Functions of the ON and OFF channels of the visual system

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In the mammalian eye, the ON-centre and OFF-centre retinal ganglion cells form two major pathways projecting to central visual structures from the retina. These two pathways originate at the bipolar cell level: one class of bipolar cells becomes hyperpolarized in response to light, as do all photoreceptor cells, and the other class becomes depolarized on exposure to light, thereby inverting the receptor signal. It has recently become possible to examine the functional role of the ON-pathway in vision by selectively blocking it at the bipolar cell level using the glutamate neurotransmitter analogue 2-amino-4-phosphonobutyrate (APB)[1]. APB application to monkey, cat and rabbit retinas abolishes ON responses in retinal ganglion cells, the lateral geniculate nucleus and the visual cortex but has no effect on the centre-surround antagonism of OFF cells or the orientation and direction selectivities in the cortex[2–5]. These and related findings[6–11] suggest that the ON and OFF pathways remain largely separate through the lateral geniculate nucleus and that in the cortex, contrary to some hypotheses, they are not directly involved in mechanisms giving rise to orientation and direction selectivities. We have examined the roles of the ON and OFF channels in vision in rhesus monkeys trained to do visual detection and discrimination tasks. We report here that the ON channel is reversibly blocked by injection of APB into the vitreous. Detection of light increment but not of light decrement is severely impaired, and there is a pronounced loss in contrast sensitivity. The perception of shape, colour, flicker, movement and stereo images is only mildly impaired, but longer times are required for their discrimination. Our results suggest that two reasons that the mammalian visual system has both ON and OFF channels is to yield equal sensitivity and rapid information transfer for both incremental and decremental light stimuli and to facilitate high contrast sensitivity.

Six monkeys were anaesthetized with halothane and given more than 50 vitreal injections by sterile procedures. The volume of APB used was 75 μl (4–20 mM APB in sterile saline) to yield estimated concentrations of 100–500 μM in the eye. The effects of such injections were assessed in separate experiments with the electroretinogram, since our previous studies had shown that when the ON channel is blocked as determined by single-cell recordings in the lateral geniculate nucleus, the b-wave of the electroretinogram is eliminated[12]. Although there is some variability in the exact time-course of APB action with the intravitreal injection method, we found that a single injection was usually effective within 1 h and lasted 3–8 h. With the concentrations used in this study, recovery was complete by the following day. In all cases only one eye was injected and the other was patched.

Monkeys were deprived of water and rewarded with apple juice. Their eye movements were monitored with the scleral search coil technique, and they were rewarded for correctly making saccades to visual stimuli presented on a colour monitor. A PDP 11/73 computer was used to drive the monitor, control the experiment and record and store the eye movement and performance data. All trials began with the appearance of a small central spot. In the detection paradigm, after the animal had made saccades to this spot and maintained fixation on it for 400–800 ms, a target stimulus appeared at one of several randomly chosen locations, and the animal's task was to make saccades to it; the stimulus remained on until it was foveated. Trials on which saccades were made to locations other than the target were aborted. When the saccade brought the fovea to within 2° of the target centre, it was judged by the programme to be successful and the animal was rewarded with a drop of apple juice. This paradigm, which permits accurate placement of stimuli on selected portions of the retina, is learned rapidly and performed accurately. Trials can be run in close succession without fatigue (with inter-trial intervals of 2–3 s), and monkeys regularly perform 1,500–2,000 trials per day. This permits relatively speedy generation of psychophysical functions. Figure 1*a* shows eye movement data collected for 48 successive errorless trials in which a target appeared 8 times at each of 6 target locations, showing the normal animal's characteristic, disciplined performance.

To test the hypothesis that the ON channel contributes predominantly to the detection of stimuli seen by virtue of light increment while the OFF channel contributes to the detection of light decrement, we trained monkeys to make saccades to targets which were either lighter than or darker than the background. Figure 1*b* shows the distribution of saccadic latencies on a set of light and dark stimuli in the normal and APB-injected monkey. One to six hours after APB administration (75 μl of 8 mM APB), there was a pronounced deficit in the detection of light incremental stimuli, accompanied by a large increase and spread in saccadic latencies. Performance on light decremental stimuli was unaffected. Figure 1*c* shows the monkey's performance over 14 successive days on this task, plotting the saccadic reaction times and the per cent correct performance on one set of light and dark stimuli. The APB was injected on day 7 during this sequence, showing the selective impairment for stimuli brighter than background, and also showing that saline injection of the same volume on day 12 did not affect the animal's performance. Similar effects were obtained using a range of target stimuli measuring 17–220 cd m^{-2}. We also obtained thresholds for the detection of light stimuli in dark-adapted animals: when the ON channel was blocked, detection thresholds were raised by 1.5–2.0 log units, suggesting that APB has a dramatic effect on the eye's rod system.

