Synaptic Regulation of L-Type Ca^{2+} Channel Activity and Long-Term Depression during Refinement of the Retinocollicular Pathway in Developing Rodent Superior Colliculus

Fu-Sun Lo[1] **and R. Ranney Mize**[1,2]

[1]*Department of Cell Biology and Anatomy and* [2]*Department of Ophthalmology and Neuroscience Center of Excellence, Louisiana State University Health Sciences Center, New Orleans, Louisiana 70112*

The retinocollicular pathway undergoes activity-dependent refinement during postnatal development, which results in the precise retinotopic order seen in adults. This process is NMDA- and nitric oxide-dependent. Recent studies have shown that L-type Ca^{2+} channels may also play a role in synaptic plasticity, but such channel activity has not previously been reported in the developing superior colliculus (SC). Here we report the presence of a postsynaptic plateau potential mediated by L-type Ca^{2+} channels using whole-cell current clamp of the SC in an isolated brainstem preparation of rats. Seventy percent of SC neurons showed these potentials as early as postnatal day 0 (P0)–P2. The potential was blocked by nitrendipine and/or APV and facilitated by bicuculline, showing that the channel is activated by NMDA receptor-mediated EPSPs and deactivated by $GABA_A$ receptor-mediated IPSPs. Blockade of L-type Ca^{2+} channels also diminished long-term depression, which we could induce in the retinocollicular pathway in neonatal animals. The incidence of plateau potentials decreased to 39% of neurons by P10–P14, suggesting that L-type calcium channels may contribute to retinocollicular pathway refinement in the developing SC.

Key words: voltage-gated Ca^{2+} channels; brain development; retinotectal pathway; sensory systems; synaptic plasticity; NMDA; GABA

It is well established that the pathway from the retina to the superior colliculus of rodents undergoes activity-dependent modifications to produce a topographically organized map of visual space in the adult (Simon and O'Leary, 1992). The NMDA glutamate receptor is involved in this process because blockade of the receptor disrupts the refinement of contralateral retinocollicular axons in rat superior colliculus (SC) (Simon et al., 1992). Recently, it also has been shown that refinement of the ipsilateral retinocollicular pathway is mediated by nitric oxide, because its retraction is disrupted in knock-out mice in which the endothelial and neuronal isoforms of nitric oxide synthase have been deleted (Wu et al., 1999). This refinement appears not to be mediated by the NMDA receptor, because a noncompetitive inhibitor, MK-801, does not prevent refinement of the pathway (Davis et al., 2000).

Recent studies have demonstrated that voltage-gated calcium channels are an alternative source of Ca^{2+} influx involved in synaptic plasticity. Thus, there are NMDA-independent forms of long-term potentiation (LTP; for review, see Johnston et al., 1992), which can be mediated by L-type Ca^{2+} channels (Grover and Teyler, 1990, 1992; Cavus and Teyler, 1996; Kurotani et al., 1996; Kapur et al., 1998). These channels could also be responsible for the Ca^{2+} influx required to release nitric oxide (Garthwaite, 1991). In the present study, we have examined whether L-type calcium channel activity is present in the neonatal rodent superior colliculus and whether the onset and development of this activity corresponds to the period of retinocollicular pathway refinement.

MATERIALS AND METHODS

Sprague Dawley rat pups ranging in age from postnatal day 0 (P0) to P14 were anesthetized with Fluothane (Halothane) and killed by decapitation. The brain was removed and immersed in an artificial CSF (ACSF) bubbled with 95% O_2 and 5% CO_2, and an *in vitro*-isolated brainstem was prepared (Xia and Lo, 1996; Lo and Mize, 1999). The brain was cut along the midline and glued onto a piece of silver plate. Using a dissection microscope, the lateral surface of the thalamus was exposed by gently removing the forebrain. This "isolated brainstem" was then placed into a submerged-type recording chamber perfused with ACSF of 28°C at a rate of 4–5 ml/min. Experiments began after 1 hr of incubation. Whole-cell patch recordings were performed with patch electrodes filled with a potassium-based solution (7–10 MΩ). The formation of the whole-cell configuration was indicated by a sudden drop in seal resistance and a DC drop to −60 mV. After "break-in," the serial resistance was completely compensated with the bridge balance of an Axoclamp-2B amplifier. The junction potential was not corrected in this study. A pair

Received Sept. 24, 1999; revised Nov. 11, 1999; accepted Nov. 22, 1999.

This work was supported in part by US Public Health Service National Institutes of Health Grants NS-36000 and EY-02973. We thank Dr. William Guido for use of his electrophysiology facility and Dr. John Cork for assistance with the statistical methods.

