Effects of changes in systemic blood pressure on the electroretinogram of the cat: evidence for retinal autoregulation. Eva Demant, Kunihiko Nagahara, and Günter Niemeyer.

Systemic blood pressure was increased and decreased in anesthetized cats by intravenous infusion of angiotensin and by gradual exsanguination, respectively. The b- and c-wave amplitudes of the electroretinogram were used as indicators of activity of the inner retina and outer retina with pigment epithelium, which are supplied by the retinal and choroidal circulations, respectively. The amplitude of the b-wave remained stable during increases in mean arterial blood pressure (MABP) up to 225 mm Hg but decreased rapidly if the MABP was lowered below 55 mm Hg. This wide range of stability of the b-wave is likely to be brought about by autoregulation of the blood supply to the inner retina. No such stability was seen in the c-wave, the amplitude of which changed inversely to increases or decreases in the MABP. The c-wave thus appears to respond to changes in choroidal blood flow. The data provide new electrophysiologic evidence for autoregulation of the retinal vasculature and suggest that choroidal blood flow may influence the amplitude of the c-wave.

Autoregulation is defined as the ability of the vasculature to maintain constant blood flow to an organ in accordance with its needs. Autoregulation of the vasculature in the eye in response to changes in systemic blood pressure has not been studied by electrophysiologic means as yet. The electroretinogram (ERG) is suitable for this purpose because stability or change in the amplitude of its components, the b-wave and the c-wave, can be expected to reflect properties of the retinal or choroidal circulation, respectively. The b-wave represents activity of the inner nuclear layer of the retina, which is supplied by the retinal circulation. The c-wave represents hyperpolarization of the retinal pigment epithelium combined with a retinal component; both sources are supplied by the choroidal circulation. We recorded ERGs during rises and falls in the systemic blood pressure induced by intravenous infusion of angiotensin and by gradual exsanguination. We correlated changes in amplitudes of b- and c-waves with changes in the mean arterial blood pressure (MABP).

Materials and methods. Four cats weighing 2.8 to 3.8 kg were premedicated with atropine sulfate 0.1 mg/kg subcutaneously and pentobarbital sodium 50 mg/kg intramuscularly (Nembutal; Abbott Laboratories, North Chicago, Ill.). The animals were intubated, paralyzed by alcuronium chloride 0.5 mm/kg intramuscularly (Alloferin; Roche Laboratories, Nutley, N.J.) and ventilated with room air. Non-rebreathing, intermittent positive-pressure ventilation at a rate of 20/min and tidal volume of 30 ml was provided by a Harvard Model 660 respirator. Anesthesia and paralysis were maintained by repeated intramuscular injections of pentobarbital sodium and alcuronium chloride, respectively. The temperature was monitored by a rectal thermistor probe and kept stable at an average of 37.4°C by an adjustable heating pad. Intravenous infusion of Ringer's lactate solution was adjusted to maintain a normal hematocrit value. After injection of bupivicaine 0.5% (Carbostesin; Astra-Bofors) into the pressure areas, the head of the animal was mounted in a stereotactic frame.

Flashes presented by a Grass photostimulator were distributed in a Ganzfeld stimulator, 40 cm in diameter. A corneal contact lens carrying an Ag-AgCl wire was used as the active electrode, and Ag-AgCl electrodes were placed under the skin of the forehead (reference) and a hind leg (ground). The pupil was dilated with 1% atropine sulfate and the animal was dark adapted until the ERG responses to stimuli of low intensity were
stable. This usually took about 1 hr. A constant light stimulus of an intensity of 3 log units above the b-wave threshold (25 μV criterion) was then applied every 30 sec. The ERG was amplified at a bandpass of 0.03 to 300 Hz, displayed on an oscilloscope, and stored on FM tape for later analysis; it revealed a small negative a-wave and prominent positive b- and c-waves (Fig. 1). The c-wave was measured from the baseline of the ERG trace.

Systemic blood pressure was monitored via a femoral artery catheter. MABP was calculated as follows:

\[ \text{MABP} = \frac{\text{diastolic BP} + \frac{\text{systolic BP} - \text{diastolic BP}}{3}} \]

Angiotensin was infused by intermittent intravenous administration to raise MABP for periods of 2 to 10 min. After the angiotensin infusion was stopped, the MABP returned spontaneously to control levels or slightly higher. The control MABP and the steepness and height of the blood pressure rises varied between individual infusions of angiotensin, and the MABP reached a maximum of 225 mm Hg. Decreases in blood pressure were produced by repeated reversed exsanguination.

