Update Article

Sensory-to-motor processing of the ocular-following response

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Abstract

The ocular-following response is a slow tracking eye movement that is elicited by sudden drifting movements of a large-field visual stimulus in primates. It helps to stabilize the eyes on the visual scene. Previous single unit recordings and chemical lesion studies have reported that the ocular-following response is mediated by a pathway that includes the medial superior temporal (MST) area of the cortex and the ventral paraflocculus (VPFL) of the cerebellum. Using a linear regression model, we systematically analyzed the quantitative relationships between the complex temporal patterns of neural activity at each level with sensory input and motor output signals (acceleration, velocity, and position) during ocular-following. The results revealed the following: (1) the temporal firing pattern of the MST neurons locally encodes the dynamic properties of the visual stimulus within a limited range. On the other hand, (2) the temporal firing pattern of the Purkinje cells in the cerebellum globally encodes almost the entire motor command for the ocular-following response. We conclude that the cerebellum is the major site of the sensory-to-motor transformation necessary for ocular-following, where population coding is integrated into rate coding. © 2002 Elsevier Science Ireland Ltd and the Japan Neuroscience Society. All rights reserved.

1. Introduction

While moving through the environment, the visual world flows around us in a pattern. Recent studies in primates have revealed three distinct visual tracking systems that deal with these visual disturbances (Kawano, 1999; Miles, 1998). These three systems process sensory information (i.e. visual motion) and generate eye movements that stabilize images on the retina during self-motion. One of these systems is called *ocular-following*, and in primates it is elicited by sudden drifting movements of a large-field visual stimulus. The system generates slow-tracking eye movements to help stabilize the eyes on the visual scene. Behavioral experiments using monkeys have revealed many features of ocular-following (Kawano and Miles, 1986; Miles and Kawano, 1986; Miles et al., 1986); the most interesting is

that the system operates in a machine-like fashion to generate eye movements with ultra-short latencies.

To understand how the brain contributes to appropriate movements in the aggregate, it is necessary to understand the complex neuronal circuit involved and how individual neurons at each level represent sensory/motor information during natural motor behavior. Most movements of the limbs involve multiple joints and multiple muscles, whereas eye movements involve no joints and only three complementary pairs of muscles. The ocular-following system is essentially regulated by visual motion at ultra-short latency (~ 50 ms), and we can measure the sensory input and motor output signals quantitatively. Furthermore, when visual processing by the retina (~ 30 ms) and the delay by the ocular motor plant (~ 5 ms) are considered, the number of intervening neural elements must be limited, suggesting that the sensory-to-motor transformation for ocular-following is elicited during the residual time (~ 15 ms). Therefore, we conducted systematic research into the role of the ocular-following system in the motor control mechanism.

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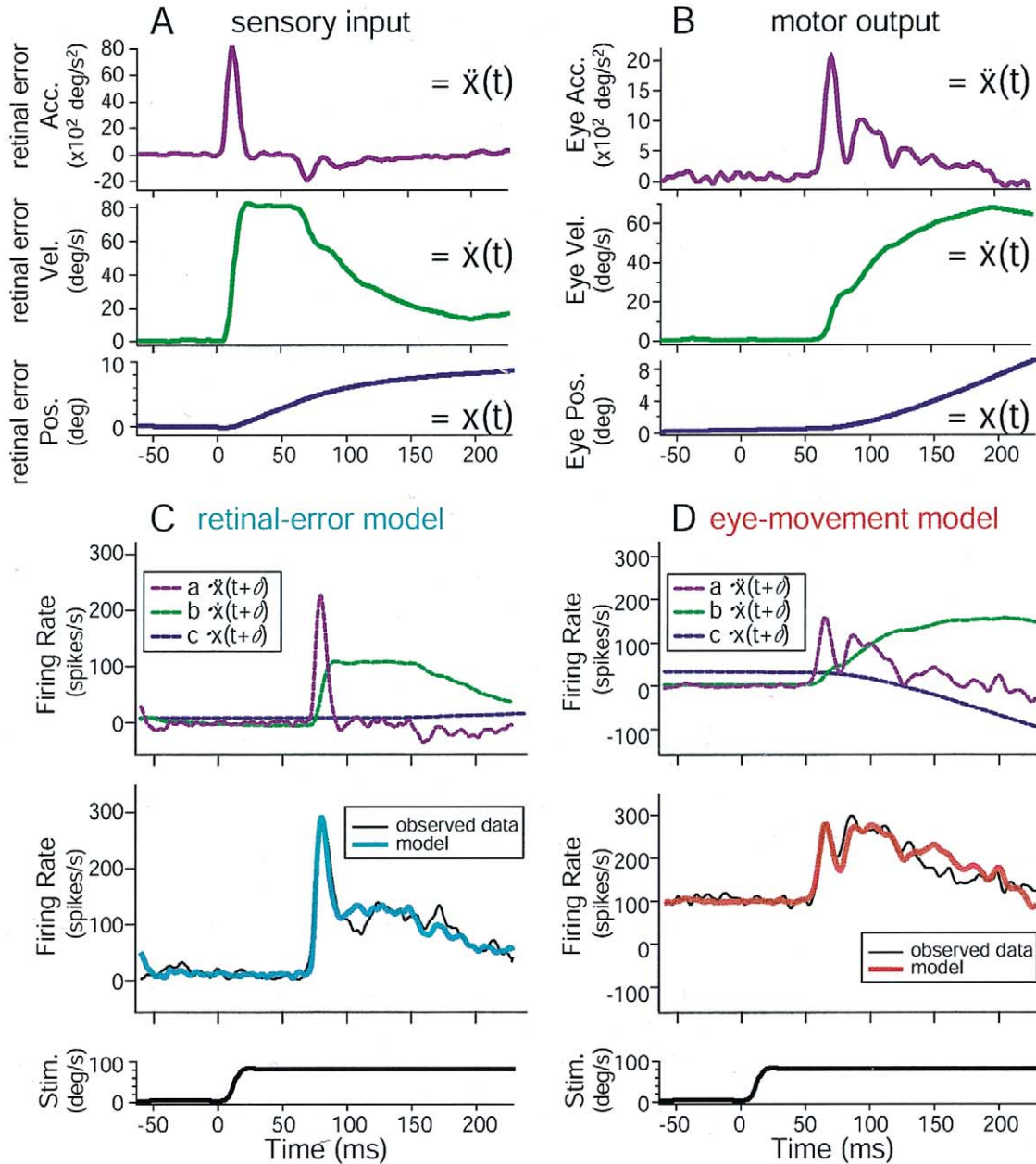*E-mail address:* a.takemura@aist.go.jp (A. Takemura).

