Dependence of Retinogeniculate Transmission on Membrane Voltage in the Cat

Differences between X and Y cells

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Abstract

The mammalian lateral geniculate nucleus seems organized to gate or control the gain of retinogeniculate transmission, the result of which is then relayed to the visual cortex. We have performed in vivo intracellular studies of retinogeniculate transmission along these retino-geniculo-cortical pathways in cats by recording the retinally evoked excitatory postsynaptic potential (EPSP) in geniculate neurons. In cats, these pathways are organized into two parallel and functionally distinct channels, the X and Y pathways. We found that nearly all geniculate X cells display a fairly conventional voltage dependency for their retinally evoked EPSPs, because the amplitudes of these EPSPs decrease fairly linearly with membrane depolarization as the EPSP reversal potential is approached. Rare X cells and all Y cells, however, show an unconventional response: over a wide range of membrane potentials, their EPSP amplitudes increase with membrane depolarization. This increase does not result from alterations in neuronal input resistance and instead seems due to changes in synaptic conductance. The underlying cause of this voltage dependency remains to be determined. None the less, it does afford an interesting means by which retinogeniculate transmission can be gated, since non-retinal inputs (e.g., corticogeniculate axons) that can control a relay Y cell's membrane potential can also modulate the cell's EPSP amplitude.

Introduction

The cat's retino-geniculo-cortical pathways are organized into several parallel, functionally independent neuronal channels (Stone et al., 1979; Sherman, 1985; Shapley and Lennie, 1985). The best understood of these are the X and Y channels that pass through the A-laminae of the lateral geniculate nucleus. Although X and Y relay cells in the A-laminae possess receptive field properties that closely match those of their retinal inputs (Stone et al., 1979; Sherman, 1985; Shapley and Lennie, 1985), such retinal innervation accounts for only 10–20% of the synapses found on these geniculate cells (Guillery, 1969a,b; Wilson et al., 1984). The remaining 80–90% of synaptic input derives mostly from local inhibitory neurons, from the visual cortex, and from the brainstem (Singer, 1977; Sherman and Koch, 1986). Rather than elaborate receptive field properties, these non-retinal inputs seem to gate or control the gain of retinogeniculate transmission (Sherman and Koch, 1986). Many different forms of such gating can occur, and these may be neuronal substrates for various categories of visual attention (Crick, 1984; Sherman and Koch, 1986; Koch, 1987). We now report evidence for a type of such gating that is based on an unusual voltage dependency for retinally evoked EPSPs and that is largely limited to the Y pathway.

Materials and Methods

Our experiments were conducted in cats with techniques that have been previously described in detail (Bloomfield et al., 1987; Bloomfield and Sherman, 1988). The cats were initially anaesthetized with 2–3% Halothane for all surgery, including the introduction of venous and tracheal cannulae and the formation of craniotomies. We then paralysed and anaesthetized the cats (paralysis: 5 mg gallamine triethiodide followed by 3.6 mg/h gallamine triethiodide plus 0.7 mg/h of d-tubocurarine; anaesthesia: a 70/30 N_{2}O/O_{2} mixture plus 1 mg/kg/h of Nembutal) and artificially ventilated them. End-tidal CO_{2} was monitored and kept near 4%, and body temperature was monitored and kept near 37°C. Heart rate and electroencephalogram were also monitored.

We used fine-tipped micropipettes (filled with 3 M potassium acetate
Retinogeniculate transmission

Fig. 1. Traces of intracellular recording from 2 X and 2 Y cells showing the relationship between membrane voltage and the amplitude of the retinally evoked EPSP. The scale represents 2 ms for all traces and 2 mV (for A and D) or 4 mV (for B and C).

We identified the receptive field centre type (on or off) for all cells studied. However, in earlier experiments in the series, we made no attempt to identify recorded cells as X or Y before impaling them, although the EPSP response latency from optic chiasm stimulation is a useful index of the cell's class (Stone et al., 1979; Sherman, 1985; Bloomfield and Sherman, 1988). In later experiments, we identified all cells as X or Y on the basis of a battery of tests, including linearity of summation in response to visual stimulation as well as the above-mentioned EPSP response latency to optic chiasm stimulation (Stone et al., 1979; Sherman, 1985; Shapley and Lennie, 1985).

