the image of the moth. While this learned detection might justifiably be called a specific search image, we prefer to limit use of this term to changes in detection due to consecutive encounters with the same prey item (*2*).

2) Although both substrate choice and body orientation contributed to crypticity in our results, they were interdependent. Detection of moths on the proper substrate was seriously reduced when the moth was placed in a vertical rather than horizontal position, whereas orientation had very little effect for moths placed on a nonmatching substrate. This indicates that body orientation is an important component of crypticity for these moths. Although the effects of substrate choice are apparent to the human eye, the effects of orientation are not. Finally, the effects of distance accord well with the observations of field workers that distance affects detection of prey most quickly and consistently under cryptic conditions (*2*).

3) The procedures developed in this study could easily be adapted for use in future studies of prey detection with a wide variety of avian and mammalian visual predators. Although the method seems artificial in some respects, it offers many advantages as a laboratory simulation of predator-prey interactions. It provides excellent control of the parameters of prey preference and the appearance and palatability of the prey. The effects of prey density and polymorphisms could be examined by varying the slides shown to the subjects. Furthermore, the data already generated with the technique reflect the operation of at least some of the processes that undoubtedly affect the detection of prey in the field. Thus, these procedures have great potential for the study of many aspects of predator-prey interactions.

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8. Details of acquisition will be described (A. T. Pietrewicz, in preparation). The jays trained on set 1 required a mean of 22.3 sessions for performance to stabilize at a mean percentage correct of 84.7. Corresponding data for jays trained on set 2 were 30.3 sessions and 74.8 percent correct. When transferred to the subsets of set 3, all birds showed a significant degree of transfer, which increased with each subset. At asymptote, mean percentages correct on the three subsets of set 3 were 74.4, 83.9, and 83.7 for positive and negative trials combined, which did not differ significantly.
9. The effects of moth species, substrate, and orientation on the speed of responding to slides were also analyzed. Response speed was defined as the reciprocal of the number of seconds between the initial peck at the stimulus key or CO key after the slide had been projected. In general, these analyses were consistent with those of percentage of correct responses; that is, those conditions which produced poorest accuracy of detection also produced the slowest response speeds. Finally, the average speed of responding to positive slides was significantly faster than that for negative slides ($P < .001$). The mean response speed for positive slides corresponds to a response latency of 2.1 seconds, while the mean response speed for negative slides corresponds to a response latency of 4.1 seconds.
10. Based in part on a thesis submitted to the University of Massachusetts by A.T.P. We thank T. D. Sargent for supplying the moths and for advice, and M. Novak for her helpful comments on the manuscript. Supported in part by NSF grant GB 30501.

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Lithium: Effects on Subjective Functioning and Morphine-Induced Euphoria

Abstract. *The therapeutic usefulness of lithium in decreasing the euphoria and other symptoms associated with manic behavior and the hypothesis of a common final mechanism for elevations in mood have led to speculation that lithium may block the euphoria induced by drugs of abuse. In this study, lithium alone was antieuphoric in drug-free opiate addicts and, further, did not block morphine-induced euphoria.*

Bunney and colleagues (*1*) speculate that a common mechanism may underlie the euphoria induced by drugs of abuse and the sudden onset of euphoria observed in mania or certain other medical illnesses. The therapeutic usefulness of lithium salts in decreasing acute manic symptomatology and decreasing the intensity of recurrent mania and depressive episodes led Bunney to further speculate that lithium might block drug-induced euphoria. Reports indicating that lithium blocks the effects of amphetamine (*2*) support this view. In this study, we report (i) the subjective effects of lithium itself and (ii) the influence of lithium on morphine-induced euphoria.

Subjects were eight federal prisoner volunteers with documented long-term histories of narcotic abuse and concomitant antisocial behavior but without history or evidence of a psychotic disorder. Each was informed as to the drugs involved and the purpose and design of the experiment. Subjects knew that the initiation and termination of lithium administration would be without their knowledge and that before and after lithium administration they would be ingesting placebo capsules. Further, they were aware that a narcotic and blank (placebo) would be administered subcutaneously under double-blind conditions during the period of placebo administration and during lithium administration. The review of the protocol and the procedures for informed consent were in accordance with National Institutes of Health guidelines.

