### References and Notes

1. P. Marler and M. Tamura, *Condor* **64**, 368 (1962).
2. M. C. Baker, *Evolution* **29**, 226 (1975).
3. P. Marler and M. Tamura, *Science* **146**, 1483 (1964); L. F. Baptista and J. R. King, *Condor* **82**, 267 (1980).
4. P. Marler, *J. Comp. Physiol. Psychol.* **71**, 1 (1970); M. Konishi, *Z. Tierpsychol.* **22**, 770 (1965).
5. The female copulation display gradually intensifies over a period of weeks prior to actual copulation. During this period the interest of the male in his mate also gradually intensifies. Posturing and trilling by the female is the immediate antecedent to copulation episodes. Wing fluttering and trilling are evident on other occasions of high arousal in both sexes, but males seldom elevate the tail. A female in a highly aggressive state—as in a fight with another female—displays such masculine behavior as loud song and physical attack, but not sexual posturing. These patterns have been reported in detail by B. D. Blanchard [*Univ. Calif. Berkeley Publ. Zool.* **46**, 1 (1941)].
6. A. P. King and M. J. West, *Science* **195**, 1002 (1977); M. J. West, A. P. King, D. H. Eastzer, J. E. R. Staddon, *J. Comp. Physiol. Psychol.* **93**, 124 (1979); M. J. West, A. P. King, D. H. Eastzer, *Am. Sci.* **69**, 56 (1981); *Anim. Behav.* **29**, 490 (1981).
7. P. Marler, *Ibis* **94**, 458 (1952); R. J. Andrew, *Science* **137**, 585 (1962); F. Nottebohm, *ibid.* **167**, 950 (1970); W. H. Thorpe, in *The New Systematics*, J. Huxley, Ed. (Clarendon, Oxford, 1940).
8. F. Nottebohm, *Condor* **71**, 299 (1969).
9. M. Milligan and J. Verner, *ibid.* **73**, 208 (1971). Audible trill vocalizations and not copulation postures were reported. The data were not presented numerically and there was no statistical analysis.
10. R. B. Payne, in *Natural Selection and Social Behavior: Recent Research and New Theory*, R. D. Alexander and D. W. Tinkle, Eds. (Chiron, New York, 1980). Payne's "genetic adaptation model" is a more rigid statement of forms of the same model discussed by other authors. Electrophoretic evidence from populations of white-crowned sparrows in coastal California [(*2*); M. C. Baker, in preparation] indicates that dialects are genetically differentiated. For a review, see M. C. Baker, in *Evolutionary and Ecological Aspects of Acoustic Communication in Birds*, D. E. Kroodsma and E. H. Miller, Eds. (Academic Press, New York, in press).
11. S. Wright, *Variability Within and Among Natural Populations* (Univ. of Chicago Press, Chicago, 1978); A. H. Miller, *Evolution* **1**, 186 (1947).
12. One subject was a nestling, and the fledglings had been out of the nest for 7 to 10 days when captured. The habitat in which the fledglings were captured is island-like, with the nearest known alien dialect located about 24 km away. Considering their age and geographic isolation, it is safe to assume that the juveniles were locally hatched. The young and adult females were housed individually in Hendrix cages (45 cm long by 23 cm wide by 25 cm high) and fed a diet of mixed finch seed, mealworms, and supplemental vitamins. The birds were tutored with tape-recorded songs played on a Revox A77 recorder through a Realistic SA-2001 amplifier and broadcast with an Altec 755-E speaker mounted in a cabinet. The songs were played at a rate of one each 15 seconds, approximating the natural singing rate of an individual male.
13. The test area was 2 m long by 1 m wide by 3 m high and shrouded with black plastic. It contained an entry door and a table on which rested a 20-cm loudspeaker mounted in a cabinet located 50 cm from a test cage containing an experimental subject.
14. M. C. Baker, K. J. Spitler-Nabors, D. C. Bradley, in preparation.
15. J. L. Brown, *Wilson Bull.* **81**, 293 (1969).
16. Mating between different species often occurs in zoos when normal choice of sexual partners is frustrated.
17. J. A. Feduccia, *The Age of Birds* (Harvard Univ. Press, Cambridge, Mass., 1980); P. Broadkorb, in *Avian Biology*, D. S. Farner and J. R. King, Eds. (Academic Press, New York, 1971), vol. 1; M. C. Baker, *Heredity* **46**, 209 (1981).


