Electroretinogram of the Visually Deprived Cat

Abstract. Cats kept in darkness from birth show a subnormal *b*-wave in the electroretinogram to 4 weeks of age but quickly develop the full response upon stimulation. When the cats are kept without light for 1 year, the response recovers slowly after intense stimulation. A 2-day exposure to light is sufficient to reverse this diminution in response.

Zetterström (*1*) reported that the appearance of the electroretinogram can be delayed considerably by rearing animals in darkness. She found that the electroretinogram was suppressed in dark-reared kittens or, if present, was of longer latency than that of light-reared controls during the first 4 weeks of life. A striking finding was that differences between the electroretinograms of light-reared and of dark-reared animals vanished if the dark-reared animals were subjected to one testing session, which consisted of about 30 flashes of light distributed over a period of 3 hours. It was not possible to delay the appearance of the electroretinogram beyond 4 weeks of age by dark rearing; kittens kept in darkness until they were more than 4 weeks old before being exposed to light showed an electroretinogram comparable to that of controls of the same age. Zetterström's measurements were all confined to the *b*-wave; the *a*-wave is not recorded until a later age. The effects of long-term dark rearing were not investigated.

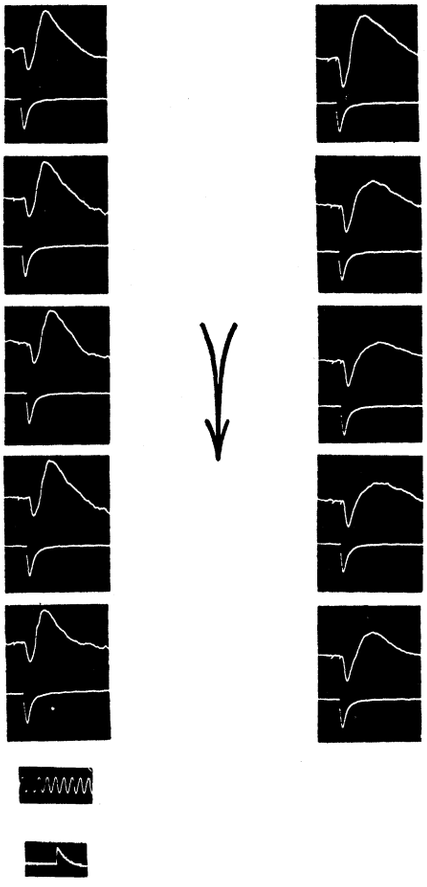

Fig. 1. (Left) An electroretinogram from a control animal: (from top) five recordings taken at 10-second intervals. (Right) Recordings obtained, under the same conditions, from an animal reared in darkness for 1 year. The change in amplitude of the *b*-wave (upward deflection) during the series is evident. Time calibration, 50 cy/sec; amplitude calibration, 200 μv. The break in the bottom line of each record indicates onset of the light flash.

In the study reported here, ten kittens were raised from birth in the laboratory, five in continuous darkness and five controls in the normally lighted animal room. At 1 year of age all the animals were anesthetized with sodium pentobarbital (Nembutal) and electroretinograms were obtained with a corneal electrode. Stimuli at five different intensities (see Fig. 1) were produced with a Grass PS-1 photic stimulator. All the animals were first light-adapted and then dark-adapted for 1 minute before testing began.

It was found that there were no significant differences between the electroretinograms of the two groups of animals when 1 minute elapsed between stimuli. When, however, a series of five flashes at the higher intensities was presented at the rate of one every 10 seconds, there was a diminution in the amplitude of the *b*-wave following the earlier flashes (Fig. 1). The effect was not observed with flashes at the two lowest intensities.

The differences between the groups at the three highest intensities were shown by rank analysis of variance to be significant at better than the .01 level. Averaged results for the two groups are shown in Fig. 2. No significant differences in either latency or amplitude were found for the *a*-waves of light-reared and dark-reared animals. When the dark-reared animals were placed in the lighted animal room it was found that exposure to 48 hours of illumination was sufficient to eliminate the diminution of the *b*-wave response to a train of high-intensity stimuli.

