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Research Note

In vivo recording of postsynaptic potentials and low threshold spikes in W cells of the cat's lateral geniculate nucleus

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Summary. We obtained good intracellular recording from 5 W cells in the C-laminae of the cat's lateral geniculate nucleus. The recordings were made from an anesthetized and paralyzed in vivo preparation. We found a consistent pattern for the postsynaptic potentials evoked from activation of the optic chiasm: first was an IPSP followed by an EPSP. This is very different from the pattern seen in X and Y cells, for which an EPSP always appears first and is then followed by an IPSP. We interpret the pattern for W cells as follows. The initial IPSP is disynaptic; this involves retinogeniculate conduction over very fast *Y* axons and a relay through an interneuron. The EPSP is monosynaptic, reflecting retinogeniculate conduction over very slow W axons. A possible implication for this is that activity over the Y pathway may generally inhibit geniculate W cells before these W cells can be excited by their retinal afferents. Finally, we elicited from each of these W cells voltage-dependent, low threshold spikes, which are very similar to those displayed by X and Y cells. These spikes can interrupt normal retinogeniculate transmission, and they are prevented by maintaining relatively depolarized membrane potentials.

Key words: Thalamus – Visual system – Calcium conductance – Cat

Introduction

Compared to X and Y cells in the A-laminae of the cat's lateral geniculate nucleus, relatively little is known about the geniculate W cells in the C-laminae (reviewed in Sherman 1985). This is partly because their poor responsiveness to visual stimulation and to activation of the optic chiasm make it difficult to establish their response properties. This is unfortunate, because the W pathway clearly represents a significant component of the retino-geniculo-cortical system along with the more prominent and better understood X and Y pathways.

In the course of our other intracellular studies of geniculate X and Y cells recorded in the A-laminae (Lo and Sherman 1989; Lo et al. 1989), we occasionally obtained good intracellular recordings from W cells in the C-laminae. This provided us with the opportunity to test several features of W cells that have been previously documented for X and Y cells. Although the observations we obtained from W cells do not represent a systematic study and are based on relatively few cells, we thought the novelty of the observations warrants a brief report, particularly in view of our poor understanding of these cells.

In our studies of W cells, we concentrated on two features: the pattern of initial postsynaptic potentials evoked by stimulation of the optic chiasm (Eysel 1976; Bloomfield and Sherman 1988), and the presence of a mechanism for generating low threshold spikes (Jahnsen and Llinás 1984a, b; Lo et al. 1990; see also the "delayed depolarizing potential" of McIlwain and Creutzfeldt 1967), which in *X* and *Y* cells are generated by a voltage-dependent Ca^{2+} conductance. The low threshold spike is particularly interesting, because it seems to play an important role in the transmission of retinal signals through geniculate relay cells to visual cortex (for a review, see Sherman and Koch 1986, 1990). It is a triangular depolarization of 10–20 mV in amplitude and roughly 40 ms in duration. At membrane levels more depolarized than about −65 mV, this low threshold spike is *inactivated;* the membrane must be held at a more hyperpolarized level to *de-inactivate* the spike so that a subsequent depolarization can *activate* it. Its threshold for activation is lower than that of a conventional action potential, thus it is called "low threshold". Finally, a high frequency burst of 2–7 action potentials typically rides its crest, and such bursty periods are followed by refractory periods at regular intervals. This creates a rhythmical cyclic discharge pattern that no longer reflects retinal input and thus poorly relays retinal information to cortex. This is said to be the *burst response mode.* In the

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absence of low threshold spikes, a relay cell is said to be in the *relay response mode,* and retinal information is relatively faithfully relayed to cortex.

