Saccade-Related Activity of Periaqueductal Gray Matter of the Monkey

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Single unit activity was recorded extracellularly from the periaqueductal gray matter (PAG) and the superior colliculus of three monkeys during spontaneous saccades and fixation. Most saccade-related cells were found in the dorsal and lateral regions of the PAG and they paused with saccades. The pause preceded the onset of saccades by 34.5 ± 6.8 msec (n = 31). In 90% of the 31 PAG cells, the saccade-related modulation in activity occurred in all directions. There was a linear relationship between pause duration and saccade duration with correlation coefficients larger than 0.70 in most cells. Superior colliculus cells showed bursts preceding onset of saccades. The lead times averaged 25.3 msec (n = 35). There was no linear relationship between burst duration and saccade duration. These results suggest that the dorsal and lateral regions of PAG play an important role in the saccadic system, probably through long lead burst units in the deep layer of the superior colliculus and/or pontine reticular formation.


Lesions of the periaqueductal gray matter (PAG) are known to induce abnormal eye movements (periaqueductal gray syndrome). Although the PAG is surrounded by important structures related to eye movements, such as the superior colliculus, interstitial nucleus of Cajal, and nucleus of Darkschewitsch, it is not known whether the PAG itself takes part in eye movement control.

Anatomical data concerning the connections between the PAG and eye movement-related structures are still obscure, but degeneration and autoradiographic transport experiments indicate that the dorsal and lateral regions of PAG below the pretectum and superior colliculus send axons to the ipsilateral superior colliculus. Also, the PAG receives inputs from the fastigal nuclei which are related to oculomotor function.

In this study, we have analyzed the activity of PAG cells in association with eye movements and compared it with the activity of neurons in the superior colliculus. The data show a clear temporal relation between PAG neural activity and saccades. A preliminary report of these results has been presented elsewhere.

Materials and Methods

The experiments were performed on three alert monkeys (macaca fascicularis). First, under general anesthesia EOG-electrodes were implanted bilaterally, and above and below the left orbit for recording eye movements in the horizontal and vertical planes, respectively. A stainless steel recording chamber was placed over the parietal bone at anterior plane 5 mm according to the stereotaxic atlas by Kusama and Ma-buchi. Transverse tubes were fixed to the skull with dental acrylic. Neural activity and ocular movements were then investigated for about 3 months. During recording sessions, the monkey sat in a specially designed primate chair. The head was painlessly immobilized. The animal viewed a rear projection screen subtending 60° of the visual field horizontally and 45° vertically.

Stainless steel microelectrodes (Elgiloy 0.25 mm) insulated with Isonel 31 were introduced into the brain through the recording chamber. They were guided to just above the superior colliculus through a 23-gauge cannula and were driven from the cannula into the PAG by a hydraulic microdrive.

Extracellular action potentials and horizontal and vertical EOGs were displayed on a polygraph, recorded on magnetic tape, and photographed. Lead times of at least 20 saccades were measured from film records with errors of less than half a millisecond. Spontaneous mean discharge rates were calculated during 10 fixation periods which lasted for more than 2 sec. This investigation was carried out in adherence to the principles
Localization of Saccade-Related Units

Histological reconstruction of the brain stem showed that recording sites for the two classes of saccade-related units were different: most pause units were clustered in a limited dorsolateral region of the PAG underlying the pretectum and the superior colliculus. None were in the ventral PAG region or in the mesencephalic reticular formation (Fig. 1). Antero-lateral locations corresponded to the anterior 5 mm–7 mm stereotaxic planes of Kusama and Mabuchi atlas10 (corresponding to the posterior 0 mm to 2 mm planes of the stereotaxic Snider and Lee atlas11). No burst units were found in the PAG. They were located more superficially and laterally in the deep layer of the superior colliculus and dorsal mesencephalic reticular formation.

