press on either lever started the intertrial interval.

In later sessions, the procedures were similar except that the required number of presses at the rear lever was increased in steps, from an fixed-ratio 1 schedule to a

fixed-ratio 4 schedule. When all subjects had met the fixed-ratio 4 requirement, the illumination duration of the rear lamp was reduced to 25, 20, and then 15 s.

As training progressed, illumination time of the front lamp was also gradually decreased to 8, 5 and 2 s. Next, a pre-signal interval with three different durations (a random sampling without replacement among 1, 3 and 6 s) was incorporated between the offset of the rear lamp and the onset of a front lamp and a variable intertrial interval of 10 ± 3 s (a random sampling without replacement among 7, 8, 9, 10, 11, 12 and 13 s intervals) was introduced. Thus, after completing the four presses on the rear lever, the subjects were to make a 180° turn to face the front panel, and wait for the onset of the signal.

At the final training sessions, the illumination time of the front lamp was varied according to a random sample without replacement routine among 100 ms, 500 ms, 1 and 2 s. In addition, a tone was incorporated simultaneously with the onset of the front lamp. Overall, each trial included a rear-pressing phase (15 s), a pre-signal interval (1, 3 or 6 s), a signal (100 ms, 500 ms, 1 or 2 s), and a variable intertrial interval (10 ± 3 ms). A press at the cued lever during the cue or 3 s afterwards led to the termination of the tone, and delivery of the reward. A press at the non-cued lever or a failure to respond within the 3-s limited-hold periods switched off the tone and marked the onset of the intertrial interval. Neither error responses nor choice omissions were rewarded, and these error trials were not repeated. All subjects were trained on this final procedure until at least 40 trials were completed during a 40-min session, and the accuracy of signal detection at the longest stimulus duration was greater than 90%. An additional 10 sessions were collected for assessment of baseline performance, before the subjects were exposed to three successive testing conditions.

2.4. Pre-session water access

In order to systematically alter the degree of deprivation, the subjects were allowed 0, 1, 2, or 5 min water access 10 m before the beginning of the testing session, in a Latin-square order. Baseline sessions intervened between water access sessions.

2.5. Effects of interference by a flashing houselight

Without changing any other parameters, a background visual "noise" was introduced by flashing the houselight at 0.5 Hz during one 40-min session (after McGaughy and Sarter, 1995). The prior baseline session served as a comparison condition.

2.6. Intraperitoneal administrations of MK-801

(+)-MK-801 hydrogen maleate (RBI, Natick, MA) (0.0317, 0.0625 and 0.083 and 0.25 mg/kg) was dissolved in saline solution. These injection doses were based on the results of Presburger and Robinson (1999). The 0.25 dose was chosen because it was shown to produce duration-independent effects in their experiment. The 0.0625 mg/kg dose and the slightly larger 0.083 mg/kg dose was chosen to determine whether smaller doses that have little or no effect on secondary performance measures would affect choice accuracy in the present version of the task. The injected volume was 1 ml/kg. Injections were administered on Tuesday and Thursday, with intervening no-injection days to ensure stable baseline performance. Each rat received one injection of every drug dose or saline in a counterbalanced order. All test sessions began 10 min after the pharmacological treatment.

2.7. Performance assessment

Measures of the subject's performance were drawn from three phases: the rear press phase, the pre-signal delay phase, and the choice phase. During the rear press phase, a subject's failures of responding to the rear lever during the 10-s illumination period of the rear lamp were counted as an *error of rear omission*. *Errors of discontinuity* were defined as failures of a subject to complete all four required presses at the rear lever. In addition, the time from the onset of the rear lamp to the subject's first press at the rear lever was recorded as *initiation latency*.

At the pre-signal phase, the responses emitted prior to the onset of one of the front cues were counted as *anticipatory responses*, and were sorted based on the length of the pre-signal interval. During the last choice phase, the failure of a subject to respond within 3 s of the termination of the cue lamp was counted as a *choice omission*. A correct response was a press at the cued lever during the front cue presentation or within 3 s afterwards. An incorrect response was a press at the non-cued lever during the cue or within 3 s afterwards. When the left cue was on, presses on the left lever were correct responses (a), and presses on the right lever incorrect responses (b). Similarly, with the right cue, right lever presses were correct responses (d) and left lever presses were incorrect responses (c). A mathematical transformation $[x = (x + 0.5)^{1/2}]$ was applied to a, b, c and d, so that dividing by zero was avoided when computing the relative number of hits (h) $[h = a/(a + b)]$ and false alarms (f) $[f = b/(b + d)]$ (Sokal and Rohlf, 1995). For each stimulus duration, a primary performance measure, the *sensitivity index*, was computed using the relative number of hits (h) and false alarms (f) {sensitivity index $= [h - f]/[2(h + f) - (h + f)^2]$} (Frey and Collier, 1973; Sahgal, 1987). Therefore, the sensitivity index ranged from -1 to $+1$, where 0 indicated chance performance, 1 indicated perfect performance, and -1 indicated perfectly inaccurate performance. Furthermore, since the probabilities of left cue and right cue were equal, the *response bias* (Y) for each stimulus duration was defined as the absolute difference

