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Dark rearing reveals the mechanism underlying stimulus size tuning of superior colliculus neurons

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Abstract

Neurons in the superficial layers of the midbrain superior colliculus (SC) exhibit distinct tuning properties for visual stimuli, but, unlike neurons in the geniculocortical visual pathway, most respond best to visual stimuli that are smaller than the classical receptive field (RF). The mechanism underlying this size selectivity may depend on the number and pattern of feedforward retinal inputs and/or the balance between inhibition and excitation within the RF. We have previously shown that chronic blockade of NMDA receptors (NMDA-R), which increases the convergence of retinal afferents onto SC neurons, does not alter size selectivity in the SC. This suggests that the number of retinal inputs does not determine size selectivity. Here we show, using single unit extracellular recordings from the SC of normal hamsters, that size selectivity in neurons selective for small stimulus size is correlated with the strength of inhibition within the RF. We also show that dark rearing causes concomitant reductions in both inhibition and size selectivity. In addition, dark rearing increases the percentage of neurons non-selective for stimulus size. Finally, we show that chronic blockade of NMDA-R, a procedure that does not alter size tuning, also does not change the strength of inhibition within the RF. Taken together, these results argue that inhibition within the RF underlies selectivity for small stimulus size and that inhibition must be intact for size tuning to be preserved after developmental manipulations of activity. In addition, these results suggest that regulation of the balance between excitation and inhibition within the RF does not require NMDA-R activity but does depend on visual experience. These results suggest that developmental experience influences neural response properties through an alteration of inhibitory circuitry.

Keywords: Rodent, Retinotectal, Receptive field properties, Stimulus tuning, Visual deprivation, Size tuning, Inhibitory circuit, Superior colliculus, Dark rearing

Introduction

The capacity of neural systems to reorganize following altered developmental experience or injury is well recognized (for recent reviews see Foeller & Feldman, 2004; Grubb & Thompson, 2004; Ruthazer, 2005; Pallas et al., 2006). How such plasticity influences subsequent behavior depends on how neural response properties are affected. Visual response properties such as orientation tuning (Sillito, 1975; Eysel et al., 1998; see Shapley et al., 2003 for review), direction selectivity (Barlow & Levick, 1965; Murthy & Humphrey, 1999; see Vaney & Taylor, 2002 for review), and velocity tuning (Goodwin & Henry, 1978, Patel & Sillito, 1978; Razak & Pallas, 2005) depend on the spatiotemporal integration of excitatory and inhibitory inputs for their construction. The role of developmental experience in shaping inhibitory circuitry has been documented in the visual cortex (reviewed in Hensch & Fagiolini, 2005; Hensch, 2004). However, few studies have examined the extent to which experience-dependent modulation of the balance between excitation and inhibition affects behaviorally relevant response properties (Humphrey & Saul, 1998). One possible mechanism through which developmental experience could influence response selectivity is through shaping the strength and/or timing of interactions between excitatory and inhibitory inputs. In this study, we provide evidence for the operation of this mechanism. We show that chronic dark rearing reduces stimulus size selectivity in superior colliculus (SC) neurons selective for small stimulus size by reducing the strength of inhibition inside the classical receptive field (RF).

Selectivity for stimulus size plays an important role in object identification for visual control of movement (Murata et al., 2000), but the mechanisms underlying size selectivity is unclear. Most neurons in the superficial SC respond best when the stimulus occupies only a small portion of the RF (Stein & Dixon, 1979; Pallas & Finlay, 1989; Razak et al., 2003), suggesting that size selectivity involves interactions between inhibition and excitation

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within the RF (Stein & Dixon, 1979). The first goal of this study was to determine if a relationship exists between the strength of inhibition within the RF and stimulus size selectivity.

If inhibition within the RF is important for selectivity for small stimulus size, then decreasing inhibition should decrease size selectivity. Long-term dark rearing (DR) increases the size of the RF and decreases the strength of inhibition within the RF of SC neurons in the hamster (Carrasco et al., 2005; Carrasco & Pallas, 2006). Early but not late light exposure protects against the effects of adult visual deprivation on the SC. We hypothesized that those SC neurons with selectivity for small stimulus size in DR hamsters would have reduced size selectivity because of the reduction in inhibition in the RF caused by the visual deprivation. In a previous study, we showed that chronic NMDA-R blockade does not affect size selectivity (Razak et al., 2003). As an additional test of the role of inhibition in size selectivity, we hypothesized that inhibition within the RF of SC neurons would not be affected by NMDA-R blockade, resulting in preserved size selectivity following this manipulation. These two developmental manipulations not only address the contributions of normally patterned neural activity to development of size selectivity, but also provide insights into the development of the balance between excitation and inhibition in the RF.

