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RESEARCH NOTE

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Motor dynamics encoding in the rostral zone of the cat cerebellar flocculus during vertical optokinetic eye movements

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Abstract The complex spike (CS) and simple spike (SS) activities of Purkinje cells in the rostral zone of the cerebellar flocculus were recorded in alert cats during optokinetic responses (OKR) elicited by a stimulus sequence consisting of a constant-speed visual pattern movement in one direction for 1 s and then in the opposite direction for 1 s. The quick-phase-free trials were selected. Ninety-eight cells were identified as rostral zone cells by the direction-selective CS activity that was modulated during vertical but not horizontal stimuli. In most of the majority population (88 cells), with an increasing CS firing rate during upward OKR and an increasing SS rate during downward OKR, the inverse dynamics approach was successful and the time course of the SS rate was reconstructed (mean coefficient of determination, 0.70 and 0.72 during upward and downward stimuli, respectively) by a linear weighted superposition of the eye acceleration, velocity, position, and constant terms, at a given time delay (mean 10 ms) from the unit response to the eye-movement response. Standard regression coefficient (SRC) analysis revealed that the contribution of the velocity term (mean SRC 0.98 for upward and 0.80 for downward) to regression was dominant over acceleration (mean SRC 0.018 and 0.058) and position (–0.14 and –0.12) terms. The velocity coefficient during upward stimuli (6.6 spikes/s per degree/s) was significantly ($P<0.01$) larger than that during downward stimuli (4.9 spikes/s per degree/s). In most of the minority population (10 cells), with both CS and SS firing rates increasing during upward OKR, the inverse dynamics approach was not successful. It is concluded that 1) in the cat rostral zone Purkinje cells, in which the preferred direction is upward for CS and downward for SS, eye velocity and acceleration information is encoded in SS firing to counteract the viscosity and inertia forces, respectively, on the eye during vertical OKR; 2) the eye position information encoded in SS firing is inappropriate for counteracting the elastic force; 3) encoding of eye velocity information during upward OKR is quantitatively different from that during downward OKR: SS firing modulation is larger for upward than for downward OKR of the same amplitude; and 4) encoding of motor dynamics is obscure in cells in which the preferred direction is upward for both CS and SS.

Key words Vertical optokinetic response · Cerebellum · Purkinje cell · Cat

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Introduction

Based on the climbing fiber input and Purkinje cell output, Sato et al. (1982a, 1982b, 1983) divided the cerebellar flocculus of the cat into three anatomical zones: the rostral, middle, and caudal zones. Subsequent studies have clarified the neural pathways from the Purkinje cells of each zone to the extraocular motoneurons, and have suggested that the middle zone is a functional module for eye-movement control in the horizontal plane, and the rostral and caudal zones are functional modules for the vertical planes (Sato et al. 1988, 1991; Sato and Kawasaki 1987, 1990, 1991). In addition, using the inverse dynamics approach (Kawato et al. 1987; Shidara et al. 1993; Gomi et al. 1998), Kitama et al. (1999) have demonstrated that the middle zone encodes eye velocity and acceleration information in its Purkinje cell simple spike (SS) firing frequency during the horizontal optokinetic response (OKR), and have concluded that the middle zone provides motor dynamics information to motoneurons to counteract viscosity and inertia forces during horizontal OKR. On the basis of the above evidence, it

may be reasonable to suggest that the rostral zone of the cat flocculus encodes motor dynamics information in SS firing frequency during vertical OKR.

Although the response properties of the SS activity of Purkinje cells in the cerebellar flocculus of cats during OKR have been reported (Fukushima et al. 1996), in the present study we have adopted a different approach, i. e. a multiple regression analysis based on the inverse dynamics model, to reveal the functional properties of these Purkinje cells. The inverse dynamics approach has the following advantages. First, it enables us to reconstruct single cell firing from the movement if its output contributes to the final motor command. In contrast, the forward dynamics approach (Krauzlis and Lisberger 1994) predicts the movement from cell firing. To predict the movement, all transfer functions of the system need to work for the movement in question and all inputs must converge on the final motor plant. However, it is difficult to know all transfer functions related to the OKR and all inputs that converge on the motor plants. Second, Fukushima et al. (1996) investigated eye velocity sensitivity of the flocculus Purkinje cells during vertical OKR in the cat and calculated this from the peak-to-peak firing frequency divided by peak-to-peak eye velocity of the sinusoidal configuration. In contrast, the inverse dynamics approach utilizes the complete records of firing rate and estimates multiple motor sensitivities (acceleration, velocity and position) simultaneously on the basis of moment-by-moment data: SS firing rates with a time resolution of 1 ms (Shidara et al. 1993; Gomi et al. 1998) or 4 ms (Kitama et al. 1999) were reconstructed from the time course of eye acceleration, velocity and position.

Upward OKR is reported to have a larger gain than downward OKR in response to the same stimulus amplitude in the human subject (Van den Berg and Collewijn 1988; Murasugi and Howard 1989), in the monkey (Matsuo et al. 1979; Matsuo and Cohen 1984), and in the cat (Collins et al. 1970; Evinger and Fuchs 1978; King and Leigh 1982). The neural mechanism responsible for the up/down asymmetry has not yet been elucidated. In the present study, using the inverse dynamics approach, the SS rates of the rostral zone Purkinje cells were reconstructed from eye acceleration, velocity, and position during vertical OKR. We will present three new findings in this paper. 1) The majority population of the rostral zone Purkinje cells, with an increasing CS rate during upward OKR and an increasing SS rate during downward OKR, encode information about eye movement dynamics in their SS firing pattern during vertical OKR. 2) There is up/down asymmetry in the velocity coefficients for vertical OKR. 3) The encoding of motor dynamics information is obscure in the minority population, whose preferred direction is upward for both CS and SS responses.

