

THE ROLE OF SPECIFIC RETINAL CELL TYPES IN VISUAL FOLLOWING RESPONSES IN CHICKS (*GALLUS GALLUS DOMESTICUS*)

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ABSTRACT: Deficits in visually guided behavior, particularly the optomotor response, are found to follow treatment of the chicken retina with a range of toxic agonists of glutamate and aspartate receptors. These agonists include kainic acid, quisqualic acid, homocysteic acid and N-methyl D-aspartic acid, given either alone or in combination with chemicals which antagonise some aspects of their neurotoxic actions and so cause cell loss of various degrees of specificity. Glutamate itself, when given at a high dose, causes non-specific lesions of the retina but has less effect on the optomotor response than kainate, which causes loss of a specific class of cells. Using these retinotoxins as tools of varying specificity, it is deduced that loss of the optomotor response, together with other visual impairments, is due to loss of amacrine cells and/or displaced ganglion cells. The paper includes discussion of the cellular and neurochemical organisation of the retina, retinal projections involved in the optokinetic response, as well as a summary of the modes of action of the toxins used.

For many years, there has been speculation about the possible role played by certain retinal cell types in the perception of moving visual stimuli. This speculation has been based on the anatomical arrangement of cell connections in the retina and, somewhat more recently, on evidence gained from electrophysiological recording from the different cell types in the retina. Now an increasing number of toxins which lesion specific neuronal types are becoming available, and their use is not only assisting in the interpretations which can be made from electrophysiological studies, but also providing a new means of investigating whether particular behavioural functions, in terms of the whole animal, can be linked to specific cell types in the retina.

Following the recognition that the amino acids glutamate and aspartate are putative neurotransmitters, particularly in the visual system (Bondy & Purdy, 1977), and that they have both excitatory and toxic actions on nerve cells (Olney, Ho & Rhee, 1971), an increasing number of their analogues have been tested for neuroexcitatory and neurotoxic properties (McGeer, Olney & McGeer, 1978). Kainic acid (KA), a conformationally restricted analogue of glutamate prepared from a marine

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alga, is one to two thousand-fold more potent than glutamate in its neurotoxic action, and it is now widely used as a tool for lesioning in the central nervous system, as it destroys cell bodies in the region of its application and spares axons passing through the region (McGeer et al., 1978). N-methyl D-aspartic acid (NMDA), an analogue of aspartate, and quisqualic acid (QA) are also neurotoxins, to name just two more.

It is generally thought that the neuronal cell death ensues by over-excitement of the cells to the extent that their energy supplies are exhausted. This is the "excitotoxic" hypothesis proposed by Olney (1969), and there is evidence to support it, at least in the case of KA. Although high doses of KA have multiple effects both postsynaptically and presynaptically, the latter affecting neurotransmitter uptake and release, at lower doses the action of KA appears to be confined to a stimulation of postsynaptic receptors (Poli et al., 1985). Neurones with more of this specific receptor-type are therefore more vulnerable to KA, these being neurones normally stimulated by glutamate *in vivo* (i.e. glutamatergic neurones). Other neurones which are stimulated by aspartate are more vulnerable to the toxic actions of NMDA and QA. KA appears to act on a sub-type of glutamate receptors, and NMDA on a sub-type of aspartate receptors. Thus, there are differences in the site and extent of lesions caused by equipotent doses of KA, NMDA and QA, apparently due at least in part to the fact that each is selective for a different sub-type of glutamate or aspartate receptors. In most areas of the brain, however, neural specificity is difficult to determine as loss of specific cell types can not be easily assessed. For this reason, the retina has emerged as the prime site in which to study the specificity and mechanisms of action of neurotoxins. Neurones in the retina are organized into distinct layers and this, together with the presence of certain rather unique morphological characteristics (e.g., ribbon synapses in receptor and bipolar cells) allows identification of specific neurone types.

There are three layers of cell bodies in the retina, the outer nuclear layer (containing the cell bodies of the photoreceptors), the inner nuclear layer (largely comprised of the cell bodies of bipolar cells but also of horizontal cells on its outer aspect and amacrine and displaced ganglion cells on its inner aspect), and the ganglion cell layer on the innermost side of the retina. Between these layers of cell bodies there are two layers comprised of axons and dendrites, the outer plexiform layer (in which connection is made between the photoreceptors and bipolars and horizontal cells) and the inner plexiform layer (in which bipolars, amacrines and ganglion cells interconnect).