We report here that a correlation exists between the strength of inhibition within the RF and selectivity for small stimulus size in the normal SC. Developmental manipulations that reduce inhibition within the RF, such as dark rearing, also reduce size selectivity in these neurons, whereas NMDA-R blockade leaves both properties intact. These results are consistent with the interpretation that (1) selectivity for small stimulus size depends on within-field inhibition, that (2) the balance between excitation and inhibition within the RF is dependent on experience with patterned light, and that (3) the long periods of visual deprivation result in decreased size selectivity through a loss in the strength of inhibition.

Materials and methods

Experimental animals (Syrian hamsters—*Mesocricetus auratus*) were bred in the Georgia State University vivarium from breeding stock purchased from Charles River Laboratories (Wilmington, MA). Some animals used in this study also provided data for a previous study (Razak et al., 2003). All procedures used on animals were reviewed and approved by the Institutional Animal Care and Use Committee, and were consistent with National Institutes of Health and USDA guidelines.

Electrophysiological recordings were obtained from adult hamsters (≥2 months of age) following anesthetization with urethane (0.7 g/mL, 0.03 mL/kg i.p. in 3–4 aliquots spaced at 20 min intervals). Urethane is advantageous for this purpose because it affects different neurotransmitter systems more uniformly than ketamine, which potentiates NMDA receptors, or pentobarbital, which suppresses GABAergic responses selectively (Maggi & Meli, 1986). Pupils were dilated with a 10% ophthalmic atropine solution. Respiration rates and withdrawal reflexes were monitored to ensure a deep level of anesthesia appropriate for surgery, with supplemental doses of urethane given as warranted. After performing a craniotomy over the SC, the visual cortex was bilaterally aspirated to eliminate influences of corticocollicular inputs (Rhoades & Chalupa, 1978) and to facilitate viewing the surface of the SC for electrode placement. Hamsters do not exhibit noticeable eye movements under anesthesia, but nonetheless a suture was placed in the conjunctivum to stabilize the left eye during the recording session. The eye was covered with a fitted plano contact lens for protection, and the brain was kept covered with sterile saline throughout the recording session.

All of the neurons included in this study were isolated within 200 μm of the SC surface. For extra-cellular single-unit recording, tungsten microelectrodes (FHC, Bowdoinham, ME) with an impedance of 1–3 MΩ were used. Using a penlight as a search stimulus, electrode penetrations were made perpendicular to the surface of the SC to locate visually responsive cells in the retino-recipient superficial gray layer (sSC). Upon isolation of a single neuron from the right SC, the approximate location of the excitatory receptive field (eRF) was determined using the penlight. A 14-inch computer monitor was then moved to the location of the eRF at a distance of 40 cm from the left eye. A Sergeant Pepper graphics board (Number Nine, Cambridge, MA) was used in conjunction with "STIM" software (developed by Kaare Christian at Rockefeller University, New York, New York) to generate visual stimuli. Data were acquired by CED 1401 hardware and processed by Spike2 software (Cambridge Electronic Design, Cambridge, UK).

The excitatory receptive field (eRF) diameter of each neuron was determined by sweeping a single spot of light (1° diameter) from the top to the bottom of the computer monitor screen. Successive sweeps started 2° lateral to the previous sweep, allowing a determination of the nasotemporal extent of the eRF. The light spot was swept at either 5°/s or 30°/s velocity, depending on whether the neuron responded better to slowly or rapidly moving stimuli. Most SC neurons in the hamster respond poorly to stimuli moving with a velocity >50°/s (Stein & Dixon, 1979; Pallas & Finlay, 1989; Razak et al., 2003; Razak & Pallas, 2005). The estimated RF size did not change with the velocity of the stimulus used.

In order to determine the strength of inhibition within the RF, two spots of light (diameter 1° each) were swept from the top to the bottom of the monitor. The second spot of light started 2.6° further away from the center spot either on the temporal or the nasal side of the center with respect to the hamster. This allowed us to determine the amount of suppression of the response to the first spot evoked by the second spot. The time interval between each sweep was set at 10 s to avoid adaptation. Each stimulus pair was repeated three to seven times.

Comparative size tuning data from NORMAL and D-APV groups were taken from Razak et al. (2003). The method used to determine size tuning in the SC of DR hamsters was identical to that published in Razak et al. (2003). Briefly, size tuning of SC neurons was measured by presenting a moving spot of light whose diameter was increased from 2.5° to 15° over successive sweeps. This approach was used instead of changing the diameter of a stationary stimulus because SC neurons respond better to moving stimuli. The spot of light was moved in the temporal-to-nasal direction with a speed of 5°/s or 30°/s. The choice of stimulus speed and the range of stimulus sizes were guided by previous observations regarding optimal stimuli for most hamster SC neurons (Pallas & Finlay, 1989; Razak et al., 2003). Neurons were classified according to stimulus size preference as low-pass (LP), band-pass (BP), high-pass (HP), and non-selective (NS). Neurons that responded with at least twice the number of spikes to the smallest sized stimuli than to the largest tested stimuli were classified as LP neurons. Stimuli that elicited at least twice the number of spikes to an intermediate size than to the smallest and the largest size were classified as BP neurons. Neurons that responded with at least twice the number of spikes to the largest stimuli than to the smallest were called HP neurons. Non-selective

neurons were those that responded within 50% of maximal response at all stimulus sizes.