Materials and methods

Animal preparation, recording, stimulation, and histological procedures

Three adult cats were used. The experimental procedures were performed in accordance with the Guidelines for Animal Experiments, Yamanashi Medical University. The methods for animal preparation, recording, stimulation, and histological procedures are the same as those described in our previous paper (Kitama et al. 1999). In brief, the cat was chronically prepared for extracellular recording of the flocculus Purkinje cells on both sides. Simple spikes (SS) and complex spikes (CS) from the recorded cells were discriminated to construct CS and SS density histograms. Eye movements were measured using a magnetic search coil system described by Remmel (1984). For optokinetic stimulation a random dot pattern (diameter, 0.2–1.0°) was projected through a fish-eye lens to a half-cylinder screen in front of the animal. Optokinetic stimuli were applied as a sequence of a constant-speed (5°/s) visual pattern movement in one direction for 1 s and then in the opposite direction for 1 s. Data were recorded on a hard disc. We kept the cat alert by making a noise. When necessary, caffeine and sodium benzoate (0.2–0.3 mg/kg) mixed with food were given.

At the termination of the experiments, some of the recording sites were marked by electrophoretic injection of Pontamine sky blue (3 μA, 15 min). After perfusion of the animal with deep sodium pentobarbital anesthesia, the cerebellum was cut in sagittal sections and stained with neutral red. Based on dye spot location and stereotaxic electrode tracks the recording sites were reconstructed on enlarged drawings.

Data preparation

The OKR is composed of quick and slow phases (nystagmus). To avoid SS activity related to the quick phase, we selected only the trials in which quick phases did not occur. A total of 5219 quick-phase-free trials were obtained from 10,412 trials recorded during horizontal stimuli, and a total of 3954 from 10,335 trials recorded during vertical stimuli. Data analysis was performed for cells for which more than 20 quick-phase-free trials were obtained.

"Horizontal modulation" was defined as the difference in average firing rate between ipsiversive and contraversive stimuli, and "vertical modulation" as that between upward and downward stimuli. A plus sign for horizontal modulation indicates that firing increases during stimuli ipsiversive to the recording side, and a plus sign for vertical modulation means that firing increases during upward stimuli. As in Kitama et al. (1999), the intervals over which firing rates were averaged were shifted 100 ms relative to the changes in stimulus direction, since the abrupt changes in stimulus direction meant there was a latency in the spike response (e.g. Fig. 2 A). A modulation of >0.29 spikes/s in CS activity was defined as a significant response because 1) we constructed the spontaneous CS density histograms when the awake animal was seated in front of the stationary visual pattern, 2) in the histograms from 2-s recordings the absolute value of the difference in CS rates between the first second and the second second of the recording was 0.11 (mean)±0.09 (SD) spikes/s in the 32 Purkinje cells investigated, and 3) the mean+2 SD was 0.29 spikes/s.

For multiple regression analysis of the averaged data the eye position signal was low-pass-filtered by a 2-pole digital Butterworth filter with a cutoff frequency of 20 Hz and then differentiated using five points to obtain the eye velocity signal. Similarly, the eye acceleration signal was obtained by digital differentiation of the eye velocity signal. The SS density histogram was also low-pass-filtered by a 2-pole digital Butterworth filter with a cutoff frequency of 20 Hz. The computer program was written by us using MATLAB (Mathworks).

Regression with the inverse dynamics model

The regression procedures were essentially the same as those described in our previous paper (Kitama et al. 1999). In brief, linear

multiple regression analysis was performed to reconstruct the time course of SS firing frequency (criterion variable) with a linear function of the eye position and its first and second time-derivatives (explanatory variables). The equation is:

$f(t-\Delta)=a\,e''(t)+b\,e'(t)+c\,e(t)+d$

where $f(t)$, $e''(t)$, $e'(t)$, $e(t)$, and Δ are the SS rate at time t, the eye acceleration, velocity, position at time t, and the time delay between the firing rate and the eye movement, respectively. Coefficients (a, b, c), the constant term (d), and the time delay were estimated by the ordinary least squares method (OLS). The search range for Δ was from –40 to 40 ms.

A modeling check was performed as follows. First, we calculated the variance inflation factor (VIF) to check the multicolinearity (e.g. multiple equally good solutions) that would be caused by a high correlation between explanatory variables. The VIF of a given explanatory variable is:

$VIF=1/(1-R^2)$

where R is a multiple correlation coefficient of a given explanatory variable fitted by the remaining explanatory variables. The data are unreliable if the VIF is >=10 (Chatterjee and Price 1977). In the present study the sinusoidal stimulus pattern, which would result in a strong correlation between explanatory variables (i.e. eye position versus eye acceleration), was not used. We adopted the velocity step stimulus pattern to reduce the correlation between explanatory variables. Second, the residual error (difference between the actual and reconstructed SS rates at time t) was plotted against the reconstructed SS rate. It is a basic assumption underlying the application of the OLS that the mean is close to 0, and the variance takes a constant value. To fulfill the OLS assumption, the distribution of the residual error should take a pattern of roughly uniform thickness along the horizontal axis. The assumption of constant variance would be violated if the range of the residual error increased with an increase in the reconstructed SS rate. The model is inapplicable for data that do not fulfill this OLS assumption.