18. We thank A. E. M. Baker, L. C. Deutsch, M. A. Cunningham, D. F. Tomback, W. A. Searcy, D. B. Thompson, J. S. Augustine, P. Greco, and G. L. Sherman for assistance and advice. Supported by NSF grant DEB-78-22657 to M.C.B.

19 May 1981; revised 11 August 1981


# Melatonin: Identification of Sites of Antigonadal Action in Mouse Brain


Abstract. *Long-term implants releasing a small quantity of melatonin (45 nanograms per day) were used to determine the brain sites of the hormone's antigonadal action in a photoperiodic species, the white-footed mouse (*Peromyscus leucopus*). Implants in the medial preoptic and supra- and retrochiasmatic areas elicited complete gonadal regression after 7 weeks. Implants in other brain regions had little effect on the animals' reproductive state.*


The importance of photoperiodism in the control of reproductive cycles has been demonstrated in a variety of mammalian species (*1, 2*). In rodents, photoperiodic control of reproductive state is mediated by the central nervous system through the retinohypothalamic tract, the suprachiasmatic nuclei (SCN), and the superior cervical ganglia (*3*). There is also evidence that the pineal gland and its hormone product melatonin are regulated by these neural pathways (*4*) and that the pineal gland mediates changes in seasonal breeding. In the Syrian hamster and the European vole, pinealectomy renders the animals incapable of responding to a photoperiod with short days, thus preventing regression (*5*). Conversely, daily melatonin injections provoke gonadal regression in the Syrian hamster and the white-footed mouse, *Peromyscus leucopus* (*6*).

Various studies have implicated the ovary, uterus, and anterior pituitary as the sites of melatonin's antigonadal activity (*7*), but there is also evidence for a site in the brain. Melatonin administration induces behavioral and electroencephalographic changes (*8*), and melatonin crystals implanted into the brain reduce the secretion of pituitary luteinizing hormone in castrated rats (*9*). Recently, the hypothalamus was shown to be a putative site of melatonin action. Melatonin is specifically bound in the rat hypothalamus (*10*), and endogenous melatonin has been localized in the SCN by fluorescence immunohistochemistry (*11*).

In a previous study we demonstrated that implants releasing small quantities of melatonin (90 ng/day) were effective in eliciting gonadal regression when implanted in the anterior hypothalamus of *P. leucopus* (*12*). The present study shows that the antigonadal effects of melatonin may be confined to the anterior hypothalamus.

Under chloropent anesthesia (16 mg per gram of body weight; Fort Dodge Laboratories), sexually mature female *P. leucopus* (*13*) were stereotaxically implanted with a melatonin-containing beeswax pellet (*12*) in a predetermined brain region. The pellets released a nearly physiological amount of melatonin (45 ng/day, or 2.4 times that produced by the pineal gland of the Syrian hamster) (*14*). Some mice were implanted with a blank beeswax pellet in the anterior hypothalamus to determine the effects of the implantation procedure on the animals' reproductive state. Correct placement of the pellets was determined histologically at the end of the experiment (*15*). Animals in another group received a subcutaneously implanted pellet of beeswax and melatonin to ascertain whether peripheral release of similar quantities of melatonin has an antigonadal effect. The mice were maintained at 23°C on a photoperiod with 16 hours of light and 8 hours of darkness.

After 7 weeks the mice were killed and the reproductive tract (vagina, uterus, oviducts, and ovaries) was removed and weighed. The mice were also examined for an imperforate vagina, which indicates reproductive regression (*16*). The functional condition of the ovaries was determined by histological examination of the state of follicular development (*17*). The extent of melatonin diffusion from the pellet into the surrounding neural tissue was determined by autoradiography (*18*).

