metabolism cages, and blood and urine samples were taken from five rats. Of the 18 remaining animals, three were offered water to drink for 8 hours before the test was terminated, and seven were returned to their home cages with food and water freely available for 4 days. The eight remaining animals given NaCl were subjected to an additional 24-hour period of deprivation, after which four were killed; the other four animals were offered water to drink for 8 hours before terminating the test.

Significantly more lithium was excreted when water was available from 8 to 16 hours after the rat was given LiCl than when water was absent ($P < .005$) (Table 1). The volume of urine excreted during the 8-hour period of deprivation (after administration of the salt) was significantly elevated in animals given LiCl as compared to the animals given NaCl ($P < .01$).

The hematocrit of rats given LiCl was elevated above that of rats given NaCl after both the 8-hour period of fluid deprivation ($P < .005$) and the 8-hour period of water intake ($P < .005$). After the 32-hour period of water deprivation, the volume of urine and the hematocrit of the rats given NaCl did not differ significantly from that of the rats deprived for 8 hours after being given LiCl. Nevertheless, significantly more water was drunk by the rats given LiCl and deprived for 8 hours than by the rats given NaCl and deprived for 32 hours ($P < .01$). The water intake of the rats deprived for 32 hours after the administration of NaCl was significantly higher than that of the animals deprived for only 8 hours after administration of NaCl ($P < .025$). The average daily intake of water of the rats given LiCl exceeded that of the rats given NaCl for the 4 days after administration of the salt ($P < .05$). No consistent differences were observed in the serum osmolality of the various groups.

The concentration of lithium in the serum of the rats receiving LiCl was significantly elevated 8 hours after administration as compared to that after 16 hours ($P < .005$), regardless of whether water was available for the last 8 hours of testing. Of the lithium administered to the rats who were thereafter deprived for 16 hours, an average of 40 percent was excreted in the urine, 10 percent was in the intestine, and an estimated 25 percent was in the extracellular fluid and the rest probably was distributed throughout the intracellular space (*3*).

This experiment demonstrates that a single load of LiCl in the stomach can consistently and markedly increase the water consumption of rats. Although lithium given in the manner described causes an increase in the urine volume and an elevation of the hematocrit, these changes alone were not responsible for the magnitude of the thirst shown by the test animals. After the rats given NaCl were deprived for 32 hours, their urine volumes and hematocrits were comparable to those of rats given LiCl and deprived for 8 hours. However, they only drank half as much water during the 8-hour intake test as did the animals given LiCl.

The rats excreted more lithium when they had access to water than when water was withheld, even though only one-half of the lithium administered was excreted in 16 hours by rats allowed to drink water for the last 8 hours of the test period. If lithium is passively excreted by the kidney, as suggested (*4*), then considerably more time would be required for the elimination of the entire lithium load. This could account for the increased daily intake of water shown by the animals given LiCl. Lithium excretion increased when patients under treatment with lithium carbonate increased their water intake (*5*). These findings provide experimental evidence in support of the forced hydration procedure used in the treatment of lithium intoxication in man (*6*).

Alterations in the blood volume and tonicity of the rats receiving LiCl cannot account for the magnitude of their thirst. Rather, the increased water intake of the rats given LiCl may constitute a mechanism serving to facilitate the renal elimination of the toxic lithium ions. By increasing their water intake, the rats given LiCl accelerated the renal excretion of lithium as well as the detoxification of their bodies. We propose that this phenomenon be called "antidotal thirst," to distinguish it from thirst induced by hypovolemia or hyperosmolarity (*7*). Antidotal thirst may be another example of a homeostatic mechanism (*8*).

DONALD F. SMITH
SAUL BALAGURA
Department of Psychology, University of Chicago, Chicago, Illinois 60637
MYER LUBRAN
Department of Pathology, University of Chicago

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Photoperiodically Significant Photoreception in Sparrows: Is the Retina Involved?

Abstract. *Blind house sparrows (150 birds) and normal ones (199 birds) were subjected to various photoperiodic treatments consisting of cycles of 12 hours light, 12 hours dark and 16 hours light, 8 hours dark at intensities ranging from 20 to 500 lux. The testicular response of the blind birds was found to be indistinguishable from the response of normal birds under these conditions. The data show that a functional extraretinal photoreceptor exists in this species which is fully capable of mediating the gonadal response to photoperiodic stimuli.*

Annual variation in the length of days is the most reliable of the seasonal environmental cues available to an organism and is used by many avian species to time the reproductive period. Since the discovery by Rowan in 1926 that artificial, long, daily photoperiods stimulate testis growth in juncos during a period when the testes are normally in a resting state in the field, evidence

has accumulated for the photoperiodic control of gonadal cycles in at least 50 species of mid- and high-latitude birds (*1*).