between left and right correct responses divided by their sum [$Y = |a - d|/(a + d)$]. The range of Y was 0 to 1, where 0 indicated no preference, and 1 indicated complete preference for one lever over the other (Sahgal, 1987). Finally, the number of trials completed was counted for every session. A trial were considered as completed when a subject made four presses on the rear bar during the 15-s rear phase, emitted no anticipatory response during the pre-signal interval, and made a press at either front lever during the cue or 3 s afterwards.

2.8. Statistical analyses

The measures of trials completed per session, errors of rear omissions, errors of discontinuity and response latency of initiation were assessed with one-way analyses of variance. The sensitivity index, choice omissions, response bias and anticipatory responses were analyzed with two-way repeated measures analyses of variance. If a main effect was significant, Tukey's Honestly Significant Difference Test was conducted. In case of a significant interaction, a means comparison (an unpaired t-test) was carried out to compare the effects of manipulations at each stimulus duration or pre-signal interval (Keppel, 1991). All analyses were conducted with Statistica (Statsoft, version 5.0).

3. Results

3.1. Baseline performance

Several measurements provided general assessment of the overall performance. An average of 66.47 ± 2.59 trials were completed per session. The response latency of initiation was 3.96 ± 0.43 s. There were three main types of errors prior to cue presentation: errors of rear omissions (35.00 ± 1.93/session), errors of discontinuity (2.44 ± 0.33/session), and anticipatory responses, which all resulted in the cancellation of the trial. Anticipatory responses per opportunity were a positive function of pre-stimulus interval ($0.72 + 0.01$ for the 1 s pre-stimulus interval, $0.84 + 0.01$ for the 3 s pre-stimulus interval, and $1.34 + 0.10$ for the 6 s pre-stimulus interval; $F(2,94) = 31.40$, $p < 0.001$). Tukey's test indicated that there were significantly more anticipatory responses at 6 s than those at 1 s ($p < 0.001$) and 3 s ($p < 0.001$) pre-signal interval, and the anticipatory responses did not differ between 1 and 3 s pre-signal intervals.

The sensitivity index increased significantly as stimulus duration increased. The scores were 0.33 at the 100 ms duration, 0.49 at the 500 ms duration, 0.51 at the 1 s duration, and 0.52 at the 2 s duration [$F(3,141) = 32.26$, $p < 0.001$]. Tukey's Honestly Significant Difference test revealed that sensitivity index of the shortest stimulus duration (100 ms) was significantly different from those at longer stimulus durations (all $p < 0.001$), but the sensitivity index scores at the three long durations were comparable. In addition, choice omissions significantly decreased as stimulus duration lengthened, $F(3,141) = 7.78$, $p < 0.001$, with more errors both at 100 ms ($p < 0.001$) and 500 ms ($p < 0.01$) than those at 1 and 2 s. In contrast, response bias was not affected by changes of signal length, $F(3,141) = 0.38$, n.s.

3.2. Effects of pre-session water access

Errors of initiation increased significantly [$F(3,99) = 24.27$, $p < 0.001$] following pre-session water access, which produced a substantial reduction of the number of trials completed per session, $F(3,99) = 24.11$, $p < 0.001$ (Fig. 1A). Tukey's Honestly Significant Difference test showed that subjects with any length of water pre-load committed more errors of initiation than without water access (all $p < 0.001$), and more errors after 2 and 5 min water than those after 1 min (both $p < 0.001$), similar numbers of errors after 2 or 5 min of pre-session water access ($p > 0.05$). The same pattern held for the number of trials completed per session. Water access also increased the subject's latency of initiation of responses, $F(3,99) = 4.68$, $p < 0.01$. Means comparisons indicated that after 5 min water access, the subjects' latencies of initiation were significantly longer than after 1 and 2 min pre-load (both $p < 0.01$), and the latency differences between 5 min water access and after no water access approached significance ($p = 0.053$). However, water access did not affect errors of discontinuity, $F(3,99) = 1.28$, n.s. Data from the 5-m water access condition were excluded from further analysis because the number of trials completed were so few that it was impossible to accurately calculate the sensitivity index, choice omissions, response bias and anticipatory responses measures. Fig. 1B shows that significantly fewer anticipatory responses were committed after water pre-load, $F(2,62) = 11.83$, $p < 0.001$. This reduction interacted with the duration of pre-signal interval, as revealed by a significant interaction of Access Time × Pre-signal Interval, $F(4,124) = 8.93$, $p < 0.001$. Specific comparisons showed that, after both 1 and 2 m water access periods, significantly fewer anticipatory responses occurred at the two longer per-signal intervals, 3 s ($p < 0.05$) and 6 s ($p < 0.001$). However, at 1 s pre-signal interval, no effect of water access on anticipatory responses was found.