When high doses (6,000 nmoles) of glutamate are applied to the retina by injection into the vitreous humour, widespread damage is caused to all layers of the retina (Rogers, Zappia & Ehrlich, 1985), probably reflecting an ubiquitous role for glutamate as a neurotransmit-

ter in the visual system. The organization of the ganglion cells is disrupted and there is a reduction in the thickness of the inner plexiform layer and the inner nuclear layer (Plate 1), this effect being greater in some regions of the retina than in others. Rogers et al. (1985) suggested that the irregular distortion of the retina by such a high dose of glutamate may be due to loss of Muller cells which provide structural support for the retina and have uptake mechanisms for glutamate.

The analogues of glutamate or aspartate cause more specific lesions in the retina, indicating that the action of each is confined to a specific sub-type of receptor (Morgan, 1983; Fagg, 1985). Receptors for KA have been demonstrated to occur on bipolar cells (Morgan & Dvorak, 1984), and toxic effects on these cells are first manifest within 5 min of injection as a swelling of the cytoplasm and a pyknotic appearance of the nuclei (see Figure 1). By 12 h after injection one can see cells which are clearly necrotic (Morgan, 1983) and these later disappear leaving the inner nuclear layer much reduced in thickness (Rogers et al., 1985). The effect of KA appears to be consistent across all regions of the retina.

There is a sub-population of bipolar cells situated on the outer aspect of the inner nuclear layer which is highly susceptible to KA. Administering a dose as low as 5 nmoles KA into the eye of the chicken causes these cells to swell (Sattayasai, Rogers & Ehrlich, 1985; although this paper originally incorrectly characterized these cells as horizontal cells). They appear to be the type I bipolar cells formerly characterized by Yew and Meyer (1975) as morphologically distinct from the other bipolars. Morgan and Millar (1986) suggest that they are possibly off-bipolars.

KA also affects amacrine cells, situated along the inner aspect of the inner nuclear layer. This may, however, be an indirect effect following KA's excitotoxic action on bipolar cells, as the first signs of swelling in amacrine cells is delayed by some 10 min after swelling in bipolars (Morgan, 1983). Also, pre-treatment with diazepam or phenobarbitone protects the amacrine cells, but not the bipolars, from KA toxicity (Di Chiara et al., 1981; Imperato, Porceddu, Morelli, Fossarello & Di Chiara, 1981). In other words, KA may excite bipolars directly which, in turn, excite amacrine cells. The presence of phenobarbitone would suppress this secondary excitation (and therefore toxicity), while diazepam may provide a counteracting inhibitory effect by enhancing GABAergic mechanisms.

There are a variety of amacrine cell types each stimulated by a different neurotransmitter (cholinergic, GABAergic, glycinergic, serotonergic and dopaminergic amacrine cells). The dopaminergic amacrine cells do not receive bipolar cell input and these amacrine cells are largely resistant to KA (Coyle, Biziere & Schwartz, 1978; Morgan, 1983), providing further evidence that KA's effect on amacrine cells is mediated via bipolars. Presumably these dopaminergic amacrine cells are not connected to other

amacrines which are stimulated by bipolars, otherwise one might expect them to be destroyed by indirect activation. The cholinergic amacrines are destroyed by low doses of KA; 8 nmoles per eye has been shown to cause loss of half the cholinergic amacrines in the chicken retina (Morgan, 1983).

In some species the ganglion cells are susceptible to KA, but in the chicken the ganglion cells proper (in the ganglion cell layer) are affected by only very high doses of KA (200 nmoles per eye causes a 40% loss of ganglion cells; Tung, Morgan & Ehrlich, 1987). At doses of KA some ten-fold lower than this it is only the displaced ganglion cells which are destroyed, apparently also an indirect effect via stimulation of bipolars.

The displaced ganglion cells are movement sensitive and directionally selective (Karten, 1979). Their dendritic trees are in close register with the cholinergic amacrines (Morgan, pers. comm.), from which they receive their only input (Morgan, 1983). That is, they have no direct input from bipolars, but may be stimulated via the route, bipolars to cholinergic amacrines to displaced ganglion cells. There is considerable evidence that they drive the optokinetic or optomotor response (Karten, Fite & Brecha, 1977; and see discussion below). In the pigeon, the displaced ganglion cells have been shown to be the only ganglion cells with input to the nucleus of the basal optic root (nBOR), which forms part of the accessory optic system and, via its efferent out-put to the vestibulo-cerebellum and oculomotor nuclear complex, drives to the optokinetic response preferentially in the vertical and torsional directions (Karten, Fite & Brecha, 1977; McKenna & Wallman, 1985a; see Figure 1).