Methods

We performed in vivo intracellular recording of cells in the cat's lateral geniculate nucleus. To do this, we used methods identical to those we have recently described (Bloomfield et al. 1987; Bloomfield and Sherman 1988; Lo and Sherman 1989; Lo et al. 1989), and we shall thus only briefly outline them here. We initially anesthetized the cats with 4% Halothane plus a 50/50 mixture of N_2O/O_2 for all surgery, including the introduction of venous and tracheal cannulae and the formation of craniotomies. We then paralyzed and artificially ventilated the cats for the remainder of the recording session, maintaining anesthesia via 0.3–1.0% Halothane in a 70/30 mixture of N_2O/O_2. We used fine-tipped micropipettes, filled with 3M KAc and beveled to a final impedance of 30–60 MΩ at 100 Hz, to record intracellularly from the geniculate neurons. Perhaps because of their small size, we found it much more difficult to obtain stable intracellular recording from W cell than from X or Y cells, and we thus slightly relaxed our criteria for acceptable intracellular recording (Bloomfield and Sherman 1988). We deemed a W cell impalement suitable for further analysis if we observed a rapid DC drop to a resting membrane potential of -40 mV or more negative, a stable resting membrane potential, and action potentials of >20 mV. Finally, we inserted a pair of bipolar stimulating electrodes into the brain to straddle the optic chiasm, and we applied single pulses (0.1 ms duration, 100–500 μA) across these electrodes.

Results

We obtained reasonable intracellular recording from five W cells in the lateral geniculate nucleus. We identified these as W cells on the basis of three main criteria (reviewed in Stone 1983; Sherman 1985). First, each was located in the C-laminae, as judged by ocular dominance shifts of the X and Y cells recorded more dorsally along the electrode track in the A-laminae and magnocellular lamina C. Second, these cells responded with action potentials only sporadically to activation of the optic chiasm, and when they did, their response latencies were relatively long (2.9–4.4 ms). Third, they exhibited poor or sluggish responses to visual stimulation.

Responses to optic chiasm stimulation

Figure 1A–C shows examples of the postsynaptic potentials elicited from activation of the optic chiasm in three of the W cells. The pattern shown here is very different from that observed for X and Y cells (Eysel 1976; Bloomfield and Sherman 1988). In these other cells, chiasm shock always evokes a monosynaptic excitatory postsynaptic potential (EPSP) that occurs first and that is almost always closely followed by a multisynaptic inhibitory postsynaptic potential (IPSP). In contrast, the pattern is reversed in W cells: the IPSP occurs before the EPSP (Fig. 1A–C). In the five W cells, the IPSP latencies occur at 1.5–1.7 ms and the EPSP latencies occur at 2.9–4.4 ms. The question of whether these EPSPs and IPSPs are monosynaptic or multisynaptic is considered in Discussion.

For the same three W cells as are illustrated in Fig. 1A–C, Fig. 1D–F provides addition evidence that the early hyperpolarizations evoked by chiasm shock are indeed IPSPs. A slight, 5–10 mV depolarization of the membrane achieved by current injection through the recording electrode increases the amplitude of the hyperpolarization. On three of the five W cells, we were able to reverse these hyperpolarizations at about -70 mV (not illustrated, but see also below); we did not test this feature on the other two cells. This voltage behavior strongly suggests that these initial hyperpolarizations induced by chiasm shock are indeed IPSPs. Furthermore, the reversal potential suggests that they are mediated by an increased conductance to Cl^-, which is the result of γ-aminobutyric acid (GABA) operating via a $GABA_A$ receptor (Dingledine and Langmoen 1980; Dunlap 1981; Segal and Barker 1984; Bloomfield and Sherman 1988).

Low threshold spikes

We have shown elsewhere (Lo et al. 1989) with in vivo intracellular recording that geniculate *X* and *Y* cells display a voltage sensitive, low threshold spike that seems to be the analogous Ca^{2+} spike described from in vitro recordings (see Introduction). We found that all five W cells of the present study were capable of generating essentially the same type of low threshold spike. This was revealed via injections of hyperpolarizing current pulses (>100 ms duration and 1–2 nA amplitude) through the electrode. The onset of the pulse hyperpolarizes the cell membrane to de-inactivate the low threshold spike, and cessation of the pulse passively depolarizes the membrane to activate the spike. Although not illustrated here, this activation of low threshold spikes is remarkably like that seen for geniculate X and Y cells (Lo et al. 1989).