Water access did not produce significant main effects on the sensitivity index, $F(2,62) = 1.09$ (Fig. 1C), choice omissions, $F(2,62) = 1.39$, or response bias, $F(2,62) = 0.74$. Furthermore, none of the interactions of Water Access × Stimulus Duration on either sensitivity index, $F(6,186) = 0.86$, choice omissions, $F(6,186) = 0.96$, or response bias, $F(6,186) = 0.55$, were statistically significant.

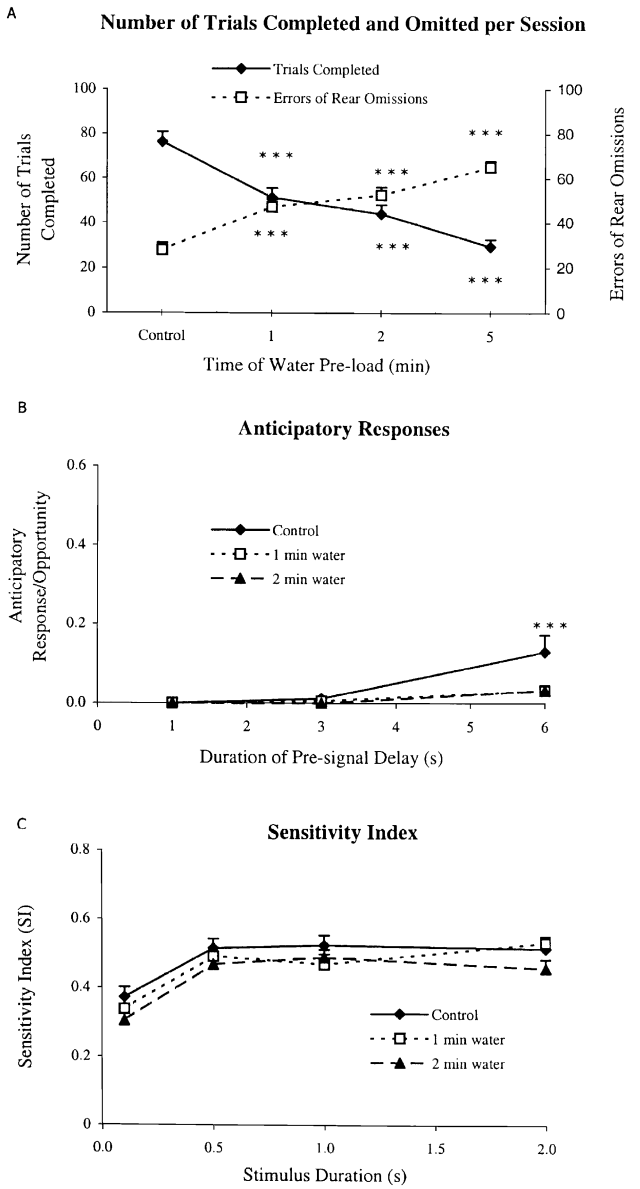

Fig. 1. Effects of pre-session access to water (i.e. pre-loads) in the homecage. (A) The number of trials completed per session was significantly decreased, and the errors of rear omissions were significantly increased by 1, 2 or 5 min pre-loads ($^{***}p < 0.001$). (B) The rate of anticipatory responding was reduced by 1 and 2 min water pre-loads ($^{***}p < 0.001$). (C) One or two minutes water pre-loads did not affect the accuracy of signal detection.

3.3. Effects of interference by flashing houselight

Fig. 2A shows that flashing the houselight reduced the number of trials completed $F(1,43) = 9.61$, $p < 0.01$. This effect was mainly due to more errors of initiation, $F(1,43) = 4.87$, $p < 0.05$, and more errors of discontinuity, $F(1,43) = 6.63$, $p < 0.05$ (not shown).