Until recently the only attempts to identify the photoreceptor responsible for photoperiodic stimulation of testis growth in birds have been those of Benoit and his co-workers (*2*). Numerous experiments by Benoit *et al.*, beginning in 1934 and continuing to the present, have established a number of facts about the photoperiodic control of testis growth in the domestic duck. In this bird it is possible to stimulate testis growth with light even after the optic nerves have been severed or both eyes removed. Localized illumination of specific areas of the brain of the duck suggests that the pituitary, the hypothalamus, and some areas of the rhinencephalon may participate in photoperiodic stimulation. Some of his data, however, led Benoit to conclude that not only a "deep receptor" in the brain but also a retinal photoreceptor is involved in what he has termed the optosexual reflex in ducks.

Recently Menaker and Keatts (*3*) demonstrated that an extraretinal photoreceptor also participates in the testis response of a passerine bird. They exposed both normal and bilaterally enucleated house sparrows (*Passer domesticus*) to 16 hours light and 8 hours dark (LD 16:8) for 61 days. At the end of this time the testes of both groups were greatly enlarged. Further, there was no significant difference in the testicular response of the birds with and without eyes. These workers suggest that retinal participation may not be involved in the normal testis response of house sparrows. However, they state, "the distinct possibility remains that the testes of both the blind and the normal birds on LD 16:8 have different growth curves and we have simply assayed them at a point in time where the two curves have leveled off together."

The study reported here was conducted to determine whether the testis growth curves of blind and normal house sparrows exposed to long days are, in fact, the same. House sparrows were field caught, approximately half were blinded, and all were subsequently exposed to various photoperiods (*4*).

Examination of the testis response

Table 1. The testicular response of blind and normal birds to various stimulatory photoperiods. The column headed "Day" gives the number of days, after the beginning of the experiment, on which samples were taken. Under the "Treatment" column, controls refer to birds killed immediately before beginning each experiment; "N" refers to normal birds, "B" to blind birds. The column headed *N* gives the sample size (number of birds). The fourth column shows the mean testis weight (both testes) in milligrams, ± 1 standard error (S.E.). The last column gives the probability derived from Student's two-tailed *t*-test. The letter designations of the experiments correspond to the parts (A to F) of Fig. 1.

Day	Treatment	*N*	Mean testis wt. ± S.E.	*P*
	Experiment A; started 15 Nov. 1967			
	Lighting conditions: LD 12 : 12; intensity, 500 lux			
0	Control	30	5 ± 1	
17	B	0*	0*	
	N	6	15 ± 7	
27	B	6	56 ± 15	$.8 < P < .9$
	N	6	50 ± 21	
37	B	6	46 ± 32	$.6 < P < .7$†
	N	6	14 ± 5	
61	B	8	142 ± 34	$.8 < P < .9$
	N	9	133 ± 37	
76	B	9	133 ± 45	$.5 < P < .6$
	N	10	173 ± 52	
	Experiment B; started 15 Nov. 1967			
	Lighting conditions: LD 16 : 8; intensity, 460 lux			
0	Control	30	5 ± 1	
17	B	0*	0*	
	N	6	94 ± 24	
26	B	8	168 ± 48	$.05 < P < .1$
	N	12	278 ± 30	
	Experiment C; started 15 Nov. 1967			
	Lighting conditions: LD 16 : 8; intensity, 46 lux			
0	Control	30	5 ± 1	
17	B	0*	0*	
	N	6	97 ± 10	
26	B	7	185 ± 61	$.8 < P < .9$
	N	7	197 ± 51	
33	B	6	190 ± 44	$.05 < P < .1$
	N	6	293 ± 20	
	Experiment D; started 21 Dec. 1967			
	Lighting conditions: LD 16 : 8; intensity, 460 lux			
0	Control	10	8 ± 2	
17	B	5	53 ± 5	$.005 < P < .01$†
	N	6	182 ± 31	
26	B	5	229 ± 64	$.5 < P < .6$
	N	6	281 ± 60	
40	B	6	421 ± 92	$.2 < P < .3$
	N	8	307 ± 35	
	Experiment E; started 21 Dec. 1967			
	Lighting conditions: LD 16 : 8; intensity, 20 lux			
0	Control	10	8 ± 2	
17	B	5	29 ± 17	$P > .9$
	N	6	31 ± 16	
41	B	12	288 ± 30	$.1 < P < .2$
	N	13	207 ± 47	
	Experiment F; started 7 Feb. 1968			
	Lighting conditions: LD 12 : 12; intensity, 470 lux			
0	Control	25	14 ± 3	
8	B	10	22 ± 5	$.6 < P < .7$
	N	10	18 ± 5	
17	B	10	70 ± 16	$.3 < P < .4$
	N	10	98 ± 26	
24	B	10	175 ± 31	$.6 < P < .7$
	N	12	200 ± 36	
31	B	10	217 ± 33	$.2 < P < .3$
	N	12	282 ± 41	
38	B	11	283 ± 58	$.6 < P < .7$
	N	12	315 ± 36	
45	B	11	307 ± 37	$.4 < P < .5$
	N	15	340 ± 23	

