Spatial Distribution and Discharge Characteristics of Superior Colliculus Neurons Antidromically Activated From the Omnipause Region in Monkey

NEERAJ J. GANDHI AND EDWARD L. KELLER
Graduate Group in Bioengineering, University of California, San Francisco 94122, and University of California, Berkeley 94720; and Smith-Kettlewell Eye Research Institute, San Francisco, California 94115

Gandhi, Neeraj J. and Edward L. Keller. Spatial distribution and discharge characteristics of superior colliculus neurons antidromically activated from the omnipause region in monkey. J. Neurophysiol. 78: 2221 ± 2225, 1997. One proposed role of the superior colliculus (SC) in oculomotor control is to suppress or excite the activity of brain stem omnipause neurons (OPNs) to initiate or terminate saccades, respectively. Although connections from the SC to the OPNs have been demonstrated, the spatial distribution and discharge characteristics of the projecting neurons from the SC remain unknown. We mapped the spatial distribution of the deeper-layer neurons of the SC by stimulating the region of the OPNs to identify antidromic projections and found that the density of direct projections from the SC to the OPNs was greatest in the most rostral region and decreased gradually for more caudal sites. On the basis of saccade-related discharge characteristics, the antidromically driven neurons were predominantly fixation and buildup neurons. The spatially distributed SC projections to the OPNs and the discharge characteristics of the SC neurons suggest that the direct projections from SC to OPNs are excitatory. Finally, we propose how excitation and disfacilitation from SC activity can contribute to modulation of OPN response and control saccades.

INTRODUCTION

The superior colliculus (SC) has long been considered an integral component of the saccadic system, although its exact contributions to control of rapid eye movements remain controversial. All proposed mechanisms of SC function require that it suppress or excite the activity of omnipause neurons (OPNs), located in the nucleus raphe interpositus on the midline of the brain stem, to initiate or terminate saccades, respectively. Fixation neurons, a specific subset of neurons found only in the rostral pole (equivalently, the most rostral 0.72 mm or up to the 2° amplitude meridian) of SC (Munoz and Wurtz 1995b), have been hypothesized to project to the OPNs and modulate the activity of the latter cells via excitatory connections because of similarities in their discharge characteristics; both types of neurons are tonically active during fixation but pause their discharge during saccades (Keller 1974; Luschei and Fuchs 1972; Munoz and Wurtz 1993a).

Anatomic and electrophysiological studies have demonstrated that the rostral SC, relative to caudal regions, projects more heavily to the OPN region (Büttner-Ennever and Horn 1994; Paré and Guitton 1994). However, neither study demonstrated the discharge characteristics of the output neurons. Studies that did characterize the output neurons of the SC (Istvan et al. 1994; Moschovakis et al. 1988) showed that the neurons project via the predorsal bundle but did not determine which axons terminated on the OPNs. On the other hand, an examination of the arborization onto the OPNs failed to stain the somata in the SC (Scudder et al. 1996). Other studies focused globally on connections between SC and OPNs (Langer and Kaneko 1984, 1990). Overall, a detailed spatial distribution of the density of SC projections to the OPNs and the discharge characteristics of these SC neurons have not been determined, except in a preliminary study (Gandhi and Keller 1996).

To address these issues, we used electrophysiological methods to antidromically activate and characterize SC neurons projecting to the OPNs. We found that the probability of antidromically activating SC neurons from the OPN region was indeed greatest in the rostral pole of the SC but decreased gradually for more caudal sites. On the basis of one classification scheme (Munoz and Wurtz 1995a), these cells were predominantly buildup and fixation neurons.

METHODS

Data presented in this report are pooled from three Macaca mulatta and two Macaca fuscata male juvenile monkeys. All experimental protocols were approved by the Institute Animal Care and Use Committee at the California Pacific Medical Center and complied with the guidelines of the Public Health Service policy on Humane Care and Use of Laboratory Animals.

The surgical and experimental methods of the present investigation have been described recently (Keller and Edelman 1994). Briefly, two stainless steel chambers were placed stereotaxically on the skull, one slanted posteriorly at an angle of 38° in the sagittal plane and aligned on the SC and another slanted laterally at an angle of 25° in the frontal plane and aligned on the OPN region. A recording tungsten microelectrode (Frederick Haer) was lowered through the lateral chamber into the region of the OPNs. The microelectrode was positioned such that OPNs were isolated and interrupted horizontal saccades (Keller 1977; King and Fuchs 1977) were produced with minimal stimulation parameters (usually 15 μA, 15 ms, 400 pulses/s).