In young chicks the nBOR is involved in the optokinetic response triggered by both vertical and horizontal retinal slip, as shown by a study measuring metabolic activity in nBOR neurones (by their uptake of radioactive 2-deoxyglucose) when the chick is performing vertical or horizontal optokinetic nystagmus (McKenna & Wallman, 1985b). In chickens treatment with KA might, therefore, be expected to eliminate the optomotor response to large field movement in both the horizontal and vertical directions, and possibly also impair detection of other types of moving visual stimuli.

The toxic actions of NMDA and QA, studied in chicken retina, appear to be confined to a direct effect on amacrines (Sattayasai & Ehrlich, 1987; Morgan, 1987), which may also indirectly cause loss of displaced ganglion cells. Bipolar cells are not affected. While QA causes an initial swelling of horizontal cells, as well as the amacrine cells, the former cells appear to recover (Sattayasai & Ehrlich, 1987). Ganglion cells are also transiently affected, but recover. Yazulla and Kleinschmidt (1980) have reported a similar short-term swelling of horizontal cells followed by recovery after KA treatment of the retina in goldfish.

Several sulphur-containing amino acids, such as cysteine and homocysteic acid (HCY), also have neurotoxic properties by acting on glutamate and/or aspartate receptors, but their actions appear to be less specific than those of KA, NMDA or QA.

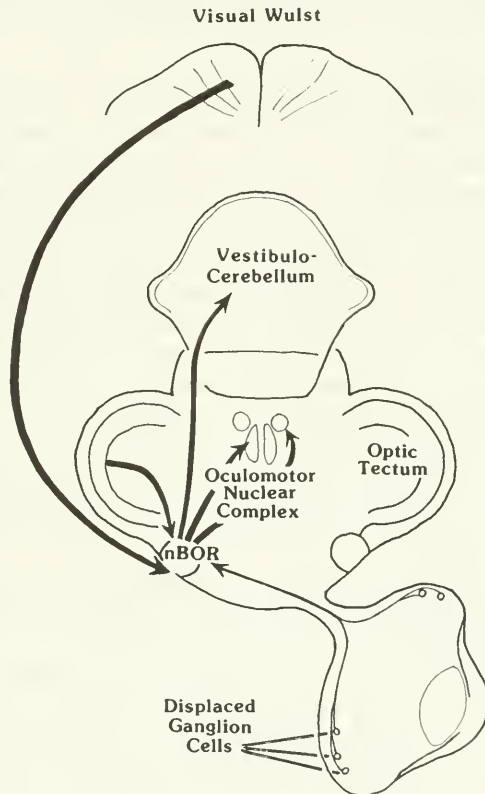


FIGURE 1. Diagrammatic representation of the connections of the nucleus of the basic optic root (nBOR). The nBOR receives inputs from the displaced ganglion cells in the retina of the contralateral eye, the visual Wulst of the forebrain and the optic tectum. Its efferent out-puts go to the vestibulo-cerebellum and the oculomotor nuclear complex.

Despite the now rather considerable amount of anatomical and histochemical research which is investigating the detailed aspects of these retinotoxins, few steps have been made to see how these lesions affect visually guided behaviour. This paper reports some of the first attempts to tie deficits in visually guided behaviour (in particular, the optomotor response) to loss of specific cell types in the retina, the latter being achieved by using a range of toxic agonists of glutamate/aspartate receptors either alone or in combination with other chemicals which antagonise their action.

EXPERIMENT 1

One day old posthatch australorp x leghorn chickens were treated intraocularly with either saline (controls) monosodium L-glutamate, N-methyl D-aspartic acid (NMDA), kainic acid (KA), quisqualic acid for (QA) or homocysteic acid (HCY) (all of the acids adjusted to pH 7 with sodium hydroxide). Each drug was administered in a range the optomotor of doses chosen on the basis of their relative potencies to excite neurones (Watkins, 1978). The doses, expressed in absolute amounts injected response in the horizontal plane (see below). The saline, were 600 to 6,000 nmoles glutamate, 0.6 to 20 nmoles KA, 600 nmoles glutamate, 6,000 nmoles glutamate, 0.6 nmoles KA and 6 nmoles KA NMA, 50 to 1,000 nmoles QA and 50 to 2,000 nmoles HCY. The cgroups were selected for further tests of visually gntrols received 6,000 nmole saline per eye to match the highest dose of drug administered. These were given in a 10:1 volume into the vitreous humour of the chickens, anaesthetised briefly with ether. (N = 6 to 8 per group). Each chick received the same treatment in both eyes.

