Post-Inhibitory Rebound of the *b*-Wave of the Pigeon ERG

DOWLING[1] has shown that the *b*-waves of the electroretinogram (ERG) exhibit the first signs of normal adaptation changes in the visual system, and has proposed that this adaptation is produced by a simple inhibitory feedback loop involving bipolar and amacrine cells of the retina. In support of this hypothesis electron microscope studies by DOWLING and BOYCOTT[2] indicate that reciprocal synapses occur between bipolar terminals and amacrine processes, which could function to produce such inhibitory feedback or gain control. If adaptation is produced by inhibition of bipolar cells then some of the signs of this action should be seen in the *b*-waves of the ERG, since they presumably originate from the bipolar cell layer of the retina[3]. Evidence is presented in this report which indicates that bipolar cells are inhibited during light adaptation, since a post-adaptation rebound effect occurs in the *b*-waves of the ERG.

Ten pigeons, *Columba livia*, were anesthetized with sodium pentabarbital, and their pupils were dilated with atropine sulphate. Silver-silver chloride electrodes were used in conjunction with a DC preamplifier, oscilloscope and polygraph to record ERGs.

The method consisted of presenting a flickering light to the pigeon's right eye until the ERGs so produced were of constant magnitude. This indicated that an equilibrium had been reached between adaptation produced by each flash and recovery between successive flashes. Then the flicker was replaced momentarily by a steady adapting light, and reintroduced in synchrony with adaptation offset, as shown in the inset in Figure 1. The course taken by the post-adaptation *b*-waves in recovering their pre-adaptation equilibrium level was the prime interest of this study.

The flickering light and the continuous adapting light originated from separate optical systems and were focused on the same area of the pigeon's right retina. The illuminance of both beams was 983 ft candles, and the relative intensity was changed by adding neutral density filters. Flicker rate and percentage of light to cycle were kept constant throughout these experiments at 4/sec and 25% respectively.

In the first experiment 5 birds were presented with adaptation periods of 0.5, 1, 2 and 4 sec. The intensity of the flickering light was reduced to 25% of the intensity of the adapting light. In the second experiment involving the other 5 birds, the duration of adaptation was kept constant at 10 sec, while the relative intensity of the adapting light was varied from 1 log unit above the intensity of the flickering light to 1 log unit below, in 0.4 log unit steps. A control condition, where 10 sec of darkness replaced the flicker, was also presented.

The *b*-waves produced by the 3 flashes immediately preceding adaptation were measured to the nearest 3 μV, together with those produced by the first, second, third, sixth and twelfth post-adaptation flashes. Post-adaptation *b*-waves, expressed as a percentage of mean pre-adaptation *b*-waves, are presented in Figure 1 for the first experiment and in Figure 2 for the second experiment. From Figure 1 it can be seen that a post-adaptation rebound effect occurs in the *b*-waves of the pigeon ERG. Although this effect is relatively small, a Wilcoxen Matched-Pairs Signed-Ranks Difference Test[4] reveals that the *b*-waves produced by the third post-adaptation flash are significantly larger than those produced by the sixth ($T = 2$, $N = 33$, $p = 0.0014$, for a 2-tailed test). This transient increase in the *b*-waves appears to be related to light adaptation, with shorter periods of adaptation resulting in increases above the mean pre-adaptation level.

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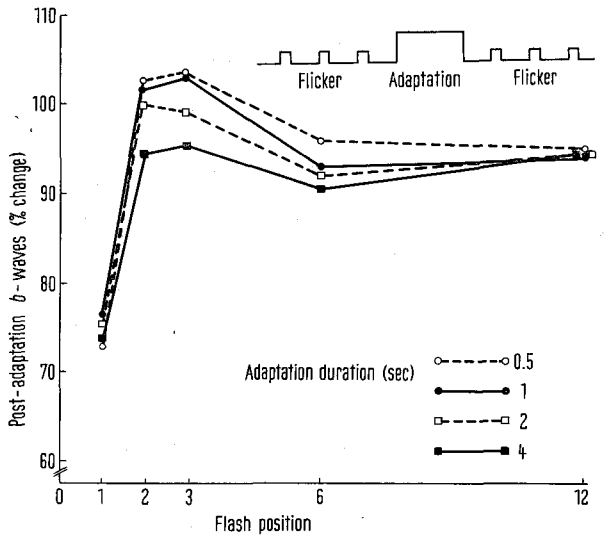

Fig. 1. Post-adaptation *b*-waves as a function of duration of light adaptation. *b*-Waves are expressed as a percentage of their mean pre-adaptation value. Flash position indicates the ordinal position of flashes following the offset of adaptation. Flash rate 4/sec. The temporal pattern of stimulation shown in the inset is explained in the text.