For comparison with normal (NORMAL group) SC neurons, excitatory RF size, strength of inhibition inside the RF, and stimulus size tuning were determined in both dark-reared (DR group) animals and in animals with chronic blockade of NMDA-R (D-APV group). For dark rearing, pregnant hamster dams were moved to a dark room three to seven days before parturition. Hamster pups stayed in the dark until the day of recording. NMDA receptors were blocked with the antagonist D-APV embedded in a slow-release polymer (Elvax, DuPont Chemicals, Wilmington, DE) with a small amount (1:100,000) of tritiated APV. A small piece of the polymer was placed on the surface of the SC on the day of birth, and was retrieved for scintillation counting on the day of recording to estimate drug release. Details of the surgical procedures and Elvax release characteristics are provided elsewhere (Huang & Pallas, 2001). The same batch of Elvax polymer described in Razak et al. (2003) was used in this study. We determined the mean D-APV release based on scintillation counts to be 534 pmol/mm^2. This is comparable to that seen previously (Huang & Pallas, 2001).

Results

Sixty-two Syrian hamsters were used in this study. Twenty seven hamsters were reared under a normal light cycle without pharmacological blockade of NMDA-Rs (NORMAL group), 23 hamsters had the ELVAX polymer containing D-APV implanted on the SC on the day of birth, and 12 hamsters were raised in the dark from birth. Table 1 shows the number of neurons from which size tuning and inhibition within the RF were determined in each group of animals.

Stimulus size selectivity is correlated with the strength of inhibition within the RF

To determine if selectivity for small stimulus size was correlated with the strength of inhibition inside the RF, both properties were assessed in 18 neurons in the NORMAL group. This population consisted of 14 LP and 4 non-selective neurons. We found that the degree to which a LP neuron was selective for stimulus size was dependent on the strength of inhibition within its RF (Fig. 1). Figs. 1A to 1C shows data from a representative neuron that responded best to the smallest stimulus used (Fig. 1A), and a response that decreased below 50% of maximum for stimuli that were larger than 9° in size. The RF diameter of this neuron was approximately 10° to 12°, showing that the neuron responded best to stimuli that were smaller than the excitatory RF (Fig. 1B). Probing with dual stimuli confirmed that inhibition was present within the RF. The response of the neuron to a single stimulus swept through the center of the RF was reduced by approximately 25% if a second stimulus was swept simultaneously through the RF (Fig. 1C). Another neuron with a LP size tuning profile is shown in Figs. 1D to 1F. It was weakly tuned to stimulus size, with its response falling to 50% of maximum only when stimulus size exceeded 14° (Fig. 1D). It had a RF size similar to that of the neuron in Fig. 1A but exhibited weak inhibition within the RF (Fig. 1E, 1F). The response of the neuron to the center spot of light was not significantly affected by the presence of a second spot of light within the RF. The neuron shown in Figs. 1G to 1I exhibited facilitation inside the RF. This neuron was non-selective for stimulus size (Fig 1G). In the presence of two spots of light, the neuron's response was higher than that for the center spot of light (Fig. 1I). These data suggest that preferred stimulus size is influenced by the strength of inhibition within the RF in these three neurons.

Table 1. *Number of neurons in each experimental group in which inhibition within the RF and size tuning were measured*

Group	Inhibition in RF	Size Tuning
Normal	52	42
D-APV	48	46
DR	49	48

When we compiled data from LP neurons from the NORMAL population, we found that the strength of inhibition inside the RF was correlated with stimulus size selectivity (Fig. 2). The strength of inhibition within the RF was determined by calculating the ratio of the response to a single stimulus to that of the response to dual stimuli. The higher this ratio, the stronger the inhibition is within the RF. To quantify size selectivity for LP neurons, the stimulus size for which the response decreased to 50% of maximum (termed "50% stimulus size") was determined. The smaller the 50% stimulus size, the stronger is the size selectivity. The 50% stimulus size of the neuron shown in Fig. 1A is 9°, whereas it is 15° for the neuron in Fig. 1D. The neuron in Fig. 1C is non-selective for stimulus size because the response does not decline below 50% for the range of stimulus sizes used. Fig. 2 shows that, as the strength of inhibition inside the RF increased, the 50% stimulus size decreased ($r^2 = 0.6$, $P = 0.002$). That is, the stronger the inhibition, the more selective the neuron is for stimulus size. All four neurons that were non-selective for size either had no inhibition within the RF or showed facilitation to dually presented spots of light. These results support the hypothesis that within-RF inhibition is necessary for stimulus size selectivity in LP neurons.