Correspondence should be addressed to Dr. R. Ranney Mize, Department of Cell Biology and Anatomy and Neuroscience Center of Excellence, Louisiana State University Health Sciences Center, 1901 Perdido Street, New Orleans, LA 70112. E-mail: rmize@lsumc.edu.

This article is published in *The Journal of Neuroscience*, Rapid Communications Section, which publishes brief, peer-reviewed papers online, not in print. Rapid Communications are posted online approximately one month earlier than they would appear if printed. They are listed in the Table of Contents of the next open issue of JNeurosci. Cite this article as: JNeurosci, 2000, 20:RC58 (1–6). The publication date is the date of posting online at www.jneurosci.org.

http://www.jneurosci.org/cgi/content/full/3891

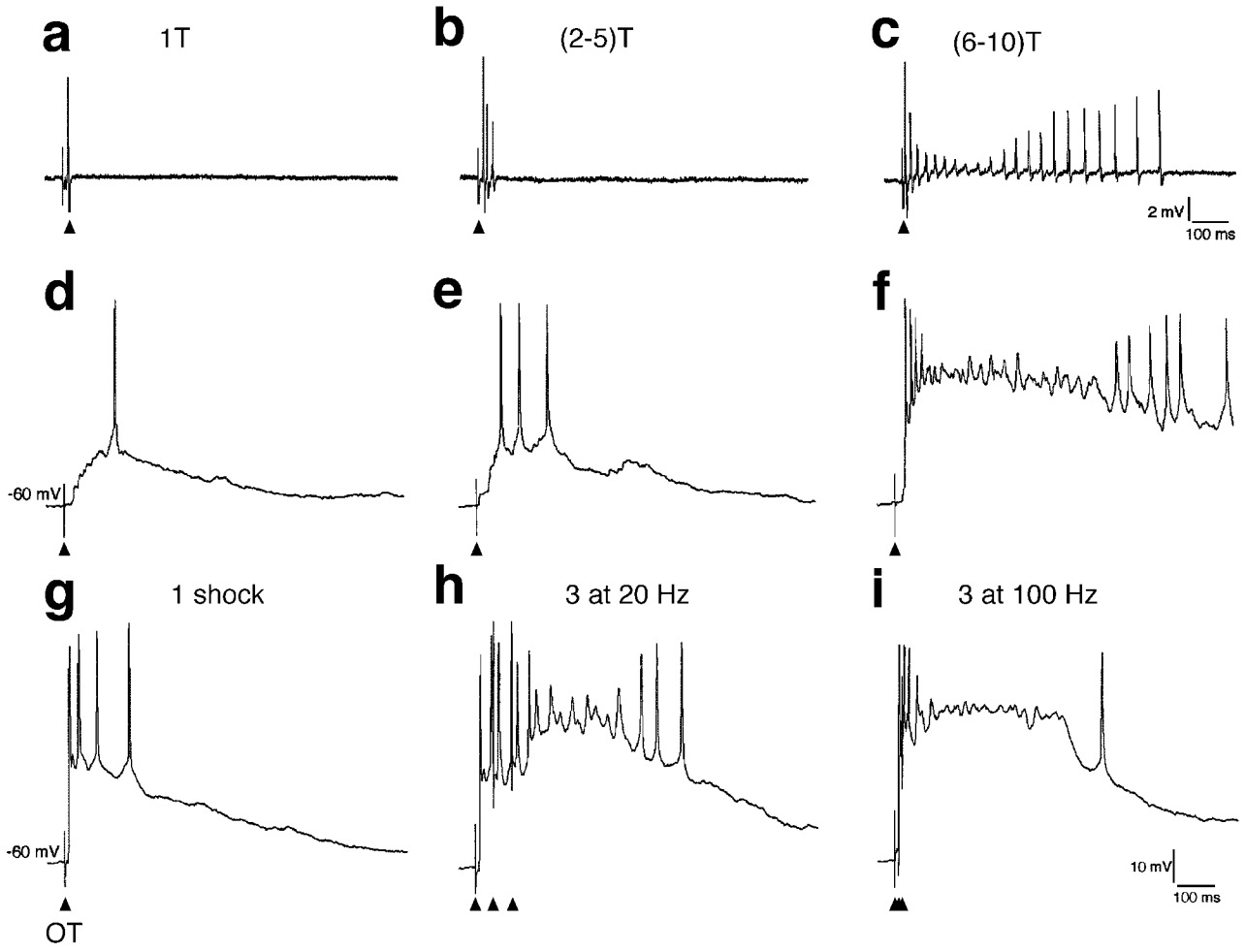

Figure 1. Responses in neurons to stimulation of optic tract (*OT*) fibers at different intensities. *a*, Stimulation of OT at threshold intensity (*1T*), moderate intensity (*b*) (2–5 times that of threshold, *2–5 T*), and strong intensity (*c*) (6–10 times that of threshold, *6–10 T*). Note that the early spikes gradually decreased in amplitude, whereas the late spikes increased in amplitude. *d*, Whole-cell recording showed that a stimulus at threshold intensity evoked a small EPSP. *e*, A moderate stimulus induced a larger EPSP. *f*, A strong stimulus elicited a long-lasting plateau potential characterized by a large amplitude (>30 mV from the resting potential), slow decay, and a long train of partially inactivated spikes. *g*, A moderate stimulus evoked an EPSP. *h*, Three stimuli of the same intensity at 20 Hz elicited a plateau potential. *i*, Three stimuli at 100 Hz induced a more prominent plateau potential, as judged by inactivation of Na^+ spikes. Membrane potential always held at −60 mV. *Arrowheads,* Electrical shocks to OT.

of iridium stimulating electrodes (0.5 MΩ; WPI) were placed on the surface of the optic tract (OT) to induce postsynaptic potentials by passing single electrical pulses (0.1–0.3 msec, 50–700 μA). We collected current-clamp data from neurons in superficial SC (depth < 200 μm) and measured the amplitude and slope of decay within 200 msec from the peak of the postsynaptic potential.