* Zero means that no blind birds were sampled on these dates. † In these two cases an approximate *t*-test was used since the testis weight variances were significantly different between blind and normal birds (*10*).

Table 2. Maintenance of testis weights under a long photoperiod. For explanation of the headings, see Table 1.

Day	Treatment	*N*	Mean testis wt. ± S.E.	*P*
	Experiment G; started 7 June 1967			
	Lighting conditions: LD 16 : 8; intensity, 500 lux			
1	B	0*	0*	
	N	9	355 ± 34	
44	B	5	489 ± 128	$.8 < P < .9$
	N	6	461 ± 99	

* Zero means that no blind birds were sampled on these dates.

to LD 12 : 12 and LD 16 : 8 at several different intensities showed no differences between the responses of blind and normal birds (see Fig. 1). This apparent lack of difference has been confirmed by statistical analysis. Table 1 shows the results obtained from comparing each group of blind and normal birds by the Student's two-tailed *t*-test. In only one sample was there a significant difference between blind and normal birds at the 5 percent level, normal birds having the larger testis weight in this case (experiment D, day 17 in Table 1). This is also the only point that was significant ($P < .01$) when the data were tested by a nonparametric statistic, Wilcoxon's two sample test (two-tailed).

Although in the majority of the experiments the growth of the testes of blind and normal birds was examined under stimulatory photoperiods and intensities, in one experiment, performed during the summer of 1967, the ability of a long photoperiod to maintain testis weights in blind and normal birds was tested. Birds that had been brought into full breeding condition in the field were taken into the laboratory and placed on an LD 16 : 8 photoperiod having an intensity of 500 lux. The data clearly show that, under these conditions, blind birds can maintain testis weights as well as normal birds (Table 2).

The testis response of blind birds is not distinguishable from the response of normal birds under the light cycles and intensities examined. However, this response was examined only down to an intenstiy of 20 lux. Although the eyes do not appear necessary for the testis response at intensities above 20 lux, it is possible that they are involved in the photoperiodic response to light of lower intensities—intensities that the extraretinal receptor may not be able to perceive. Bartholomew (*5*) showed that the minimum intensity needed to elicit a measurable testis response in the house sparrow is about 7 lux. While the data presented here cannot rule out the possibility that the eyes might be involved in the range of 7 to 20 lux, there is clearly no evidence of such involvement at the intensities examined. The response of blind birds to 20 lux is clearly as strong as the response of normal birds to this intensity (Fig. 1E). Although the eyes do not appear necessary for a normal testis response, the present data cannot exclude the possibility that either the extraretinal receptor (receptors) or the eyes are capable of mediating this response.