Results

We have investigated the dependence of the retinally evoked EPSP on membrane voltage in a total of 40 geniculate neurons. We saw no differences in the EPSP characteristics we studied between cells with on-centre receptive fields and those with off-centre fields, and thus
centre type is not considered further. Of the sample of 40 neurons, the complete battery of tests was used to identify between the X and Y cells in the quality of recordings. With the exception of 2 provisionally defined X cells (see below), all of the cells showed the increase in EPSP amplitude with membrane depolarization as illustrated in Figures 1C, D, and 2B. Finally, two neurons with response latencies to optic chiasm stimulation of 2.2 and 2.0 ms (thereby suggesting that they were X cells), also showed an increase in EPSP amplitude with membrane depolarization. Thus, except for these cells, which have been only provisionally identified, our results suggest a distinct difference between X and Y cells as regards the voltage dependency of retinally driven EPSPs.

Figure 1 illustrates the typical effect of membrane voltage on the retinally evoked EPSPs in these geniculate neurons. For the X cells increasing depolarization of the membrane over the ranges tested (i.e. typically \(-120 \text{ mV} \text{ to } -10 \text{ mV}\) resulted in a progressively smaller EPSP (Fig. 1A,B). The voltage dependency for these X cells was thus similar to that described for most neurons, and it can be explained as follows. As the membrane approaches the reversal potential of the EPSP, which must be positive with respect to the resting potential to produce a depolarization, the electromotive force driving the EPSP diminishes, resulting in a smaller EPSP. Most surprisingly, however, the Y cells showed precisely the reverse relationship: increasing membrane depolarization increased EPSP amplitude (Fig. 1C,D). Only when the Y cells were depolarized sufficiently did their retinally evoked EPSPs begin to decrease in amplitude (see also below).

Figure 2 shows for an additional 4 X and 4 Y cells the representative relationships between membrane voltage and EPSP amplitude over an extensive range of membrane voltages. Notice the nearly linear relationship for the X cells (Fig. 2A). Each of the Y cells showed a prominent and broad peak in EPSP amplitude as a function of membrane voltage (Fig. 2B). For these cells, the membrane voltage at which the maximum retinal EPSP amplitude occurred ranged from \(-35 \text{ mV}\) to \(-75 \text{ mV}\), with a mean and standard deviation of \(-56 \pm 10 \text{ mV}\).

Each of the 13 completely identified X cells and 6 of the 8 cells with longer response latencies to optic chiasm stimulation displayed the reduction in EPSP amplitude with membrane depolarization as illustrated in Figures 1A, B, and 2A. Every Y cell and every cell with a shorter response latency to optic chiasm stimulation in our sample showed the increase in EPSP amplitude with membrane depolarization as illustrated in Figures 1C, D, and 2B. Finally, two neurons with response latencies to optic chiasm stimulation of 2.2 and 2.0 ms (thereby suggesting that they were X cells), also showed an increase in EPSP amplitude with membrane depolarization. Thus, except for these cells, which have been only provisionally identified, our results suggest a distinct difference between X and Y cells as regards the voltage dependency of retinally driven EPSPs.

Two features concerning the voltage dependency of these EPSPs as illustrated in Figures 1 and 2 bear elaboration. First, prior data from our laboratory indicate that retinal synapses are located electronically quite close to the somata of these geniculate neurons (Wilson et al., 1984; Bloomfield et al., 1987; Hamos et al., 1987). Therefore, it seems likely that the shifts in membrane voltage created by current injection are only slightly smaller at the retinal synaptic locations than are those we have induced and measured at the somata. Second, although the current injections used to manipulate membrane voltage sometimes led to slight changes in neuronal input resistance, these changes were not of sufficient size or duration to explain the curious voltage dependency of EPSP amplitudes in Y cells. In fact, except for one Y cell, we saw no evidence of anomalous rectification, whereby neuronal input resistance decreases with membrane hyperpolarization, although such rectification has been reported for geniculate neurons recorded in vitro (Crunelli et al., 1987; 1988; see also Discussion). Even for the Y cell showing decreased input resistance with depolarization, the resistance change was insufficient to explain the changes in EPSP amplitude.
Figure 3 shows for 4 X cells and 4 Y cells the observed EPSP amplitudes as well as those that would be predicted on the basis of the observed changes in input resistance. Our measurements of neuronal input resistance fluctuated slightly (typically less than 25%; but for 2 of the Y cells the changes were approximately 50%) but randomly with respect to membrane voltage, and we calculated expected EPSP values for each cell based on these fluctuations (see below). Two sets of EPSP values were actually calculated for each neuron: one based...
on an EPSP reversal potential of 0 mV and the other based on a reversal of +55 mV. These were chosen as likely to bound the actual reversal potentials, and as illustrated, even such widely different values for the reversal point do not substantially alter the picture. Our estimates of the expected EPSP values are based on the assumption that synaptic conductance is not dependent on membrane voltage. We know that

