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A CHOLINERGIC-SENSITIVE CHANNEL IN THE CAT VISUAL SYSTEM TUNED TO LOW SPATIAL FREQUENCIES

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Visually evoked responses to counterphased gratings were recorded from the cat visual cortex before and after physostigmine administration. Physostigmine markedly reduced the responses to low spatial frequencies, but minimally affected the response to high frequencies. This effect is considered cholinergic since it could be reversed by atropine. These results support at least a two-channel model of spatial frequency responsivity.

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periments have been conducted to elucidate the existence and nature of the channels.

According to the multichannel model, psychophysically obtained contrast sensitivity functions (*6*) are thought to represent the sensitivity of more than one detection mechanism and not the output of a single detector channel. In support of this model, visual cortical cells have been shown to be tuned relatively narrowly to spatial frequency (*5*). Problems are encountered, however, in trying to extrapolate single-unit response characteristics to their role in visual perception, for perception presumably represents the combined activity of populations of cells. Stronger agreement is observed between psychophysical results and results from experiments with visual evoked responses (VER's), which represent the sum of massed neural events. For example, psychophysically obtained contrast sensitivity functions are positively correlated with curves derived from VER measures (*7*).

Cholinergic influences have been found at various stages of processing within the primary visual pathway (*8*). Altering the normal cholinergic activity at these stages and measuring a physiological response which is correlated with results from a psychophysical detection task may provide clues to the types of cells involved in the perceptual task. We wish to show that the carbamate physostigmine, which binds acetylcholinesterase (AChE) and thus prevents the hydrolysis of acetylcholine (ACh) at synaptic sites, preferentially reduces the response to low spatial frequencies. We used the VER as a measure of responsivity.

A Cholinergic-Sensitive Channel in the Cat Visual System Tuned to Low Spatial Frequencies

Abstract. *Visually evoked reponses to counterphased gratings were recorded from the cat visual cortex before and after physostigmine administration. Physostigmine markedly reduced the responses to low spatial frequencies, but minimally affected the response to high frequencies. This effect is considered cholinergic since it could be reversed by atropine. These results support at least a two-channel model of spatial frequency responsivity.*

The application of Fourier theory to the analysis of the visual system has revealed quantitative and systematic information about its dynamics and organization. Campbell and Robson (*1*) suggested that the human visual system contains channels that are sensitive to different bands of spatial frequency (*2*). Since then, numerous psychophysical (*3*) and single-unit electrophysiological (*4, 5*) ex-