We also recorded field potentials (FPs) from superficial SC (depth = 100 μm) with patch electrodes filled with 1 M NaCl (1–2 MΩ) to determine whether long-term changes in synaptic efficacy could be induced in SC. An electrical stimulus was applied every 30 sec, and the intensity (0.5–1.0 mA) was adjusted to induce an FP with an amplitude of three-fourths maximal response. After 15 min of control recordings, we applied a train of high-frequency pulses (50 Hz, 20 sec) (Okada, 1993) at the same intensity. Then we collected FPs for another 90 min. The effect of the tetanus was determined by comparing the average amplitude of control FPs with that of the post-tetanic period of 80–90 min. All numerical values were expressed as mean ± SE. A Student's paired *t*-test and χ^2 were used to determine statistical significance. Electrophysiological signals were collected by an Instrutek VR10B interface unit and stored on a Macintosh Power PC (9500/132) with the Pulses (HEKA) software program.

The ACSF contained (in mM): NaCl, 124; KCl, 2.5; NaH_2PO_4, 1.25; $MgSO_4$ 0.1; $NaHCO_3$, 26; glucose, 10; $CaCl_2$, 2, pH 7.4 after saturation by gases. The potassium-based solution for patch micropipettes contained (in mM); K-gluconate, 140; HEPES, 10; EGTA-Na, 1.1; $CaCl_2$, 0.1; $MgCl_2$, 2; ATP-Na, 2; GTP-Na, 0.2, PH 7.25. Different antagonists including D-APV (100 μM) and bicuculline (10 μM) to block NMDA and $GABA_A$ receptors were applied to the bath. We also applied nitrendipine (10 μM) to block L-type Ca^{2+} channels.

RESULTS

Extracellular recordings (n = 71) showed that OT stimulation at different stimulus intensities produced three response patterns. An electrical shock at threshold intensity evoked only one spike in SC neurons (Fig. 1*a, 1T*). A moderate stimulus (two to five times threshold) induced a short train (<250 msec) of spikes [Fig. 1*b, (2–5)T*]. A strong stimulus (6–10 times threshold) elicited a long train (>300 msec) of spikes with a specific change in spike amplitude [Fig. 1*c, (6–10)T*] such that initial spikes gradually decreased, whereas later spikes gradually increased in amplitude. Whole-cell recordings showed similarly that a weak stimulus (*1T*) evoked a small EPSP with one spike riding on it (Fig. 1*d*), whereas a moderate stimulus [*(2–5)T*] induced a larger EPSP that resulted in several spikes (Fig. 1*e*). A strong stimulus [*(6–10)T*] elicited a