Third, the auto-correlation function of the residual error was calculated, and a check was made for possible periodicity using a threshold level of ±0.25 over 100 ms of τ. Periodicity would not be observed if the model is applicable. Fourth, the coefficient of determination (CD) was used as an indicator of the goodness of fit of the regression. The value of CD increases both with the goodness of fit and with the signal/noise (S/N) ratio of the SS firing data. To increase the S/N ratio, the data were averaged at a bin width of 4 ms. Fifth, coefficient reliability was estimated by the 95% confidence interval (CI). The coefficient ranges, with 95% certainty, from A–B to A+B, where A is the coefficient and B is the 95% CI. Sixth, the standard regression coefficient (SRC) was calculated to evaluate the relative contribution of each explanatory variable to the regression of the criterion variable. The SRC is the coefficient of an explanatory variable calculated by the regression of the standardized criterion variable (mean=0, SD=1) with the standardized explanatory variables. Finally, the statistical significance of the contribution of each explanatory variable to the regression was tested by the forward selection method. The model started as a no-explanatory variable model, and a simple regression analysis was performed (step 0). A one-variable model was then applied using each of the explanatory variables in turn. The explanatory variable whose F-value for the regression was the largest was chosen (step 1). Additional variables were selected similarly in steps 2 and 3 if the F-value was >2.62. If at any step the largest F-value was <2.62 (P>0.05), the test was finished without an additional variable being selected. If all velocity, position, and acceleration variables are selected, we call the cell type the velocity-position-acceleration type (VPA). Similarly, if the velocity and position variables are selected, we call the cell type the velocity-position (VP) type. In addition, velocity-acceleration (VA) and velocity (V) types were found.

In the present study, regression analysis was performed during upward and downward stimulus periods.

Results

Identification of rostral-zone Purkinje cells

Rostral-zone Purkinje cells were identified anatomically and physiologically. Anatomically, the recording site was determined with reference to the dye spot and the electrode track, and was confirmed to be located in the flocculus in an area corresponding to the rostral zone (Fig. 1). Physiologically, the direction selectivity of the CS response to large-field visual pattern movement was investigated according to Fushiki et al. (1994), as follows. In response to constant speed (5°/s) visual stimuli in the upward direction for 1 s and then downward for 1 s (Fig. 2A, 3rd trace), the vertical OKR eye movement was elicited (Fig. 2A, 4th trace). The retinal slip velocity (stimulus velocity minus eye velocity) was in the appropriate low-speed range (<8°/s in Fig. 2A, bottom trace) for eliciting vigorous CS responses in the cat (Fushiki et al. 1994). CS activity was deeply modulated (0.79 spikes/s; a positive sign indicates that the CS rate increases during upward stimuli) during vertical stimuli (Fig. 2A, 1st trace), while it was only weakly modulated (–0.07 spikes/s; a negative sign indicates that the CS rate increases during contraversive stimuli) during horizontal stimuli (Fig. 2B). The direction selectivity of SS responses during OKR was in the opposite direction to that of CS responses in this cell: the SS firing rate increased during downward stimuli and decreased during upward stimuli (vertical modulation was –39.1 spikes/s in Fig. 2A, 2nd trace). The horizontal modulation of SS activity

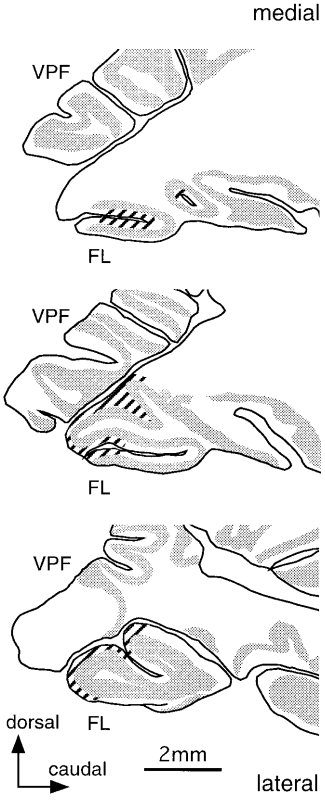

Fig. 1 Line drawings in a one in ten series of 0.1 mm sagittal sections through the flocculus (*FL*) and the adjacent ventral paraflocculus (*VPF*). The cells were recorded in the *diagonally striped area* which corresponds to the rostral zone of the FL. The *gray areas* represent the granular layer

