method gives a lift coefficient $C_L = 0.34175$ and an induced-drag coefficient $C_{D_i} = 0.00531$, where $C_L = 2L/(\rho U_\infty^2 S)$ and $C_{D_i} = 2D_i/(\rho U_\infty^2 S)$, and S is the planform area. When these values are substituted in the induced-drag formula, an induced efficiency $e = 1.0$ is obtained, as expected. The spanwise load distribution for wing 1 (Fig. 4) shows good agreement with the elliptical load distribution plotted.

Next, two wings with different amounts of sweep are analysed to examine the effect of backward curvature on their induced-drag characteristics when compared with a wing of 'optimal' planform (Fig. 3). The two aft-swept wing shapes are obtained from the original wing shape by 'shearing' it so that the chord lengths parallel to the centreline, the wing span and the planform area are all unchanged. In addition, panel number and distribution are held constant. Wing 2 has a backward-curved leading edge and straight trailing edge. At constant $\alpha = 4°$, $C_L = 0.34236$ and $C_{D_i} = 0.00510$ resulting in $e = 1.045$; a 4.5% increase in induced efficiency compared to wing 1. For wing 2 the spanwise load distribution is no longer elliptical (Fig. 4). For a constant chord distribution, backward sweep produces an increase in aerodynamic loading outboard towards the tip (decrease inboard towards the root) of the lifting surface. Wing 3 has both leading edge and trailing edge curved backwards. The change in trailing edge from straight to curved backwards has relatively little influence on the load distribution (Fig. 4), but causes a slight reduction in lift-curve slope and a significant reduction in induced drag. At constant $\alpha = 4°$, $C_L = 0.33714$ and $C_{D_i} = 0.00475$ resulting in $e = 1.088$; an 8.8% increase in induced efficiency over wing 1. The spanwise chord distribution and the resulting load distribution are not considered to be optimal. The problem of determining the optimal load distribution for crescent-shaped lifting surfaces is still being studied.

In conclusion, this steady-flow analysis of lift and drag characteristics of crescent-shaped wings indicates that aerodynamic efficiency is improved as a result of increased backward curvature. The combination of high induced efficiency and large wing span results in low drag from lift for a given loading. This may help explain why fast marine animals and efficiently flying birds have evolved long crescent-shaped lifting surfaces.

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Dopamine enhances excitatory amino acid-gated conductances in cultured retinal horizontal cells

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In the teleost retina, cone horizontal cells receive extensive innervation from dopaminergic interplexiform cells[1], and possess dopamine receptors whose activation stimulates adenylate cyclase[2,3]. Exogenously applied dopamine modifies several aspects of horizontal cell activity in the intact retina, including the responsiveness of these neurons to light[4-6] and the strength of electrical coupling between them[7-9]. We have used whole-cell voltage clamp methods to examine whether dopamine can alter the light-responsiveness of horizontal cells by changing their sensitivity to the neurotransmitter released by the photoreceptors. We report that dopamine and cyclic AMP, although having little direct effect on resting membrane conductance, greatly enhance ionic conductances gated by kainate, an agonist of the transmitter released by the photoreceptors, and by L-glutamate, the agent proposed to be the photoreceptor transmitter[10-14]. Our results provide the first direct evidence for dopaminergic regulation of excitatory amino-acid neurotransmission in the vertebrate nervous system and suggest a possible mechanism to explain the reduction in the responsiveness of horizontal cells observed when retinas are treated with dopamine.

Experiments were performed on retinal horizontal cells isolated from the white perch (*Roccus americana*). These neurons retain their distinctive morphologies in short-term culture (Fig. 1, legend) allowing identification of rod-driven as opposed to cone-driven cells (ref. 15 and unpublished data). In agreement with voltage clamp[9] and current clamp[13] studies, we found that application of a pulse of Ringer's containing dopamine (200 μM) to isolated horizontal cells had no consistent effects on resting membrane conductance (Fig. 1*a*). In 42% of the cone horizontal cells studied ($n = 38$), dopamine caused a small outward current, whereas in 24% of cells we observed a similarly small inward current. In the remaining 34% of the cells, dopamine either produced no discernible current or biphasic responses. Similar results were obtained over a wide range of holding potentials (data not shown). Dopamine receptors on these neurons thus do not appear to be directly linked to ionic conductances. In contrast, application of a pulse of Ringer's containing kainate (50 μM) to isolated horizontal cells invariably caused a large (0.3-5.0 nA) inward current accompanied by an increase in conductance and in membrane current noise (Figs 1*b*, *c* and 3*a*). This inward current was reduced at depolarized potentials and reversed to an outward current near 0 mV (0.57 ± 2.1 mV, mean ± s.e.m., $n = 7$), suggesting that kainate opens cation channels in the horizontal cell membrane[16].