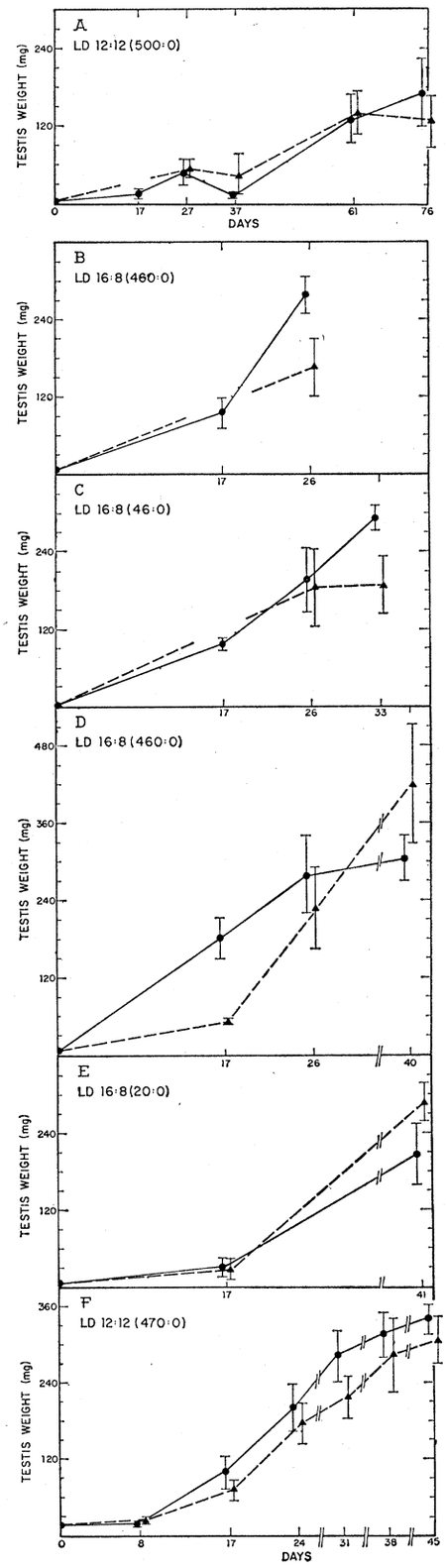

Fig. 1. The testicular response of blind and normal sparrows to various experimental regimens. Points are means of the combined weights of the two testes of all birds in each sample. Dashed lines connect the means of the blind birds; solid lines, the means of the normal birds. The vertical lines represent 1 standard error to either side of these means. Day "zero" shows the mean testis weight of birds killed immediately before beginning each experiment. Parts (B) to (F) are drawn to a similar scale. LD 12:12 (500:0) means a light-dark cycle of 12 hours light and 12 hours dark followed (in parentheses) by the intensity of the light phase: intensity of the dark phase (in lux). Notation is similar for the other parts of the figure.

Benoit's conclusion that the retina is involved in the testis response of ducks is based on data from two types of experiments. In one, Benoit deposited around the eye, in the posterior part of the orbit, slats or sheets of opaque material in ducks with both sectioned and intact optic nerves (*6*). In this way he attempted to study the action of the retinal receptor by blocking the diffusion of light behind the eye. Benoit concluded that the eye itself must be capable of participating in the testis response because, when the back of the orbit was partially masked, there was less testis growth in ducks with severed optic nerves than in those with intact nerves. In the second type of experiment, Benoit *et al.* (*7*) exposed normal ducks and ducks with sectioned optic nerves to equal intensities of light and demonstrated a stronger testis response in the normal birds.

In the duck, the route by which light reaches the extraretinal receptor may be via the orbit (*8*). If this is the case, then Benoit's interpretation of his experiments is open to question. Masking the posterior part of the orbits of intact ducks would involve positioning the slats of material around the intact nerve. Such a procedure would seem to prohibit the amount of shielding that could be accomplished if the optic nerve did not have to be respected. If more light were able to diffuse past the shields in the intact ducks to the extraretinal receptor, there would be a stronger response. Also, sectioning the optic nerves may produce degenerative changes in the eye and adjacent tissues, which could reduce the amount of light reaching the extraretinal receptor as compared to the amount of light reaching the extraretinal receptor in normal birds.

We have demonstrated the existence of a functional extraretinal photoreceptor that is fully capable of mediating the testis response in the house sparrow. Our data offer no support for the hypothesis that the retina is involved in this response. Ducks and house sparrows may of course have

different mechanisms for perceiving photoperiodically active light. However, in view of our data, we feel that Benoit's conclusions should be regarded with caution.

Several recent papers have shown that other species of birds utilize extraretinal light perception in the timing or control of other physiological responses as well as in those directly concerned with photoperiodism (*9*). Extraretinal light perception, in all likelihood performed directly by one or more areas of the brain, may well be a universal component of the sensory repertoire of birds.