It is interesting to note that the change in amplitude of the *b*-wave during a train of stimuli found in the dark-reared animal is similar to the change found by Horsten and Winkelman (*2*) to be produced in the cat during impaired oxygen supply and referred to by them as the "exhaustion phenomenon." Thus, it is suggested that exclusion of adequate stimulus to the cat retina during post-partum maturation produces some sort of deficiency in retinal metabolism, but one which is reversed upon surprisingly short exposure to light.

Glucose and oxygen were once thought to be the primary, if not the exclusive, requirements for the functional metabolism of retinal and central neurons. More recently, ribonucleic acid and protein have been found to participate in such metabolism (*3*). Hellström and Zetterström suggest specifically that a primary correlation may exist between the level of the sulfhydryl groups in the retina and the appearance of the electroretinogram. Levels of ribonucleic acid in the nuclei and cytoplasm of ganglion cells are quickly altered by variations in the functional demands imposed by stimulation. Chronic depression of protein and ribonucleic acid follows prolonged visual deprivation, but the study under discussion and others carried on in our laboratory (*4*) lead to the conclusion that, until such depression is extreme, normal physiological functions of neu-

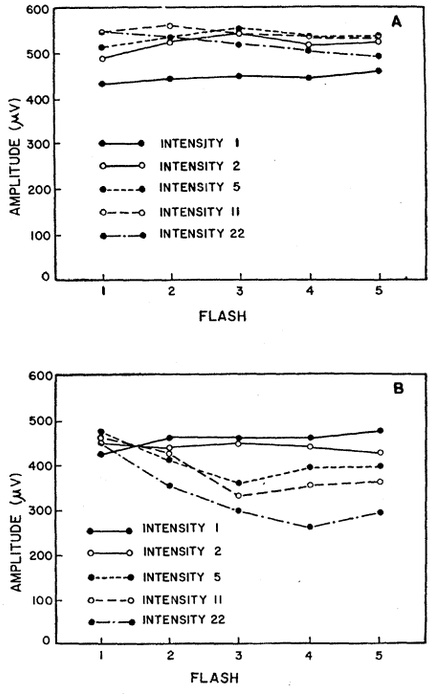

Fig. 2. (*A*) Averaged data for control group: amplitude of *b*-wave as a function of the order of flash in a series. (*B*) Averaged data for dark-reared group: the change in amplitude of the *b*-wave during a series at high intensities of stimulation is clear. Intensity of stimulus light is given in lumen-seconds per square foot (data from manufacturer).

ral transmission may not be impaired. The more intimate relations between neurons may, however, be affected in such a way that only tests of complex perceptual processes will reveal the visual deficits produced by visual deprivation (*5*).

BRUCE L. BAXTER
AUSTIN H. RIESEN

Department of Psychology,
University of Chicago,
Chicago, Illinois

References and Notes

1. B. Zetterström, *Acta Physiol. Scand.* **35**, 272 (1955 → B. Hellström and B. Zetterström, *Exptl. Cell Research* **10**, 248 (1956).
2. G. P. M. Horsten and J. E. Winkelman, *A.M.A. Arch. Ophthalmol.* **57**, 557 (1957).
3. K. Bech, *Anat. Skr.* **2**, 59 (1955); S. O. Brattgård, *Acta Radiol. Suppl.* **96**, 1 (1952); H. Hydén, in J. Brachet and A. E. Mirsky, *The Cell* (Academic Press, New York, 1960), vol. 4.
4. B. Baxter, thesis, Univ. of Chicago (1959); A. H. Riesen, *Am. J. Orthopsychiat.* **30**, 23 (1960).
5. A. H. Riesen, *J. Nervous Mental Disease* **132**, 21 (1961). This investigation was supported by grant No. B-1590 from the National Institute of Neurological Diseases and Blindness.

3 July 1961

Predictions of the Growth Model for Normal Chicken Growth

Abstract. The model of growth control advanced by Weiss and Kavanau has been further evaluated with an I.B.M. 7090 computer. Predictions for the concentration of growth-inhibiting substances and their quantitative distribution in the animal are in good agreement with known developmental changes. Results are being used to predict the course of compensatory organ growth in the immature animal.