Kainate-gated currents were stable in the absence of dopamine. In the experiments reported here, the amount of kainate ejected was first adjusted to give a nonsaturating response (typically, 0.5-1.5 nA for cone horizontal cells, 1.0-2.5 nA for rod horizontal cells); repeated applications of the same quantity of kainate to a cell yielded responses that rarely varied in amplitude by more than 30%. In 10 cone horizontal cells that received only kainate, the mean response to the first application was 1.04 ± 0.15 nA ($n = 10$); subsequent responses averaged 0.90 ± 0.07 nA ($n = 18$). Following administration of a pulse of Ringer's containing dopamine (200 μM), however, currents evoked by applications of kainate were markedly larger (Fig. 1*b* and Table 1). In 22 cone horizontal cells to which dopamine was applied, responses increased significantly ($P < 0.01$, two-tailed t-test) from 0.90 ± 0.21 nA ($n = 22$) to 1.95 ± 0.16 nA ($n = 82$). In 20 of these cells, dopamine increased kainate currents by more than 100% over control levels (mean maximal response 2.74 ± 0.34 nA) and changes of >10-fold were occasionally observed.

That dopamine stimulates the production of cyclic AMP (cAMP) in fish retinas[2,3], and that dopamine has no significant

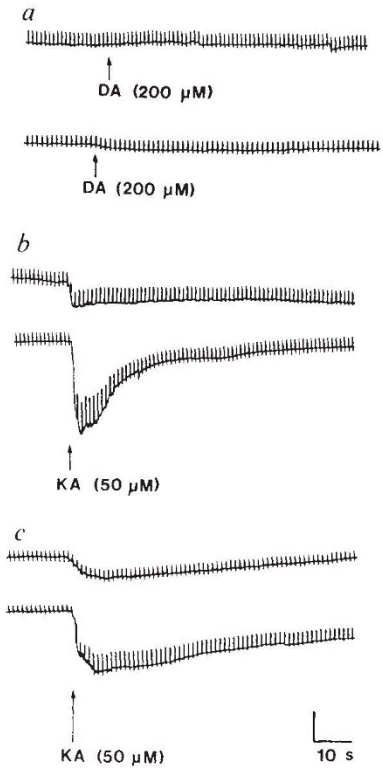

Fig. 1 Effects of dopamine (DA) on resting and kainate (KA)-gated conductances of cone horizontal cells. *a*, Voltage clamp records from two cells illustrating the lack of effect of dopamine on resting conductance. Membrane potential was clamped at −60 mV and 20 mV voltage pulses were applied throughout the record to monitor membrane conductance. Dopamine (200 μM in Ringer's) was applied by pressure ejection in a pulse lasting 0.5–1.0 s at the times indicated by the arrows. Downward deflections denote inward transmembrane current. *b*, Voltage clamp records from another cell illustrating currents evoked by a pulse of Ringer's containing kainate (50 μM) before (upper trace) and 8 min after (lower trace) administration of 200 μM dopamine. Both kainate and dopamine were applied by pressure ejection as in *a*. *c*, Kainate currents in another cell before (upper) and 4 min after (lower trace) administration of 8-bromo-cAMP (500 μM). Vertical calibration, 1.0 nA for *a* and *b*; 2.0 nA for *c*.

Methods. Horizontal cells were enzymatically and mechanically dissociated from white-perch retinas[15], and maintained in culture for 1–10 days. During this time, four morphological classes of horizontal cells can be distinguished, three of which correspond to cone horizontal cells (unpublished data). Similar results were obtained from all three types of cone horizontal cell. The culture conditions used here do not affect the sensitivity of the dopamine-dependent adenylate cyclase in teleost horizontal cells (R. Van Buskirk and J.E.D., unpublished data), nor does this cyclase exhibit denervation supersensitivity[21]. Cells were voltage clamped using low resistance (5–14 MΩ) patch electrodes in the whole cell recording configuration[17,18], using a Dagan 8900 clamp amplifier with a 100 MΩ headstage (Dagan Corporation). In most experiments, the holding potential was set at −60 mV and membrane conductance assessed by monitoring the instantaneous currents evoked by 100 ms depolarizing 20 mV voltage steps. This potential range was chosen to minimize voltage-dependent sodium and potassium currents[19], which were not otherwise blocked. The external medium was an oxygenated teleost Ringer's solution containing (mM): NaCl, 145; KCl, 4; $CaCl_2$, 2.4; $MgSO_4$, 1.7; $MgCl_2$, 1.5; Na_2HPO_4, 2.5; KH_2PO_4, 0.4; glucose, 10; HEPES, 10; *p*H 7.6. The pipette contained (mM): Potassium gluconate, 120; KCl, 4; $MgCl_2$, 2; $CaCl_2$, 1; EGTA, 11; HEPES, 10; *p*H 7.5. Except for haloperidol, which was added directly to the bath, drugs were dissolved in Ringer's applied in brief (0.5–1.0 s) pulses by pressure ejection (100–400 nl) from small-bore triple-barrel pipettes placed 50–100 μm from the cell. All concentrations reported are those in the pipettes; we estimate that the concentration at the cell was lower by ~25% (ref. 13).