Another recording microelectrode was lowered through the posterior chamber until SC neurons with visuomotor discharge properties were recorded. Next, bipolar single-pulse stimulation (0.25 ms in duration) was applied to the OPN region while activity of the SC neuron was sampled at 20 kHz. Stimulation intensity was initially set to 50 μA and was raised or lowered until a threshold defined as antidromic activation on 50% of the trials was found. Intensity was increased up to a maximum of 150 μA. If an SC...
neuron was driven, we attempted to obtain a collision by triggering the stimulation when the discharge rate of the SC neuron reached a threshold (typically 50 spikes/s). Otherwise, the antidromic test was confirmed by a constant latency of neuron activation; a latency jitter \( \leq 0.2 \) ms was considered tolerable in making the judgment of constant latency.

Discharge characteristics of isolated neurons before and during saccades were then determined by recording window-discriminated spikes at 1 kHz as the monkey made delayed saccades to several eccentricities in the preferred direction. Spike density traces were then produced by convolving the spike trains with a gaussian waveform (\( \sigma = 10 \) ms) (Richmond et al. 1987). Recording penetrations were made uniformly along the rostral-caudal dimension of the SC.

To map the spatial distribution of the antidromically activated SC neurons, their location within the SC needed to be determined. At the bottom of each track, \( \sim 2.5 \) mm from the SC surface, a brief stimulation train (range of parameters: 25–35 \( \mu \)A, 25–75 ms, 400 pulses/s) was applied during fixation to produce a fixed-vector or site-specific maximal amplitude saccade (Robinson 1972; Stanford et al. 1996). This vector was always similar to the optimal saccade associated with the most vigorous neural response in the delayed saccade task. The amplitude of the fixed vector saccade was used to compute the cell’s location in the SC by the formulas provided by Ottes et al. (1986).

**RESULTS**

Irrespective of whether or not they were antidromically driven from the OPN region, only the SC neurons that exhibited visuomotor and motor responses and were typically found deeper than 1 mm from the surface were included in the analysis. On the basis of one classification scheme (Munoz and Wurtz 1995a), the cell types included in our study were burst neurons, buildup neurons, and fixation neurons. We often tested superficial layer neurons with only visual responses for antidromic activation from the OPNs and were unable to drive any.

**Spatial distribution of SC neurons antidromically activated from the OPN region**

We tested a total of 101 SC neurons for antidromic activation from the OPNs; of these, 47 were considered driven on the basis of either collision tests (25 of 47) or constant latency measures (22 of 47). The probability of antidromically activating SC neurons from the OPNs depended on the location of the cell along the rostral-caudal dimension. Figure 1 summarizes the spatial distribution of antidromically activated SC neurons. All neurons tested for antidromic activation were placed in one of five spatial bins on the basis of their location in the SC, and data in each bin were pooled from at least two monkeys. Binwidth was set to 0.72 mm, restricting fixation neurons to the first bin only (Munoz and Wurtz 1995b). The abscissa is the rostral-caudal spatial position in SC coordinates as well as the corresponding fixed vector saccade amplitude, and the ordinate shows the percentage of antidromically driven cells within each bin. A linear regression through the distribution indicates that \(~70\)% of the most rostral neurons are antidromically activated from the OPNs; this value gradually decreases to \(~10\)% for caudal cells. The trend in the density of projections to the OPNs is significantly different from a uniform distribution of antidromic activation at all SC sites (\( P < 0.01 \)). The analysis indicates that neurons outside the rostral pole of the SC also contribute directly to controlling OPN activity, although this influence diminishes for caudal regions.

**Discharge characteristics of tested SC neurons**

Neural activity of the isolated SC neurons was recorded as the monkeys made delayed saccades in the preferred direction. We characterized a total of 63 neurons; of these, 30 were identified as antidromically activated from the OPN region. Figure 2 illustrates the antidromic activation and the saccade-related discharge characteristics of five driven neurons, one from each spatial bin of Fig. 1, for saccades of optimal and larger-than-optimal amplitude. The most striking observation of Fig. 2 is that many SC neurons antidromically activated from the OPN region displayed weak bursting or tonic activity, instead of suppression, during optimal saccades.