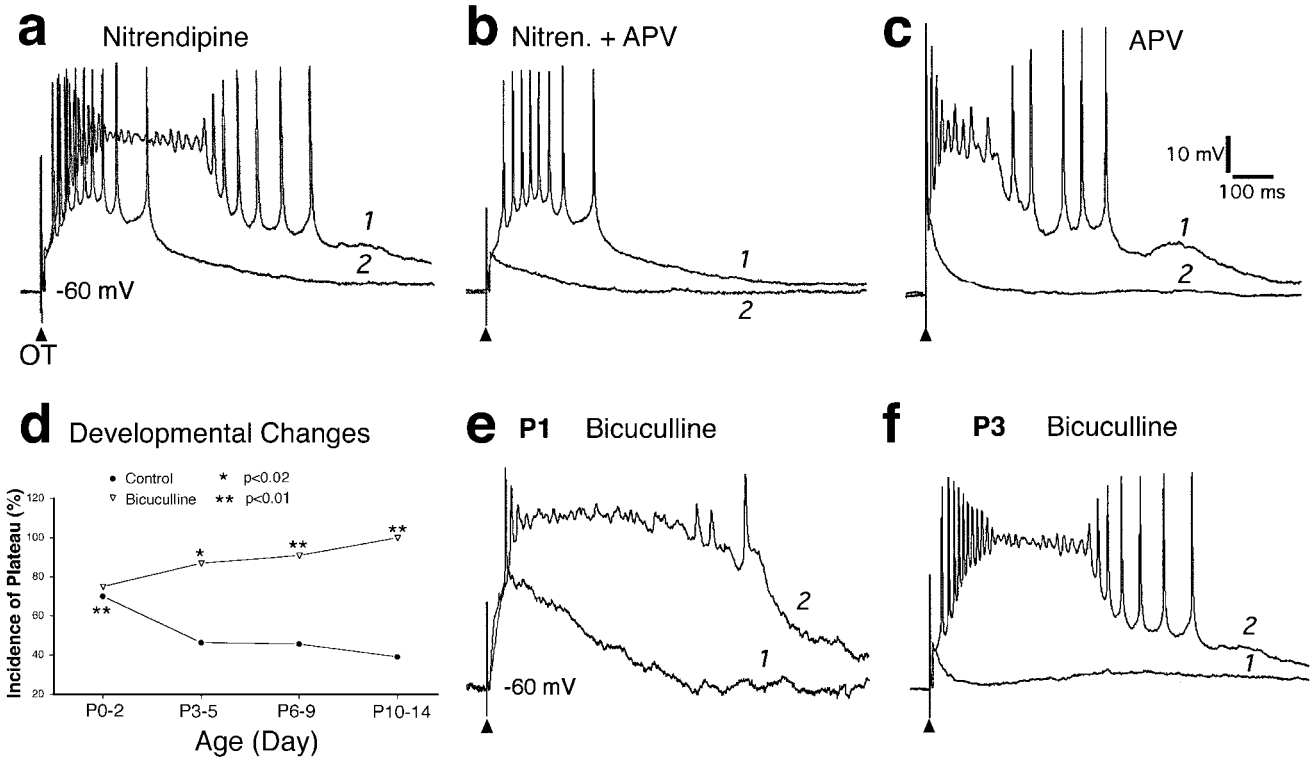

Figure 2. Interaction between postsynaptic potentials and plateau potential. *a*, Application of 10 μM nitrendipine blocked the plateau potential, leaving the underlying EPSP intact (*trace 1* before, *trace 2* after drug application). *b*, Additional application of 100 μM D-APV blocked the late component of the EPSP. *c*, Application of D-APV also blocked the plateau potential. *d*, The incidence of plateau potentials at different ages (*filled circles*) and after blocking $GABA_A$ receptors by bicuculline (*open triangles*). *e, f*, Application of 10 μM bicuculline converted EPSPs into plateau potentials, regardless of whether the EPSP was followed by a definite IPSP (*e* vs *f*).

long-lasting membrane depolarization that was characterized by a large amplitude (>30 mV from the resting potential), slow decay (slope < 0.01 mV/msec), and a long train of spikes with decreases followed by increases in amplitude, a response pattern called a plateau potential (Fig. 1*f*).

The plateau potential depolarized the membrane above −40 mV for >200 msec, which partially inactivated Na^+ channels and explains the decrease in spike amplitude. The plateau potential is likely evoked by spatial summation of multiple retinal inputs, which converge on the neuron and can also be induced by temporal summation. As shown in Figure 1*g*, one moderate stimulus evoked an EPSP, whereas three stimuli of the same intensity at 20 Hz elicited a plateau potential (Fig. 1*h*), and three stimuli at 100 Hz induced a more prominent plateau potential as judged by inactivation of Na^+ spikes (Fig. 1*i*).

To determine the contribution of various channels to the plateau potential and EPSPs, we applied a variety of blockers. Application of 10 μM nitrendipine, a potent blocker of L-type Ca^{2+} channels, did not affect the EPSP evoked by either weak or moderate stimuli (data not shown) but did block the plateau potential ($n = 12$), leaving the underlying EPSP intact (Fig. 2*a, 1* vs *2*), indicating that the plateau potential is mediated by L-type Ca^{2+} channels and triggered by the EPSP. Because the underlying EPSP depolarized the membrane above −40 mV for tens of milliseconds, the threshold of the plateau potential was likely approximately −40 mV. Na^+ spikes that depolarized the membrane above 0 mV could not trigger the plateau potential (Fig. 1*d,e,g*). In addition, after blocking K^+ channels, Na^+ spikes always triggered plateau potentials (Contreras et al., 1997; Lo et al., 1998). Thus, the regenerative activation of L-type Ca^{2+} channels, which is the origin of the plateau potential, was dependent on both amplitude and duration of membrane depolarization. To test the voltage and time dependencies of the plateau potential, we applied depolarizing current pulses at different amplitudes and durations. The depolarization of the cell body that we recorded from could not induce a plateau potential but did induce a train of regular spikes without specific changes in amplitude.