Fig. 2B shows that more anticipatory responses were observed in the flashing houselight condition [main effect: $F(1,43) = 10.10$, $p < 0.001$; interaction: $F(2,86) = 4.35$, $p < 0.05$]. Means comparisons indicated that at the 3 s ($p < 0.001$) and 6 s ($p < 0.05$) pre-signal intervals there were significantly more anticipatory responses with flashing houselight than with no houselight.

Fig. 2C shows that flashing the houselight impaired the accuracy of signal detection. The sensitivity index was significantly reduced, $F(1,43) = 12.53$, $p < 0.001$, but the interaction of Houselight Condition × Stimulus Duration only approaching significance, $F(3,129) = 2.34$, $p = 0.07$. A means comparison revealed that sensitivity index scores at both 100 ms ($p < 0.01$) and 500 ms ($p < 0.05$) were significantly lower with flashing houselight than those with no houselight.

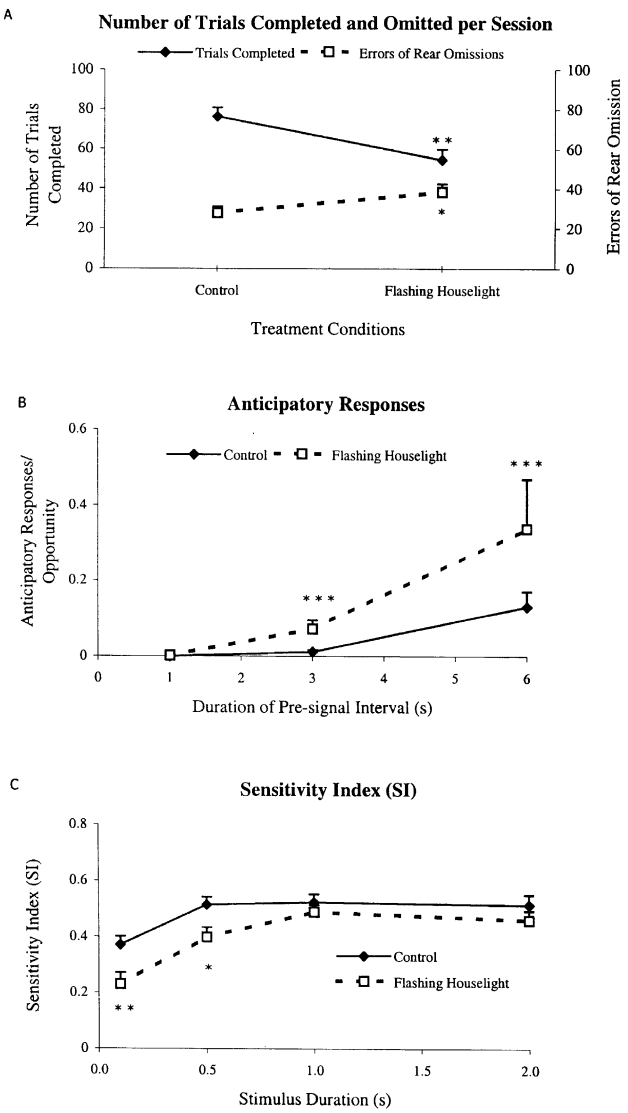

Fig. 2. Effects of flashing the houselight. (A) The addition of the flashing houselight resulted in more errors of rear omission ($^{*}p < 0.05$), and reduced the number of trials completed per session ($^{**}p < 0.01$). (B) More errors of anticipation were committed than when the duration of pre-signal interval was 3 and 6 s ($^{***}p < 0.001$). (C) The flashing houselight impaired choice accuracy in a stimulus duration-dependent manner. The impairments occurred at the 100 ms ($^{**}p < 0.01$) and 500 ms ($^{*}p < 0.05$), but not at 1 and 2 s stimulus durations.

Flashing the houselight did not alter the latency of response initiation [$F(1,43) = 1.10$] or response bias [main effect, $F(1,43) = 0.00$; interaction of Houselight Condition $\times$ Stimulus Duration, $F(3,129) = 1.54$]. While the main effect of flashing houselight on choice omissions was not significant, $F(1,43) = 0.10$, there was a significant interaction between houselight condition and stimulus duration on choice omissions, $F(3,129) = 3.31$, $p < 0.05$. Means comparisons showed that significant difference of choice omissions existed only at the shortest stimulus duration under the flashing houselight condition ($p < 0.05$).