Dark rearing reduces the strength of inhibition within the RF and reduces size tuning

Sensory deprivation provided an additional way to test the relationship between inhibition and size tuning. Dark-rearing from birth results in a reduction in surround inhibition in hamster SC (Carrasco et al., 2005). It seemed likely that deprivation could also cause a loss of inhibition within the RF, and if so, a direct test of the necessity of within-RF inhibition to size tuning of LP neurons could be performed. Thus we measured the size selectivity and strength of inhibition within the RF of neurons in DR animals and compared the data to data from NORMAL animals.

We found that dark-rearing profoundly affected both the strength of inhibition within the RF and the size selectivity of SC neurons. Similar to the NORMAL group, LP neurons in the DR group also had strong inhibition within the RF (e.g., Figs. 3A to 3C), and neurons that were not size selective either exhibited facilitation (e.g., Fig. 3D to 3F) or showed no inhibition within the RF (e.g., Fig. 3G to 3I). The neuron shown in Fig. 3B exhibited two peaks in its RF. Similar effects of DR on RF structure have been reported before (Carrasco et al., 2005). When the population of neurons in the DR group was considered, the average strength of inhibition inside the RF was significantly lower than in the NORMAL group (Fig. 4A, $P < 0.001$, *t*-test). We next analyzed how this reduction

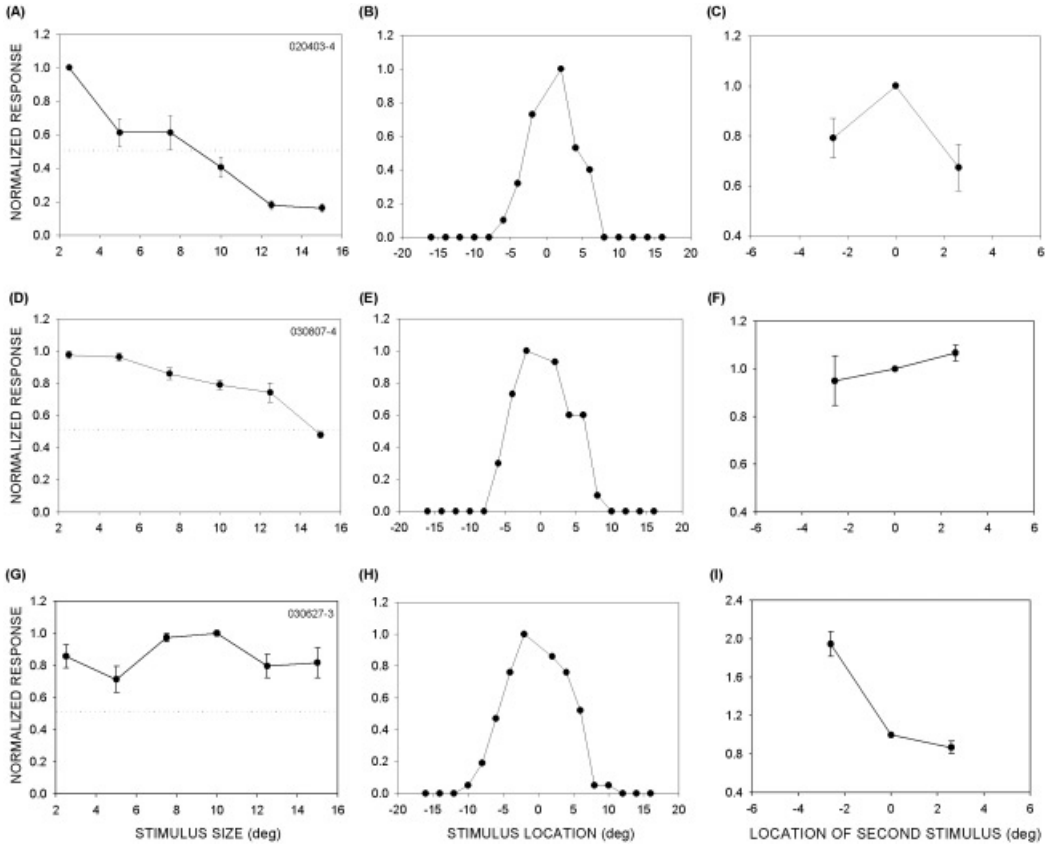

Fig. 1. Inhibition within the receptive field predicts size selectivity in single neurons from NORMAL animals. (A, D, G) Size tuning was determined by measuring the response to a spot of light of increasing size. These data were normalized to the maximum response. The dotted lines show the stimulus size at which the response declined to 50% of maximum (50% stimulus size). The neurons in (A) and (D) were size selective, whereas the neuron in (G) was not size selective. (B, E, H) The RF diameter of individual neurons was determined by vertically sweeping a single spot of light through different locations in the visual field. (C, F, I) Inhibition within the RF was determined by measuring the reduction in response to a single spot of light moving through the center of the RF (at 0) by the addition of a second spot of light on either side of the center.