Application of 100 μM D-APV blocked the late but not the early component of the EPSP (Fig. 2*b, 1* vs *2*), showing that it consisted of both NMDA and non-NMDA components. Because the NMDA component had a larger amplitude and longer duration than the non-NMDA component (Fig. 2*b*), the NMDA receptor-mediated EPSP might contribute to the activation of L-type Ca^{2+} channels. To test this, we applied 100 μM D-APV alone ($n = 10$), which also blocked the plateau potential (Fig. 2*c, 1* vs *2*), indicating that it is triggered by the NMDA receptor-mediated EPSP.

The incidence of plateau potentials decreased during development (Fig. 2*d*). At the age of P0–P2, 70% (21 of 30) of tested neurons had plateau potentials. At P3–P5, only 46.4% (13 of 28) of tested neurons showed plateau potentials. This incidence decreased further to 45.7% (16 of 35) at P6–P9 and to 39.1% (9 of 23) at P10–P14 (Fig. 2*d, filled circles*). The decrease in incidence of the plateau potential from P0–P2 to P3–P14 was statistically significant ($\chi^2, p < 0.01$).

The decrease in incidence of the plateau potential was probably not caused by a decrease of input resistance during development,

because there was no significant difference in input resistance between neurons with and without plateau potentials in each age group ($p > 0.05$). However, it probably did result from an increase in GABA receptor-mediated inhibition (Shi et al., 1997). Application of 10 μM bicuculline, an antagonist of $GABA_A$ receptors, transformed EPSPs into plateau potentials at the same stimulus intensity. At P0–P2, 75% (6 of 8) of tested neurons showed this transformation. The percentage gradually increased, rising to 87% (7 of 8) at P3–P5, 91% (10 of 11) at P6–P9, and 100% (8 of 8) at P10–P14. In the presence of bicuculline, the incidence at P3–P14 was significantly different from that without bicuculline ($\chi^2, p < 0.01 \sim 0.02$; Fig. 2d, *open triangles*) and presumably reflects the development of GABAergic inhibition in SC.

We examined this further by studying the development of the IPSP. Although the EPSP was not frequently followed by an IPSP at early ages, the decay slope at these ages varied from 0.05 to 0.95 mV/msec, suggesting that the rapidly declining EPSP was curtailed by a "hidden" IPSP. Application of bicuculline converted the EPSP into a plateau potential in some neurons (Fig. 2*e, 1* vs *2*), supporting the existence of an invisible IPSP (Fig. 2*e*). At P0–P2, bicuculline failed to convert EPSPs into plateau potentials in 25% (2 of 8) of the tested neurons, suggesting that inhibitory circuits or $GABA_A$ receptors may be relatively sparse at this age. By P3, however, a typical IPSP could be observed (Fig. 2*f, trace 1*) in some collicular neurons, and blocking the IPSP with bicuculline produced a typical plateau potential (Fig. 2*f, trace 2*). This suggests that the $GABA_A$ receptor-mediated IPSP prevents activation of L-type Ca^{2+} channels either via its shunting mechanism or because of its hyperpolarizing effect as early as P0.

We next studied what the function of this potential may be during development. Retinal ganglion cells show spontaneous high-frequency bursts of spikes before eye opening (Galli and Maffei, 1988). The rhythmic activity among neighboring cells produced by these bursts is highly correlated and progresses as a traveling wave across the retina (Meister et al., 1991; Wong et al., 1993). Blockade of such activity blocks formation of ocular dominance columns in visual cortex and laminar segregation in the lateral geniculate nucleus (Shatz, 1994, 1996). High-frequency spontaneous retinal activity may also be sufficient to activate L-type Ca^{2+} channels, which would provide evidence that these channels participate in retinocollicular refinement. To mimic burst activity, a train of electrical shocks (50 Hz, 0.5 sec) was applied to OT of isolated brainstem. This train evoked a depolarization that lasted for several seconds in most SC neurons (Fig. 3*a*). The depolarization was primarily blocked by application of nitrendipine (Fig. 3*b*), showing that synaptic activation of L-type Ca^{2+} channels mediates this sustained depolarization.

