Saccade-related Purkinje cell activity in the oculomotor vermis during spontaneous eye movements in light and darkness

Abstract  Saccade-related Purkinje cells (PCs) were recorded in the oculomotor vermis (lobules VI, VII) during spontaneous eye movements and fast phases of optokinetic and vestibular nystagmus in the light and darkness, from two macaque monkeys. All neurons (n=46) were spontaneously active and exhibited a saccade-related change of activity with all saccades and fast phases of nystagmus. Four types of neurons were found: most neurons (n=31) exhibited a saccade-related burst of activity only (VBN); other units (n=7) showed a burst of activity with a subsequent pause (VBPN); some of the units (n=5) paused in relation to the saccadic eye movement (pause units, VPN); a few PCs (n=3) showed a burst of activity in one direction and a pause of activity in the opposite direction. For all neurons, burst activity varied considerably for similar saccades. There were no activity differences between spontaneous saccades and vestibular or optokinetically elicited fast phases of nystagmus. The activity before, during, and after horizontal saccades was quantitatively analyzed. For 24 burst PCs (VBN, VBPN), the burst started before saccade onset in one horizontal direction (preferred direction), on average by 15.3 ms (range 27-5 ms). For all these neurons, burst activity started later in the opposite (non-preferred) direction, on average 4.9 ms (range 20 to -12 ms, P<0.01) before saccade onset. The preferred direction could be either with ipsilateral (42% of neurons) or contralateral (58%) saccades. Nine burst PCs had similar latencies and burst patterns in both horizontal directions. The onset of burst activity of a minority of PCs (n=5) lagged saccade onset in all directions. The pause for VBPN neurons started after the end of the saccade and reached a minimum of activity some 40-50 ms after saccade completion. For all saccades and quick phases of nystagmus, burst duration increased with saccade duration. Peak burst activity was not correlated with saccade amplitude or peak eye velocity. PCs continued to show saccade-related burst activity in the dark. However, in 59% of the PCs (VBN, VBPN), peak burst activity was significantly reduced in the dark (on average 28%, range 15–36%) when saccades with the same amplitude (but longer duration in the dark) were compared. For VBP neurons, the pause component after the saccade disappeared in the dark. The difference in peak burst activity (light vs darkness) is similar to that seen for saccade-related neurons in the fastigial oculomotor region (FOR, the structure receiving direct input from vermal PCs) and suggests that the oculomotor vermis also might affect saccade acceleration and/or deceleration. The findings indicate that in the oculomotor vermis – in contrast to the FOR – several different types of saccade-related neurons (PCs) are found. However, the vast majority of PCs behave qualitatively similar to FOR neurons with regard to the burst activity pattern and a direction-specific burst activity onset starting well before saccade onset. This latency will allow these neurons to influence the initiation of saccades in the saccadic brainstem generator through multisynaptic pathways. At present, it has to be determined how (saccade-related) PC activity determines FOR activity.

Key words  Saccades · Oculomotor vermis · Single-unit activity · Light and darkness · Monkey

Introduction

As far as saccades are concerned, the cerebellum is thought to be primarily involved in saccadic accuracy. Based on the results of lesion, microstimulation, and recording studies, two cerebellar structures turned out to be crucial for the control of saccade metrics: the posterior vermis (lobule VI, VII) and its underlying structure, i.e. the caudal part of the fastigial nucleus (Keller 1989). Lesions in the cerebellar posterior vermis (Aschoff and Cohen 1971; Ritchie 1976) and the deep cerebellar nu-
clei, i.e., the caudal fastigial nucleus (Optican and Robinson 1980), lead to pulse step mismatch dysmetria (review in Leigh and Zee 1991). Saccades may fall short of reaching the visual target (hypometric) or may be too large (hypermetric). The dysmetria may be related to the initial or the final eye position in the orbit (Ritchie 1976) and may be direction-specific (Aschoff and Cohen 1971). However, the saccade velocity/amplitude and duration/amplitude relationship (main sequence) was thought to be unaffected by cerebellar lesions (Keller 1989).

Unilateral lesions in the posterior vermis (lobule VI and VII), referred to as the oculomotor vermis (Noda and Fujikado 1987), lead to hypermetric saccades to the contralateral side and hypometric saccades to the ipsilateral side (Aschoff and Cohen 1971), whereas hypermetric centripetal and hypometric centrifugal saccades have been described after bilateral lesions (Ritchie 1976). In the caudal fastigial nucleus (fastigial oculomotor region, FOR), the immediate output structure of the vermal Purkinje cells (PC; Yamada and Noda 1987), unilateral lesions cause hypermetric saccades to the ipsilateral side and hypometric saccades to the contralateral side (Robinson et al. 1993). Bilateral FOR lesions produce hypermetric saccades regardless of initial eye position (Optican and Robinson 1980, Robinson et al. 1993). Recent evidence also shows that – in contrast to earlier findings – the saccade velocity profiles are altered after FOR lesions (Robinson et al. 1993).