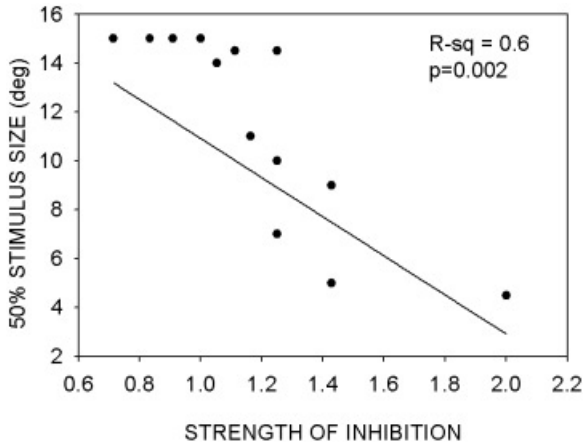

Fig. 2. The 50% stimulus size is correlated with inhibition within the RF in LP neurons. This plot shows that the population of LP neurons exhibits a strong relationship between size selectivity and the strength of within-field inhibition. Size selectivity was quantified by measuring the stimulus size for which the response declines below 50% of maximum response (50% stimulus size). The strength of inhibition is the ratio of response to the single stimulus through the center of the RF and the response to the dual stimuli.

in inhibition affected stimulus size tuning in the population of neurons in the DR group.

Dark-rearing significantly altered the distribution of size tuning categories in the SC (Fig. 4B). In NORMAL SC a vast majority of neurons preferred small-sized stimuli (LP). Most of the remaining neurons were either tuned to intermediate-sized stimuli (BP) or preferred larger stimuli (HP). Less than 10% of NORMAL SC neurons were non-selective for size. Fig. 4B shows that close to 30% of neurons in the DR group were non-selective for size. The increase in non-selective neurons appeared to be mainly at the expense of LP tuned neurons, because the percentage of BP and HP neurons was less affected. The difference in distribution of size tuning categories was significant ($\chi^2 = 12.25$, $P < 0.01$).

The responsiveness of the population of SC neurons in DR animals to different-sized stimuli was also significantly affected by the lack of visual experience. By pooling normalized size tuning data from individual neurons, it was possible to compare the overall size selectivity of the population of SC neurons in NORMAL and DR animals. Although in the NORMAL group the average response declined with increasing stimulus size, DR caused the neuronal population to be non-selective for size (Fig. 4C). The difference in average response was significant at every stimulus size (two-way ANOVA, Tukey test for pairwise comparison,