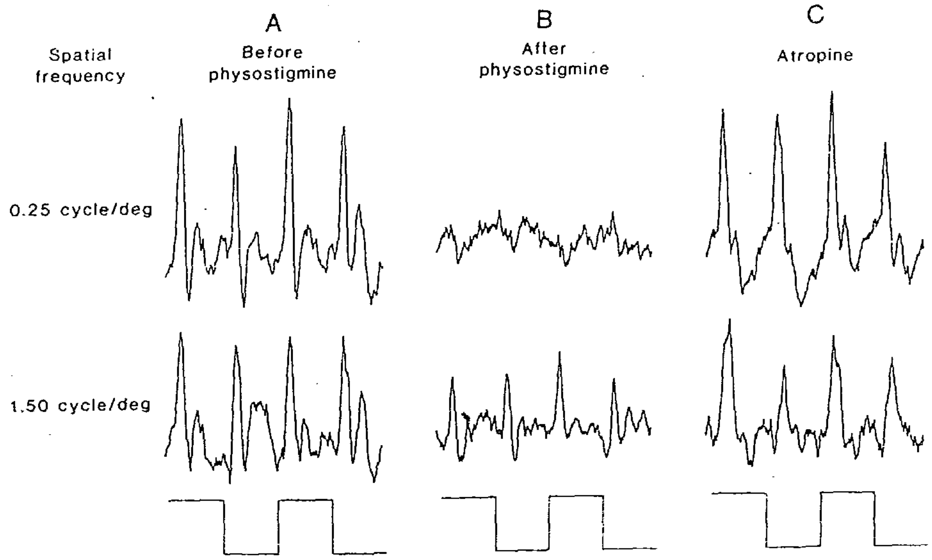

Fig. 1. Peristimulus histogram averages (120-second collection period with a 1-msec sampling interval) for two spatial frequencies from a single experiment (cat 24). (A) Baseline VER's. (B) VER's after an injection of physostigmine (0.5 mg/kg). (C) Recovery VER's after injection of atropine sulphate (0.5 mg/kg). The bottom row depicts the 2-Hz square-wave alternation of the grating pattern. All response averages were collected with sine-wave gratings of 0.40 contrast $[(L_{max} - L_{min}) \div (L_{max} + L_{min})$, where L is luminance$]$.

Anesthesia was induced in adult cats by ventilation of 3 to 4 percent halothane in a 3:1 gas mixture of nitrous oxide and carbogen and maintained with 1 to 2 percent halothane during surgical preparation. Cannulas were inserted into the trachea, one of the femoral arteries, and the two saphenous veins. To reduce eye movements, the two sympathetic trunks were cut and the animal was paralyzed by an infusion of Flaxedil (30 mg kg^{-1} $hour^{-1}$) in an isotonic glucose solution. End-tidal CO_2 was maintained near 4 percent by adjusting the stroke volume of the respirator. The cat was held in a stereotaxic headholder, and core temperature was maintained at 37°C. During the experiment, halothane was removed from the gas mixture. Heart rate, blood pressure, lung resistance, and electroencephalogram (EEG) were continuously monitored. Arterial blood gas and cholinesterase concentrations (9) were measured periodically.

Atropine and Neo-Synephrine were instilled in the cat's eyes to dilate the pupils, retract the nictitating membranes, and relax accommodation. The eyes were fitted with contact lenses with artificial pupils (diameter, 3 mm). The right or left eye was focused with an appropriate lens on a cathode-ray tube (CRT) 12.7 cm in front of the cat's eye. The other eye was occluded.

Sine-wave or square-wave luminance gratings subtending a visual angle of 50° by 42° were generated on the face of the CRT (*10*). The phases of grating patterns were alternated in square-wave fashion at 2 Hz. Care was taken to ensure that the 82-cd/m^2 mean luminance did not change during phase alternation.

The VER's were recorded with appropriate filtering and differential amplification (×5000) from stainless steel bone screws over the visual (area 17) and parietal cortex. A computer averaged responses and controlled stimulus presentation. Six spatial frequencies were presented quasirandomly. Frequencies were presented for 10 seconds each and followed by a 1-second equivalent luminance exposure. This was continued until all frequencies elicited cumulative response averages of 2 minutes, that is, twelve 10-second collection periods for each frequency. Our response measure was the sum of the amplitudes of the first five even Fourier harmonics of the fundamental (2 Hz) less the sum of the first five odd harmonics (*11*).

Results were obtained from five cats. Prior to physostigmine administration, four to five repetitions of the response averages were collected with each of six spatial frequencies to establish baseline. During the 1-second epoch, four primary peaks are seen in the response average (Fig. 1A). In agreement with earlier results (*11*), secondary peaks were often present and were generally most predominant at higher spatial frequencies. After intravenous administration of physostigmine, responses to low spatial frequencies were often abolished (Fig. 1B). Responses to higher spatial frequencies were minimally affected, although alterations in response shape were often noted (not shown). To be sure that the effect we observed was due to cholinergic activity (*12*), we administered atropine sulphate. Atropine, a muscarinic antagonist, competes with ACh for postsynaptic cholinergic receptor sites, thus reducing the influence of an abundance of ACh. Responses after atropine administration recovered markedly (Fig. 1C), typically, to within baseline variation.

Figure 2A shows the results of a complete experiment in one cat. Physostigmine administration led to significant reductions in response to low spatial frequencies. Responses to the two lowest spatial frequencies were completely abolished. Pooled data from the four cats presented with the same spatial frequencies demonstrate the contrasting response decrement at low and high spatial frequencies (Fig. 2B). The effect was the same whether sine-wave (Fig. 1) or square-wave (Fig. 2) gratings were used.