To determine the role of sustained depolarization on retinocollicular synaptic transmission, we tested the effect of tetanic stimulation on the evoked field potential of superficial SC. Tetanic stimulation that induces LTP in adult rat SC (Okada, 1993) induced a long-term depression (LTD) in amplitude of the field potential (FP) in neonatal rat SC (Fig. 3*c*). The mean amplitude of FP between 80 and 90 min after tetanus was 71.73 ± 2.33% (mean ± SE) of the pretetanic baseline ($n = 37$; *t* test; $p < 0.01$). Application of 10 μM nitrendipine did not change the amplitude of control FPs, but it partially blocked the LTD. The mean amplitude of FP after tetanus in the presence of nitrendipine was 84.97 ± 4.85% ($n = 10$) of the baseline, which was significantly different ($p < 0.02$) from the control (Fig. 3*c*). Thus, Ca^{2+} influx via L-type Ca^{2+} channels contributes to induction of LTD in the developing SC. By contrast, application of 10 μM bicuculline had no effect on the magnitude of LTD (data not shown).

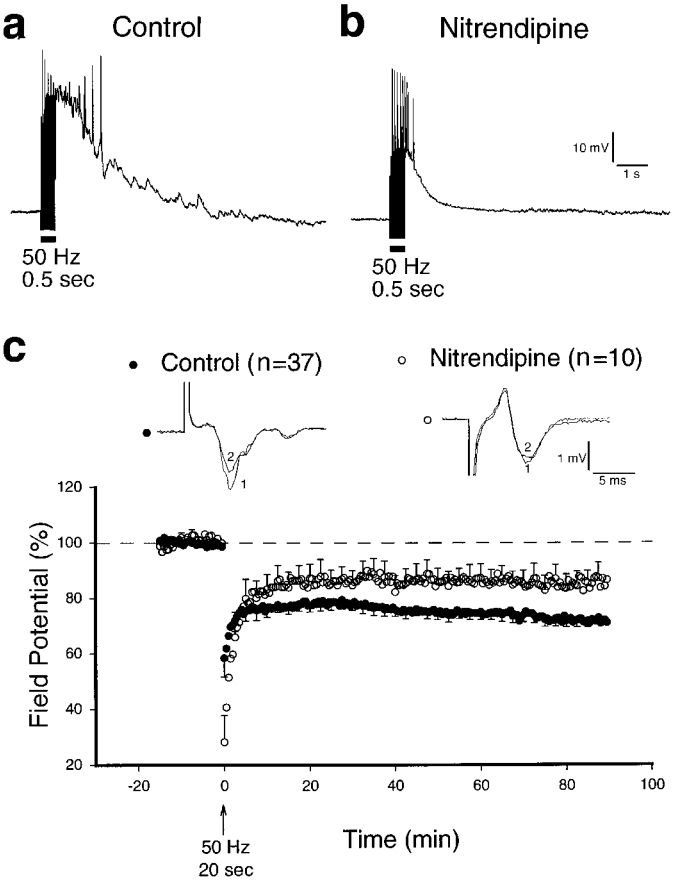

Figure 3. Functional significance of the activation of L-type Ca^{2+} channels in SC neurons. *a*, A train of high-frequency stimuli (50 Hz, 0.5 sec) induced a long-lasting depolarization. *b*, The long-lasting depolarization was largely blocked by application of 10 μM nitrendipine. *c*, High-frequency stimulation (50 Hz, 20 sec) of OT induced an LTD in the amplitude of field potentials ($n = 37$; *filled circles*). The LTD was partially blocked by application of 10 μM nitrendipine ($n = 10$; *hollow circles*). Error bars indicate SE. *Insets* give example records before (*1*) and after (*2*) tetanic stimulation.

DISCUSSION

Our results are important because they are the first to show, using current-clamp techniques, that NMDA receptor-mediated EPSPs, if large enough, can activate L-type Ca^{2+} channels to produce a plateau potential in SC neurons of neonatal rats, and that $GABA_A$ receptor-mediated IPSPs can prevent these potentials. A synaptically evoked sustained depolarization, i.e., plateau potential, has been reported in a few types of neurons in invertebrates (Kiehn and Harris-Warrick, 1992; Dicaprio, 1997) and vertebrates (Russo and Hounsgaard, 1996; Di Prisco et al., 1997; Rekling and Feldman, 1997; Morisset and Nagy, 1998). However, the amplitude of these plateau potentials is much smaller than the plateau potential found in SC neurons (>30 mV). In addition, the plateau potential in other brain structures induces a long train of regular spikes (afterdischarges) without inactivation of Na^+ spikes, and depolarizing current pulses can evoke the plateau potential in these studies, whereas current injection never induced the plateau potential in SC neurons. These differences are probably attributable to different ionic bases for plateau poten-