The results indicate that brain sites for the antigonadal action of melatonin are located in the rostral brainstem, notably in supra- and retrochiasmatic areas. Mice with melatonin-containing implants in these regions exhibited a degree of regression of the reproductive tract (Fig. 1 and Table 1) similar to that induced by 12 weeks of exposure to a photoperiod with short days (*2, 19*). Reproductive tract weight decreased 61 percent in mice implanted with pellets in the suprachiasmatic area and 59 percent in mice receiving pellets in the retrochiasmatic area (Fig. 1). A majority of the mice receiving pellets in these areas also exhibited imperforate vaginas and had ovaries that lacked preovulatory follicles (Table 1). Animals with melatonin-containing implants in other brain areas maintained normal reproductive tract weight (Fig. 1). The one exception was a



0036-8075/81/1113-0821$01.00/0

Table 1. Effect of location of melatonin-containing implants on the reproductive state of female *Peromyscus leucopus* maintained for 7 weeks on a photoperiod with 16 hours of light and 8 hours of darkness.

| Location of implant | *N* | Mean weight (mg) of reproductive tract ± standard error | Mice with imperforate vaginas | Mice with preovulatory follicles |
|---|---|---|---|---|
| Suprachiasmatic area | 7 | 37 ± 3* | 7* | 0* |
| Retrochiasmatic area | 5 | 39 ± 3* | 3 | 1* |
| Posterior hypothalamus | 9 | 85 ± 10 | 1 | 8 |
| Preoptic area | 9 | 86 ± 10 | 2 | 8 |
| Basal forebrain | 7 | 91 ± 15 | 1 | 5 |
| Cortex | 3 | 91 ± 17 | 0 | 3 |
| Internal capsule–striatum | 8 | 107 ± 13 | 0 | 8 |
| Midbrain reticular formation | 6 | 107 ± 5 | 0 | 6 |
| Blank implant in hypothalamus | 5 | 106 ± 18 | 0 | 5 |
| Subcutaneous implant | 7 | 88 ± 9 | 1 | 6 |

*Significantly different from value for mice implanted with blank pellets at $P < .01$ (one-way analysis of variance). Comparisons between means were made by using the error term from the analysis of variance and the *t* distribution. A chi-square test for independence was used to establish the effect of pellet location on the number of mice with an imperforate vagina and the number of mice lacking preovulatory follicles.

mouse with an implant in the medial preoptic area. It is unlikely that the surgical procedure influenced this response to melatonin, since blank implants in the hypothalamus did not elicit regression. In earlier studies on castrated rats (*9*), crystals of melatonin were effective in reducing the secretion of pituitary luteinizing hormone when implanted in the midbrain reticular formation and median eminence, but the quantities of melatonin released were not measured and possible diffusion to other brain or peripheral sites was not assessed. In *P. leucopus*, melatonin implants in and near these regions had no effect on reproductive state.

Two lines of evidence indicate that melatonin did not act at a distance from the site of implantation. First, autoradiography of brain sections indicated that [$^3$H]melatonin diffused into the surrounding tissue over a distance of less than 0.2 mm. Data from mice with pellets implanted in or against the third ventricle were discarded. Second, subcutaneous melatonin-containing implants of similar size did not elicit gonadal regression (Table 1).

The sites of melatonin action were located medially, 0.1 to 0.4 mm lateral to the third ventricle. This location could facilitate uptake of melatonin from the ventricular system. Immunohistochemical localization of endogenous melatonin in such medial hypothalamic sites as the SCN (*11*) is consistent with a ventricular mode of transport of pineal secretions (*20*); there is a close association between the pineal gland and the third ventricle in the Syrian hamster and the white-footed mouse (*21*).

The SCN are thought to regulate endogenous rhythms associated with reproduction and activity (*22*). Hamsters with lesions of the SCN remain reproductively active regardless of length of photoperiod (*23*). Our demonstration that melatonin acts in the suprachiasmatic area is significant because the SCN may be a critical target of pineal secretions (*20*). This is supported by the observation that the SCN contain melatonin (*11*) and that in Syrian hamsters the antigonadal effect of long-term melatonin implants is abolished by SCN lesions (*24*). Experimental evidence showing the