In one of the W cells, we were able to activate the low threshold spike from the depolarization evoked from activation of the optic chiasm. This is illustrated in Fig. 1G, H. To do this, we first had to de-inactivate the low threshold spike by holding the cell's membrane at -80 mV. Notice that, at -80 mV, there is no sign of an early hyperpolarization. This is because the early IPSP is reversed and actually creates a depolarization beginning at 1.7 ms after the chiasm shock. Thus the depolarization that activates the low threshold spike begins with a reversed IPSP that has added to it the later EPSP.

Discussion

The W cells we have studied from the C-laminae of the cat's lateral geniculate nucleus show two interesting features. First, in response to activation of the optic chiasm, they initially exhibit an IPSP that is then followed by an EPSP. This is very different from geniculate X and Y cells, which first show an EPSP that is followed by an

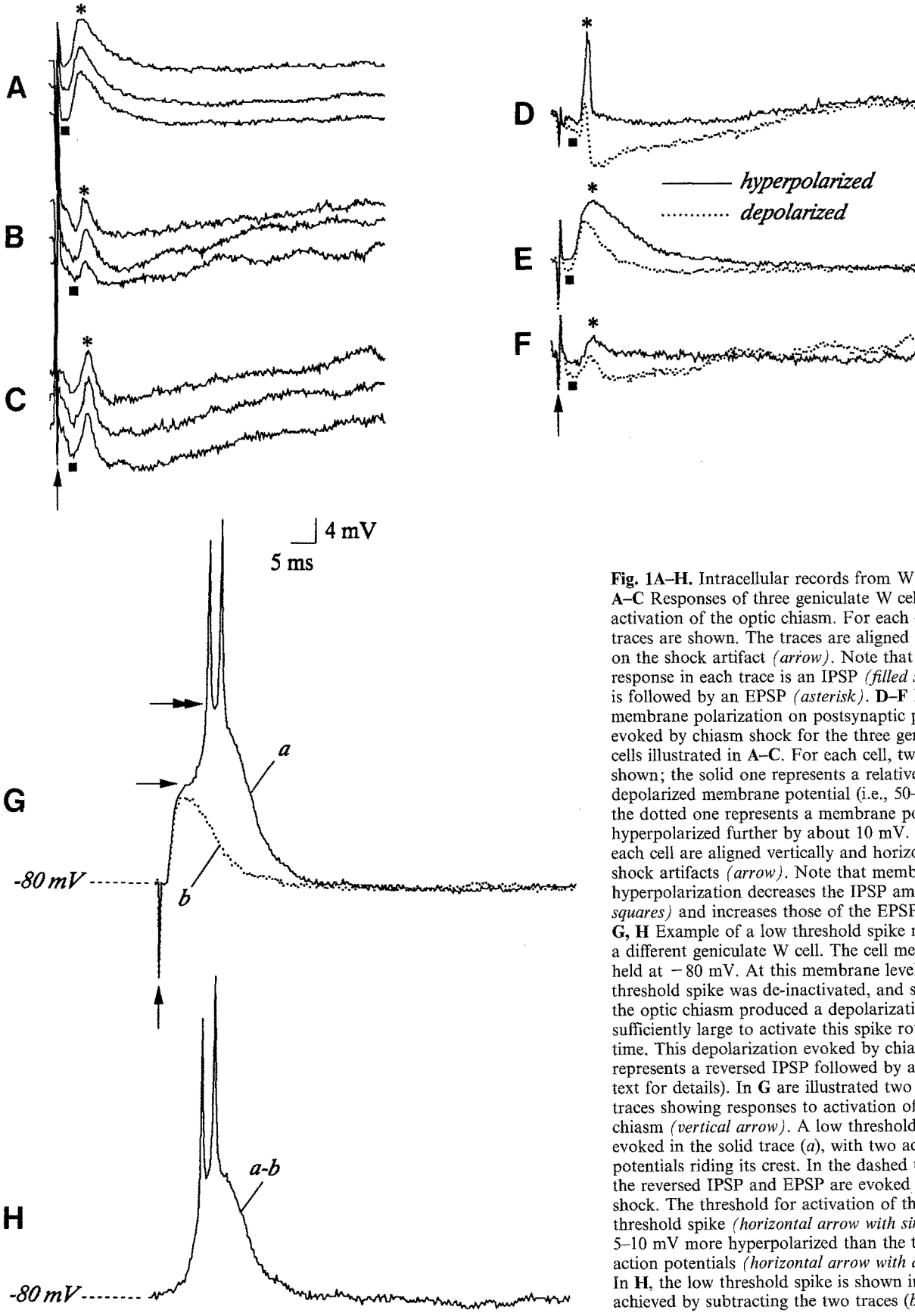

Fig. 1A–H. Intracellular records from W cells. **A–C** Responses of three geniculate W cells to electrical activation of the optic chiasm. For each cell, three traces are shown. The traces are aligned horizontally on the shock artifact *(arrow)*. Note that the earliest response in each trace is an IPSP *(filled square)*, which is followed by an EPSP *(asterisk)*. **D–F** Effects of membrane polarization on postsynaptic potentials evoked by chiasm shock for the three geniculate W cells illustrated in **A–C**. For each cell, two traces are shown; the solid one