The underlying neuronal mechanisms which prevent cerebellar dysmetria are not well understood, although saccade-related neurons have been isolated in both cerebellar structures, including PCs in the oculomotor vermis (Kase et al. 1980; McElligott and Keller 1982).

Recently, however, considerable progress has been made in analyzing saccade-related activity in the FOR (Ohtsuka and Noda 1991; Fuchs et al. 1993; Helmchen et al. 1994). The main features are that the vast majority of neurons have a preferred direction to the contralateral side, with an activity increase 15–20 ms before saccade onset, early enough to affect saccade initiation. All neurons burst with all types of saccades (visually guided, spontaneous saccades in light and darkness, fast phases of vestibular and optokinetic nystagmus). The difference between centripetal and centrifugal saccades had no major effect on the activity pattern (Fuchs et al. 1993). The activity pattern for saccades in light and darkness was different and could be best explained by comparing the altered amplitude/duration relationship for saccades in light and darkness (Helmchen et al. 1994).

Since the vermal PCs project mainly to the FOR, precise knowledge about the activity pattern in both structures under identical conditions is mandatory in order to understand the contribution of the oculomotor vermis to the activity pattern in the FOR. Previous studies on PC activity in the oculomotor vermis are not sufficient to allow a comparison with the recent results from FOR neurons. In oculomotor vermis studies, either directional aspects have not been considered (McElligott and Keller 1982) or their latency conclusions (Kase et al. 1980) are different from other studies (McElligott and Keller 1982, Sato and Noda 1992). The differences in saccade activity in light and darkness have either not been considered or were not analyzed.

Therefore, we decided to use the same experimental paradigm and type of analysis as in our previous study on FOR neurons (Helmchen et al. 1994). It will be shown that there is a larger variety of types of saccade-related PCs in comparison with the FOR. However, the majority of neurons had an activity pattern similar to the FOR neurons. Based on this, it will be difficult to explain FOR activity on the basis of the PC input, particularly since this input is inhibitory (Ito 1984); other inputs to the FOR, such as mossy fiber collaterals, must play a major role.

### Materials and methods

The two monkeys in this study (Macaca fascicularis) were prepared for single-unit recordings (for details see Boyle et al. 1985). With the monkeys under general anesthesia, and in aseptic conditions, a recording chamber for single-unit recordings was implanted. Bolts were attached to the skull to maintain stable head position during the experiments. Horizontal and vertical eye position was recorded by electrooculography (EOG) in one monkey and by the search coil technique in the other monkey (Judge et al. 1980). For calibration, the horizontal vestibulo-ocular reflex (VOR) gain at 0.2 Hz, ±40°/s in the light was set equal to 1. For vertical eye movements the relationship between saccade amplitude and duration in the light was used (King et al. 1986). The midposition of the eye was determined by repeatedly attracting the monkey’s attention to look at defined fixation points. For the monkey being used for EOG recordings, calibration was repeated several times during the experiments to minimize the effects of gain fluctuations (Gonschor and Malcolm 1971). During the course of the experiments, the two monkeys were also trained to fixate and follow a target. Consequently, calibration was also taken from the fixation performance to defined target steps. Both methods yielded the same results.

During the experiments, the monkeys sat upright in a primate chair with their heads fixed to the chair on a servo-controlled vestibular turntable surrounded by an optokinetic cylinder (Toennies, Würzburg). The oculomotor vermis (lobules VI and VII) was approached at a 15° angle (posterior from the vertical axis in the sagittal or parasagittal plane) by stereotaxic coordinates, using the atlas of Shantha et al. (1968).

Neuronal activity was recorded with varnished tungsten microelectrodes. The position of the electrode with respect to the cerebellar layers was determined by the characteristic neuronal activity as the electrode was advanced by a hydraulic stepping motor device. The PC layer was identified by the complex spike activity intermingled within the simple spike activity; 65% of the PCs had clear complex spikes (Fig. 1). The remaining neurons without typical complex spike activity, but very similar simple spike activity, were found intermingled between these PCs. Since their response characteristics were the same, they will be treated together. Activity of afferent fibers (mossy fiber) and cerebellar cortical interneurons (i.e., granule cells) were excluded from this study.

Spontaneous eye movements were recorded in light and darkness. In addition, saccades were sampled during optokinetic and vestibular stimulation in the horizontal plane (yaw axis). This included sinusoidal vestibular stimulation (0.2 Hz, ±40°/s) in the dark and light as well as constant velocity optokinetic stimulation (60°/s) and optokinetic afternystagmus (OKAN), i.e., the nystagmus which continues in the dark after optokinetic stimulation. The latter stimulation proved to be useful for generating a large num-