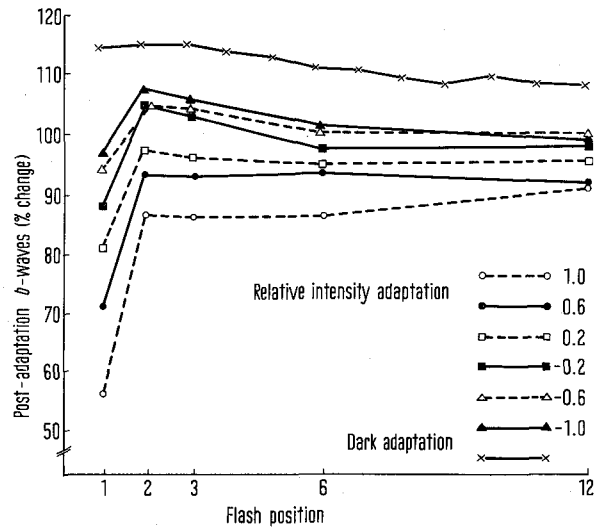

Fig. 2. Post-adaptation *b*-waves as a function of relative intensity of light adaptation. Adaptation intensity values are expressed in log units relative to the flicker intensity. Duration of adaptation 10 sec, flash rate 4/sec.

The results of the second experiment show that although the post-adaptation *b*-waves generally are diminished more with increased intensity of adaptation, a non-monotonic recovery curve is still obtained. Since no rebound effect was obtained for the dark adaptation control, it can be concluded that light is necessary to produce this effect, which in turn adds weight to the argument that these are post-inhibitory rebound effects. The prominence of the *b*-wave rebound at lower levels of adaptation suggests that 2 processes may be involved, one an initial rapid transient effect producing the rebound, and a second slower and more gradual recovery. As in the early stages of dark adaptation the slow process may be ascribed to photochemical changes, and the rapid transient effect to neural processes[5].

Several control observations were made which ruled out the possibility that these rebound effects resulted from a mere summation with other waves of the ERG, or from real differences in the intensity of the post-adaptation light flashes.

These results, together with a similar observation made by GARCIA-AUSTT and PATETTA-QUEIROLO[6] on the ERGs of neonatal chickens, lend support to DOWLING's view that visual adaptation results from inhibitory feedback to retinal bipolar cells[7].

Zusammenfassung. Im ERG von Tauben zeigen die *b*-Wellen einen Rückpralleffekt, «rebound effect», nach der Lichtadaptation. Dies scheint darauf hinzuweisen, dass während der Lichtadaptation die bipolaren Zellen gehemmt werden.

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Zur Frage der Beziehungen zwischen enddiastolischem Ventrikeldruck und dp/dt bzw. d^2p/dt^2 der Ventrikeldruckkurve des Herzens

Die Differentialquotienten dp/dt und d^2p/dt^2 der Ventrikeldruckkurve des Herzens informieren über dessen Kontraktionsdynamik. Diese ebenso wie die Kontraktilität werden durch inotrope Faktoren und enddiastolische Faserlänge bzw. -spannung bestimmt. Als Ausdruck der Faserspannung kann der enddiastolische Ventrikeldruck gelten, der durch enddiastolisches Volumen und Myokarddehnbarkeit determiniert ist.

Da der enddiastolische Druck teilweise als wesentlicher, die Kontraktilität bestimmender Faktor angesehen wurde[1–3], haben wir die Beziehungen zwischen enddiastolischem Druck sowie dp/dt und d^2p/dt^2 unter verschiedenen hämodynamischen bzw. kontraktilen Situationen des Herzens untersucht.