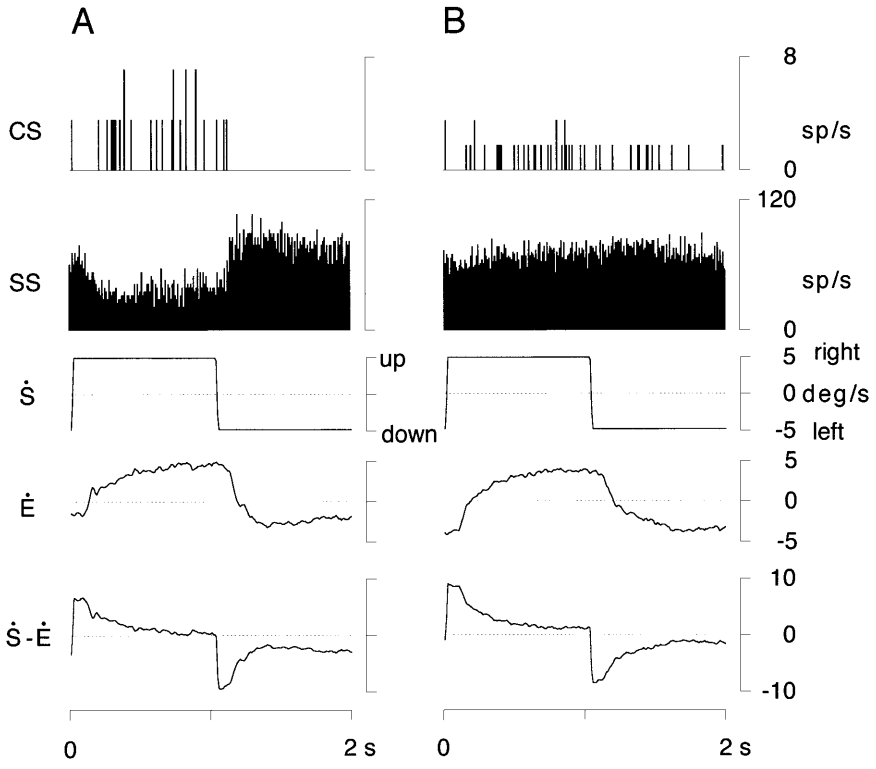

Fig. 2 Direction selectivity of a left flocculus rostral-zone Purkinje cell during vertical (**A**) and horizontal (**B**) optokinetic response (OKR) at a stimulus velocity of 5°/s. The mean of 57 quick-phase-free trials selected from 184 trials is shown in **A**, and mean of 28 from 138 trials is shown in **B**. Top to bottom: complex spike (*CS*) and simple spike (*SS*) histograms, surround velocity (*S'*), eye velocity (*E'*), and retinal slip velocity (*S'-E'*). Bin width is 10 ms. Note that the CS firing frequency increases during upward stimuli and decreases during downward stimuli, and that the SS response is reciprocal to the CS response. Horizontal stimuli are not effective for evoking CS and SS responses

was only –0.8 spikes/s (SS rate increased during contraversive stimuli) in the cell represented in Fig. 2.

We selected 98 rostral-zone Purkinje cells as vertical-type cells whose vertical modulation of CS activity was >0.29 spikes/s and larger than the horizontal modulation. Fifteen rostral-zone Purkinje cells were not selected as vertical type cells because of the low (<0.29 spikes/s) vertical modulation. In all 98 cells the preferred direction of CS was upward. On the other hand, the preferred direction of SS was downward in most cells (88 of the 98) and upward in a small number of cells (10). SS rate modulation in the 10 cells with the upward preferred direction was weak (mean vertical modulation, 9.7± 4.6 spikes/s, range 1.6–16.2 spikes/s). Figure 3 summarizes the direction selectivity of the 88 cells (SS preferred direction is downward), with vertical modulation plotted as a function of horizontal modulation. The mean vertical and horizontal modulation of CS activity was 1.3±0.6 (SD) and –0.15±0.26 (SD) spikes/s, respectively, and the mean vector points were in the upward direction with a small contralateral inclination of 6.8°. The mean vertical and horizontal modulation of SS activity was –22.1±14.1 (SD) and 2.1±4.6 (SD) spikes/s, respectively, and the mean vector points were in the downward direction with a small ipsilateral inclination of 5.5°. Thus, the mean directional preferences of the CS and SS responses are nearly in the vertical meridian and in opposite directions to each other in most rostral zone cells (Fig. 3, thick lines).

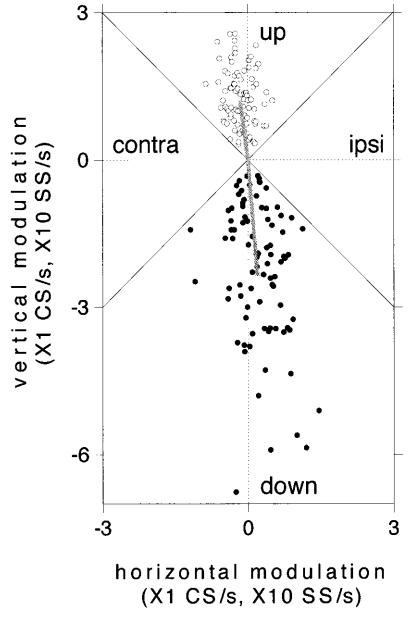

Fig. 3 Direction selectivity of rostral-zone Purkinje cells (*n*=88) during OKR at a stimulus velocity of 5°/s. Vertical modulation (difference in spike rate between upward and downward visual stimuli) versus horizontal modulation (difference between ipsiversive and contraversive stimuli) is plotted for each cell. Taking account of the latency of the spike responses from the onset (0.0 s) of the ipsiversive and upward stimuli, the calculation phase was shifted 100 ms: 0.1–1.1 s for upward and ipsiversive stimuli and 1.1–2.0 and 0.0–0.1 s for downward and contraversive stimuli. A plus sign for vertical modulation means that the firing rate increases during upward stimuli, while a plus sign for horizontal modulation indicates that the firing rate increases during ipsiversive stimuli. Note that the mean vectors (*thick lines*) of the CS response (*open circles*) and the SS response (*solid circles*) are nearly in the vertical meridian and in opposite directions