The design of the experiment was based on the protocol for lithium treatment of acute mania. Usually lithium carbonate (300 mg) is administered by mouth three or four times daily to such

Table 1. Scales of the ARCI before, during, and after lithium administration. Numbers represent the mean raw scores and standard deviations for eight subjects. Superscripts represent the probability value of the t calculated for the significance of the mean difference from predrug control scores. Mean serum lithium values on the morning of ARCI testing were 0.81 ± 0.25 meq/liter during lithium stabilization and 0.15 ± 0.05 meq/liter during withdrawal.

Scale	Before lithium	Lithium stabilization	Lithium withdrawal
General drug effect	15.9 ± 2.9	$20.5 \pm 3.3^{.02}$	$22.8 \pm 7.2^{.05}$
Pentobarbital-chlorpromazine-alcohol group (PCAG)	10.5 ± 3.3	$12.6 \pm 4.9^{.40}$	$15.8 \pm 6.04^{.05}$
Tired	7.5 ± 1.8	$9.0 \pm 2.4^{.05}$	$9.6 \pm 2.6^{.10}$
Drunk	3.6 ± 0.9	$5.4 \pm 1.1^{.02}$	$6.6 \pm 2.8^{.05}$
Morphine-benzedrine group (MGB)	17.5 ± 4.6	$12.2 \pm 3.5^{.01}$	$12.5 \pm 3.7^{.02}$
Excitement	11.9 ± 3.3	$8.9 \pm 1.6^{.05}$	$8.5 \pm 2.5^{.05}$
Efficiency	28.0 ± 5.6	$22.0 \pm 3.4^{.05}$	$19.8 \pm 4.9^{.02}$
Popularity	12.4 ± 3.2	$9.2 \pm 3.9^{.02}$	$9.4 \pm 3.9^{.05}$

Table 2. Scale scores and pupillary changes produced by morphine and placebo in eight subjects during lithium administration and during the control period (before and after lithium treatment). For scales, numbers represent mean total 5-hour scores (sum of six observations) and standard deviation. The data for pupils are the mean total 5-hour change in pupillary diameter (sum of six observations, in millimeters) and standard deviation, with negative sign indicating constriction and positive, dilation. Superscripts represent the probability values of the t calculated for the significance of the mean difference between control and lithium scores.

Measure	Placebo		Morphine (15 mg)		Morphine (7.5 mg)	
	Lithium	Control	Lithium	Control	Lithium	Control
Morphine-benzedrine group	$1.2 \pm 2.3^{.30}$	5.1 ± 8.8	$16.0 \pm 17.5^{.40}$	20.6 ± 29.1	$11.0 \pm 15.7^{.20}$	7.1 ± 12.7
Subjects' liking	0 ± 0	0 ± 0	$6.8 \pm 2.1^{.05}$	4.5 ± 3.2	$2.6 \pm 2.1^{.50}$	1.9 ± 2.7
Opiate symptoms	0 ± 0	0 ± 0	$10.5 \pm 9.4^{.50}$	9.2 ± 8.8	$3.2 \pm 2.6^{.70}$	4.1 ± 7.0
Observers' liking	$2.9 \pm 8.1^{.40}$	0 ± 0	$13.0 \pm 2.0^{.70}$	12.1 ± 4.5	$9.1 \pm 4.4^{.40}$	6.9 ± 4.4
Opiate signs	$0.8 \pm 2.1^{.40}$	0 ± 0	$33.2 \pm 4.8^{.90}$	32.1 ± 9.8	$17.0 \pm 12.1^{.20}$	28.5 ± 13.9
Pupils	$+0.1 \pm 2.6^{.20}$	$+1.7 \pm 2.1$	$-7.2 \pm 2.5^{.30}$	-5.2 ± 3.2	$-3.4 \pm 3.0^{.50}$	-4.3 ± 2.8

patients to maintain serum levels at 0.6 to 1.2 meq/liter. Levels of 1.5 meq/liter are regarded as toxic. The calming effect of lithium is not immediate but occurs 5 to 10 days after initiation of therapy. Abrupt termination of lithium results in a recurrence of acute manic symptomatology 3 to 5 days later.

Initially, one placebo capsule (lactose) was administered orally at 9 a.m., 4 p.m., and 10 p.m. daily for 5 days. From days 6 through 10, this was increased to two placebo capsules three times daily. On day 11, one 300-mg lithium capsule was substituted for one placebo capsule at each medication time for a total daily dose of 900 mg. Subsequent doses (up to 1500 mg daily) were adjusted to maintain serum lithium levels at 0.8 to 1.0 meq/liter. After 20 days of lithium administration, placebo capsules were substituted for 4 days without knowledge of subjects or observers to determine if abrupt lithium withdrawal produced any affective changes in these nonpsychotic subjects. Serum lithium was detectable in decreasing concentrations through 8 days after withdrawal.