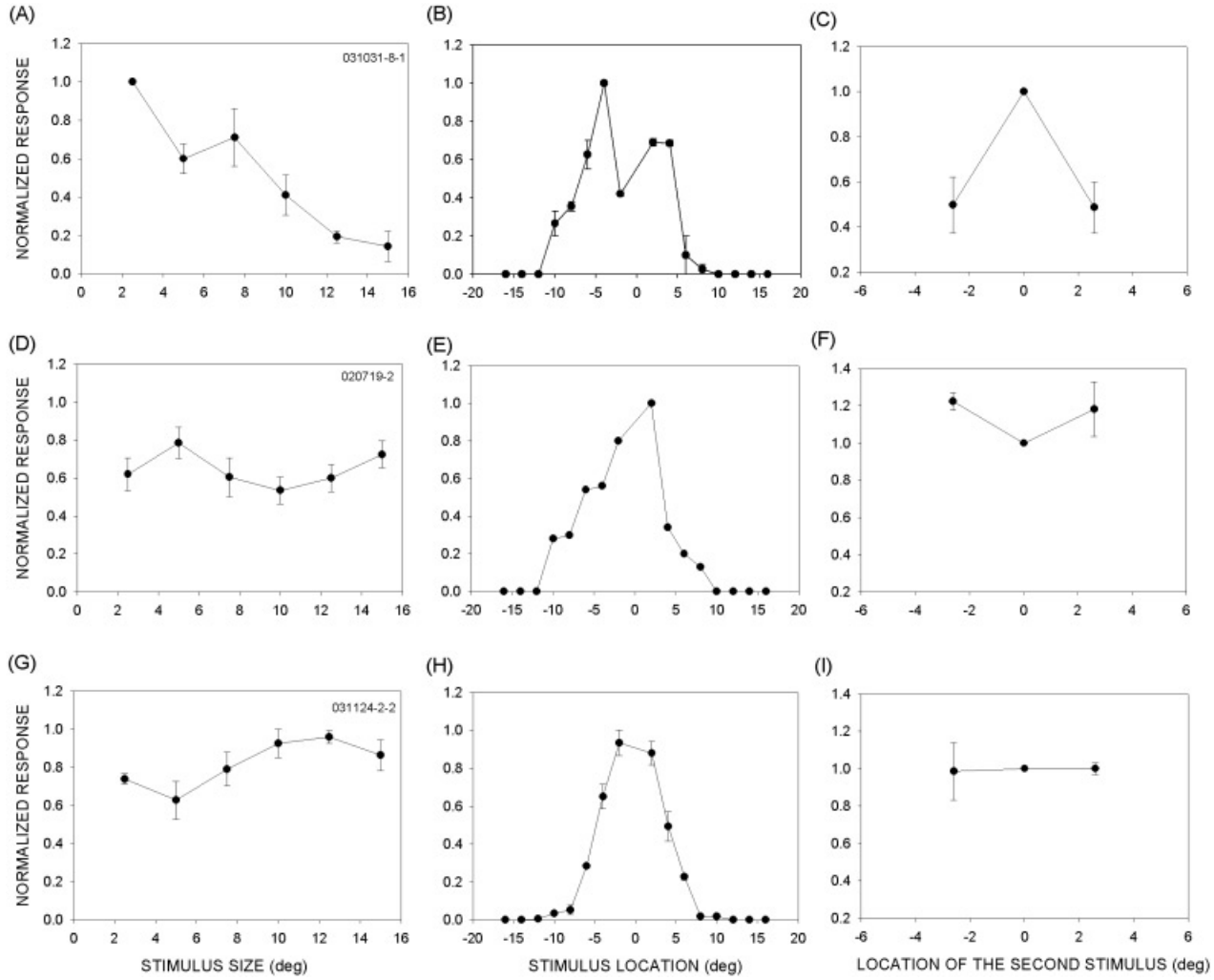

Fig. 3. Inhibition within the RF predicts size selectivity of SC neurons in DR hamsters. (A, D, G) Stimulus size selectivity functions. (B, E, H) RF diameters. (C, F, I) Inhibition within the RF. Details as in Fig 1.

$P < 0.05$). These results provide further support for the hypothesis that within-RF inhibition is necessary for stimulus size tuning in sSC neurons.

Comparison with the D-APV group

As a further test of the connection between size tuning and inhibition, we measured inhibition within the RF in the D-APV group. Because size selectivity is not affected by chronic NMDA-R blockade (Razak et al., 2003), we hypothesized that inhibition within the RF would be preserved in the D-APV group. In SC neurons from animals with chronic NMDA-R blockade of the SC during development, we found that the simultaneous presence of a second stimulus within the RF reduced the response to a similar extent as it did in NORMAL animals ($P > 0.05$, *t*-test) (Fig. 4A), suggesting that the strength of inhibition within the RF does not depend on NMDA receptors. We have previously shown that size tuning categories and size selectivity were similar between the D-APV and the NORMAL groups (Razak et al., 2003). This finding provides additional support for the hypothesis that changes in strength of inhibition inside the RF underlie changes in size tuning.

Discussion

Neurons in the SC are highly selective for stimulus size. This study sought to determine if selectivity for small stimulus size depends on inhibition within the RF, and if the development of this inhibition and size selectivity could be influenced by visual experience. We report that the presence of within-field inhibition is correlated with stimulus size selectivity of LP neurons in the SC. Neurons that did not exhibit inhibition within the RF were not selective for stimulus size. The evidence for the importance of inhibition within the RF is strengthened by the observation that inhibition within the RF and size selectivity was reduced by dark rearing hamsters into adulthood. In addition, chronic blockade of NMDA-Rs did not affect the strength of inhibition within the RF, and as predicted from the normal and DR data, also had no effect on size tuning. This study focuses on the mechanisms underlying size selectivity in LP neurons, the most dominant category of size-tuned neurons in the SC. The mechanisms underlying BP and HP selectivity were not addressed in this study. However, the percentage of BP and HP neurons was not affected by DR, suggesting that mechanisms in addition to within-RF inhibition are also involved in shaping size selectivity in the SC.