We examined several other perceptual functions for which we used discrimination rather than detection tasks. The paradigm was quite similar to that used for the detection of light increment and decrement, but instead of one target, several stimuli appeared after the central spot was fixated. One of these stimuli was different from the rest and the animal's task was to make saccades to this target. The physical characteristics of the stimuli could be varied systematically and were presented in randomized sequences. These tests assessed thresholds for the detection of colour stimuli of different degrees of saturation, the maximal temporal rate of flicker discrimination, minimal stereoscopic depth perception using random-dot stereograms, grating acuity, movement perception using random dot displays and the discrimination of gratings having different orientations. Only mild deficits were found on these tasks when the ON channel was blocked with APB. On all of the tasks, however, there was a consistent increase in the latency to performance, averaging 50 ms.

We also examined the contrast sensitivity of animals following APB administration and found considerable impairment using a variety of contrast sensitivity tests. Figure 2 shows the results from one of these. Monkeys were shown six stimuli, five of which were checkerboards while one was a homogeneous stimulus of the same flux. The animal was trained to make saccades to this homogeneous stimulus. Checkerboards of six different spatial frequencies were used, all at the same contrast, randomized over successive trials within a single block. Different contrasts were used in successive blocks. The stimuli appeared at equally spaced locations around the fixation spot at a distance of 8°. The results show a significant loss in contrast sensitivity particularly at optimal spatial frequencies, as seen in both the per cent correct and the reaction time data. In other tests a