represents a relatively depolarized membrane potential (i.e., 50–60 mV), and the dotted one represents a membrane potential hyperpolarized further by about 10 mV. The traces for each cell are aligned vertically and horizontally on the shock artifacts *(arrow)*. Note that membrane hyperpolarization decreases the IPSP amplitudes *(filled squares)* and increases those of the EPSPs *(asterisks)*. **G, H** Example of a low threshold spike recorded from a different geniculate W cell. The cell membrane was held at −80 mV. At this membrane level, the low threshold spike was de-inactivated, and stimulation of the optic chiasm produced a depolarization that was sufficiently large to activate this spike roughly half the time. This depolarization evoked by chiasm shock represents a reversed IPSP followed by an EPSP (see text for details). In **G** are illustrated two superimposed traces showing responses to activation of the optic chiasm *(vertical arrow)*. A low threshold spike is evoked in the solid trace (*a*), with two action potentials riding its crest. In the dashed trace (*b*), only the reversed IPSP and EPSP are evoked from chiasm shock. The threshold for activation of the low threshold spike *(horizontal arrow with single head)* is 5–10 mV more hyperpolarized than the threshold for action potentials *(horizontal arrow with double head)*. In **H**, the low threshold spike is shown in isolation, achieved by subtracting the two traces (*b* from *a*) in **G**

IPSP. Second, these W cells exhibit low threshold spikes, as do geniculate X and Y cells.