Fig. 1. The ensemble averaged temporal patterns of 40 trials under the same stimulus conditions, and reconstruction using linear regression models based on retinal error or eye movement. The temporal patterns are aligned with the stimulus onset. (A): the temporal pattern of retinal error (sensory input signals). From top to bottom, the vertical retinal error acceleration, velocity, and position profiles. An upward deflection in the figure indicates a downward retinal error. (B): the temporal pattern of ocular-following (motor output signals). From top to bottom, the vertical eye acceleration, velocity, and position profiles. An upward deflection in the figure indicates a downward eye movement. The temporal patterns for retinal error (A) were obtained by subtracting eye movements (B) from stimulus movements. (C): reconstruction of the temporal pattern of an MST neuron using the retinal-error model with data at a stimulus velocity of 40°/s for downward ramps. The upper panel shows that the retinal error profiles were shifted by the delay time (δ). The acceleration (purple line), velocity (green line), and position (blue line) components are shown. In the lower panel, the reconstructed firing pattern of an MST neuron (cyan line) is superimposed on the observed firing pattern. (D): reconstruction of the temporal pattern of a P-cell (80°/s in downward ramps) using the eye-movement model with combined data for stimulus velocities of 10, 20, 40, 80, and 160°/s. The upper panel shows that the eye movement profiles were shifted by the delay time (δ). The acceleration (purple line), velocity (green line), and position (blue line) components are shown. In the lower panel, the reconstructed firing pattern of a P-cell (red line) is superimposed on the observed firing pattern.

In this review, we propose a hypothesis that explains the spatio-temporal and sensory-to-motor transformations involved in ocular-following. To this end, we first

review the neural pathway for ocular-following, and then describe the response properties and neural representation at each level of the information-processing

circuitry by reconstructing the temporal firing patterns using linear regression models based on retinal error or eye movement (Takemura et al., 2001).

2. Neural pathway for the ocular-following response

Chemical lesions in the medial superior temporal (MST) area of the cortex produced by local injections of ibotenic acid severely attenuate initial ocular-following (Shidara et al., 1991; Takemura et al., 2002), which strongly supports the idea that ocular-following responses are cortically mediated by a pathway that includes MST. Anatomical studies have reported that MST sends strong projections to the dorsolateral pontine nucleus (DLPN) (Brodal, 1978; Glickstein et al., 1980, 1985 Maunsell and Van Essen, 1983; Ungerleider et al., 1984; May and Andersen, 1986), and DLPN sends projections to the cerebellum, mainly to the ventral paraflocculus (VPFL) and dorsal paraflocculus of the cerebellum (Glickstein et al., 1994; Nagao et al., 1997). In fact, previous reports mention that lesions of VPFL impair early ocular-following (Miles et al., 1986), and that local injections of lidocaine to DLPN reduce the amplitude of initial ocular-following towards the side of the lesion (Kawano et al., 1990). Recent electrophysiological studies have examined the discharges of single neurons during ocular-following in MST (Kawano et al., 1994), DLPN (Kawano et al., 1992), and VPFL (Shidara and Kawano, 1993) in the monkey, and it was reported that the neurons in these regions responded with directional selectivity to movements of a large-field visual stimulus. In most cases, they increased their firing rate before the associated eye movement, some soon enough to have a causal role in producing even the earliest ocular-following responses. This evidence from previous studies suggests that early ocular-following responses are mediated by a pathway that includes MST, DLPN, and VPFL.