\[ I_s = G_s \cdot (V_m - V_r) \]  

(1)

where \( I_s \) is the synaptic current, \( G_s \) is the synaptic conductance (i.e., the product of \( n \), the number of channels open, and \( g \), the conductance of each channel), \( V_m \) is the membrane potential, and \( V_r \) is the reversal potential. By our calculations, the increase in conductance due to synaptic activation of each channel), where \( G \) is the membrane resistance. Strictly speaking, equation 2 refers to the values of \( V_{EPSP} \) and \( R_N \) at the location of the synapse, and we have measured these at the soma; however, retinal synapses are so close to the soma electronically (see above) that our observed values of \( V_{EPSP} \) and \( R_N \) can be used in equation 2 to obtain a reasonable approximation of \( I_s \).

It then follows by substitution that

\[ V_{EPSP} = I_s \cdot R_N \]  

(2)

where \( V_{EPSP} \) is the amplitude of the EPSP and \( R_N \) is the neuronal input resistance. Strictly speaking, equation 2 refers to the values of \( V_{EPSP} \) and \( R_N \) at the location of the synapse, and we have measured these at the soma; however, retinal synapses are so close to the soma electronically (see above) that our observed values of \( V_{EPSP} \) and \( R_N \) can be used in equation 2 to obtain a reasonable approximation of \( I_s \).

\[ V_{EPSP} = G_s \cdot (V_m - V_r) \cdot R_N \]  

(3)

and

\[ G_s = V_{EPSP} / (V_m - V_r) \cdot R_N \]  

(4)

We can thus calculate \( G_s \) for each of the \( V_r \) values from our conjoint measures of \( V_{EPSP} \), \( V_m \), and \( R_N \). This then permits an estimate of the expected \( V_{EPSP} \) for other paired values of \( V_m \) and \( R_N \) by using formula 3. We have arbitrarily chosen to obtain our estimate of \( G_s \) from the EPSP evoked at the most negative membrane potential. The actual EPSP amplitude chosen as the basis for these estimates and ensuing normalization has no effect on our basic conclusions. The X cells when analysed in this fashion showed no evidence of any voltage dependent changes in synaptic conductance for the retinal EPSP (Fig. 3A), while the Y cell response patterns suggest that their retinally evoked synaptic conductances were strongly dependent on membrane voltage (Fig. 3B).

Discussion

The phenomenon we have described above represents a dramatic difference between the X and Y pathways, at least of retinogeniculate synapses. We found that the EPSP amplitude displayed an unusual voltage dependency for all Y and perhaps some rare X cells. For these cells, the EPSP amplitude grew with membrane depolarization over a large range, in spite of the fact that such depolarization bore the membrane towards its reversal potential for the EPSP. Limited control experiments indicate that this voltage dependent increase in EPSP amplitude is probably due to an increase in synaptic conductance. The remaining X cells showed a more conventional voltage dependency for which EPSP amplitude decreased with membrane depolarization.

Implications for retinogeniculate transmission

The voltage dependency of retinal EPSPs in Y cells suggests an interesting means of gating retinogeniculate transmission in the Y pathway, and our suggestion essentially follows that of Koch (1987). That is, the Y cell’s membrane potential will effect the size of retinal EPSPs, and EPSP amplitude controls the extent to which the postsynaptic cell responds with action potentials that can be transmitted to visual cortex. Non-retinal inputs that are in a position to control the membrane potential of Y cells can thus set the gain of retinogeniculate transmission through these cells. It seems plausible that the extrinsic inputs to the lateral geniculate nucleus from visual cortex and/or brainstem can effectively control the membrane potential of geniculate Y cells, either by direct excitation or indirectly by their control of local inhibitory neurons (Sherman and Koch, 1987).