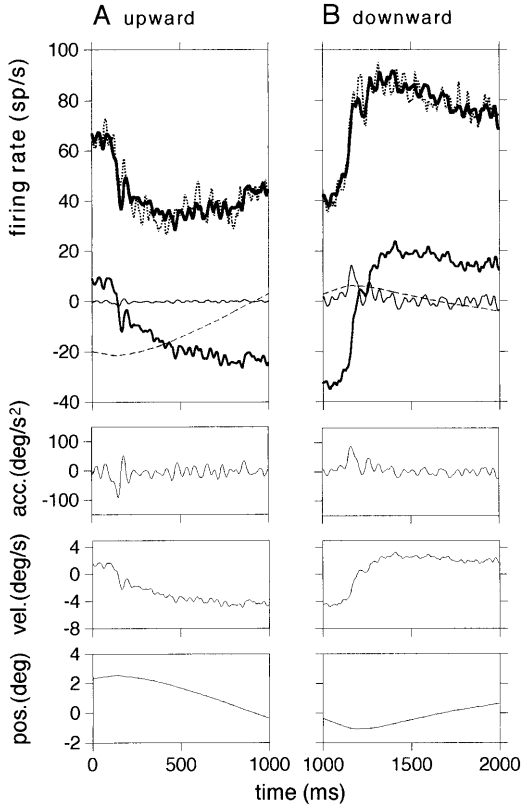

Fig. 4 Multiple regression analysis during upward (**A**) and downward (**B**) stimuli at a stimulus velocity of 5°/s in the unit shown in Fig. 2. Top traces: actual (*dotted lines*) and reconstructed (*thick solid lines*) SS frequency together with eye position (*broken lines*), velocity (*medium solid lines*), and acceleration (*thin solid lines*) components of the reconstruction. Second, third, and bottom traces: time course of eye acceleration, velocity, and position, respectively. Bin width is 4 ms. Time 0 indicates the onset of a trigger pulse which drives a sequence of optokinetic stimuli. Upward direction in eye movement traces means that the eye movement is in the downward direction, which is the preferred direction of the SS response. For superposition, SS profiles were shifted by the delay time (4 ms) between the SS response and eye movement response

Inverse dynamics analysis on the cells with downward preferred direction

Figure 4 shows the results of multiple regression analysis in a cell whose SS preferred direction is downward. The SS firing frequency (criterion variable) was reconstructed from the eye position, velocity, and acceleration (explanatory variables). In Fig. 4 the downward eye movement has a positive sign because the preferred direction of the SS response is downward. Up/down asymmetry of eye velocity was found and should be described here. Upward eye velocity (4.3°/s calculated as a mean eye velocity during 0.9–1.0 s) was greater than downward eye velocity (2.1°/s calculated as mean eye velocity during 1.9–2.0 s) in Fig. 4. Similar up/down asymmetry was found in all three cats tested, and the mean gain (downward/upward eye velocity) was 0.65±0.35 (n=10), 0.42±0.23 (n=10), and 0.39±0.14 (n=49), respectively.

During upward stimuli (Fig. 4A), the velocity coefficient (b) was 6.3 spikes/s per degree/s, and the contribution of the velocity term ($b\,e'(t)$, medium solid line) was dominant over most of the stimulus cycle. The position coefficient was –7.3 spikes/s per degree, and the position term ($c\,e(t)$, broken line) was of reversed sign compared with the direction of eye movements, contributing to the gradual firing change. The acceleration coefficient (a) was 0.018 spikes/s per degree/s^2, and the contribution of the acceleration term ($a\,e''(t)$, thin solid line) was negligible in this cell. The time delay was 4 ms and the constant term (d) was 74.6 spikes/s. The CD was 0.82, indicating that the regression model satisfactorily explains the time course of SS firing frequency. The size of the 95% CI of each coefficient was small (0.018 spikes/s per degree/s^2, 0.39 spikes/s per degree/s, and 0.83 spikes/s per degree for the acceleration, velocity and position coefficients, respectively). The SRC was 0.04 for the acceleration, 1.32 for the velocity, and –0.72 for the position variables, indicating that the velocity variable played a dominant role in the regression. Forward selection analysis revealed that the contribution of the velocity and position terms to the regression was statistically significant (P<0.05) but the contribution of the acceleration term was not significant (P>0.05) (VP type).

The regression analysis described just above was also performed during downward stimuli (Fig. 4B). The coefficients were 0.14 spikes/s per degree/s^2, 5.4 spikes/s per degree/s, and –5.3 spikes/s per degree for acceleration, velocity and position variables, respectively, with a time delay of 4 ms and a constant term of 65.8 spikes/s. The 95% CI of each coefficient was small (0.028 spikes/s per degree/s^2, 0.21 spikes/s per degree/s, and 0.10 spikes/s per degree for acceleration, velocity and position coefficients, respectively). The CD was 0.92. The SRC was 0.22 for the acceleration, 1.05 for the velocity, and –0.23 for the position variables. Forward selection analysis revealed that the contributions of the acceleration, velocity and position terms were all statistically significant (P<0.05)(VPA type).