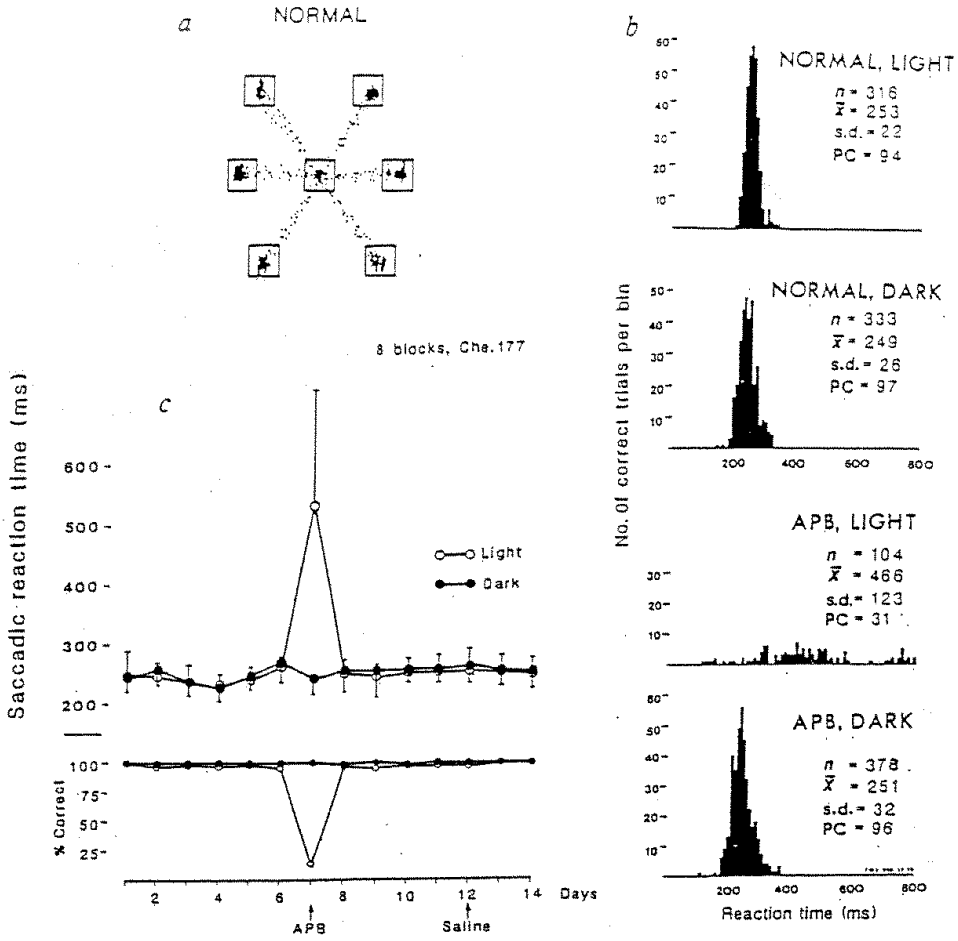

Fig. 1 *a*, An *x*–*y* frame showing traces of saccades made from a central fixation point to a target presented randomly at one of six positions. Targets are 8° eccentric and are squares subtending 1° of visual angle; data from 48 successive trials are shown. Boxes represent spatial limits set for correct acquisition. *b*, Distribution of saccadic latencies and per cent correct performance before and after APB injection (75 μl of 8 mM) to light incremental and light decremental stimuli. Base illumination set at 121 cd m^{-2}. The light stimuli measured 186 and the dark 59 cd m^{-2}. *n*, Number of trials per histogram; $\bar{x}$, mean; s.d., standard deviation. PC, per cent correct. *c*, Saccadic reaction times and per cent correct performance on 14 successive days for incremental (circles) and decremental (disks) stimuli. APB (75 μl of 8 mM) was injected on day 7 and saline (75 μl) on day 12. Vertical bars show standard deviations, upward for incremental and downward for decremental stimuli.

two-alternative forced-choice staircase procedure was used in which sinusoidal gratings had to be discriminated from homogeneous stimuli; injections of 450 μM APB resulted in a loss of foveal contrast sensitivity of up to 25%.

These results suggest two possible reasons for the existence of both an ON and an OFF channel in the mammalian visual system. One is to provide a means for transmitting information about both light increment and light decrement with an excitatory process to the central nervous system. Since the maintained activity of retinal ganglion cells is relatively low, the information conveyed by a decrease in activity (for example, the effect of light increment on OFF cells) is difficult to utilize effectively by central visual system neurones, particularly since their maintained activity is even lower than that of retinal ganglion cells. Having both an ON and an OFF channel therefore makes possible efficient information transfer for either sign of contrast change. This is necessary because of the high premium that exists on the speed of information processing in the animal kingdom, both for appetitive and for avoidance behaviours. The second reason for the existence of the ON and OFF channels is to provide increased contrast sensitivity, probably as a result of some form of push–pull interaction between the ON and OFF channels at higher levels in the visual system. High contrast sensitivity is undoubtedly a most desirable attribute for optimal visual function. Neither of these considerations identifies a unique solution to a biological problem. Rapid information transfer and high contrast sensitivity could probably also be accomplished by having a single channel with a rather high maintained discharge throughout the visual system. Such a solution, however, would probably require an unacceptably high rate of metabolic activity.

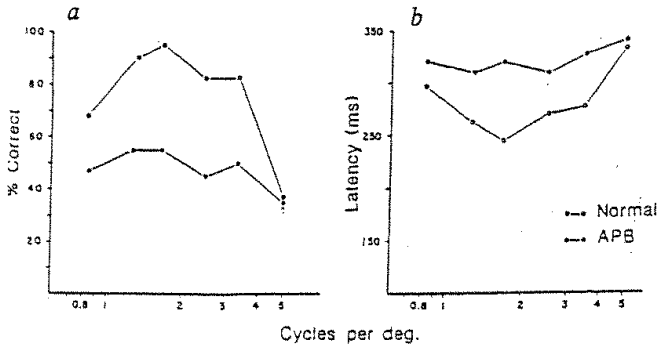

Fig. 2 Per cent correct (*a*) and mean saccadic latencies (*b*) on a discrimination task requiring an animal to make saccades to a homogeneous stimulus paired with a set of five checkerboard stimuli; sets were of different spatial frequencies but of the same contrast. Background illumination was 25 cd m^{-2}, the homogeneous stimulus was 68 cd m^{-2} and the high- and low-contrast checkerboards were 88 and 48 cd m^{-2}, respectively. Each point is based on 60 trials.

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1. Slaughter, M. M. & Miller, R. F. *Science* 211, 182–184 (1981).
2. Schiller, P. H. *Nature* 297, 580–583 (1982).
3. Horton, J. C. & Sherk, H. *J. Neurosci.* 4, 374–380 (1984).
4. Sherk, H. & Horton, J. C. *J. Neurosci.* 4, 381–393 (1984).
5. Knapp, A. G. & Mistler, L. A. *J. Neurophysiol.* 50, 1236–1245 (1983).
6. Conway, J. L. & Schiller, P. H. *J. Neurophysiol.* 50, 1330–1342 (1983).
7. LeVay, S. & McConnel, S. K. *Nature* 300, 350–351 (1982).
8. Norton, T. T., Rager, G. & Kretz, R. *Brain Res.* 327, 319–323 (1985).
9. Ratzkowski, D. & Fitzpatrick, D. *Neurosci. Abstr.* 68(9), 227 (1985).
10. Stryker, M. P. & Zahs, K. R. *J. Neurosci.* 3, 1943–1951 (1983).
11. Waessle, H., Boycott, B. B. & Illing, R. B. *Proc. R. Soc.* B212, 177–195 (1981).
12. Knapp, A. G. & Schiller, P. H. *Vision Res.* 24, 1841–1846 (1984).