KA and 6 nmoles KA groups were selected for further tests of visually guided behaviour to ascertain how specific any effects of the treatment conditions on vision might be. On day 10 they were deprived of food for 3 to 4 hours and tested for ability to discriminate food grains from a background of small pebbles of a similar range of colour, shapes and sizes but differing in texture and brightness (for details of method see Rogers, Drennan & Mark, 1974).

Between day 10 and 19 they were tested for ability to detect and peck at a small, red bead (3 mm in diameter) mounted on a rod moved slowly across the floor of the cage. Detection was also scored by moving the bead slowly in a horizontal plane from behind the head towards the beak at a distance of approximately 6 cm from the eye. When the chick detects the bead it gives a startle response, an obvious jerk of the head sometimes accompanied by a trill call (for details see Low, Rogers, Brumley & Ehrlich, 1985). The angle of detection (from the beak) was then estimated for each eye to within the nearest 10°. A mean was calculated from three trials given to each eye.

The experimenter scoring behaviour on the visual tasks was unaware of the drug condition which each animal had received.

The Optomotor Test

The chick was placed in a small glass cylinder centred in the middle of a drum 30 cm in diameter and 68 cm high. The inner wall of the drum

had vertical black and white stripes of 2.5 cm width. It was rotated in an anticlockwise direction at frequency of 0.4 Hz. Tracking ability was assessed by measuring slow, tracking head movements in the direction of rotation of the drum made over two revolutions of the drum and while the chick was standing stationary with its eyes open. This was repeated five times and an average taken.

The optomotor response involves slow tracking movements of the head followed by rapid saccades against the direction of movement of the drum. Only head, and not eye movements were scored, eye movements being minimal in birds. A certain number of random (or, at least, non-tracking) head movements were present in animals which did not show obvious saccades; these were scored when they were in the direction of the drum's rotation, and adherence to this rigid criterion biased the results against finding a visual deficit in the optokinetic response.

The effect of drug treatment was calculated in terms of the difference between the mean number of tracking movements made before treatment and that obtained after treatment. For presentation in the figures the 'optomotor deficit' was calculated as a ratio of this difference of the 'before' minus 'after' score over the score before treatment and expressed over a range with a maximum value of 10 (an optomotor deficit of 10 therefore means complete elimination of the optomotor response).

The raw data were analysed by a one-way analysis of variance followed by a limited number of paired t-tests (one tailed) with degrees of freedom corrected for heterogeneity of variance when a significant ($P < 0.05$) effect of treatment was found.

EXPERIMENT 2

From the data of experiment 1 it was possible to choose (at least within the limits of the doses tested) the lowest dose of each toxin which causes maximal deficits in the optokinetic response. These respective doses of each toxin were then co-administered with 5,000 nmoles magnesium chloride, as Mg^{++} ions antagonise the binding of agonists at NMDA receptors (Watkins, 1981). This antagonism of Mg^{++} at NMDA receptor sites is thought to be due to a reduction in the affinity of the receptors for NMDA (Fain, Ishida & Callery, 1983).

The co-administration of diazepam (1.25 g in 10 l) with 6 nmoles of KA was also tested, on the basis that diazepam blocks the indirect effects of KA and so spares amacrine and displaced ganglion cells (see above).

These chicks were tested for optomotor response only, before and after treatment.

RESULTS

Optomotor Response

As illustrated in Figure 2, treatment with either 600 or 6,000 nmoles of glutamate per eye failed to have any dramatic effect on the optomotor

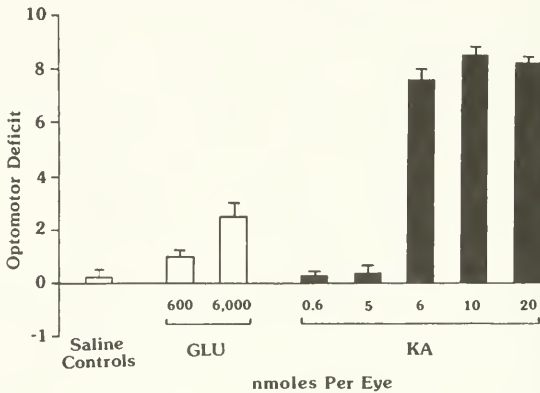


FIGURE 2. Means and standard errors of the deficits in the optomotor responses.