Table 1 Coefficients of the acceleration, velocity, and position terms (a, b, c, respectively), of the reconstructed SS firing rates. Values are means ±SD from 52 cells. *CI* confidence interval, SRC standard regression coefficient

		Coefficient	95% CI	SRC
Upward stimuli	a, (spikes/s)/(°/s^2)	0.008±0.133	0.017±0.089	0.018±0.155
	b, (spikes/s)/(°/s)	6.6±3.5	0.57±0.19	0.98±0.23
	c, (spikes/s)/°	–5.70±5.3	1.3±0.56	–0.41±0.35
Downward stimuli	a, (spikes/s)/(°/s^2)	0.065±0.171	0.060±0.22	0.058±0.186
	b, (spikes/s)/(°/s)	4.9±2.9	0.39±0.13	0.80±0.17
	c, (spikes/s)/°	–3.4±10.3	2.3±1.1	–0.12±0.30

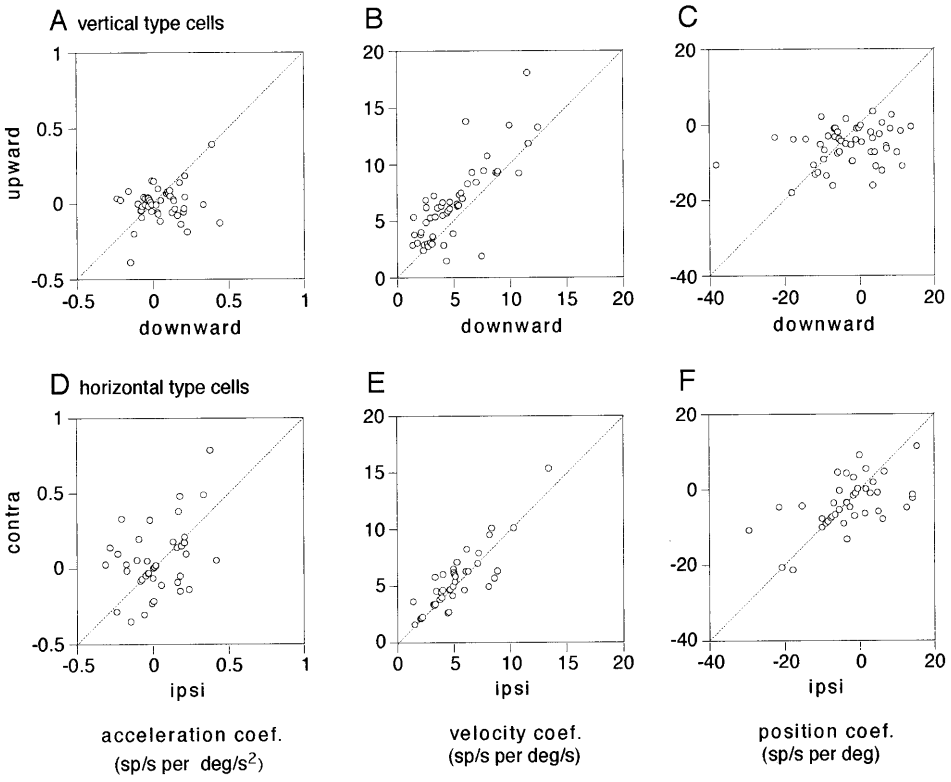

Fig. 5 Acceleration (**A**), velocity (**B**), and position (**C**) coefficients (n=52) during upward stimuli were plotted against those during downward stimuli (data from the rostral zone Purkinje cells in this study). Acceleration (**D**), velocity (**E**), and position (**F**) coefficients (n=41) during contralateral stimuli were plotted against those during ipsilateral stimuli (data from the middle zone Purkinje cells in Kitama et al. 1999). Note that the velocity coefficients during upward stimuli are larger than those during downward stimuli. A positive coefficient means that the unit's SS rate tended to increase with downward or ipsilateral eye movement

Of the 88 rostral zone cells whose preferred direction of SS activity was downward, 69 had SS firing that was well modulated (vertical modulation >10 spikes/s). In these 69 cells regression analysis and the modeling check were performed. First, the correlation between the explanatory variables was examined using the VIF, which was 2.1±0.2 (SD) and 1.5±0.2 for the position, 2.0±0.2 and 1.2±0.1 for velocity, and 1.2±0.1 and 1.5±0.1 for acceleration variables during upward and downward stimuli, respectively. Because the VIF was at most 2.7 and <10, we concluded that the stimulus pattern adopted in the present study was adequate for avoiding multicolinearity. Second, based on the distribution pattern of the residual errors plotted against the reconstructed firing rate, all 69 cells were judged to satisfy the basic assumption of the OLS. Third, the autocorrelation function of the residual error was calculated, and periodicity was found at the threshold level of ±0.25 in 14 cells. In these 14 cells, our regression model was judged to be inapplicable to the regression analysis. In addition, in three cells during upward stimuli the SS reduction-response was very large and the SS firing rate became saturated at zero spike level, forming a flat firing pattern. We judged that the saturated flat firing pattern at zero level was inappropriate for regression analysis. Thus, we show the results from the 52 remaining cells in Table 1: 1) the mean velocity and acceleration coefficients were positive and the mean position coefficient was negative, 2) the 95% CI was small, and 3) based on the SRC, the velocity term is dominant over the acceleration and position terms during both upward and downward stimuli. In addition, forward selection analysis revealed that the contribution of the velocity term to the regression was significant (P<0.05) in all 52 cells investigated, but the acceleration and position terms were not significant (P>0.05) in some cells: 17 and 16 cells for acceleration terms, and 4 and 5 cells for position terms during upward and downward stimuli, respectively. Thus, 32 and 31 cells are the VPA type, 16 and 16 cells are the VP type, 3 and 5 cells are VA type, and 1 and 0 are the V type during upward and downward stimuli, respectively. The CD was high (mean and SD, 0.70±0.18 and 0.72±0.17 during upward and downward stimuli, respectively) in the 52 cells, showing that the reconstructed SS rate fit the actual data well. The mean time delay was 10±11 ms during both upward and downward stimuli.