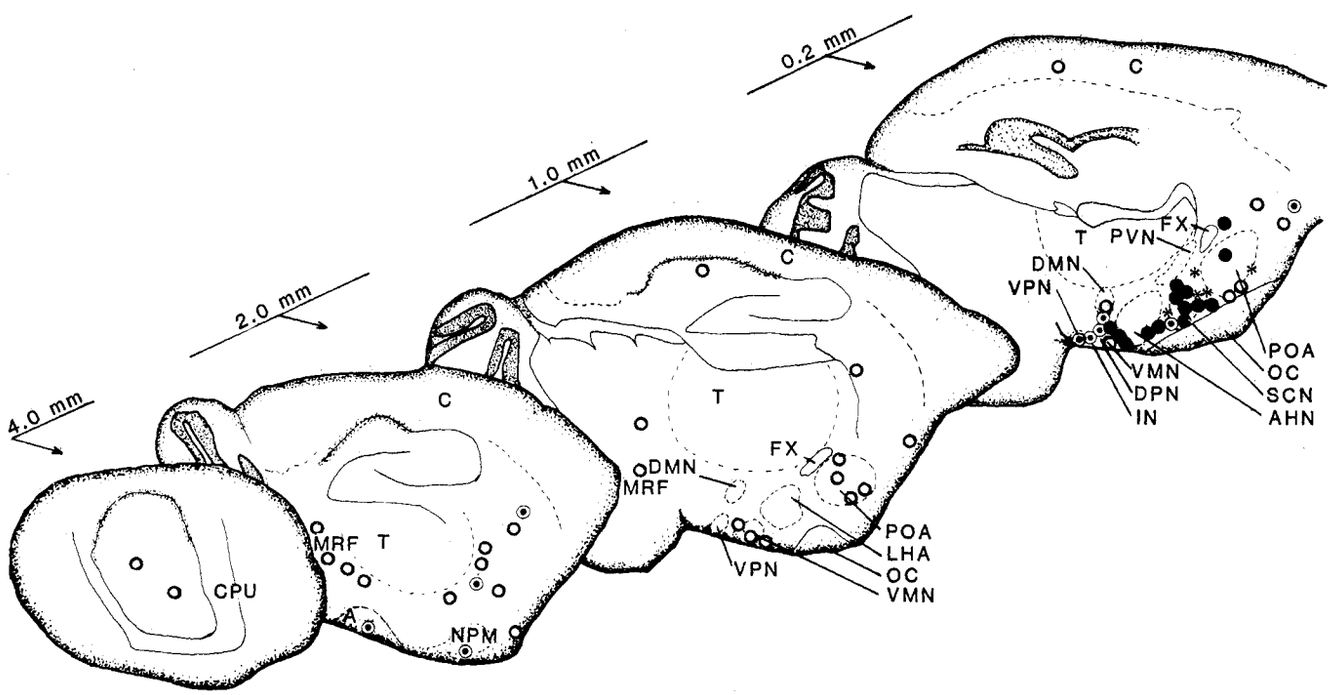


Fig. 1. Diagrams of sagittal sections of female *P. leucopus* brain, showing the effects of long-term intracranial implants of melatonin-containing pellets on reproductive tract weight (RTW). Symbols indicate the location of each implant as well as the magnitude of the response: (●) RTW < 45 mg, (⊙) RTW 45 to 70 mg, and (○) RTW > 70 mg. Asterisks show the location of blank pellets (RTW > 70 mg). The distance between each sagittal section and the midline is shown above the drawings. Abbreviations: *AHN*, anterior hypothalamic nucleus; *A*, amygdala; *C*, cerebral cortex; *CPU*, caudate-putamen; *DMN*, dorsomedial nucleus; *FX*, fornix; *IN*, infundibular nucleus; *LHA*, lateral hypothalamic area; *MRF*, midbrain reticular formation; *NPM*, nucleus preopticus magnocellularis; *OC*, optic chiasma; *DPN*, dorsal premammillary nucleus; *VPN*, ventral premammillary nucleus; *POA*, preoptic area; *PVN*, paraventricular nucleus; *SCN*, suprachiasmatic nucleus; *T*, thalamus; *VMN*, ventromedial nucleus.