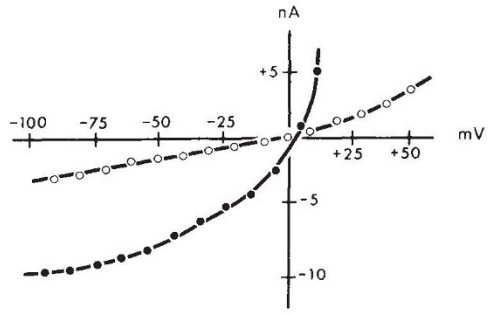

Fig. 2 Kainate current as a function of membrane potential for a cone horizontal cell that received only kainate (○) and for another cone horizontal cell following treatment with 500 μM 8-bromo-cAMP (●). Membrane potential was changed in a rampwise fashion (50 mV s^{-1}), and current–voltage relations for kainate were determined by subtracting currents recorded in the absence of kainate from currents recorded at the peak of a response to 50 μM kainate. Before exposure to 8-bromo-cAMP, the response of the treated cell to kainate was 1.63 nA at a holding potential of −60 mV.

Table 1 Effects of test agents on responses of cone horizontal cells to 50 μM kainate

	Initial response (nA)	Response after drug (nA)	Time after administration of drug (s)	*n*
Control	1.04 ± 0.15	0.94 ± 0.08	183.5 ± 8.4	10
Dopamine (200 μM)	0.90 ± 0.21	2.24 ± 0.32**	195.2 ± 8.3	22
Dopamine (200 μM) + Haloperidol (20–50 μM)	0.92 ± 0.16	0.90 ± 0.23	165.0 ± 6.0	7
8-bromo-cAMP (500 μM)	0.82 ± 0.21	2.37 ± 0.67*	181.0 ± 11.2	10
Serotonin (500 μM)	1.40 ± 0.24	1.42 ± 0.36	154.3 ± 9.1	5

* $P < 0.05$, ** $P < 0.01$, two-tailed *t*-test.

Values given are mean ± s.e.m. For each cell tested, the amount of kainate ejected was first adjusted to give a nonsaturating response (0.3–2.5 nA). This dose was used in all subsequent applications of kainate to that cell. A pulse of Ringer's containing dopamine (200 μM), 8-bromo-cAMP (500 μM), or serotonin (500 μM) was then applied, followed by repeated applications of the initial dose of kainate. For quantitative comparisons, the initial kainate response of each cell has been compared with a response obtained 2–4 min after application of the various test agents. For the control condition, where no drug was applied, a response obtained 2–4 min after the end of the initial response was chosen.

effects on membrane conductance, together suggest that cAMP mediates the enhancement phenomenon reported here. In support of this possibility, application to cone horizontal cells of a pulse of Ringer's containing 500 μM 8-bromo-cAMP, a membrane permeable analogue of cAMP, also increases the amplitude of subsequent kainate responses (Fig. 1*c* and Table 1). The degree of enhancement produced by 8-bromo-cAMP is similar to that produced by dopamine (mean initial response 0.82 ± 0.21 nA, $n = 10$; mean response after 8-bromo-cAMP, 2.21 ± 0.34 nA, $n = 32$; $P < 0.05$). Neither 8-bromo-cAMP nor dopamine cause any obvious changes in the reversal potential for kainate (Fig. 2), indicating that the increases in current reported here do not result from the activation of additional ionic conductances.

We have also examined whether dopamine affects the responses of cone horizontal cells to L-glutamate, which may be the transmitter released by photoreceptors[10–14]. As for other species of fish[16–20], we found that perch horizontal cells were much less sensitive to glutamate than to kainate. Nevertheless,