The acceleration, velocity, and position coefficients during upward stimuli were plotted against the corresponding coefficient during downward stimuli in Fig. 5 (A–C). The mean velocity coefficient during upward stimuli was significantly (P<0.01) higher than that during downward stimuli (B) but the mean acceleration (A) and position (C) coefficients during downward stimuli were not significantly different (P>0.01) from those during upward stimuli. In marked contrast, during horizontal OKR, the mean acceleration, velocity, and position coefficients during contralateral stimuli were not different (P>0.01) from those during ipsilateral stimuli when data shown in Fig. 5D–F were taken from Purkinje cells recorded in the middle zone of the flocculus (Fig. 5D, acceleration coefficients 0.028±0.179 vs 0.053± 0.226 spikes/s per degree/s^2 during ipsilateral vs contralateral stimuli; E, velocity coefficients 5.2±2.5 vs. 5.4±2.6 spikes/s per degree/s; F, position coefficients

–3.0±9.5 vs. -3.8±6.7 spikes/s per degree) (data from Kitama et al. 1999).

Examination of Fig. 5 also reveals the difference that exists among the Purkinje cells with regard to sign constancy of the position and acceleration coefficients. The coefficient for a given cell often has an opposite sign for upward compared to downward movement. This is not the case for the velocity coefficients, which all have the same sign for both movement directions. If the cell's performance is consistent, the sign of the coefficient should be the same whether the movement is upward or downward. A lack of sign consistency was found in 14 cells for the acceleration coefficient and 15 cells for the position coefficient, in which the contribution to regression was statistically significant.

Inverse dynamics analysis on the cells with upward preferred direction

As mentioned above, the minority population of the rostral zone Purkinje cells (10 cells) have an upward preferred direction of SS activity. These cells were characterized by a small vertical modulation in most cells (<10 spikes/s in six cells). Regression analysis was performed in the remaining four cells in which the vertical modulation was >10 spikes/s. A modeling check was performed and one cell was rejected for regression analysis because the periodicity was more than ±0.25 in the autocorrelation function of the residual error. Thus, we show the results of regression analysis for three cells.

In two cells the CD was low (0.35 and 0.32 during upward stimuli and 0.55 and 0.50 during downward stimuli), indicating that reconstruction of the SS time course was not satisfactory. In the remaining cell, the CD was 0.78 and 0.85 during upward and downward stimuli, suggesting that a large part of the time course of SS activity was reconstructed. In this cell, the velocity, position, and acceleration coefficients and the time delay were 7.59 (CI 0.72) and 5.80 (0.40) spikes/s per degree/s, –1.02 (1.60) and 6.95 (2.35) spikes/s per degree, 0.03 (0.06) and –0.11 (0.06) spikes/s per degree/s^2, and –32 and –28 ms during upward and downward stimuli, respectively. The velocity, position, and acceleration SRC were 0.93, –0.06, and 0.03 during upward stimuli and 0.80, 0.17, and –0.10 during downward stimuli, suggesting that the contribution of the velocity term is dominant over the remaining terms. Forward selection analysis revealed that this contribution was statistically significant ($P<0.05$) in all terms during downward stimuli but was not significant ($P>0.05$) in position and acceleration terms during upward stimuli.

Discussion

Fushiki et al. (1994) have shown that CS activity of the rostral-zone Purkinje cell is modulated direction selectively during movement of a large-field visual pattern: CS firing rate increases during upward movement and decreases during downward movement, and is not modulated by horizontal stimuli. In the present study, by making use of the results of Fushiki et al. (1994), the rostral-zone Purkinje cells (Fig. 1) were identified by direction-selective CS activity during movement of a large-field visual pattern that elicits the OKR in the alert cat (Fig. 2, Fig. 3). The present study has shown that SS firing of an identified Purkinje cell is also modulated in a direction-selective manner during the stimuli. In the majority cell population (88 of the 98 cells) SS modulation was reciprocal to CS modulation: the CS rate increased during upward and decreased during downward stimuli, and the SS rate increased during downward and decreased during upward stimuli (Fig. 2, Fig. 3). With the inverse dynamics approach, reconstruction of the SS time course from eye movement was successful in most of these cells (Fig. 4, Fig. 5), indicating that motor dynamics information is clearly encoded in SS firing in this majority population. In contrast, in the minority cell group (10 cells), both CS and SS responses have an upward preferred direction, that is, both CS and SS increased during upward stimuli and decreased during downward stimuli. In most of these minority population cells SS modulation was small during vertical OKR, and the inverse dynamics approach (reconstruction of the SS time course from movement) was unsuccessful, suggesting that encoding of motor dynamics information on the SS firing rate is obscure in this minority population.