Lithium itself produced complaints of nausea, sleepiness, irritability, relaxation, and sluggishness. Two subjects reported difficulty playing basketball because of inability to react quickly; however, no neurological abnormalities were found. One subject was constantly thirsty and had polyuria, which has been repeatedly documented as an effect in some patients (*3*). Following lithium withdrawal, symptoms abated as serum lithium levels decreased. Subjects first reported being fully normal 7 to 10 days after lithium withdrawal.

Subjective effects of lithium itself were determined with the Addiction Research Center Inventory (ARCI), which subjects completed on day 9 of placebo administration, on day 10 of lithium administration, and on day 4 of lithium withdrawal (when subjects still received placebo capsules). The ARCI is a 550-item questionnaire for which 38 scales have been derived to measure acute and chronic drug effects, opiate and alcohol withdrawal, as well as personality and psychiatric disorders (*4*). One scale, the morphine-benzedrine group (MBG), measures drug-induced euphoria in narcotic addicts and also appears to distinguish manic from depressed patients, which supports observations that mania is in part a euphoric state (*5*). In this regard, the MBG scale of the ARCI and the mania scale of the Minnesota Multiphasic Inventory are significantly correlated in the opiate addict population under a no-drug condition ($r = .379$) (*6*). However, only the MBG scale (*6, 7*) and not the mania scale (*8*) shows increased scores with acute morphine administration and decreased scores with withdrawal of morphine (*9*) after long-term administration; this indicates that the MBG measures mania as a state and the mania scale measures mania as a trait. Significant subjective effects were detected during lithium administration and also 4 days after withdrawal, as would be expected from the persistent serum levels of lithium (Table 1). There was no evidence of any distinct changes in affect produced by lithium withdrawal.

Lithium significantly increased scores on the general drug effect, pentobarbital-chlorpromazine-alcohol group, tired, and drunk scales of the ARCI and significantly decreased scores on the MBG, excitement, efficiency, and popularity scales. This pattern indicates that the subjective effects included (i) feelings of sluggishness, weakness, and tiredness, (ii) lessened motivation for cognitive and physical activity, (iii) slight dysphoria, (iv) lessened excitement, feeling of popularity, and euphoria, and (v) decreased social and cognitive efficiency. The significant decreases in MBG scale scores indicate that lithium itself is antieuphoric.

To further characterize the subjective effects of lithium, the profile of scale scores was compared with profiles of scores obtained with various drug conditions in previous studies (*4*). A prior discriminate function analysis of 1321 completed ARCI tests indicated that the following drug conditions could be distinguished from each other: no drug, acutely administered morphine, amphetamine, lysergic acid diethylamide, nalorphine or cyclazocine, alcohol, pentobarbital, chlorpromazine, and chronically administered opiates. The sum of the squares of differences between scores for lithium (adjusted for scale intercorrelations) and those for each of the various drug conditions from previous studies was least with those for chlorpromazine. Thus, the overall profile of subjective effects produced by lithium most closely resembles that produced by a small dose of chlorpromazine.

The effects of lithium on morphine-induced euphoria were determined by administering test doses of morphine sulfate before, during, and after the administration of lithium. During the prelithium control period while the subjects were ingesting placebo capsules, each subject was given a 15-mg dose of morphine, a 30-mg dose of morphine, and a saline placebo subcutaneously under double-blind conditions. The three treatments, each a single injection, were administered to each subject at 4-day intervals in random order. Between days 10 and 15 of lithium administration, morphine (15 mg) and saline placebo were administered to all subjects subcutaneously in random order, again at a 4-day interval. Four to 6 hours after administration of this dose of morphine, two subjects experienced disturbing nausea and vomiting. Since both subjects had tolerated this and the 30-mg dose of morphine in the control period, it was suspected that the nausea and emetic effect of morphine was additive to nausea caused by lithium. [Nausea was reported in one study in which lithium was administered to normal controls (*8*).] As a consequence, a 7.5-mg dose of mor-

phine was administered subcutaneously in place of the 30-mg dose. Four to 6 weeks after termination of lithium administration, a 7.5-mg dose of morphine was again given to each subject. This is a near-threshold dose for detection of subjective effects in this population.