Methodik. Die Untersuchungen wurden an 28 künstlich beatmeten und thorakotomierten Katzen durchgeführt. Die Ventrikeldruckmessung erfolgte durch Metallkanülen nach vorheriger transventrikulärer Punktion des linken Herzventrikels und Stathamelelementen 23 Db. sowie entsprechenden Druckverstärkern. Es erfolgte eine elektrische Differentiation der Ventrikeldruckkurve mit 2 in Serie geschalteten RC-Gliedern (Zeitkonstante 0,25 msec). Registrierung der Druck- und RC-Signale mit einem Electronics for Medicine Research Recorder DR 8.

Elf Versuche erfolgten am isolierten Katzenherzen. Einzelheiten der Methodik bei KOHLHARDT et al.[4] Perfusion der spontan schlagenden Präparate bei 35–37 °C über den linken Vorhof mit einem O_2-begasten Erythrozyten-Tyrode-Gemisch. Zusammensetzung der Tyrodelösung: 8,0 g NaCl; 0,3 g KCl; 0,28 g $CaCl_2$; 0,12 g $MgCl_2$; 1,0 g $NaHCO_3$; 64,8 mg NaH_2PO_4 sowie 2,0 g Glukose in 1000 ml. Im linken Ventrikel war ein PVC-Katheter zur Druckmessung eingebunden. Druckregistrierung und elektrische Differenzierung der Ventrikeldruckkurve erfolgte wie bei den In-vivo-Versuchen. Messung des Herzzeitvolumens durch Messzylinder.

Ergebnisse. Druckbelastung des linken Ventrikels in vivo durch Aortenkompression führte zum Anstieg seines enddiastolischen Druckes. Gleichzeitig ergab sich ein Anstieg von dp/dt_{max} und d^2p/dt^2_{max} (Figur 1). Auffallend ist eine stärkere Zunahme von d^2p/dt^2_{max}.

Bei konstantem enddiastolischem Ventrikeldruck steigert K-Strophanthin (30 µg, 40 µg, 60 µg/kg) die Werte von dp/dt_{max} von $2547{,}5 \pm 261{,}4$ mm Hg $\times$ sec^{-1} bis auf $3185{,}9 \pm 86{,}6$ mm Hg $\times$ sec^{-1} ($p = 0{,}01$) und die Werte für d^2p/dt^2_{max} von $79586{,}0 \pm 8153{,}7$ mm Hg $\times$ sec^{-2} bis auf $106556{,}0 \pm 4377{,}2$ mm Hg $\times$ sec^{-2}.

Volumenbelastung mit 6prozentiger Makrodexlösung (stufenweise Injektion von jeweils 5 ml/kg bis zu einer Gesamtmenge von 25 ml/kg) erhöht den enddiastolischen Ventrikeldruck von $6{,}7 \pm 0{,}8$ mm Hg auf $17{,}1 \pm 3{,}6$ mm Hg ($p < 0{,}01$). Mit diesem enddiastolischen Druckanstieg ist eine Zunahme von dp/dt bzw. d^2p/dt^2 verbunden, wobei jedoch bei einem Teil der Versuche die Werte für dp/dt_{max} und d^2p/dt^2_{max} bei weiterer Zunahme des enddiastolischen Druckes wieder abnehmen (Figur 2).

Erfolgt am isolierten Herzen eine abrupte Füllungsdruckerhöhung von 4 auf 10 mm Hg im linken Vorhof, so steigen enddiastolischer linker Ventrikeldruck von $4{,}02 \pm 0{,}95$ mm Hg auf $9{,}02 \pm 0{,}68$ mm Hg ($p < 0{,}01$), dp/dt_{max} von $1507{,}8 \pm 36{,}5$ auf $1588{,}4 \pm 22{,}8$ mm Hg $\times$ sec^{-1} ($p = 0{,}05$), d^2p/dt^2_{max} von $35168{,}2 \pm 1740{,}0$ auf $40948{,}3 \pm 2890{,}1$ mm Hg $\times$ sec^{-2} ($p < 0{,}05$) und die

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