response, whereas a dose of KA as low as 6 nmoles per eye almost completely eliminated the optomotor response ($P < 0.01$; paired t-tests for 'before' versus 'after' treatment scores). Indeed, had a conservative measure of head movements not been adopted, there would have been a total elimination of the optomotor response by 6, 10 or 20 nmoles of KA as no saccades were seen in chicks treated thus. The dose curve for KA is exceptionally steep, 5 nmoles causing no deficit in the optomotor response while 6 nmoles causes a maximal deficit.

It should be noted that two of the 24 chicks treated with 6 or more nmoles of KA appeared to lock on to one set of stripes on the rotating drum and follow this pattern around and around by turning in circles. Occasionally, this whole body movement tracking is seen in controls but in them it rarely lasts for more than one revolution and then the chick stands stationary performing tracking and saccade movements of the head. These KA-treated chicks were unable to stop circling and they never showed the alternate tracking and saccade movement of the head.

As illustrated in Figure 3 the optomotor response is eliminated by NMDA administered in 20 and 50 nmoles doses per eye ($P < 0.05$ for the lower dose and $P < 0.01$ for the higher dose; paired t-tests). The 10 nmoles dose of NMDA caused little effect on the response, suggesting a rather steep dose curve although probably less so than for KA.

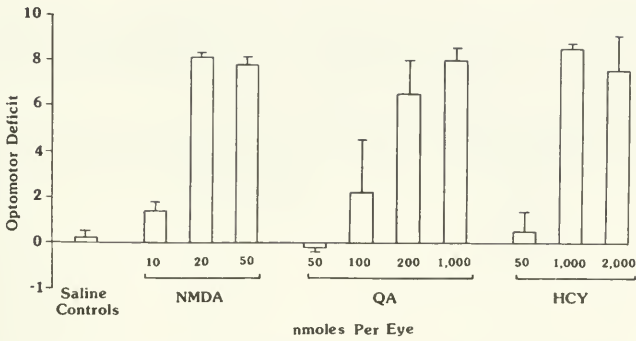


FIGURE 3. Deficits in optomotor responses as a function of drug dose level.

Higher doses of QA were required to cause a significant deficit in the optomotor response (200 and 1,000 nmoles QA; for each $P < 0.05$ paired t-tests). The 50 nmole dose of QA had no effect, and the 100 nmole dose caused a deficit in the response of some chicks and not others, as evidenced by the large variability in the mean score ($P < 0.05$ for a Levene's test, showing a significant variance effect).

HCY caused significant deficits in the optomotor response when administered at 1,000 and 2,000 nmoles per eye ($P < 0.01$ for each), but not at 50 nmoles.

The graded order of potency of these drugs on the optomotor response is therefore $KA > NMDA > QA > HCY$, with glutamate having no marked effects even at exceptionally high doses.

The lowest doses which caused a maximal deficit in the optomotor response (viz. 6 nmol KA, 20 nmoles NMDA, 200 nmoles QA and 1,000

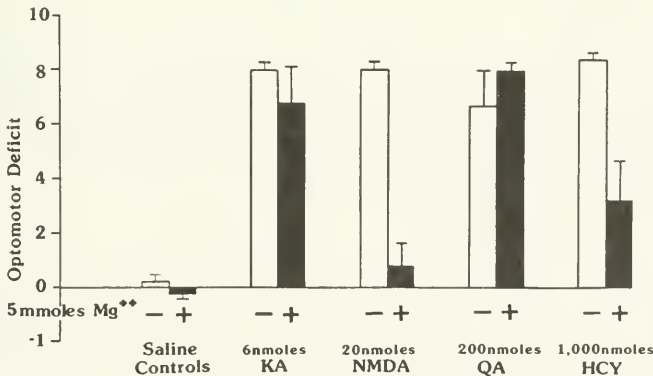


FIGURE 4. Effects of administration of 5 nmole of Mg^{++} on the means and standard errors of optomotor deficits produced by various excitotoxins.

nmoles HCY) were then chosen for co-administration with 5,000 nmoles of Mg^{++} . As seen in Figure 4 the presence of Mg^{++} ions antagonised the effect of NMDA, and to a lesser extent the effect of HCY, but had no effect on the deficits caused by KA and QA.