tials. In most other structures, the plateau potential is blocked by nonspecific high-threshold Ca^{2+} channel blockers (Co^{2+} or Cd^{2+}) or by L-type Ca^{2+} channel blockers (Zhang and Harris-Warrick, 1995; Rekling and Feldman, 1997; Russo et al., 1997), indicating that the generation of plateau potentials requires Ca^{2+} influx through the high-threshold or L-type Ca^{2+} channel. Recently, it has been demonstrated that the charge carrier for the plateau potential is a Ca^{2+}-activated, nonselective cationic current (I_{CAN}) (Zhang et al., 1995; Pearlstein and Dubuc, 1998; Morisset and Nagy, 1999; Perrier and Hounsgaard, 1999). The charge carrier for the plateau potential in SC remains to be examined.

The occurrence of the plateau potential decreases during the time that the retinocollicular pathway is undergoing refinement (Land and Lund, 1979; Simon and O'Leary, 1992), suggesting that it may be important in this process. The decrease in incidence of the plateau potential appears to be attributable both to downregulation of NMDA-mediated currents (Hestrin, 1992; Shi et al., 1997) and upregulation of $GABA_A$ receptor-mediated currents (Shi et al., 1997). The role of calcium influx through L-type Ca^{2+} channels during pathway refinement is uncertain, but our results show that one effect is the induction of long-term depression of retinocollicular transmission because blockade of L-type Ca^{2+} channels reduced LTD in neonatal SC. LTD has been considered a model for elimination of inappropriate synapses that presumably occurs during pathway refinement. Although our results are the first to report LTD in the developing SC, LTD has been demonstrated in the neonatal hippocampus (Bolshakov and Siegelbaum, 1994; McLean et al., 1996), and LTD in hippocampus has been shown to be dependent on the activation of L-type Ca^{2+} channels in rodents (Bi and Poo, 1998; Domenici et al., 1998; Norris et al., 1998). It will be important in the future to conduct additional experiments that directly link L-type Ca^{2+} current activity to pathway refinement in the developing rodent SC.

REFERENCES

Bi GQ, Poo MM (1998) Synaptic modifications in cultured hippocampal neurons: dependence on spike timing, synaptic strength, and postsynaptic cell type. J Neurosci 18:10464–10472.

Bolshakov VY, Siegelbaum SA (1994) Postsynaptic induction and presynaptic expression of hippocampal long-term depression. Science 264:1148–1152.

Cavus I, Teyler T (1996) Two forms of long-term potentiation in area CA1 activate different signal transduction cascades. J Neurophysiol 76:3038–3047.

Contreras D, Durmuller N, Steriade M (1997) Plateau potential in cat neocortical association cells in vivo: synaptic control of dendritic excitability. Eur J Neurosci 9:2588–2595.

Davis FS, Cork RJ, Pihl LG, Cao N, Mize RR (2000) The NMDA antagonist MK-801 fails to disrupt refinement of the ipsilateral retinocollicular pathway in C57/Bl6 mice. FASEB J, in press.

Dicaprio R (1997) Plateau potentials in motor neurons in the ventilatory system of the crab. J Exp Biol 200:1725–1736.

Di Prisco GV, Pearlstein E, Robitaille R, Dubuc R (1997) Role of sensory-evoked NMDA plateau potentials in the initiation of locomotion. Science 278:1122–1125.

Domenici MR, Berretta N, Cherubini E (1998) Two distinct forms of long-term depression coexist at the mossy fiber-CA3 synaptic in the hippocampus during development. Proc Natl Acad Sci USA 95:8310–8315.

Galli L, Maffei L (1988) Spontaneous impulse activity of rat retinal ganglion cells in prenatal life. Science 242:90–91.

Garthwaite J (1991) Glutamate, nitric oxide and cell-cell signalling in the nervous system. Trends Neurosci 14:60–67.

Grover LM, Teyler TJ (1990) Two components of long-term potentiation induced by different patterns of afferent activation. Nature 347:477–479.

Grover LM, Teyler TJ (1992) *N*-methyl-D-aspartate receptor-independent long-term potentiation in CA1 of rat hippocampus: input-specific induction and preclusion in a non-tetanized pathway. Neuroscience 49:7–11.

Hestrin S (1992) Developmental regulation of NMDA receptor-mediated synaptic currents at a central synapse. Nature 357:686–689.

Johnston D, Williams S, Jaffe D, Gray R (1992) NMDA-receptor-independent long-term potentiation. Annu Rev Physiol 54:489–505.

Kapur A, Yeckel MF, Gray R, Johnston D (1998) L-type calcium channels are required for one form of hippocampal mossy fiber LTP. J Neurophysiol 79:2181–2190.