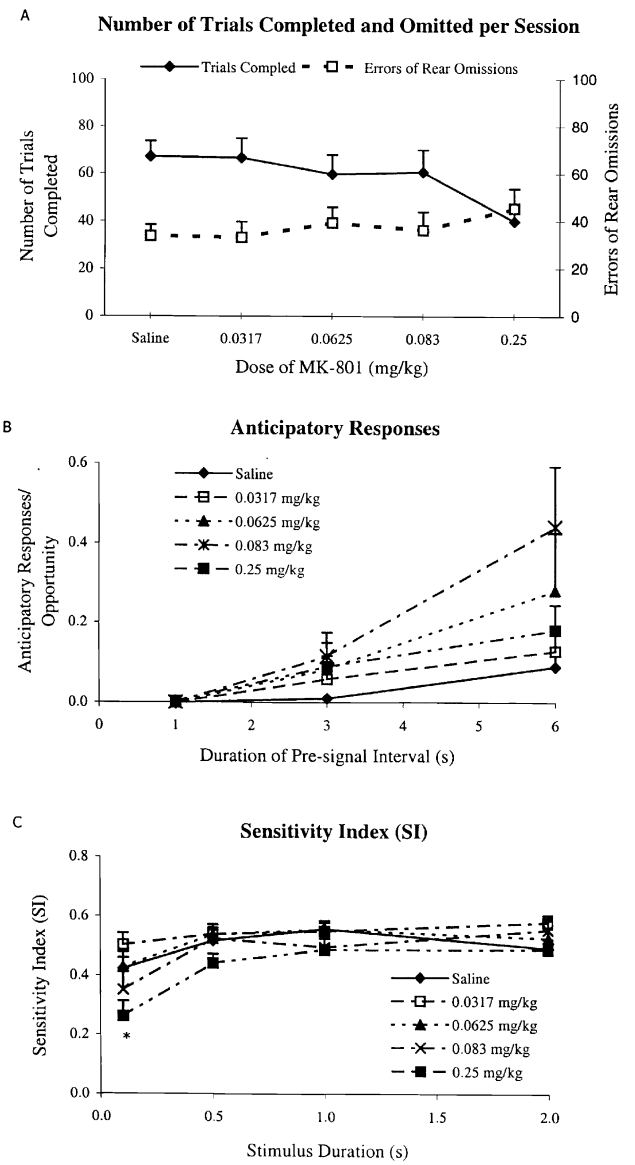

Fig. 3. Effects of glutamate *N*-methy-D-aspartate receptor antagonist MK-801 i.p. (A) Infusions of MK-801 did not affect errors of rear omissions or number of trials completed per session. Note ordinal presentation on abscissa. (B) Anticipatory responses were not affected by MK-801 injections. (C) Choice accuracy was significantly impaired by MK-801 injections at the shortest stimulus duration, 100 ms ($^{*}p < 0.05$).

3.4. Effect of intraperitoneal administration of MK-801

Fig. 3A shows that even the largest 0.25 mg/kg dose of MK-801 failed to substantially influence the measures of motivation. Injections of MK-801 did not decrease the number of trials completed per session, $F(4,51) = 1.40$, nor increased errors of initiation, $F(4,51) = 0.53$. In addition, errors of discontinuity were not affected by MK-801 injections, $F(4,51) = 2.02$.

In contrast to water pre-load and flashing houselight manipulations, the anticipatory responses were not affected by MK-801 infusions. Neither the main effect of dose, $F(4,51) = 1.88$, nor the interaction of Dose $\times$ Pre-signal Duration, $F(8,102) = 1.63$, was significant, even though, as expected, the effect of pre-signal duration on anticipatory responses was significant, $F(2,102) = 10.65$, $p < 0.001$ (Fig. 3B).

Fig. 3C shows the effects of MK-801 injections on the sensitivity index. There was no main effect of MK-801 on the sensitivity index, $F(4,51) = 1.38$, but the interaction of Dosage $\times$ Stimulus Duration was significant, $F(12,153) = 2.16$, $p < 0.05$. Means comparisons indicated that only the highest dose of MK-801 disrupted the sensitivity index at the stimulus duration of 100 ms ($p < 0.05$).

The main effect of infusions of MK-801 on choice omissions only approached significance, $F(4,51) = 2.48$, $p = 0.055$. However, the interaction of Dosage $\times$ Stimulus Duration was significant, $F(12,153) = 3.39$, $p < 0.001$. A means comparison showed that the highest dose of MK-801 increased choice omissions solely at the shortest stimulus duration, 100 ms, $p < 0.01$. Response bias was not affected by MK-801 injections [main effects of dose, $F(4,51) = 0.98$; interaction of Dose $\times$ Stimulus Duration, $F(12,153) = 1.09$]. In addition, latency of initiation was also not affected by MK-801 [$F(4,51) = 1.24$].

4. Discussion

The present experiments examined the effects of the reduction of reinforcer efficacy, a change of environmental context, and a drug known to alter sensory-attentional processes on signal detection where trials were initiated by the subject and where a variable pre-signal interval produced temporal unpredictability of the signal.