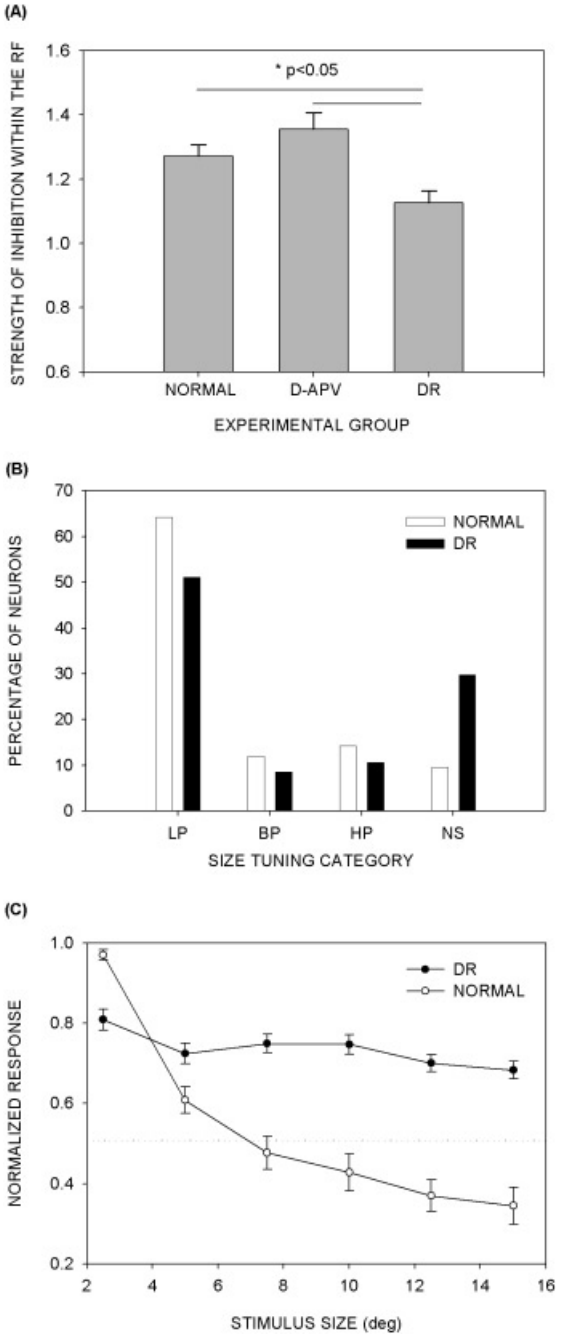

Fig. 4. Dark-rearing reduces inhibition within the RF and reduces size selectivity of SC neurons. (a) Dark-rearing from birth results in a significant reduction in inhibition within the RF. In the NORMAL group, the response to dual stimuli swept through the RF was on average around 80% of the response to the single stimulus swept through the RF center. In contrast, in the DR group, the response was unaffected by the addition of a second stimulus. Chronic blockade of NMDA-R did not significantly alter the strength of inhibition within the RF ($P > 0.1$ compared to NORMAL). (b) The distribution of size tuning categories was altered by long-term dark rearing. Specifically, the incidence of non-selective neurons was increased at the expense of neurons preferring small stimuli (χ^2 test, $P < 0.01$). (c) The recorded population of neurons in DR animals showed poor size selectivity, whereas in the NORMAL group there was a strong preference for small stimuli. The differences were significant at all stimulus sizes ($P < 0.05$, two-way ANOVA, Tukey test for pairwise comparisons). These results suggest that dark-rearing results in a loss of inhibition within the RF.

The absence of a change in within-RF inhibitory strength in the D-APV group of animals suggests that NMDA-R dependent synaptic activity is not critical for an effective balance between excitation and inhibition within the RF. We have previously shown that NMDA-R blockade has no effect on the distribution of size tuning categories or the selectivity of the neuronal population for stimulus size (Razak et al., 2003). These observations also strengthen the support for our hypothesis that inhibition within the RF is necessary for size tuning. Taken together, these results suggest that the reduction in the strength of within-field inhibition seen under DR underlies the reduction in size tuning in LP neurons. However, the possibility that a shared mechanism caused a reduction in inhibition and size tuning cannot be discounted with this experimental design.

The parallel reduction in the strength of inhibition and in size tuning does not result from a reduction in the excitatory drive in dark-reared animals, because SC neurons in both DR and normal hamsters have similar excitatory responses to moving stimuli (Carrasco et al., 2005). In addition, most neurons in the SC are size-tuned regardless of their level of excitability, arguing against any possible reduction of excitatory drive as a basis for dark rearing-induced reduction of strength of inhibition and size tuning.

It must be noted that this study does not completely characterize the properties of inhibition within the RF. The strength of inhibition within the RF was determined at one location (2.6°) each on the nasal and temporal side of the center of the RF. The correlation between size selectivity and strength of within-RF inhibition suggests that other locations in the RF might have a similar strength of inhibition as at the 2.60 location. However, the possibility that other locations within the RF show different strengths of inhibition cannot be discounted. Additional studies with a greater spatial resolution between the two spots of light, and temporal differences in the onset of the two spots, are required to describe the balance between inhibition and excitation in the RF more thoroughly.