SCN as the exclusive brain site of melatonin activity is not conclusive, however, since Syrian hamsters with SCN lesions undergo gonadal regression in response to multiple daily injections of melatonin (*25*). The basis for the antigonadal effects of melatonin might be the presence, near the SCN, of a melatonin-sensitive dopaminergic system that regulates prolactin release (*26*). In Syrian hamsters prolactin is thought to play a critical role in mediating the inhibition of gonadal function which occurs during exposure to a photoperiod with short days (*27*).

The observation that nearly physiological quantities of melatonin inhibit gonadal function to the same degree achieved by exposure to a photoperiod with short days supports the view that pineal melatonin mediates the reproductive effects of such a photoperiod by acting at a specific neural site.

J. DAVID GLASS
G. ROBERT LYNCH
*Department of Biology,*
*Wesleyan University,*
*Middletown, Connecticut 06457*

### References and Notes

1. S. Gaston and M. Menaker, *Science* **158**, 925 (1967); K. Hoffmann, *J. Comp. Physiol.* **85**, 267 (1973).
2. G. R. Lynch, *Oecologia* **13**, 363 (1973).
3. R. Y. Moore, in *The Pineal Gland and Reproduction*, R. J. Reiter, Ed. (Karger, Basel, 1978), p. 1.
4. D. C. Klein, J. L. Weller, R. Y. Moore, *Proc. Natl. Acad. Sci. U.S.A.* **68**, 3107 (1971); R. Y. Moore and D. C. Klein, *Brain Res.* **71**, 17 (1974).
5. R. A. Hoffman and R. J. Reiter, *Science* **148**, 1609 (1965); G. M. Farrar and J. R. Clarke, *Neuroendocrinology* **22**, 134 (1976).
6. B. D. Goldman, V. Hall, C. Hollister, P. Roychoudhury, L. Tamarkin, W. Westrom, *Endocrinology* **104**, 82 (1979); P. G. Johnston and I. Zucker, *Biol. Reprod.* **23**, 1069 (1980); D. J. Margolis and G. R. Lynch, *Gen. Comp. Endocrinol.*, in press.
7. M. Cohen, D. Roselle, B. Chabner, *Nature (London)* **274**, 894 (1978); J. E. Martin and C. Sattler, *Endocrinology* **105**, 1007 (1979).
8. F. C. Anton-Tay and J. L. Diaz, *Life Sci.* **10**, 841 (1971).
9. F. Fraschini, B. Mess, L. Martini, *Endocrinology* **82**, 919 (1968).
10. L. P. Niles, Y.-W. Wong, R. K. Mishra, G. M. Brown, *Eur. J. Pharmacol.* **55**, 219 (1979).
11. G. A. Bubenik, G. M. Brown, L. G. Grota, *Brain Res.* **118**, 417 (1976).
12. J. D. Glass and G. R. Lynch, *Neuroendocrinology*, in press.
13. The mice were the laboratory-reared offspring of a genetically heterogeneous stock derived from mice trapped in central Connecticut.
14. M. D. Rollag, E. S. Panke, W. Trakulrungsi, C. Trakulrungsi, R. J. Reiter, *Endocrinology* **106**, 231 (1980).
15. The brain was frozen in liquid nitrogen and 8-μm-thick sections were made with a cryostat. Standard histological procedures were used (*11*).
16. W. L. Whitaker, *J. Exp. Zool.* **83**, 33 (1940).
17. T. Pedersen and H. Peters, *J. Reprod. Fertil.* **17**, 555 (1968).
18. Light microscope autoradiograms were prepared by coating 8-μm-thick frozen sections fixed for 2 seconds in cold acetone with Kodak NTB-2 emulsion. The autoradiograms were exposed for 3 weeks before development. The extent of spread of melatonin from the implanted pellets was determined by measuring the distance from the implant at which the density of grains exposed by [$^3$H]melatonin equaled that of background.
19. G. R. Lynch and S. L. Gendler, *Oecologia* **45**, 318 (1980).
20. F. Anton-Tay, C. Chou, S. Anton, R. J. Wurtman, *Science* **162**, 277 (1968).
21. M. N. Sheridan and R. J. Reiter, *J. Morphol.* **131**, 153 (1970); J. D. Glass and G. R. Lynch, *J. Comp. Physiol.*, in press.
22. M. H. Stetson and M. Watson-Whitmyre, *Science* **191**, 197 (1976); F. K. Stephan and A. Nunez, *Behav. Biol.* **20**, 1 (1977); B. Rusak and I. Zucker, *Physiol. Rev.* **59**, 449 (1979).
23. B. Rusak and L. P. Morin, *Biol. Reprod.* **15**, 366 (1976).
24. B. Rusak, *ibid.* **22**, 148 (1980).
25. E. L. Bittman, B. D. Goldman, I. Zucker, *ibid.* **21**, 647 (1979).
26. A. Bjorklund, O. Lindval, A. Nobin, *Brain Res.* **89**, 29 (1975).
27. F. Bex, A. Bartke, B. D. Goldman, S. Dalterio, *Endocrinology* **103**, 2069 (1978); B. D. Goldman, K. S. Matt, P. Roychoudhury, M. H. Stetson, *Biol. Reprod.* **24**, 287 (1981).
28. Supported by grant NS-15503 from The National Institutes of Health.