Thus, encoding of motor dynamics information is clear in the Purkinje cell group in which direction selectivity is reciprocal for CS and SS responses, but obscure in the cell group in which it is identical. The reciprocal relationship between CS and SS responses may play an important role in encoding motor dynamics information in the SS firing rate. To draw a definitive conclusion, further investigations on the functional role of the CS would be necessary.

Using the inverse dynamics approach proposed by Kawato et al. (1987), Kitama et al. (1999) have successfully reconstructed the time course of SS frequency in middle-zone Purkinje cells by using linear weighted superposition of eye position, velocity, and acceleration during horizontal OKR in the alert cat. The present study applied the inverse dynamics approach to rostral-zone Purkinje cells, in which the SS preferred direction was downward, and SS frequency was successfully reconstructed from vertical OKR eye movements. The present results from the rostral zone are essentially the same as those of Kitama et al. (1999) from the middle zone. First, the mean velocity and acceleration coefficients are positive and the position coefficient is negative relative to the downward preferred direction of the SS response, meaning that SS rates tended to increase with downward eye acceleration, downward eye velocity and upward change in eye position. As electric stimulation of the rostral zone elicits downward eye movements (Sato and Kawasaki 1991; Sato et al. 1991), the negative position information is inappropriate for counteracting the elastic

force on the eye. Second, the velocity SRC is much larger than the acceleration and position SRCs, suggesting that velocity information dominates over acceleration and position information in the SS firing pattern. Statistically, the contribution of the velocity term to the regression is significant in all cell types (VPA, VP, VA and V), while the contribution of acceleration or position terms is not significant in some cell types (VP, VA and V). Third, SS firing precedes (mean 10 ms) the eye movement, satisfying one of the requirements that SS activity should provide motor dynamics information to the extraocular motoneurons for driving OKR eye movement. Thus, the rostral zone may encode motor dynamics information on eye velocity and acceleration to counteract viscosity and inertia forces during vertical OKR. This information would be transmitted to the extraocular motoneurons disynaptically through the target neurons, located in the central part of the superior vestibular nucleus, of the floccular Purkinje cells (Sato and Kawasaki 1990).

Fukushima et al. (1996) also reported eye velocity sensitivity of SS firing in the flocculus Purkinje cells during vertical OKR in alert cats. The most crucial difference lies in their views about the origin of the modulation related to eye movements. Fukushima et al. (1996) suggested that Purkinje cell activity related to eye velocity is caused by the positive feedback input from the vestibular nuclei forming a transfloccular positive feedback loop and making the time constant of eye movement longer. On the other hand, the present study shows that SS firing changes rapidly preceding the eye velocity in response to a change in the direction of rotation of the visual surroundings (Fig. 4). This finding, at least in the cell group in which the preferred direction is upward for CS and downward for SS, supports the view of the inverse dynamics theory that supposes that the cerebellum calculates the forthcoming motor dynamics based on visual information (Kawato et al. 1987; Yamamoto et al. 1997).

The present study shows that the mean velocity coefficient of rostral zone SS activity during upward OKR is significantly ($P<0.01$) larger than that during downward OKR, whereas such coefficient asymmetry is not present in the middle zone SS activity between rightward and leftward OKR (Fig. 5). A similar coefficient asymmetry has been reported previously in the monkey ventral paraflocculus during the vertical ocular following reflex (OFR): the acceleration, velocity, and position coefficients during downward OFR were larger than those during upward OFR (Gomi et al. 1998). These authors did not mention whether the difference was statistically significant or not, and they attributed the coefficient asymmetry to the preferred (downward) and anti-preferred (upward) directions of the SS responses (Gomi et al. 1998). The present study, for the first time, provides statistically significant evidence that coefficient asymmetry exists in the vertical OKR but not in the horizontal OKR, eliminating the idea that the coefficient asymmetry is between the preferred and anti-preferred directions. As eye movement asymmetry is present during vertical OKR (this study) but not during horizontal OKR (Kitama et al. 1999), coefficient asymmetry may be related to eye movement asymmetry. In the cat during vertical OKR, both the coefficient and eye movement were larger during upward than during downward stimuli (this study). On the other hand, in the Japanese monkey during OFR, both the coefficient and eye movement were larger during downward than during upward stimuli (Yamamoto et al. 1997; Gomi et al. 1998). It appears that the coefficient is larger during stimuli that produce larger eye responses during vertical OKR and OFR.

The larger velocity coefficient for upward stimuli means that SS modulation is larger for upward OKR than for downward OKR of the same amplitude. If neural processing for upward-OKR-generation is quantitatively the same as that for downward OKR generation, the amplitude of SS modulation should be the same during upward and downward OKR of the same amplitude. Thus, the coefficient asymmetry means that the neural response for generation of upward OKR is different quantitatively from that for downward OKR. It has been suggested that there is a neural system in the brainstem that stores eye velocity information differently during upward OKR than during downward OKR (Matsuo and Cohen 1984). The present study has provided evidence that the cerebellum also encodes eye velocity information differently during upward OKR than during downward OKR. To understand the different neural processing responsible for the up/down asymmetry of the OKR, additional studies focusing on the target neurons of rostral-zone Purkinje cells, extraocular motoneurons, and the mechanical dynamics of the eye will be needed.

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