The theory of growth control advanced by Weiss (*1*) has been formulated into a set of three simultaneous differential equations by Weiss and Kavanau (*2*). The mathematical model extends beyond a mere representation of normal growth to growth disturbances and regulation and dissects the growth problem into a series of detailed questions which lend themselves to experiment. Some of these questions concern changes in volume of body fluids and concentration of postulated growth-inhibiting substances. Predictions for these changes based upon data for normal chicken growth follow.

The basic assumptions upon which the model was predicated are:

1) The gain in mass of a living system is the net balance of mass "produced" and retained over mass "destroyed" and otherwise lost.

2) The mass M of the system consists of two functionally different components: The generative mass G, comprising the instruments of protoplasmic reproduction, and the differentiated mass D, derived from G and consisting of terminal products and other derivatives that do not reproduce.

3) Each specific cell type reproduces its protoplasm through the self-duplication and catalytic activity of "templates" characteristic of that cell type. Each cell also produces specific, freely diffusible "antitemplates" which can inhibit the activity of the corresponding templates, and which become distributed in the "dilution pool" V (which includes the blood, lymph, intercellular fluids, and other parts of the body to which they gain access).

4) The antitemplates regulate growth by a negative feedback mechanism, in which their increasing populations render an increasing proportion of the homologous templates ineffective, resulting in a corresponding decline in growth rate.

5) Attainment of terminal size represents a stationary equilibrium between incremental and decremental growth components.

6) The generative mass, and the differentiated mass including the antitemplates, undergo continual metabolic degradation and replacement.

Recently, predictions of the model were determined for compensatory organ growth in the adult (*3*). By reason of the model's explicitness, several possible mechanisms considered in the more general scheme of growth control (*2*) were ruled out as unrealistic. For example, of the various alternative sources of production of the antitemplates, all were ruled out except the generative mass.

The model reproduces a number of phenomena observed in the compensatory response to disturbance of equilibrium of organ systems. Thus it reproduces the spurt of compensatory growth of an organ system after artificial reduction and the spontaneous resumption of organ growth after artificial lowering of antitemplate concentration at terminal equilibrium [observed in liver plasmapheresis experiments with adult rats (*4*)]. It predicts that compensatory organ growth will proceed in an undulatory fashion and accounts for the heretofore unexplained secondary spurt of growth (after the first week or so) in partially hepatectomized rats. It accounts for the fact that liver cell-protein synthesis in the regenerating rat liver attains its maximum rate before plasma-protein synthesis does (*5*), and it predicts the decrease in rate of regeneration of organ mass with increasing age. Additionally, the model has directed attention to a number of questions to be decided by future experiments (*3*).

In point of fact, the model represents a class of systems controlled by negative feedback. In a formal sense it is equally valid for alternative biological systems, requiring for conversion merely simplification or reassignment of significance, or both, of variables and parameters. For this reason, and in view of the increasing weight of evidence for negative feedback control of growth processes (*1*, *6*), investigations of its predictions, stability, and general behavior after disturbances of equilibrium are significant for current studies.

Evaluation of the model for compensatory organ growth in the adult was undertaken first because the simultaneous differential equations (*2*) describing the adult system are relatively simple. Although the stability of this process in the adult has been verified for a wide range of mass reductions and other disturbances, it remains to determine predictions for compensatory organ growth in the immature animal. These are of particular interest because almost all experimentation is carried out with immature, rapidly growing animals.

In order to solve the differential equations of the model it is necessary to specify the daily rate of catabolic loss of antitemplates, k_5, and the number x of antitemplates required to inactivate each template. Since these are not known, solutions for the adult system had to be scanned with a range of biologically feasible values (*3*). These solutions, in turn, indicated probable limits for the two parameters. Accordingly, the values 10⅓, 21⅔, and 32 percent for k_5 (half lives of 6½, 3¼, and 2⅙ days), and 4, 8, and 16 for x, were chosen for the present study.

To predict the course of compensatory organ growth in the immature animal, it is necessary to fit the model to the data for normal chicken growth, for each combination of values of k_5 and x. Each value of x generates a curve for the antitemplate concentration C, and each value of k_5 a curve for the number of antitemplates I present in the system during growth (*2*, Eqs. 4, 6a, and 21). From this information, nine curves for the growth in volume of the dilution pool V can be derived ($V = I/C$).