HERBERT UNDERWOOD
MICHAEL MENAKER
Department of Zoology,
University of Texas,
Austin 78712

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Neuromuscular Contacts in Intracranial Arteries of the Cat

Abstract. *Nerves of intracranial arteries of the cat were restricted to adventitia, with neuromuscular contacts observed only at the border of adventitia and media. Axons of such neuromuscular contacts possessed at least two different populations of synaptic vesicles. One axonal type contained many small (500 angstroms in diameter) granular vesicles and occasional agranular vesicles. The other contained only agranular vesicles.*

Although gross observations and histologic studies have established the presence of nerves on intracranial arteries, their significance remains obscure (*1*). Such perivascular nerves are often thought to be of little functional significance (*2*). With fluorescence microscopy, nerves can be histologically identified as sympathetic or adrenergic (*3*). Electron microscopy permits differentiation of afferent and efferent nerve "endings," allows a detailed view of neuromuscular relationships, and, based upon the type of synaptic vesicles present, can probably allow distinction between adrenergic and cholinergic axons (*4*).

One of the authors (E.N.) had previously studied the ultrastructural features of the innervation of human cerebellar arteries obtained at autopsy after fixation in osmium tetroxide and embedding in methacrylate (*5*). One axon containing synaptic vesicles with electron-opaque cores or granules was seen. On the basis of descriptions of similar vesicles in sympathetic nerves of the pineal gland (*6*), we hypothesized that such an axon might be efferent, noradrenergic, and concerned with regulation of cerebral blood flow. In view of the conflicting physiological evidence (*7*), fluorescence microscopic studies indicating a rich adrenergic innervation to intracranial arteries were of particular interest (*8*). However, in two electron microscopic studies on intracranial arteries, granular vesicles were specifically not noted (*9*), and numerous granular vesicles have been observed in adrenergic sympathetic nerves to arteries in other organs (*10*). It was, therefore, considered worthwhile to reexamine the problem of intracranial arterial innervation; a matter of possible importance to regulation of cerebral blood flow and the occurrence of arterial spasm (*11*).

Because of demonstrations that the electron-opaque central cores of the granular vesicles in sympathetic neuromuscular contacts could be lost with slower penetrating fixatives such as osmium tetroxide and glutaraldehyde

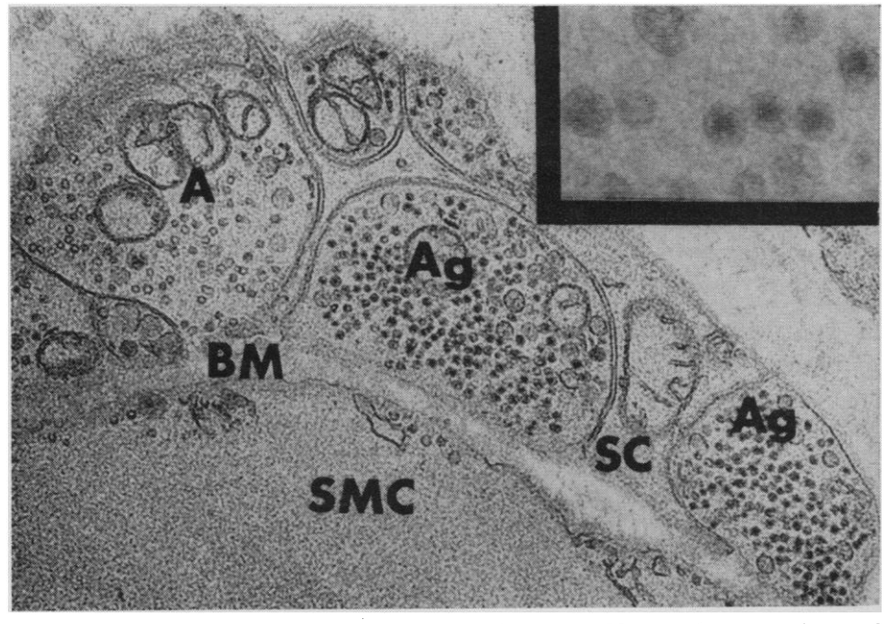

Fig. 1. A neuromuscular contact in an intracranial artery. Note coalescence of axonal and smooth muscle basement membranes (*BM*). Axon containing predominantly agranular vesicles (*A*). Axons with predominantly granular vesicles (*Ag*). Schwann cell cytoplasm investing axons (*SC*). Smooth muscle cytoplasm (*SMC*) (× 39,000). Inset: High magnification micrograph of granular vesicles shown in axons labeled *Ag* (× 122,000).