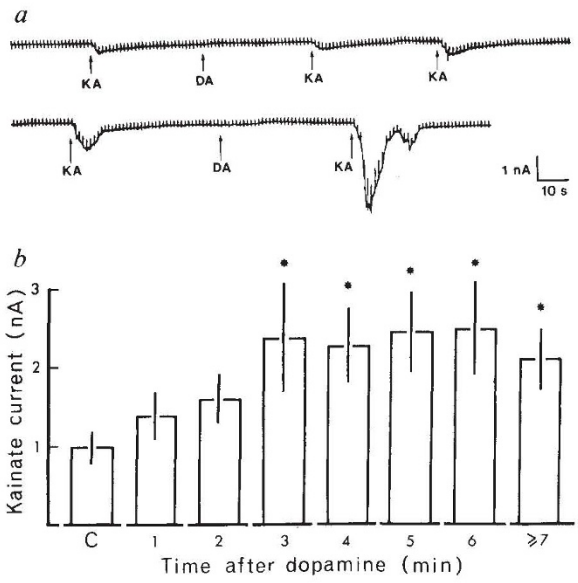

Fig. 3 Time course of the enhancement produced by dopamine. *a*, Voltage clamp record illustrating progressive increases in kainate (KA) currents after exposure to dopamine (DA). A second application of dopamine resulted in a further increase in response. Current fluctuations at the end of the largest response were not typical of responses seen after administration of dopamine. Method of drug application and other conventions as in Fig. 1. The record is continuous in time. *b*, Kainate-induced currents plotted as a function of time after application of dopamine. Data are from 12 cone horizontal cells which were all studied for ≥6 min. The experimental procedure was as described in Table 1, and all cells received only a single application of dopamine. Kainate responses were assigned to one-minute time bins depending on the interval between application of kainate and exposure to dopamine, with bin 1 containing responses obtained 0–1 min after application of dopamine, and so on. Bars, s.e.m.; asterisks, responses significantly greater than the mean control response (one-tailed *t*-test).

in eight cells studied, currents evoked by 100 μM glutamate increased from 0.06 ± 0.03 nA to 1.15 ± 0.22 nA following exposure to 200 μM dopamine ($P < 0.001$). The extent of enhancement was comparable to that seen with kainate.

The enhancing action of dopamine appeared to be specific to cone horizontal cells. The kainate-induced currents of rod horizontal cells, which lack dopaminergic innervation *in vivo*, failed to increase following treatment with dopamine (mean initial response 1.23 ± 0.54 nA, $n = 6$; mean response after treatment 0.98 ± 0.20 nA, $n = 8$) or with 8-bromo-cAMP (mean initial response 2.40 ± 0.79 nA, $n = 6$; mean response after treatment 2.22 ± 0.50 nA, $n = 10$). Furthermore, dopamine was ineffective when haloperidol (20–50 μM) was added to the external medium, and application of serotonin (500 μM) failed to alter the responsiveness of cone horizontal cells to kainate (Table 1). The evidence indicates that specific dopamine receptors on cone horizontal cells are involved in the enhancement of sensitivity to kainate.

Although the time course of the enhancement effect varied from cell to cell, it was generally consistent with the involvement of a second messenger system. As shown in Fig. 3, kainate-induced currents typically increased over the course of several minutes following the application of dopamine. In most cases, responses remained substantially elevated for as long as we could hold a cell (8–12 min). Additional applications of dopamine or 8-bromo-cAMP often resulted in additional enhancement, as was the case for the cell shown in Fig. 3*a*.

The results presented here demonstrate that dopamine, probably acting through a cAMP-dependent process, facilitates an ionic conductance gated by excitatory amino acids, possibly the same conductance used by the photoreceptor transmitter. Modulation of voltage-dependent ion channels by second messenger systems is now well established; our findings suggest that channels gated by neurotransmitters may likewise be subject to modification by regulatory biochemical pathways. Our experiments do not reveal which properties of the amino acid-gated channels (affinity for ligand, number of functional channels, unitary conductance, kinetics) are altered by dopamine. Experiments at the single-channel level may resolve these issues.

An augmentation of amino-acid sensitivity may provide an explanation for the paradoxical observation that dopamine has no consistent effect on the membrane potential or resistance of isolated horizontal cells[9,13], but usually depolarizes horizontal cells in the intact retina[4–6]. Under most experimental conditions, photoreceptors are thought to release a transmitter which tonically depolarizes horizontal cells. If dopamine facilitates the action of this transmitter, it would be expected to depolarize horizontal cells still further in the intact retina, when the transmitter is present, but to have no effect on isolated cells *in vitro*, where the transmitter is absent. Our results also suggest a possible explanation for the decrease in light responsiveness of horizontal cells observed following application of dopamine to the intact retina. Light reduces the flow of transmitter from the photoreceptors, thereby hyperpolarizing horizontal cells. If dopamine enhances the potency of the photoreceptor transmitter, as we have proposed, it may render light-induced reductions in transmitter release less effective and so decrease the amplitude of the responses of horizontal cells to light.

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Spectral sensitivity of human cone photoreceptors

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The brain computes visual colour by analysing the relative excitations of three types of retinal cones[1]. Each cone excitation is governed by a spectral sensitivity function which relates the amplitude of the neural response to wavelength at constant light intensity. The spectral sensitivities of human cones are not well characterized. We report measuring the sensitivities by recording electrical responses of human cones to stimuli of different wavelengths. Spectral sensitivities of 'green' and 'red' cones, determined over the entire visible region, show peaks near 530 and 560 nm respec-

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