The subjective, euphoric, and pupillary effects of each dose of morphine and placebo were measured at each time with a standard procedure (*7, 10, 11*). At 7 and 7:30 a.m., pupillary diameter was determined photographically. At 8 a.m., morphine or placebo was injected subcutaneously under double-blind conditions. Change in pupillary diameter was determined photographically 0.5, 1, 2, 3, 4, and 5 hours later; subjects and observers answered questionnaires at the same six times. From these questionnaires, scores were calculated on scales measuring the subjective, euphoric, and behavioral effects of morphine. From subject responses, these were scores on the opiate symptom and subject liking scales (*10, 11*) and on a subset of items from the MBG scale (*7*). Opiate sign and observers' liking scale scores were obtained from observers' responses (*9, 11*). The six scores after drug injection for change in pupillary diameter and for each scale were summed (total 5-hour scores) to serve as the measure of drug response.

Comparison of the responses to morphine during lithium administration to those before and after lithium administration indicates that lithium did not block the euphoric, subjective, or miotic effects of morphine (Table 2). In fact, morphine (15 mg) was significantly more euphoric during lithium administration, as measured by subjects' liking scores. The slight decrease in MBG scores and increase in observers' liking and opiate sign scale scores with placebo response during lithium administration (Table 2) is attributed to the effects of lithium itself.

These studies indicate that (i) lithium itself is antieuphoric in nonmanic subjects, and its profile of subjective effects most closely resembles that for a small dose of chlorpromazine; and (ii) lithium does not block morphine-induced euphoria. Further, these observations argue against a common mechanism for euphoria.

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Basal Ganglia Cooling Disables Learned Arm Movements of Monkeys in the Absence of Visual Guidance

Abstract. *Unilateral local cooling in the region of the globus pallidus of Cebus monkeys produced a severe breakdown in the performance of learned flexion-extension elbow movements when animals had no visual information about arm position but not when such information was displayed to them. This result indicates that visual information enables an animal to compensate to a large degree for the motor disorder produced by globus pallidus dysfunction, and it may explain why some previous workers have failed to see motor impairments in monkeys with lesions in the globus pallidus who were observed in their cages.*

The globus pallidus (GP) (a major efferent nucleus of the basal ganglia) has recently been implicated in motor control. For example, a correlation has been found between firing of single units in the GP and movements of the contralateral limbs (*1*). This finding is in keeping with anatomical studies (*2*) that have emphasized the functional significance of the input to basal ganglia from all areas of cerebral cortex and the output from the GP to thalamic nuclei, which project to cerebral motor cortex. However, the exact function of the GP in motor control is still not clear. In the early ablation studies in animals, lesions of the GP were found to produce no obvious motor defects (*3*). It was only when large bilateral lesions were made in the GP that monkeys were found to adopt a flexion posture of the limbs and to lose placing and righting reactions (*4*). From his studies on human patients with diseases that produced lesions in the basal ganglia, Martin (*5*) concluded that bilateral lesions of the GP produced loss of postural reflexes. In one test for motor defects, patients were asked to reach out with their arm at shoulder height and touch alternately the tips of the examiner's two forefingers, which were held about a foot apart. With their eyes open the patients continued to perform well for several minutes, ". . . but if after the first movements he closes his eyes, the hand almost immediately falls away and the movement peters out" (*5*, p. 13).

In an attempt to produce an animal model of such diseases we have implanted cooling sheaths in the GP in four Cebus monkeys (*6*). Some preliminary results have been reported as abstracts (*7*). Cooling through cryoprobes inserted into these sheaths produced a temporary functional lesion, which was restricted to the brain region surrounding the sheath (Fig. 1). Motor performance of these monkeys was tested in a behavioral situation similar to that of the patients. Monkeys were trained to move a handle in a horizontal arc of about 60° between two target positions by making alternate flexion and extension movements at the elbow. Animals were rewarded with a drop of fruit juice for making three alternate movements during which the handle had to be held in each of the 20° targets for 0.2 second. The animals' view of their limbs was blocked by an opaque plate. At the start of each experimental session, flexion and extension targets were indicated by lights that lit when the handle was in target, thus providing the animals with proprioceptive cues for the position of the targets. After about 10 minutes of practice, the lights were removed and animals continued the alternating movements without any visual cues as to target position. The first monkey tested (M29L) never learned the significance of the visual cues and was rewarded for simply moving the handle from side to side and passing through the targets.

Cooling the right GP in these four monkeys impaired the performance of this simple arm movement task. The monkeys normally made smoothly executed