4.1. Baseline performance measures

In baseline conditions, detection accuracy was sensitive to signal duration. At the shortest stimulus duration, the subjects were least accurate, and made the most choice omissions. This is what would be expected if the duration of the stimulus affected their discriminability. The subjects also showed an increase in anticipatory responses and a decrease in choice omissions as a function of increasing pre-signal interval length. These two measures may repre-

sent a tendency to emit superfluous responses with a fixed probability. Alternatively, they may meaningfully correspond to a "false alarm" and "miss" of the classic signal detection 2×2 matrix (where a "hit" and "correct reject" represent the other two alternatives). In this latter case, then, the responses are emitted to produce a reinforcer, and a rough ratio of the two may estimate a response bias measure.

4.2. Reward efficacy and sustained attention

In the first condition, subjects were allowed a brief period of water access prior to a session, which acutely reduced the degree of deprivation. Indeed, these subjects committed more rear omissions, completed fewer trials, and took longer to initiate a trial. However, their vigilance measure (the sensitivity index) was not altered by water pre-loads, nor was response bias-altered.

Theses results are consistent with those reported by McCarthy and Davison (1979, 1981). After studying pigeons' performance of signal detection with discrete two-choice procedure, these authors concluded that when two identical reinforcers were used for both correct responses, neither response bias or discriminability was affected by the degree of deprivation.

One interpretation of the lack of effects of water pre-loads on discriminability and bias observed presently is that they illustrate an independence between the measurement of motivation or motor capability and the measure of vigilance. Alternatively, the pre-commitment of having made four presses at the beginning of each trial may maximize the subject's attentiveness during the stimulus presentation period of the task. Since only a single last press on a front lever was needed to earn the reward, subjects would have "pre-committed" to receiving the reward. This supposition was supported by the observation that once a trial was started, its probability of being completed was not affected by water pre-loads.

In contrast, signal-detection performance was impaired in a duration-dependent manner in the flashing houselight condition. We can offer three explanations for this. First, the flashing houselight may have altered the stimulus context, dishabituating the subjects from attending to many environmental cues to which the subject had previously habituated. Second, the houselight may have produced stimulus competition by drawing the rat's gaze away from the cue lamps to the houselight. The flashing houselight also increased errors of discontinuity, which may indicate that it was difficult for the subjects to maintain focus to only one component of the task. Finally, the illumination produced by the houselight may have decreased the detectability of the cuelamp. Short duration cuelamp illumination would be most likely to be fully concurrent with a 1.0-s houselight, whereas longer duration stimuli would be more likely to be partially concurrent with the houselight and partially not, perhaps creating greater detectability than fully obscured, shorter duration stimuli. In any case, because the biggest load of attention was demanded at the shortest stimulus duration, it was not surprising that the most detrimental effects on the sensitivity index and increases of false alarms were observed with the briefest cue duration.

These findings are partially consistent with those of McGaughy and Sarter (1995). On one hand, the flashing houselight presently produced an increase in anticipatory responses and errors of omission regardless of the stimulus duration, which was consistent with results reported by McGaughy and Sarter (1995). However, in their experiment, the flashing houselight impaired the vigilance index, misses, and false alarms, all independently of stimulus duration. The more profound disruption observed by these authors suggest that increased task complexity might be an important factor moderating distractibility.

4.3. N-methyl-D-aspartate receptors and attention

The effects of MK-801 are far more selective in the present paradigm than previously reported (Buffalo et al., 1994; Hoffman, 1992; Presburger and Robinson, 1999; Tan et al., 1989; Whishaw and Auer, 1989; Wozniak et al., 1990). The 0.25-mg/kg dose of MK-801 disrupted the sensitivity index and choice omissions, and these effects were significant only at the shortest stimulus duration. No increase in errors of initiation and only a trend toward a reduction of trials completed was detected. This duration-dependent impairment on sensitivity index and choice omissions was comparable to that produced by the flashing houselight. Under these two manipulations, both the disruption of the sensitivity index and the increase in choice omissions were a function of stimulus duration. Such a comparison suggests that the subjects might have been more readily distracted at the time when they were required to maintain visual orientation.