Co-administration of diazepam with 6 nmoles of KA did, however, reverse the deficit in the optomotor response caused by KA (Fig. 5).

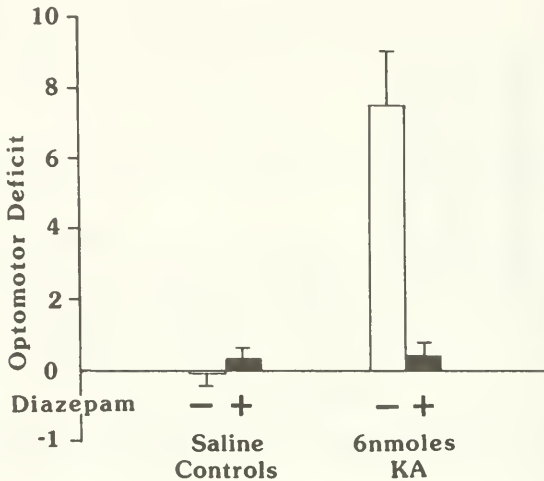


FIGURE 5. Effects of diazepam administration on the toxicity of KA on optomotor responses.

Visual Discrimination Performance

In the last 20 pecks of the task requiring the chicks to discriminate grain from pebbles, the control, saline-treated chicks made a mean of less than one error, errors being pecks at pebbles, whereas those treated with 6,000 nmoles glutamate and 6 nmoles KA failed to discriminate grains from pebbles (Table 1). The 0.6 nmoles KA had no effect on performance in this task and the 600 nmoles glutamate caused only a slight increase in the number of errors.

Detection of a Moving Bead

All of the control chicks detected the moving bead at an angle greater than 100° from the beak (Table 1). In each of the groups treated with 600 nmoles of glutamate or 0.6 nmoles KA there was only one chick which had less ability to detect the bead than did controls. The 6,000 nmoles dose of glutamate had a variable effect: half of this group detected the bead at greater than 100° from the beak, as controls, but the other half either failed to respond or detected it at an angle of less than

TABLE 1
Visual Discrimination Performance

<i>Treatment</i>	<i>Visual Discrimination (Errors in last 20 pecks)</i>	<i>Detection of moving bead</i>	<i>Pecking aim</i>
Saline controls	0.7 (0.4)	> 100°	+
600 nmoles glutamate	3.5 (0.9)	> 100°	+
6,000 nmoles glutamate	10 (± 2.4)*	variable (see text)	-
0.6 nmoles KA	1.1 (0.4)	> 100°	+
6 nmoles KA	11 (1.2)*	no response	-

Note: Visual discrimination performance is scored in terms of the number of errors (pecks at pebbles) in the last 20 pecks of the task, given on day 10 (first column). Means (with standard errors) are given. Asterisks indicate a significant difference from controls ($P < .05$; one-tailed t-tests). Detection of a moving bead advanced towards the beak from behind the head in a horizontal plane 6 cm from the eye was scored in terms of the angle from the beak at the point of detection (second column). Pecking aim was scored by moving the same bead at floor level (+ means good aim, - poor aim, often 2 cm out).

30° (i.e. in the binocular field). All of the chicks treated with KA failed to respond to the moving bead by giving a startle response; yet they made vague following movements of the bead when it was moved in the binocular field.

Pecking Aim

The ability to peck at the bead when moved slowly across the floor was grossly impaired in the chicks treated with 6 nmoles KA. None of the latter were able to make beak contact with the stimulus and they often pecked up to 2 cm to one side of it or short of the floor (Table 1). They did, however, attempt to follow and peck at the bead indicating at least partial vision. More than half of the group treated with 6,000 nmoles glutamate had a similar inability to aim. The lower doses did not impair aiming ability.

DISCUSSION

Although the high dose of glutamate (6,000 nmoles) caused poor pecking aim, inability to discriminate grain from pebbles and impaired

ability to detect the moving bead, it did not cause more than a marginal deficit in performance of the optomotor response. Given the patchy distribution of glutamate's effect on the retina, it may be that large field movement, as in the optomotor test, can be detected while small stimuli, moving or not moving, cannot. Using biochemical techniques, Lund Karlsen and Fonnum (1976) have shown that systemic treatment of neonatal rats with glutamate reduces the number of GABAergic and cholinergic neurones in the retina, but this loss may occur in some regions and not others. The results for glutamate are difficult to assess, but it is worth noting that a glutamate-treated retina, which looks more distorted and damaged than a KA treated retina (Plate 1) or, indeed, a NMDA- or QA-treated retina (Sattayasai & Ehrlich, 1987), actually has less functional loss of vision.

