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CHAPTER 3.4

Vergence eye movement signals in the cerebellar dorsal vermis

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Abstract: We examined simple-spike activity of Purkinje cells (P-cells) that responded during a search task which required both vergence- and frontal-pursuit. Of a total of 100 responding P-cells, 16% discharged only for frontal-pursuit, 43% only for vergence-pursuit, and 41% for both. Thus, the majority of vermal pursuit P-cells modulated their activity during vergence-pursuit. These P-cells also discharged for vergence eye movements induced by step target-motion in-depth. The majority of vergence related P-cells carried convergence signals with both eye velocity and position sensitivities, and they discharged before the onset of convergence eye movements. Muscimol infusion into the sites where convergence P-cells were recorded resulted in a reduction of peak convergence eye velocity, of initial convergence eye acceleration, and of frontal-pursuit eye velocity. These results suggest specific involvement of the dorsal vermis in vergence eye movements.

Keywords: cerebellum; vermis; Purkinje cell; vergence; pursuit; muscimol

Introduction

The cerebellar dorsal vermis has been known to be related to conjugate eye movements, such as saccade and smooth pursuit in fronto-parallel planes (i.e., frontal-pursuit). However, there is no detailed study on vermal Purkinje cell (P-cell) activity for disconjugate, vergence eye movements. Previous studies indicate that in the upstream pathways, the majority of pursuit neurons in the frontal eye fields (FEF) carry not only frontal-pursuit signals but also vergence signals (Fukushima et al., 2002; Akao et al., 2005). To understand the role of the cerebellar dorsal vermis in vergence eye movements, we examined discharge characteristics of vermal pursuit P-cells.

Materials and methods

Three Japanese monkeys were trained to pursue a virtual target through polarized shutter glasses with their head restrained. Eye movements were monitored using the scleral search coil method. In our search task, a virtual target was moved sinusoidally at 0.5 Hz with oblique trajectories in 3D space. The monkeys pursued the target with the combination of frontal- and vergence-pursuit. P-cells were identified by the existence of complex spikes in the dorsal vermis, and simple spike activity was recorded from single P-cells. Once responsive P-cells were encountered, their responses

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were tested during sinusoidal frontal- and vergence-pursuit, separately. To examine velocity sensitivity, the target was moved at different frequencies (0.3 Hz–1.0 Hz, at ±5°). We also used vergence ramp or step tasks and double target task (Nitta et al., 2007). In the vergence step task, the target was jumped between far point and near points, repeatedly. The monkeys were required to make rapid convergence or divergence eye movements. In a double-target task, monkeys fixated a stationary target and a second spot was sinusoidally moved in depth. The recording sites were confirmed histologically in the cerebellar dorsal vermis (lobules VI and VII). All procedures were performed in strict compliance with the guidelines for the Care and Use of Animals of NIH. Our specific procedures were approved by the Animal Care and Use Committee of Hokkaido University School of Medicine.

Results

We analysed simple-spike discharge of 100 vermal pursuit P-cells that responded during our search task. Of these, 41% responded during both vergence- and frontal-pursuit, 43% responded only during vergence-pursuit, and 16% responded only during frontal-pursuit. Thus, 84% of our pursuit P-cells responded during vergence-pursuit. Figure 1 shows representative responses. This P-cell