16 June 1981; revised 13 August 1981

## Optimization Theory Fails to Predict Performance of Pigeons in a Two-Response Situation

Abstract. *Optimization theory states that organisms behave in a way that maximizes reinforcement or "value." In a two-response situation, pigeons' response proportions approximately equaled reinforcement proportions, even when this behavior pattern substantially decreased the rate of reinforcement. Optimization or reinforcement maximization was not supported as the basic mechanism underlying choice behavior.*

A fundamental question in the study of choice behavior is what basic principle most accurately describes how an organism distributes its time among the various behaviors that are possible in a given environment. One possible answer to this question is provided by overall maximization theory or optimization theory. According to optimization theory, an organism distributes its behaviors so that, in the long run, some variable (for example, the amount of food received, the energy content of the food, or the total subjective value from all sources of stimulation) is maximized. Although characterizations of the variable to be maximized vary with different writers and different experimental contexts, the notion of maximization has become increasingly popular in a number of disciplines. Among psychologists, Rachlin and his colleagues have propounded the view that organisms allocate time so as to maximize value (*1*). Optimization theory is currently popular in behavioral ecology, where researchers have shown that members of diverse species approximate optimal choices in such behavioral realms as foraging, prey selection, diet selection, mating, and choice of group size (*2*). In economics, the notion that every consumer spends his or her income so as to maximize subjective utility is such a fundamental part of microeconomic theory that it is seldom questioned. Thus, Samuelson has claimed that the view that consumers maximize subjective utility "is not merely a law of economics, it is a law of logic itself" (*3*).

The purpose of this report is not to dispute that many organisms produce near-optimal behaviors in a variety of situations. Rather, it is to provide evidence against optimization as the basic mechanism underlying choice behavior. How such a mechanism might work can be explained with a simple example. Suppose a hungry pigeon can peck at either of two response keys, and responses at each key occasionally provide access to food. According to Rachlin's optimization theory (*1*), an animal in such a choice situation will try various methods of distributing its behavior and eventually settle on the distribution that provides the maximum rate of food delivery. For example, by testing various ways of allocating its behavior the animal may learn that distributing 30 percent of its responses on the red key and 70 percent on the green key produces the highest rate of food reinforcement. If so, the animal's behavior should stabilize around this response distribution.

A competing theory of choice behavior is Herrnstein's (*4*) matching equation, which states that the proportion of responses devoted to one alternative will match (equal) the proportion of reinforcements provided by that alternative. For the situation just described, Herrnstein's equation can be written

$$\frac{P_G}{P_G + P_R} = \frac{F_G}{F_G + F_R} \quad (1)$$

where $P_G$ and $P_R$ are the numbers of pecks on the green and red keys, and $F_G$ and $F_R$ are the numbers of food reinforcements received from the green and red keys, respectively. For many choice situations, matching theory and optimization theory predict nearly or exactly the same behavior, but in some circumstances their predictions are different. This experiment was designed to test these two theories in a simple choice situation for which the two theories make markedly different predictions.


0036-8075/81/1113-0823$01.00/0 