KA causes a consistent lesion across the retina and a dose as low as 6 nmoles causes loss of the optomotor response, impaired pecking aim, inability to perform the visual discrimination task and impaired detection of a moving bead. It is interesting to note that 5 nmoles of KA cause swelling of a sub-type of bipolar cells 2 hr after treatment (Plate 1), but this dose does not cause a deficit in the optomotor response. The amacrine and/or displaced ganglion cells must be spared at this dose, possibly because the swelling of this type of bipolars may be transient with later recovery.

The dose curve for KA's effect on the optomotor response is an extremely steep one. Coyle et al. (1978) found a similar steep dose curve

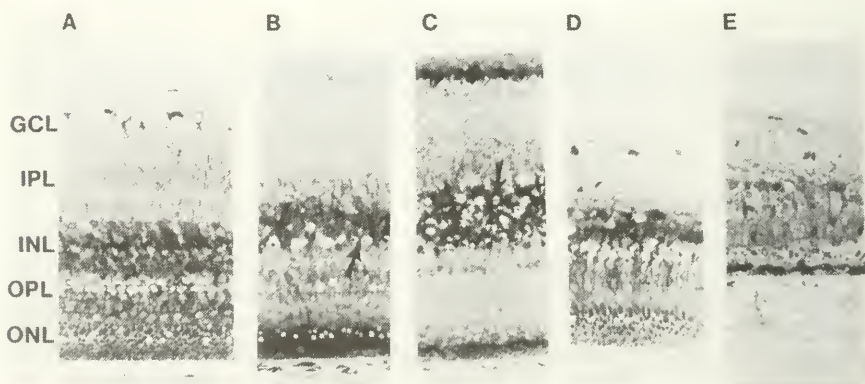


PLATE 1. Light micrographs of chicken retinae. A. Control, saline-treated retina (6,000 nmoles) sampled 10 days after treatment. B. Retina 2 hr after a 5 nmole dose of KA given intraocularly. C. As for B, 2 hr after a 10 nmole dose of KA. D. Retina sampled 10 days after a 6 nmole dose of KA. E. Retina 10 days after a 6,000 nmole dose of glutamate.

Ganglion cell layer (GCL); inner plexiform layer (IPL); inner nuclear layer (INL); outer plexiform layer (OPL); outer nuclear layer, photoreceptors (ONL). The arrows in B and C indicate bipolar cells with swollen cytoplasm and pyknotic nuclei. In D these cells, having been destroyed, are no longer present, and there is a reduction in thickness of the IPL and INL. Note the distortion of all layers in E.

for KA's reduction of activity of the enzyme chlorine acetyl transferase in the retinae of chicks. They found no effect of 5 nmoles KA but a half maximal reduction of enzymic activity with 15 nmoles KA.

The effect of KA on the optomotor response appears to be an indirect one involving amacrines and/or displaced ganglion cells, as co-administration of diazepam protects the chicks from the elimination of the optomotor response caused by KA. It would be interesting to see if diazepam can protect the chicks from the other visual deficits caused by KA.

NMDA affects a different population of receptors than does KA. This has been shown anatomically, and the data reported here illustrate the same phenomenon at a functional level. The Mg^{++} ions block the deficit in the optomotor response caused by NMDA but they afford no protection against the effect of KA. Similarly, Mg^{++} gives no protection from the effect of QA, suggesting that QA also acts at a different receptor sub-type. From previous anatomical studies, the QA receptors are confined to amacrine cells (Sattayasai & Ehrlich, 1987).

HCY appears to have a less specific effect, as Mg^{++} affords some protection from its effect on the optomotor response but the protection is not maximal. HCY is also far less potent in causing a functional deficit in the optomotor response than any of the drugs tested.