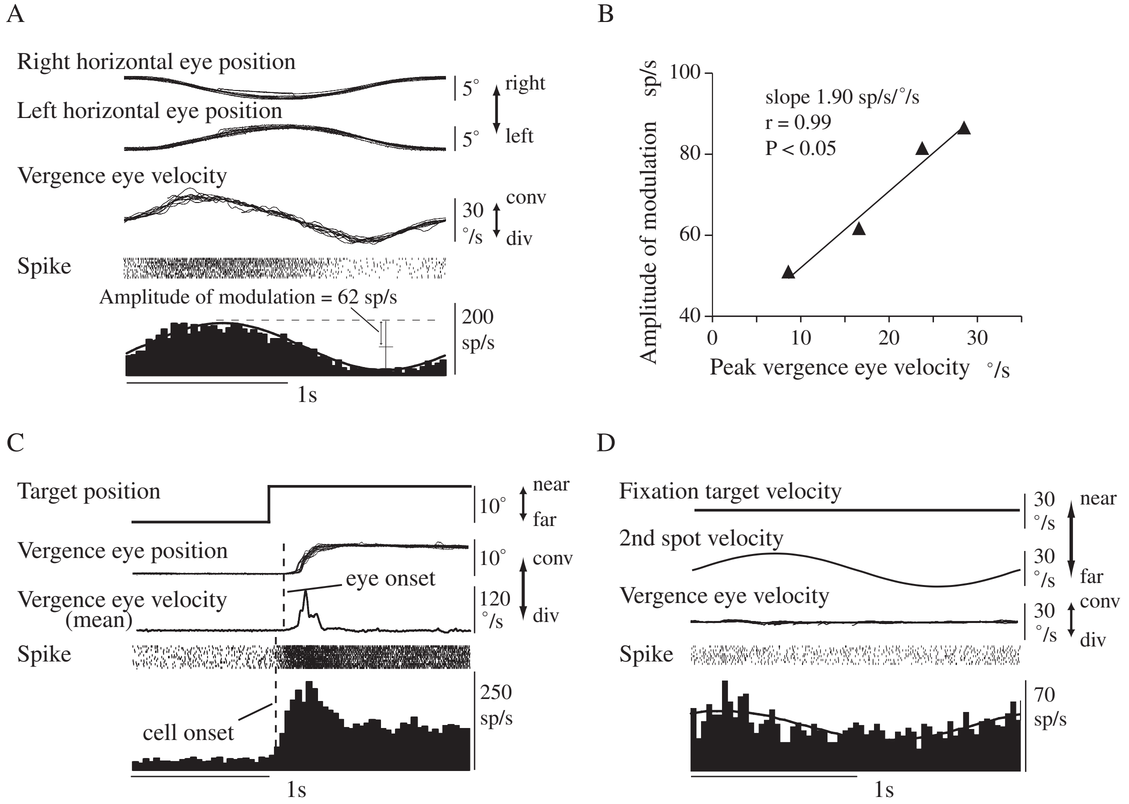

Fig. 1. Responses of a representative vergence-related vermal P-cell. Vergence eye position (velocity) was calculated as the difference between left horizontal eye position (velocity) and right horizontal eye position (velocity). Fitted sine curves are superimposed on the spike histograms (A, D). conv: convergence, div: divergence. Adapted with permission from Nitta et al. (2007).

discharged maximally during peak convergence eye velocity (Fig. 1A, 0.5 Hz, ±5°). Of the 84 vergence-related P-cells, 45 (54%) discharged during peak convergence eye velocity, 16 (19%) discharged during peak divergence eye velocity, and 23 (27%) discharged during peak vergence eye position. In Fig. 1B, the amplitude of discharge modulation of this P-cell increased as vergence eye velocity increased. Of 42 tested P-cells, the majority ($n = 28$, 67%) had significant positive linear correlation between amplitude of discharge modulation and peak vergence eye velocity.

During target step motion (Fig. 1C), this P-cell showed burst discharge during convergence eye movement followed by tonic discharge during the maintenance of convergence eye position. Of 40 tested P-cells, 8 (20%) showed only burst discharge, 25 (63%) showed both burst and tonic discharge, and 7 (17%) showed only tonic discharge. Thus, the majority ($n = 32$, 80%) had vergence eye position sensitivity. Of the 32 P-cells, 27 (81%) showed tonic discharge for convergence eye position, 5 (19%) showed tonic discharge for divergence eye position. Some vermal P-cells showed visual responses during the double-target task (Fig. 1D). Of 42 tested vergence-related P-cells, 14 (33%) had visual sensitivity in depth. In Fig. 1C, this P-cell discharged before the onset of convergence eye movements. When 40 P-cells were tested during step vergence eye movements toward their preferred directions (33 convergence, 7 divergence), the majority ($n = 29$, 73%) discharged before the onset of vergence eye movements with the median lead time of 16 ms.