Saccade-Related Cells in the PAG

All the saccade-related units in the dorsal and lateral PAG regions showed a pause that was time-locked to the onset of saccades, and they had tonic discharges were pause units which ceased firing in close temporal relation to saccadic onset; 35 cells were burst units which fired prior to saccadic onset.
during steady fixation. The average spontaneous discharge rates in 29 PAG cells were calculated during the periods of fixation, which lasted for more than 2 sec before the saccades. Tonic discharge rates varied from cell to cell (mean values from 30–79 spikes/sec, with an average of 57.8 spikes/sec). One cell showed fluctuating discharge frequencies (Fig. 2). This cell exhibited presaccadic discharges at 50–190 spikes/sec. The discharge rates did not change in relation to eye position or to slow eye movements. There was no correlation between discharge rate and period of fixation. Visual inputs, such as light on and off, proved to be ineffective to alter the discharge rates. The pause onset preceded the saccades. The cessation of firing preceded the onset of saccades with an average lead time of 34.4 msec (Fig. 2B, C), varying from 20–100 msec (Fig. 2B). The average lead time of the 31 pause cells was 34 ± 6.8 msec (mean ± SD), ranging from 20.4–53 msec (Fig. 3A). Twenty-eight of the 31 pause cells (90%) exhibited pauses for all saccades, regardless of their directions. In three cells (10%), pauses of activity occurred during ipsilateral saccades. No cells had saccade-related modulation in activity during eye movements in the other directions. The pause durations were linearly related to saccade durations, since the correlation coefficients between them were larger than 0.70 in 29 pause cells. The regression lines of typical ten cells are shown in Figure 4. Their coefficients ranged from 0.71 to 0.91.

Pause durations tended to be longer than saccade durations.

**Saccade-Related Cells in the Superior Colliculus**

Thirty-five cells were histologically identified in the deep layer of the superior colliculus or in the dorsal
mesencephalic reticular formation. These cells showed bursts starting clearly before the onset of saccades. The lead times of the bursts (n = 35) ranged from 16.7–34.1 msec with an average of 25.3 msec (Fig. 3B). Although there was an intimate temporal relationship between burst onset and saccade onset, burst durations and saccade durations were not related in the majority of these cells. Twenty-eight of the 35 burst cells (80%) were direction selective. The directional preference was oblique for 15 cells, contralateral for 11 cells, and vertical for 2 cells. Seven showed no directional preference. Their saccade-related modulations were not analyzed in detail any further because they had the same characteristics of activity as described in previous reports.12,13

Discussion

The present study has shown the existence of cells in the PAG which pause in association with spontaneous saccades. The cells were located in the dorsal and lateral PAG in a limited region at the level of the pretectum and the superior colliculus. This is in contrast with the previous report by Matsunami.14 According to him, the PAG units in the diencephalon of the monkey had bursts preceding saccadic onset by 8.4 msec. We found no burst units in the PAG of the mesencephalon, and all our burst cells were located in the deep layer of the superior colliculus and the dorsal mesencephalic reticular formation. The discrepancy between the two sets of data might result from a difference in recording sites. From the published figures of Matsunami, the majority of his burst units recorded seemed to be located in more rostral part of PAG than our recording sites.

Wurtz et al12 have described pause units that lie deep in the colliculus bordering on the deep layer, whose relation to eye movements was similar to that of pause units in the pontine reticular formation. In contrast to the pause units in the pontine reticular formation which have an average lead time of 16 msec,15,16 pause cells of the PAG in the present study had significantly longer lead times (34.8 ± 6.8 msec). This value was also substantially larger than that of pause units in the floculus17 and vestibular nuclei.18

The present study has also shown that the PAG cells stopped firing before cells in the ipsilateral superior colliculus began to fire. This suggests that there may be an inverse relationship between activity of PAG and superior colliculus cells. Anatomical data show that the efferent fibers from the dorsal and lateral regions of PAG project to ipsilateral superior colliculus.3-5 It is possible that the pause PAG cells may inhibit the superior colliculus cells during spontaneous saccades, in the same way as the pause cells in the pontine reticular formation inhibit the burst cells in pontine reticular formation,16 and substantia nigra cells exhibiting a pause during visually guided saccades inhibit the superior colliculus cells.19 However, it is anatomically known that the PAG also projects fibers to the pontine reticular formation in the monkey,6 where saccade-related long lead burst units are located. Therefore, the PAG cells may also inhibit these units.

Besides lead times, there is another difference between our PAG cells and pontine reticular formation units. The pause cells in the PAG had relatively irregular tonic discharges during intersaccadic intervals, whereas pause units in the pontine reticular formation, as well as in the flocculus and vestibular nucleus, had high and regular tonic discharges ranging from 50–200 spikes/sec. Taking lead time and discharge frequency into consideration, it seems likely that the PAG cells may regulate presaccadic activity influencing superior colliculus cells and/or long lead bursts units in the pontine reticular formation.

Key words: periaqueductal gray matter, superior colliculus, saccade, pause units, saccade-related modulation

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References

8. Hepp K, Henn V, and Jaeger J: Eye movement related neurons...