Many studies, using different animal models, also confirm the significance of *N*-methyl-D-aspartate receptors in sensory-motor gating. For instance, by presenting novel objects into an open field, Dai and Carey (1994) found that while control rats concentrated their investigating behavior around a new object, MK-801-treated rats distributed their activities over the entire apparatus. Prepulse inhibition, a suppression of a startle response by presenting a weak stimulus just before the startle-inducing stimulus, has been employed as an empirical model of sensory gating (Geyer et al., 1990; Graham, 1975; Ison and Hammond, 1971). Mansbach and Geyer (1989) and Al-Amin and Schwarzkopf (1996) found that MK-801, along with its analog phencyclidine, decreased or eliminated prepulse inhibition in rats. Like schizophrenics (Braff and Geyer, 1990; McGhile and Chapman, 1961; Venables, 1964), animals after antagonism of *N*-methyl-D-aspartate receptors displayed the inability to maintain focus and to filter irrelevant information (Swerdlow et al., 1994).

Evaluating the effects of MK-801 must also be done in the context of a large literature showing that blockade of NMDA receptors inhibits long-term potentiation in brain structures critical learning and memory such as the hippocampus (Morris et al., 1986) and impairs the acquisition of a variety of rodent tasks (e.g. Cohn et al., 1992; Murray et al., 1995). Enhanced distractibility could contribute to these learning impairments, though the reverse is also conceivable.

4.4. Conclusions

Taken together, these results suggest that one can procedurally isolate the motivation to respond to stimuli from accuracy of detection. In doing this, our experiments also revealed that stimulus duration-dependent impairment of choice accuracy was produced by MK-801 and the alteration of stimulus context, but not by explicit reduction of the degree of deprivation of the subject. These results also suggest that this paradigm might usefully protect attending from side effects of drugs that influence motivation to respond.

Acknowledgements

We thank Drs. Brenda Anderson, Jasper Brener, Dave Emmerich, Xiaoqing Liu and Peter Rapp for their constructive suggestions for the project. We also thank Bill Guethelin and Glen Hudson for technical support.

References

Al-Amin, H.A., Schwarzkopf, S.B., 1996. Effects of the PCP analog dizocilpine on sensory gating: potential relevance to clinical subtypes of Schizophrenia. Biol. Psychiatry 40, 744–754.

Braff, D.L., Geyer, M.A., 1990. Sensory gating and schizophrenia: human and animal models. Arch. Gen. Psychiatry 47, 181–188.

Buffalo, E.A., Gillam, M.P., Allen, R.R., Paule, M.G., 1994. Acute behavioral effects of MK-801 in rhesus monkeys: assessment using an operant test battery. Pharmacol. Biochem. Behav. 48, 935–940.

Bushnell, P.J., Oshiro, W.M., Padnos, B.K., 1997. Detection of visual signals by rats: effects of chlordiazepoxide. Psychopharmacology 134, 230–241.

Cohn, J., Ziriax, J.M., Cox, C., Cory-Slechta, D.A., 1992. Comparison of error patterns produced by scopolamine and MK-801 on repeated acquisition and transition baselines. Psychopharmacology (Berlin) 107, 243–254.

Dai, H., Carey, R.J., 1994. The NMDA antagonist MK-801 can impair attention to exteroceptive stimuli. Behav. Brain Res. 62, 149–152.

Davison, M., McCarthy, D., 1980. Reinforcement for errors in a signal-detection procedure. Journal of the Experimental Analysis of Behavior 34, 35–47.

Frey, P.W., Collier, J.A., 1973. Sensitivity and responsivity measures for discrimination learning. Learn. Motiv. 4, 327–342.

Geyer, M.A., Swerdlow, N.R., Mansbach, R.S., Braff, D.L., 1990. Startle response models of sensorimotor gating and habituation deficits in schizophrenia. Brain Res. Bull. 25, 485–498.

Givens, B., 1997. Effect of ethanol on sustained attention in rats. Psychopharmacology 129, 135–140.

Graham, F.K., 1975. The more or less startling effects of weak prestimulation. Psychophysiology 12, 238–248.

Green, D.M., Swets, J.A., 1974. Signal Detection Theory and Psychophysics. Wiley, New York.

Hoffman, D.C., 1992. Typical and atypical neuroleptic antagonize MK-801-induced locomotion and stereotypy in rats. J. Neural Transm.: Gen. Sect. 89, 1–10.

Ison, J.R., Hammond, G.R., 1971. Modification of the startle reflex in the rat by changes in the auditory and visual environments. J. Comp. Physiol. Psychol. 75, 435–452.

Keppel, G., 1991. Design and Analyses: A Researcher's Handbook. 3rd edn. Prentice-Hall, New Jersey.

Mansbach, R.S., Geyer, M.A., 1989. Effects of phencyclidine and phencyclidine biologs on sensory gating in the rat. Neuropsychopharmacology 2, 229–308.

McCarthy, D., Davison, M., 1979. Signal probability, reinforcement and signal detection. J. Exp. Anal. Behav. 32, 373–386.