In the visual cortex of cats and rodents, it has been demonstrated that DR causes a reduction in the effectiveness of GABAergic circuitry (Benevento et al., 1992; Gianfranceschi et al., 2003). Multiple mechanisms have been proposed to underlie the reduction in inhibitory strength. Morales et al. (2002) showed that DR from birth prevents the normal developmental increase in GABAergic input to visual cortex. Dark-rearing also changes the expression pattern of different enzymes involved in GABA synthesis (Chen et al., 2001). Although in cat visual cortex, GAD65/GAD67 immunoreactivity and the number of GABAergic cells are not altered by dark rearing, in rat visual cortex there is a decrease in the number of GABAergic cells. GABA is involved in shaping RF properties in the rodent SC as well (Binns & Salt, 1997). In the rat SC, DR causes a reduction in benzodiazepine binding (Schliebs et al., 1986), suggesting that GABAergic circuitry is altered by manipulation of sensory experience in SC as it is in cortex (reviewed in Hensch & Fagiolini, 2005). However, whether mechanisms similar to those found in the cortex underlie these changes remain unclear, and warrant further study.

Dark-rearing alters NMDA-R function in cats and rodents, and may affect inhibition and size selectivity through this indirect mechanism. For example, DR reduces the NR2A receptor subunit expression in rat visual cortex (Chen et al., 2000; Tongiorgi et al., 2003). In rat SC and cat visual cortex, DR during development causes NMDA-R to assume a larger role in generating light-driven activity in adults than AMPA-R (Fox et al., 1991; Czepita et al., 1994; Binns & Salt, 1998). It is unlikely that the effects of DR on

size tuning and inhibition were indirectly caused by altered NMDA-R function however, given our result that chronic blockade of NMDA-R does not alter either property (size tuning—Razak et al., 2003; inhibition—this study). One possible reason for the difference in the effects of DR and NMDA-R blockade on size tuning and inhibition within the RF may be that these properties depend on AMPA-R function, which is unaltered by DR in rodent SC and cat cortex (Binns & Salt, 1998; Gordon et al., 1997).

Our finding that DR reduces inhibition within the RF suggests that light-driven neural activity is necessary for developing the normal balance between inhibitory and excitatory input strength. It cannot be determined conclusively from our data whether the maturation of this balance or its maintenance in adults was affected by dark rearing. However, our recent findings on the development of excitatory RFs in the hamster SC suggest that adult maintenance can be affected. In dark-reared animals, excitatory RF diameters reach normal size at approximately 2 months of age, but prolonged rearing in the dark prevents the maintenance of this refinement (Carrasco et al., 2005; Carrasco & Pallas, 2006). Either spontaneous patterned activity during development or activity-independent processes may be sufficient for the early development of normal RF properties. If the balance between inhibition and excitation is critical for the initial establishment of normal RF diameters, then the strength of inhibition should have reached normal values at 2 months of age. Because spontaneous activity diminishes in developing SC (Itaya et al., 1995) and visual input is prevented, dark-reared animals may not receive normal levels of patterned input. This may cause a reduction in the strength of inhibition that in turn causes RF diameters to increase and size selectivity to decrease by adulthood. One prediction of this hypothesis is that size tuning in the SC of NORMAL and dark-reared hamsters should be indistinguishable at 2 months of age when RF sizes are normal.

Although the current study shows that visually driven neural activity during development is necessary for the normal maturation of inhibition and excitation and for stimulus size selectivity, age-related alterations in response properties are also caused by an age-related decrease in inhibition (Leventhal et al., 2003; Betts et al., 2005; Hua et al., 2006). Modulation in the strength of inhibition also underlies shifts in topographic maps induced by altered sensory experience (Zheng & Knudsen, 1999). In addition, injury-induced reduction of excitatory inputs causes a reduction in the strength of inhibition (Rajan, 1998; Vale et al., 2003). Taken together, these studies show that the balance between excitation and inhibition is a common and critical substrate through which developmental experience, aging, and injury can alter sensory response properties and subsequently, behavior.

Conclusion

This study shows that NMDA-R blockade does not influence inhibition within the RF. We have previously shown that NMDA-R blockade does increase the strength and spatial extent of inhibition outside of the RF (surround inhibition) in the hamster SC (Razak & Pallas, 2005). Taken together, these data suggest that different components of inhibitory inputs to SC neurons may be differentially influenced by developmental experience. Neural selectivity for velocity, direction, and size of moving stimuli contributes to SC-mediated behaviors such as detection of and orientation towards moving stimuli. We have utilized developmental plasticity as a tool to provide evidence that inhibition within the RF is important for stimulus size tuning. Other sensory response properties that depend on the balance between inhibition and excitation, such as stimulus direction and velocity selectivity, may also develop through activity-dependent effects on this balance. Studies on the potential for recovery from long-term loss of sensory input may benefit from considering the nature and malleability of interactions between inhibitory and excitatory inputs.

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