Postsynaptic potentials evoked by chiasm stimulation

We can draw several inferences from the pattern of postsynaptic potentials evoked from activation of the optic chiasm, and these are summarized in Fig. 2. The available evidence, both electrophysiological and morphological (Guillery 1971; Guillery and Scott 1971; Eysel 1976; Bloomfield and Sherman 1988), suggests that all retinogeniculate synapses are excitatory. Thus it is likely that the early IPSP evoked from chiasm stimulation represents a multisynaptic response involving inhibitory, GABAergic interneurons. However, the very short latency of the IPSP, at 1.5–1.7 ms following chiasm stimulation, limits the number of intervening synapses to two and requires a very rapidly conducting retinogeniculate component. We thus suggest that the retinogeniculate axons involved must be the fastest-conducting axons in the optic nerve and tract; that is, they must be Y axons. From chiasm stimulation, Y axons can induce a monosynaptic EPSP in geniculate neurons at a latency of 1.0 ms or less (Cleland et al. 1971; Hoffmann et al. 1972; Bloomfield and Sherman 1988). If an interneuron in the C-laminae receives this short latency, retinogeniculate *Y* input, there is just enough time for the additional synaptic delay needed for this interneuron to evoke an IPSP in a W cell. There is insufficient time for an additional synaptic delay, which would be required by other plausible inhibitory circuits, such as those involving the perigeniculate nucleus or corticofugal activity. Likewise, there is insufficient time for the retinogeniculate component of the IPSP to be other than Y cells, because both retinogeniculate X and W axons fail to evoke postsynaptic EPSPs until at least 1.4 ms after chiasm stimulation (Cleland et al. 1971; Hoffmann et al. 1972; Wilson et al. 1976; Cleland et al. 1976; Sur and Sherman 1982; Bloomfield and Sherman 1988).

The first EPSP evoked by chiasm stimulation is more difficult to interpret. Geniculate W cells clearly receive monosynaptic input from retinogeniculate axons (Raczkowski et al. 1988), and the EPSP latencies we measured are consistent with these slowly conducting retinogeniculate W axons. Thus the retinogeniculate input to the W cell depicted in Fig. 2 is present and probably at least contributes to the early EPSP. Furthermore, the evoked EPSP exhibited little latency jitter to chiasm stimulation, which also suggests a monosynaptic response. However, we cannot rule out the distinct possibility that multisynaptic excitatory inputs also contribute to this EPSP.

Geniculate W cells respond relatively poorly to visual stimulation and activation of the optic chiasm (Wilson et al. 1976; Sur and Sherman 1982). Prior explanations offered for this include the relatively poor responsiveness of retinal W cells that innervate these geniculate neurons (reviewed in Stone 1983; Sherman 1985) and the paucity of retinal synapses located on geniculate W cells (Raczkowski et al. 1988). The circuit outlined in Fig. 2 suggests

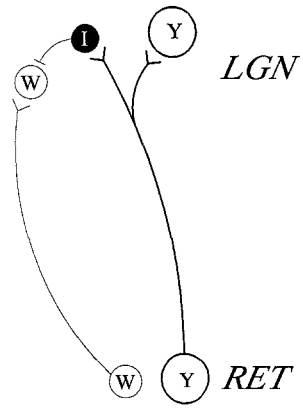

Fig. 2. Schematic diagram of circuitry suggested by the present results. The W cell in the lateral geniculate nucleus (LGN) receives a monosynaptic excitatory input from a W cell in retina (RET). A retinogeniculate Y axon innervates a GABAergic interneuron (I), which then innervates the geniculate W cell. See text for details

a potent inhibition of geniculate W cells by the Y pathway, and this, in turn, offers an additional explanation for the poor responsiveness of W cells. Since retinal Y cells are quite responsive to visual stimuli, and since the neighboring retinal W and Y cells as depicted in Fig. 2 are likely to have overlapping receptive fields, it seems likely that any visual stimulus that would activate the retinal W cell would also activate the retinal Y cell. Thus most visual stimuli likely to activate the retinal W cell would, via the Y pathway, inhibit the geniculate W cell and reduce its responsiveness to the active retinogeniculate W axons.

Low threshold spikes

We have shown that geniculate W cells, like their X and Y cell counterparts, have low threshold spikes. This is consistent with prior in vitro work indicating that practically all thalamic neurons exhibit such spikes (Jahnsen and Llinás 1984a, b). This also implies that W cells, like X and Y cells, are capable of at least two response modes, the relay and burst modes. This has significant implications for retinogeniculate transmission and the relay of retinal signals to cortex. As noted in the Introduction, the relay mode reflects faithful retinogeniculate transmission, but the burst mode, which results from the low threshold spikes, represents a breakdown in this faithful transmission.

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