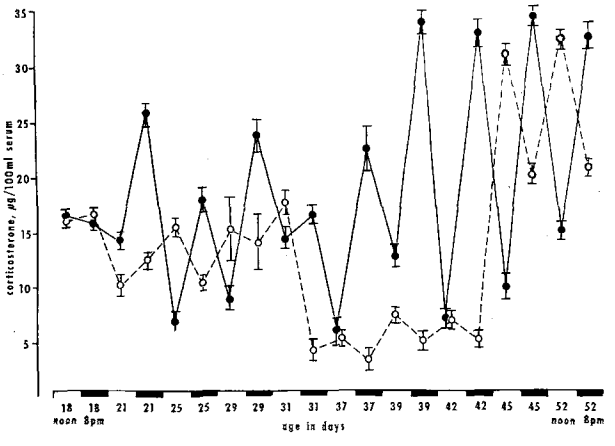
The Changes in Basal Corticosterone Secretion in Rats Blinded at Birth

Recently we have found that the onset of a daily variation in serum corticosterone is correlated in time with the development of a retinohypothalamic projection to the suprachiasmatic nucleus of the hypothalamus[1]. Light and dark have been known for a long time to influence the periodicity of a number of endocrine rhythms, including the daily cycle of corticosterone secretion[2,3]. We therefore decided to investigate whether visual input is required for the appearance of an adrenal rhythm.

Female Sprague-Dawley derived rats were obtained from Simonsen Laboratories, Gilroy, California at midgestation and were placed in a 14 h light, 10 h dark schedule (lights on at 3 h). The day after birth litters were reduced to 8 animals. The females were anesthetized with cold and half of the animals were blinded by optic enucleation. The remainder, hereafter referred to as sham-operated, were subjected to a single midline abdominal incision as a control for the stress of surgery. The animals were returned to their mothers and left undisturbed until 18 days of age. Blood samples were collected by decapitation on day 18 and day 21 at the usual time of the trough (08.00 h) and peak (16.00 h) of serum corticosterone in rats maturing under our animal room conditions[4]. The remaining litters were weaned at noon on day 21 and the weanlings placed 3 per cage. Blood samples were collected by cardiac puncture at the ages shown in the Figure. No animal was sampled more than once every 4 days. The blood was handled as previously described and corticosterone was assayed by means of a fluorometric procedure[4].



Serum corticosterone levels in sham-operated and blinded females. Samples were taken by decapitation on days 18 and 21 and by cardiac puncture on subsequent days. Each point represents mean ± standard error for 5 rats. Solid circles, intact, sham-operated females; open circles, females blinded at 1 day of age. Samples were taken at 08.00 h and 16.00 h.

The values of serum corticosterone obtained in females at different ages are shown in the Figure. At 18 days of age, the 08.00 h and 16.00 h samples were not significantly different in either intact or blinded rats. Beginning on day 21, sham-operated rats showed clear evidence of a daily rhythm (F test, $p = 0.001$), which increased in amplitude shortly after puberty (37.2 ± 1.2 days). Blind females did not show evidence of a daily rhythm until vaginal opening (45.5 ± 2.0 days). At that time (the 45 day sample) a rhythm appeared which was reversed to that of sham-operated rats. Prior to day 45, the range of serum corticosterone was first around 10–17 µg per 100 ml serum and then 2.5–7 µg per 100 ml serum.

Since only 2 sample times were chosen, it is impossible to tell whether a rhythm was absent in the blinded rats before day 45 or whether a phase shift was occurring so that by day 45 it was detectable in the 2 time periods chosen. HALBERG[2] has found that in adult mice, blinding causes a shift in both the frequency and the acrophase of the serum corticosterone rhythm so that by 3 weeks after surgery, the rhythm in blinded rats is 180° out of phase with sham-operated controls[5].

Zusammenfassung. Nachweis, dass sich bei postnatal geblendeten Ratten ein Tagesrhythmus entwickelt, der allerdings später als bei den Kontrolltieren auftritt. Der Rhythmus scheint umgekehrt zu sein.

JUDITH A. RAMALEY

Department of Physiology and Biophysics, University of Nebraska Medical Center, 42nd and Dewey Avenue, Omaha (Nebraska 68105, USA),
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COGITATIONES

On the Antagonism of Ergot Alkaloids and Dopamine by Phenothiazines

Several groups have now provided evidence for an interaction between some of the alkaloids extractable from ergot (*Claviceps purpurea*) and dopamine receptors. Some of the alkaloids may directly stimulate dopamine receptors[1–3] but some are thought to antagonize the actions of dopamine on the receptors[4–6]. It would also seem likely that the phenothiazine group of compounds, which are known to be antagonists of dopamine[7–10] can also antagonize some of the actions of ergot alkaloids[11–13] including lysergic acid diethylamide (LSD) induced hallucinations[13,14].

In an effort to understand why phenothiazines should antagonize ergot alkaloids, molecular models have been constructed of D-LSD, a potent hallucinogen known to