After muscimol injection into the right dorsal vermis (Fig. 2A), peak convergence eye velocity and initial convergence eye acceleration decreased. The maintenance of convergence eye movements was not affected. Rightward frontal-plane pursuit eye velocity also decreased. After muscimol injection into the left dorsal vermis (Fig. 2B), the monkey often made rightward saccades near the onset of vergence eye movements. When the monkey made pure vergence eye movements, the onset of

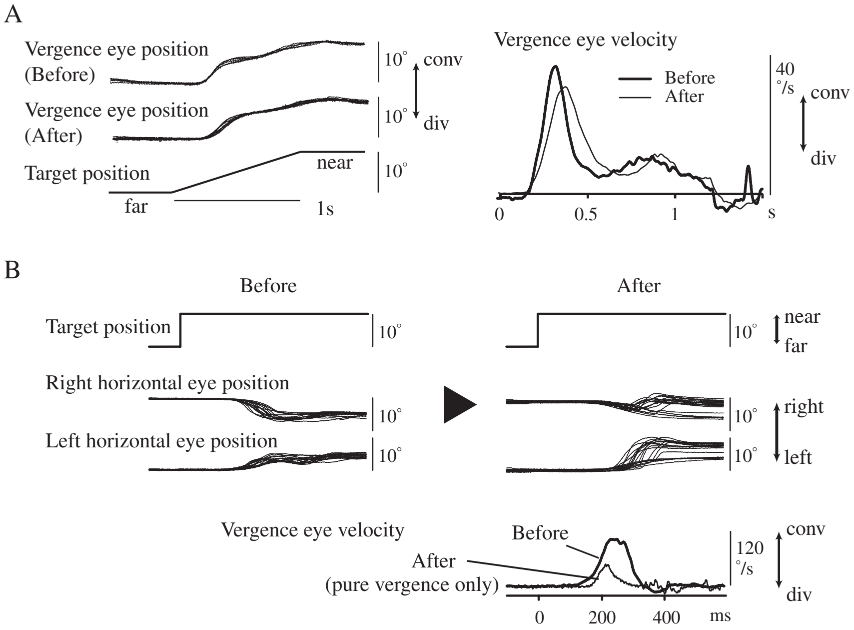

Fig. 2. Muscimol injections (0.5–1.0 μl, 10 μg/1 μl) into the recording sites. Injections were made into the right (A) and left (B) dorsal vermis, respectively. At the bottom (B), mean vergence eye velocities are compared before and after muscimol injection where only the trials without saccade intrusion were averaged. Adapted with permission from Nitta et al. (2007).

convergence eye movement was delayed and peak convergence eye velocity decreased. Divergence eye movements were less affected and ipsiversive saccades became hypometric.

Discussion

Both convergence and divergence signals are found in neurons in the FEF and the nucleus reticularis tegmenti pontis (NRTP) (Gamlin and Clarke, 1995). The NRTP receives projection from the FEF and sends axons to the cerebellar dorsal vermis. Vermal convergence signals that were found in the present study are most likely to be sent from the FEF via NRTP. It is well known that mossy fibres originating in the pontine nuclei send signals not only to the cerebellar cortex but also to the deep cerebellar nuclei with axon collaterals. In the preliminary reports, it was suggested that neurons in the caudal fastigial nucleus, that receives direct inhibitory projections from dorsal vermal P-cells, are also involved in convergence eye movements (Gamlin and Zhang, 1996; Zhang and Gamlin, 1996), suggesting that the dorsal vermis-caudal fastigial pathway may be specifically involved in the initiation of convergence eye movements. To understand the exact neural mechanisms, further studies are needed for discharge characteristics of caudal fastigial neurons.

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