This also suggests a role for the corticogeniculate pathway commensurate with its prominent size, which can be contrasted to the subtle functions suggested for this pathway by other studies (Kalil and Chase, 1970; Schmielau and Singer, 1977; Geisert et al., 1981). Thus the visual cortex, by modulating the activity in its efferent corticogeniculate axons, can control membrane voltage in geniculate Y cells and thereby affect the gain of retinogeniculate transmission in the Y pathway. In principle, this can be accomplished either globally or within various subpopulations of geniculate Y cells.

Possible causes for voltage dependence of the EPSPs

Clearly, more work is needed to determine the underlying causes for the voltage dependency of retinally evoked EPSPs in Y cells. For now, we can only speculate as to these causes, many of which can be imagined. Two fairly obvious possibilities involve anomalous rectification and glutamatergic synaptic transmission via N-methyl-D-aspartate (NMDA) receptors.

Anomalous rectification

Anomalous rectification is common to many neurons (reviewed in Llinás, 1984). It occurs with hyperpolarization and is due to an increased potassium conductance, which reduces the neuronal input resistance. A lower input resistance would result in a smaller EPSP (see equation 2), so this seems a plausible means of producing smaller EPSPs with membrane hypopolarization as seen for Y cells. Crunelli et al. (1987, 1988) have described anomalous rectification for geniculate neurons studied in vitro. However, no differences in this behaviour were described between the X and Y cells they studied (Crunelli et al., 1987, 1988), so anomalous rectification seems an implausible explanation for the EPSP differences between X and Y cells as described in the present study. In any case, our input resistance measurements do not support the notion that any such rectification was sufficiently large to account for the EPSP behaviour we observed (see Results).

NMDA receptors

The EPSP voltage dependency of Y cells in some ways resembles that reported for glutamatergic synapses employing an NMDA receptor. The NMDA receptor is voltage dependent, because the depolarizing conductance it controls can be progressively blocked as the membrane becomes more hyperpolarized (Dingledine, 1983; Mayer et al., 1984; for a review, see Mayer and Westbrook 1984). Recent examples have been published of NMDA dependent EPSPs with time courses and voltage dependencies similar to those of our Y cells (e.g. O'Brien and Fischbach, 1986; Thompson et al., 1988). This raises the possibility that the retinogeniculate Y synapse uses glutamate (or a similar substance) as the neurotransmitter and that many of its postsynaptic receptors are of the NMDA type. This is interesting in a developmental context, because a great deal of attention has recently been focused on this receptor as an important factor in synaptic plasticity and
development (e.g. Collingridge and Bliss, 1987; Collingridge, 1987; Bear et al., 1987; Cline et al., 1987), and retinogeniculate Y axons display considerably more plasticity during postnatal development than do X axons (Sur et al., 1982; Garraghty et al., 1986a,b; Raczkowski et al., 1988).

While the possibility is attractive that the Y but not X pathway uses NMDA receptors for retinogeniculate transmission, it should not be mistaken for anything but speculation at present. Prior data may be consistent with the notion that retinal synapses are glutamatergic (Kemp and Sillito, 1982) and that NMDA receptors are present on geniculate neurons (Crunelli et al., 1987; Moody and Sillito, 1988), but there is disagreement concerning the possibility that NMDA receptors are used in retinogeniculate transmission (Crunelli et al., 1987; Moody and Sillito, 1988). To further complicate matters, the existence of NMDA receptors can often be difficult to demonstrate (Salt, 1986; Herron et al., 1986), so even our failure to detect the appropriate voltage dependency for X cell EPSPs does not allow us to conclude that the retinogeniculate X pathway lacks NMDA receptors. It is also the case that many other voltage dependent conductances may be present that could account for our results. More data are clearly needed to determine the ionic and pharmacological bases of the phenomena we have described. Whatever the explanation, it is clear that, under the conditions of our experimental paradigm, retinogeniculate transmission proceeds differently for X and Y pathways, and this difference could be important for the non-retinal control of this transmission.

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Abbreviations

EPSP excitatory postsynaptic potential
NMDA N-methyl-D-aspartate

References