Overall, the results implicate a decisive role for amacrine and/or displaced ganglion cells in the horizontal optomotor response. In the chicken, ordinary ganglion cells are not affected by KA, NMDA or, at least permanently, by QA, and co-administration of diazepam with KA protects the amacrines and displaced ganglion cells, but not the bipolar cells. Thus, the bipolars and the ganglion cells proper (in the ganglion cell layer) play no essential role in the optomotor response. Amacrine cells are involved in integration across the retina and for that reason they are thought to have a role in the detection of movement. At least one population of amacrine cells, the cholinergic amacrines, would appear to sustain a role in the optomotor response via their connection to the displaced ganglion cells. As already discussed, the nucleus of the basal optic root (nBOR) receives input from displaced ganglion cells only (as shown in the pigeon) and it is involved in the optokinetic response via its output to the oculomotor nuclear complex and the vestibulo-cerebellum. In the pigeon the nBOR may be mainly involved in the optomotor response to movement in the vertical direction, but in the chicken the nBOR is active when horizontal retina slip occurs (McKenna & Wallman, 1985b). Thus, loss of the horizontal optomotor response after KA, NMDA and QA treatment may result from a specific loss of displaced ganglion cells or, rather, the cholinergic amacrines which feed on to them.

Karten et al., (1977) have suggested that the displaced ganglion cells control the fast (saccadic) phase of the optomotor response. If so, this may explain the performance of the two KA-treated chicks which

appeared to lock on to the moving stripes and follow the rotating pattern around continuously. No suppression of the slow tracking movement to perform a saccadic return of the head, and so track a new set of stripes, may have been possible.

Although lesioning the nBOR has been shown, in the pigeon, to abolish the ability to show optomotor tracking of higher velocity movement in the horizontal direction, the response can still be performed at lower velocities (Fite, 1979). The nBOR is thus not the sole region controlling optokinetic nystagmus. The other central substrate involved is the lentiform nucleus of the mesencephalon, and this is specialised for horizontal retinal slip (McKenna & Wallman, 1985b). It receives input directly from the retina (Ehrlich & Mark, 1984), indirectly from the visual Wulst (Miceli, Gioanni, Repérant & Peyrichoux, 1979) and from the nBOR (Brecha, Karten & Hunt, 1980). Loss of amacrine and/or displaced ganglion cells after treatment with KA, NMDA or QA must eliminate the ability of both the nBOR and the lentiform nucleus to drive the optomotor response. Both systems must, therefore, have the similar requirements of retinal input. It is not known which ganglion cells provide input to lentiform nucleus, but the data reported here may be taken to suggest that, as for the nBOR, the input is from displaced ganglion cells.

The visual Wulst sends efferent projections to the nBOR (Rio, Villalobos, Miceli & Repérant, 1983; see Figure 1) and it may play a role in visual following responses. Indeed, we have recent data showing that there is an increased uptake of 2-deoxyglucose in regions of the visual Wulst in chicks performing the optomotor response (Rogers & Bell, in preparation).

It is unlikely that the deficits in detecting a small moving bead caused by glutamate and KA are due to loss of displaced ganglion cells or any other impairment of input to the accessory optic system. Detection of small moving objects appears to be a property more characteristic of the optic tectum. Although the doses of KA used in these experiments had no observable toxic effect on the ganglion cells which send their axons to the tectum, amacrine cells modulate information transfer between the bipolar and ganglion cells and their loss could affect tectal input from the retina.

The amacrine cells receive efferent input from the isthmo-optic nucleus, and lesions of the isthmo-optic nucleus impair the ability of chickens to detect small moving beads in much the same way as found in these experiments, albeit to a somewhat lesser degree (Rogers & Miles, 1972). Miles (1972) showed that the feed-back loop, retina to tectum to isthmo-optic nucleus and back to amacrine cells of the retina, is important in detection of moving spots as well as moving edges. Isthmo-optic units are particularly responsive to dark edges moving obliquely down across the visual field towards the beak, the passage of which transiently

enhances responsiveness to small moving spots. Miles (1972) suggested that the system may aid visual search into dark areas as when turning the head to search for beetles in shade, and for allowing the animal to deal with the consequences of its own movement. Chicks with lesions of the isthmo-optic nucleus have impaired ability to discriminate grains from pebbles, particularly in areas of low light intensity (Rogers & Miles, 1972). This might suggest that the inability of KA-treated chicks to perform the same visual discrimination task is due to loss of amacrine cells.

Loss of one cell class in the retina, such as the amacrine cells, would, therefore, appear to disrupt visual processing in more than one of the central visual systems and lead to a collection of functional impairments in visually guided behaviour. Specificity at the retinal level does not confer specificity at the functional level, but with the possibility of placing lesions with greater specificity for cell type and sub-type in the retina, and by making comparisons across species, we have the potential to understand more about retinal and central circuitry in the visual system and how this translates into visual performance of the whole animal.

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