To classify the neurons antidromically activated from the OPN region and to compare their identity with those not projecting to the OPNs, we used the criterion established by Munoz and Wurtz (1995a). During an eye movement of the isolated SC neurons, cells with activity \(< 30 \) spikes/s at \( \geq 100 \) ms before movement onset are burst neurons, and those with activity \( > 30 \) spikes/s \( \geq 100 \) ms before movement onset are buildup neurons. Fixation neurons are the subset of buildup neurons located in the rostral pole of the SC.

Accordingly, the maximum activity during the 100–150 ms (presaccadic period), averaged over 3–20 trials, before onset of optimal movements in the delayed saccade paradigm, cells with activity \(< 30 \) spikes/s at \( \geq 100 \) ms before movement onset are burst neurons, and those with activity \( > 30 \) spikes/s \( \geq 100 \) ms before movement onset are buildup neurons. Fixation neurons were the group of buildup neurons with optimal saccade amplitude \(< 2^\circ\) (equivalently,
located in the rostral pole). Figure 3 summarizes our sample of driven and nondriven neurons in each of the three classes. Only 1 burst neuron, 18 fixation neurons, and 11 buildup neurons constituted the 30 SC neurons antidromically activated from the OPN region. In contrast, 13 burst neurons, only 4 fixation neurons, and 16 buildup neurons formed the 33 non-antidromically driven SC neurons. The spatial distribution of the burst and buildup neurons not antidromically activated, although equally interesting for the cell classification analysis, was not determined because of the small sample size ($n = 33$ neurons).

**Latency and threshold of antidromic activation**

The latency of the action potential generated in the SC neurons following a stimulus pulse to the OPNs ranged from 0.7 to 2.3 ms, with a mean $\pm$ SD of 1.13 $\pm$ 0.38 ms. The latency was not dependent on the location of the SC neuron. A threshold current at which the SC neuron was driven 50% of the time was determined for 30 of the 47 cells. The threshold values ranged from 10–120 $\mu$A with a mean $\pm$ SD of 65 $\pm$ 29 $\mu$A.

**DISCUSSION**

Uniform sampling of visuomotor and motor neurons along the rostral-caudal extent of the SC has demonstrated that the percentage of SC neurons antidromically driven from the OPNs is largest in the rostral pole of the SC and declines gradually for more caudal sites. Burst neurons, classified by the level of presaccadic discharge, were rarely observed to project to the OPNs. Thus fixation and buildup neurons constitute the majority of projections to the OPNs.

Although most fixation neurons were antidromically activated from the OPN region, a significant number of buildup neurons were not driven by the stimulation of the OPN region. The identification of buildup neurons (Munoz and Wurtz 1995a), requiring that the discharge rate be $>30$ spikes/s $\approx 100$ ms before optimal saccade onset, is an arbitrary measure and may be an inadequate classification scheme taken alone. Perhaps multiple criteria (Munoz and
SC neurons that project to the OPNs remain tonically active. The mean stimulation threshold current for antidromic activation of SC neurons from the OPNs was 65 μA, raising concern that the interpretations may be contaminated by current spread to neighboring regions or fibers passing near the stimulation region. Although we cannot completely rule out these possibilities, we believe that the effects of current spread are minimal for several reasons. 1) The spatial distribution of the SC projections to the OPNs correlates well with the observation that stimulation of the rostral 2 mm, a region 3 times wider than the rostral pole of the SC, during large saccades interrupts the ongoing movement, whereas stimulation of the caudal region at saccade onset accelerates it (Gandhi and Keller 1995). 2) The caudal SC appears to have ample projections to the burst generator region (Chimoto et al. 1996a,b; Raybourn and Keller 1977). Thus current spread laterally into this area should antidromically drive a greater proportion of neurons in the caudal SC. 3) If the stimulation current were to spread and activate the pretectal bundle, which contains the axons of output neurons of the SC and lies immediately adjacent to the OPN region, all burst, buildup, and fixation neurons would have been antidromically driven (Istvan et al. 1994).

In conclusion, the observation that the projections from
the SC to the OPNs are greatest in the rostral SC and decrease gradually for caudal regions of the SC appears not to be an artifact of current spread from the stimulated OPN region. Instead, it is a conservative estimate of the spatial distribution of SC outputs to the OPNs.

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Address for reprint requests: E. L. Keller, Smith-Kettlewell Eye Research Institute, 2232 Webster St., San Francisco, CA 94115.

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