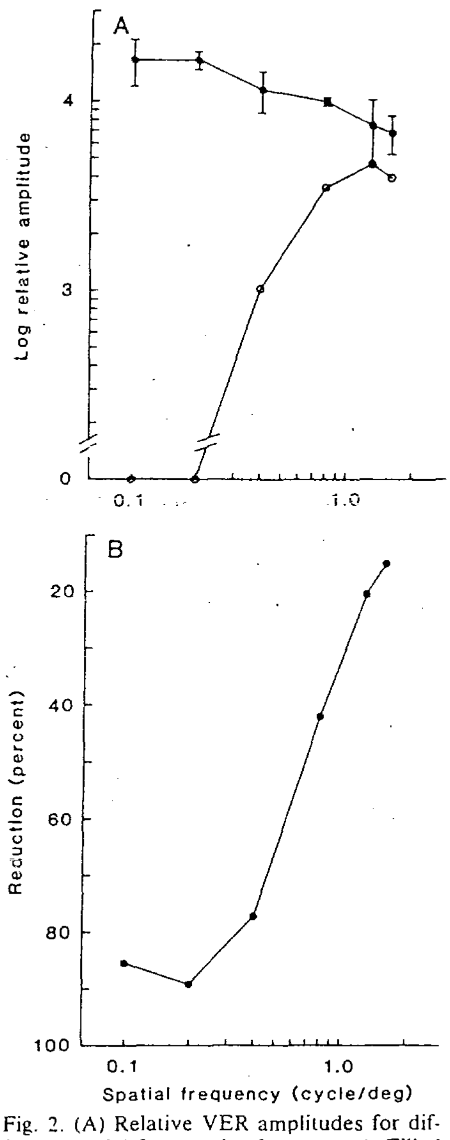

Fig. 2. (A) Relative VER amplitudes for different spatial frequencies from cat 14. Filled circles are baseline VER's with mean of four measures and 1 standard deviation. Open circles are relative VER amplitudes during the first 13.2 minutes after injection of physostigmine (0.8 mg/kg). (B) Averaged data from cats 11, 12, 13, and 14 showing VER reduction for different spatial frequencies after an injection of physostigmine. All animals received doses of 0.5 mg/kg except cat 14, which received a dose of 0.8 mg/kg. In both (A) and (B) grating alternation was 2 Hz. For all square-wave gratings, contrast was held constant at 0.40.

The nonuniformity of the VER reduction supports the hypothesis that spatial responsivity in the cat visual system is mediated by two or more detector channels.

The reduction in VER could be due to secondary effects of AChE inactivation (for example, facilitated or inhibited release of other neurotransmitters that mediate the primary response). Since atropine reverses the VER depression (Fig. 1), excessive cholinergic stimulation within a pathway must mediate the effect.

It is tempting to describe our results in terms of a change in the response properties of a particular class or classes of cells that function in a dectector-response channel, either in the cortex or subcortically. Kirby and Enroth-Cugell (*13*) have shown a pharmacological distinction in the receptive field properties between the X and Y retinal ganglion cells of the cat (*14*). Ikeda and Sheardown (*15*) have suggested that ACh enhances retinal Y cell responses while simply altering the maintained discharge of X cells. In a histochemical study of the cat lateral geniculate nucleus, Dean *et al.* (*16*) reported an abundance of AChE in layers A and A1 where X cell terminations are predominantly found. Finally, Kemp *et al.* (*17*) have reported preliminary data showing that 94 percent of the cortical cells studied responded to ACh. Lacking further information concerning cholinergic influences on functional cell classes in the cat and cortical cell contributions to the VER, we cannot ascribe our results to a loss of a subcortical input or to changes in response properties of a cortical cell class. However, our results do provide evidence for the existence of at least two detector-response channels located in the cat visual system and differentially sensitive to spatial frequency. Similarly, Snyder and Shapley (*11*) showed that the monocularly deprived eye of kittens had cortical VER's that were more depressed to low spatial frequencies than the VER's of the nondeprived eye. Although the selective depression caused by developmental manipulation was less pronounced than that reported here, consideration of the combined results suggests that cholinergic synapses failed to develop in the pathway from the deprived eye to the cortex.

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