McCarthy, D., Davison, M., 1981. Towards a behavioral theory of bias in signal detection. Percept. Psychophys. 29, 371–382.

McGaughy, J., Sarter, M., 1995. Behavioral vigilance in rats: task validation and effects of age, amphetamine, and benzodiazepine receptor ligand. Psychopharmacology 117, 340–357.

McGhile, A., Chapman, J., 1961. Disorders of attention and perception in early schizophrenia. Br. J. Med. Psychol. 34, 103–116.

Moore, H., Dudchenko, P., Bruno, J.P., Sarter, M., 1992. Toward modeling age-related changes of attentional abilities in rats: simple and choice reaction time tasks and vigilance. Neurobiol. Aging 13, 759–772.

Morris, R.G., Anderson, E., Lynch, G.S., Baudry, M., 1986. Selective impairment of learning and blockade of long-term potentiation by an *N*-methyl-D-aspartate receptor antagonist, AP5. Nature 319, 774–776.

Muir, J.L., Dunnett, S.B., Robbins, T.W., Everitt, B.J., 1992. Attentional functions of the forebrain cholinergic systems: effects of intraventricular hemicholinium, physostigmine, basal forebrain lesions and intracortical grafts on a multiple-choice serial reaction time task. Exp. Brain Res. 89, 611–622.

Murray, T.K., Ridley, R.M., Snape, M.F., Cross, A.J., 1995. The effect of dizocilpine (MK-801) on spatial and visual discrimination tasks in the rat. Behav. Pharmacol. 6, 540–549.

Nevin, J.A., 1982. Psychophysics and reinforcement schedules: an integration. In: Commons, M.C., Nevin, J.A. (Eds.), Quantitative Analyses of Behavior. Discriminative Properties of Reinforcement Schedules, vol. 1. Balliger, Cambridge.

Presburger, G., Robinson, J.K., 1999. Spatial signal detection in rats is differentially disrupted by Δ^9-tetrahydrocannabinol, scopolamine, and MK-801. Behav. Brain Res. 99, 27–34.

Robbins, T.W., Everitt, B.J., Ryan, C.N., Marston, H.M., Jones, G.H., Page, K.J., 1989a. Comparative effects of quisqualic and ibotenic acid-induced lesions of the substantia innominata and globus pallidus on the acquisition of a conditional visual discrimination: differential effects on cholinergic mechanisms. Neuroscience 28, 337–352.

Robbins, T.W., Everitt, B.J., Marston, H.M., Wilkinson, J., Jones, G.H., Page, K.J., 1989b. Comparative effects of ibotenic acid- and quisqualic acid-induced lesions of the substantia innominata on attentional function in the rat: further implications for the role of the cholinergic neurons of the nucleus basalis in cognitive processes. Behav. Brain Res. 35, 221–240.

Sahgal, A., 1987. Some limitations of indices derived from signal detection theory: evaluation of an alternative index for measuring bias in memory tasks. Psychopharmacology 91, 517–520.

Sokal, R.R., Rohlf, F.J., 1995. Biometry: The Principles and Practice of Statistics in Biological Research, 3rd Ed. Freeman, New York.

Swerdlow, N.R., Braff, D.L., Taaid, N., Geyer, M.A., 1994. Assessing the validity of an animal model of deficient sensorimotor gating in Schizophrenic patients. Arch. Gen. Psychiatry 51, 139–154.

Tan, S., Kirk, R.C., Abraham, W.C., McNaughton, N., 1989. Effects of the NMDA antagonists CPP and MK-801 on delayed conditional discrimination. Psychopharmacology 98, 556–560.

Tomporowski, P.D., Tinsley, V.F., 1996. Effects of memory demand and motivation on sustained attention in young and older adults. Am. J. Psychol. 109, 187–204.

U.S. Department of Health and Human Services, 1985. Guide for the Care and Use of Laboratory Animals (DHHS Publication No. NIH 85-23). U.S. Government Printing Office, Washington, DC.

Venables, P., 1964. Input dysfunction in schizophrenia. In: Maher, B.A. (Ed.), Progress in Experimental Personality Research. Academic Press, New York, pp. 1–47.

Whishaw, I.Q., Auer, R.N., 1989. Immediate and long-lasting effects of MK-801 on motor activity, spatial navigation in a swimming pool and EEG in the rat. Psychopharmacology (Berlin) 98, 500–507.

Wozniak, D.F., Olney, J.W., Kettinger, L., Price, M., Miller, J.P., 1990. Behavioral effects of MK-801 in the rat. Psychopharmacology (Berlin) 101, 47–56.