Kiehn O, Harris-Warrick RM (1992) Serotonergic stretch receptors induce plateau properties in a crustacean motor neuron by a dual-conductance mechanism. J Neurophysiol 68:485–495.

Kurotani T, Higashi S, Inokawa H, and Toyama K (1996) Protein and RNA synthesis-dependent and -independent LTPs in developing rat visual cortex. NeuroReport 8:35–39.

Land PW, Lund RD (1979) Development of the rat's uncrossed retinotectal pathway and its relation to plasticity studies. Science 205:698–700.

Lo F-S, Mize RR (1999) Retinal input induces three firing patterns in neurons of the superficial superior colliculus of neonatal rats. J Neurophysiol 81:954–958.

Lo F-S, Cork RJ, Mize RR (1998) Physiological properties of neurons in the optic layer of the rat's superior colliculus. J Neurophysiol 80:331–343.

McLean HA, Caillard O, Ben-Ari Y, Gaiarsa J-L (1996) Bidirectional plasticity expressed by GABAergic synapses in the neonatal rat hippocampus. J Physiol (Lond) 496:471–477.

Meister M, Wong ROL, Baylor DA, Shatz CJ (1991) Synchronous busts of action potentials in ganglion cells of the developing mammalian retina. Science 252:939–943.

Morisset V, Nagy F (1998) Nociceptive integration in the rat spinal cord: role of nonlinear membrane properties of deep dorsal horn neurons. Eur J Neurosci 10:3642–3652.

Morisset V, Nagy F (1999) Ionic basis for plateau potentials in deep dorsal horn neurons of rat spinal cord. J Neurosci 19:7309–7316.

Norris CM, Halpain S, Foster TC (1998) Reversal of age-related alterations in synaptic plasticity by blockade of L-type Ca^{2+} channels. J Neurosci 18:3171–3179.

Okada Y (1993) The properties of the long-term potentiation (LTP) in the superior colliculus. Prog Brain Res 95:287–296.

Pearlstein E, Dubuc R (1998) Cellular mechanisms underlying plateau potentials in lamprey reticulospinal neurons. Soc Neurosci Abstr 24:1669.

Perrier J-F, Hounsgaard J (1999) Ca^{2+}-activated nonselective cationic current (ICAN) in turtle motoneurons. J Neurophysiol 82:730–735.

Rekling JC, Feldman JL (1997) Calcium-dependent plateau potentials in rostral ambiguus neurons in the newborn mouse brain stem in vitro. J Neurophysiol 78:2483–2492.

Russo RE, Hounsgaard J (1996) Plateau-generating neurons in the dorsal horn in an in vitro preparation of the turtle spinal cord. J Physiol (Lond) 493:39–54.

Russo RE, Nagy F, Hounsgaard J (1997) Modulation of plateau properties in dorsal horn neurons in a slice preparation of the turtle spinal cord. J Physiol (Lond) 499:459–474.

Shatz C (1994) Role for spontaneous neural activity in the patterning of connections between retina and LGN during visual system development. Int J Dev Neurosci 12:531–546.

Shatz C (1996) Emergence of order in visual system development. Proc Natl Acad Sci USA 93:602–608.

Shi J, Aamodt SM, Constantine-Paton M (1997) Temporal correlations between functional and molecular changes in NMDA receptors and GABA neurotransmission in the superior colliculus. J Neurosci 17:6264–6276.

Simon DK, O'Leary DD (1992) Development of topographic order in the mammalian retinocollicular projection. J Neurosci 12:1212–1232.

Simon DK, Prusky GT, O'Leary DD, Constantine-Paton M (1992) *N*-methyl-D-aspartate receptor antagonists disrupt the formation of a mammalian neural map. Proc Natl Acad Sci USA 89:10593–10597.

Wong ROL, Meister M, Shatz CJ (1993) Transient period of correlated bursting activity during development of the mammalian retina. Neuron 11:923–938.

Wu HH, Cork RJ, Huang PL, Shuman DL (1999) Refinement of the ipsilateral retinocollicular projection is disrupted in double endothelial and neuronal nitric oxide synthase gene knockout mice. Brain Res Dev Brain Res, in press.

Xia J, Lo F-S (1996) IPSP-EPSP interaction on neurons in the lateral geniculate neurons of the rat. Chin Sci Bull 41:1116–1123.

Zhang B, Harris-Warrick RM (1995) Calcium-dependent plateau potentials in a crab stomatogastric ganglion motor neuron. II. Calcium current and its modulation by serotonin. J Neurophysiol 74:1929–1937.

Zhang B, Wootton JF, Harris-Warrick RM (1995) Calcium-dependent plateau potentials in a crab stomatogastric ganglion motor neuron. II. Calcium-activated slow inward current. J Neurophysiol 74:1938–1946.