Results. Typical changes in the ERG during a blood pressure increase are shown in Fig. 1, B, and the data are plotted in Fig. 2. Blood pressure increases were induced in four animals for a total of seven times, reaching an MABP of 185 to 225 mm Hg. All responses were similar, as is summarized in Table I. The b-wave amplitude remained stable even during the most rapid changes in blood pressure. The c-wave amplitude showed a biphasic change, i.e., a decrease as soon as MABP rose, followed by an increase as soon as MABP started falling. This pattern also was seen when the c-wave was measured from the troughs of the a-wave or the b-wave. During one of the seven blood pressure increases the c-wave decreased and subsequently returned to control without an overshoot.

The a-wave showed no consistent changes, ex-
**Table I. Blood pressure increases and ERG**

<table>
<thead>
<tr>
<th>Experiment No.</th>
<th>Increase in MABP* (mm Hg)</th>
<th>Initial MABP (mm Hg)</th>
<th>Maximum MABP (mm Hg)</th>
<th>b-Wave amplitude</th>
<th>c-Wave amplitude</th>
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<tr>
<td>1</td>
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<td>Stable</td>
<td>-23</td>
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<tr>
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<tr>
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<td>+129</td>
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<td>195</td>
<td>Stable</td>
<td>-25</td>
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*Expressed in percent of control values for comparison.
†Illustrated in Fig. 2.

The b-wave and autoregulation. In the cat the retinal circulation forms two to three layers of capillary nets that supply the inner retina up to the outer border of the inner nuclear layer. The retinal vessels of the cat have been shown to autoregulate in response to changes in systemic blood pressure.
Fig. 3. Typical response of the b- and c-wave amplitudes to a decrease in blood pressure.

Table II. Blood pressure decreases and ERG

<table>
<thead>
<tr>
<th>Experiment No.</th>
<th>Fall in MABP* (%)</th>
<th>Initial MABP (mm Hg)</th>
<th>Minimum MABP (mm Hg)</th>
<th>Changes in amplitude b-Wave (%)</th>
<th>c-Wave (%)</th>
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<td>40</td>
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</table>

*Expressed in percent of control values for comparison.
†Illustrated in Fig. 3.

The present data add electrophysiologic evidence for autoregulation of the retinal circulation by showing stability of the b-wave, and thus of "retinal function," during changes in MABP between 55 and 225 mm Hg. Retinal function largely depends on tissue PO₂. Under constant oxygenation in these experiments, the flow rate in the retinal vessels determines tissue PO₂. That the b-wave amplitude changes with change in retinal blood flow has been shown in man as well as in the perfused mammalian eye in vitro.

From the remarkable stability of the b-wave during wide-ranging rises and falls in systemic blood pressure in our experiments, we conclude that the blood flow in the retinal circulation is kept stable by an autoregulatory mechanism.

An upper limit of autoregulation has not been reached in our experiments; the lower limit is found at MABP of 55 mm Hg. At levels lower than this the b-wave amplitude changes in parallel with the systemic blood pressure. The lower limit of autoregulation in the retina corresponds to the lower limit of cerebral autoregulation in man and in dog, where it is given as an MABP of 50 mm Hg in response to lowering the cardiac output. In monkeys the lower limit of autoregulation in the peripapillary retinal vessels was found at perfusion pressure of 40 cm H₂O (corresponding to 30 mm Hg) in response to increases in intraocular pressure. In man, retinal autoregulation has been shown to maintain a constant blood flow in the macular capillaries during decreases in perfusion pressure to 27 ± 6 mm Hg, i.e., by as much as 36%.
The c-wave. We found that in all experiments the amplitude of the c-wave changed in the direction opposite to the change in MABP, whether the blood pressure change was primarily induced or accompanied exposure to various gas mixtures. It is likely that a rise in MABP and its subsequent fall to control levels are paralleled by an increase and decrease in choroidal blood flow. In our experiments this postulated increase in choroidal flow was consistently accompanied by a decrease in c-wave amplitude, and conversely, a decrease in choroidal flow may have induced the increase in c-wave amplitude. We suggest that the c-wave amplitude is inversely affected by the choroidal blood flow via an unknown mechanism. The changes in c-wave amplitude may occur either in the pigment epithelial component of the c-wave or in the retinal component. Due to autoregulation of the retinal circulation, it seems unlikely that the retinal component contributes to changes in the c-wave.

It is possible that the changes in choroidal blood flow are influenced by choroidal vasoconstriction via the sympathetic innervation, which was kept intact in our experiments.

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REFERENCES