3. The local and global representation of sensory/motor information

To examine how incoming sensory signals are represented in neural responses and transformed into outgoing commands (especially the dynamic aspect), we quantitatively analyzed the relationship between the temporal firing patterns of single neurons in MST, DLPN, and VPFL, and the temporal patterns of the retinal errors (the retinal-error model, Fig. 1A) or eye movements (the eye-movement model, Fig. 1B) specified by three parameters (acceleration, velocity, and position) using the following equation:

$$\hat{f}(t - \delta) = a\ddot{x}(t) + b\dot{x}(t) + cx(t) + d,$$

where $\hat{f}(t)$, $\ddot{x}(t)$, $\dot{x}(t)$, $x(t)$ and δ are the reconstructed firing frequency of a neuron; the acceleration, velocity, and position of retinal error or eye movement at time t, and the time delay, respectively. The four coefficients (a, b, c, d) and the time delay (δ) were computed using the least-squares error method.

Previous experiments reported that ocular-following was strongly dependent on stimulus speed (Miles et al., 1986), and that ocular-following-related neurons in MST, DLPN, and VPFL also changed their firing patterns in relation to the stimulus speed (Kawano et al., 1990, 1992, 1994; Shidara and Kawano, 1993). To examine the local/global representation of cell firing for information in the sensory input (retinal error) or motor output (ocular-following), we simultaneously recorded the single unit activities and ocular responses for five different ramp speeds (10, 20, 40, 80, and 160°/s) of a large random-dot pattern. To study the local representation of cell firing within the limited stimulus range, we reconstructed the temporal firing pattern of each neuron for each visual stimulus speed and computed the coefficients for each parameter using the least-squares error method for each stimulus condition. To study the global linearity and global characteristics of cell firing, we reconstructed the temporal firing patterns of each neuron for the five visual stimulus speeds and computed a single set of coefficients.

4. The representation of sensory information: MST area of the cerebral cortex

Most MST neurons showed strong directional preferences. Their preferred directions (direction of motion associated with the most vigorous discharges) were distributed throughout all directions of motion. Hence, there were no significant differences in directional preference (ipsiversive/contraversive or up/down) in MST area. The direction-selective MST neurons generally responded best to high stimulus speeds, although some neurons preferred lower stimulus speeds. When we attempted to reconstruct the temporal firing patterns of a given cell in response to all visual stimuli (five speeds) using a single set of parameters, the linear regression model was inapplicable, regardless of whether the retinal-error model or the eye-movement model was used. These results suggest that the temporal firing patterns of MST neurons were not linearly related with retinal error or eye movement under multiple stimulus conditions.

On the other hand, when we investigated how well the linear regression model reconstructed the temporal waveform of each neuronal response to each visual stimulus, MST firing patterns were successfully reconstructed by the retinal-error model (Fig. 1C) but not by the eye-movement model. The difference in the goodness

of fit of the retinal-error and eye-movement models was significant ($P < 0.0001$), indicating that the retinal-error model reflects the temporal firing patterns of MST neurons more accurately than does the eye-movement model. To understand the characteristics of the firing patterns of MST neurons, we focused on the coefficients for acceleration and velocity in the retinal-error model. Their distribution was scattered, indicating that there are various cell types—some neurons have larger acceleration coefficients relative to velocity coefficients, while some have smaller coefficients relative to velocity coefficients.

These results suggest that the temporal firing patterns of MST neurons represent dynamic properties of the visual stimulus by various combinations of the acceleration, velocity and position components of the retinal errors in the neighborhood of their preferred speed, and that the entire population of MST neurons encodes visual information for ocular-following responses.

5. The representation of motor information: VPFL of the cerebellum

Compared to the response properties of MST neurons, the simple spike responses of Purkinje cells (P-cells) in VPFL showed much narrower response ranges in terms of both directional preferences—P-cells were divided into two classes that preferred ipsiversive or downward motion—and speed preferences—responses were always best at the very highest speeds which elicited the largest ocular responses. As for the temporal patterns, the eye-movement model adequately reconstructed a large number of these P-cell firing patterns using only a single set of parameters (Fig. 1D), suggesting that P-cells have the appropriate global characteristics for motor command (Shidara et al., 1993; Gomi et al., 1998; Takemura et al., 2001). The mean ratio of the acceleration coefficient to the velocity coefficient of P-cells was 50.1, which was close to that of motor neurons (67.4). These results demonstrate that P-cells already encode the dynamic component of the motor command for ocular-following.

On the other hand, both the retinal-error and eye-movement models adequately reconstructed most of the temporal patterns of P-cells under each stimulus condition, and the difference in the goodness of fit between the models was not significant. Since the local visual information encoded in MST neurons converges on a P-cell, the temporal firing patterns at every stimulus speed locally relate to the retinal errors. These results suggest that P-cells receive the visual information represented by MST firing pattern. In comparing between the estimated acceleration coefficients of MST and VPFL, there is less need for the retinal-error acceleration component to be presented in P-cell firing patterns than in MST neuron-

firing patterns. This implies that information on retinal errors is integrated into the appropriate temporal firing pattern of P-cells. These results suggest that the temporal firing pattern of P-cells in VPFL represents the dynamic properties of the visual stimulus for the narrow range of visual information held by DLPN and MST neurons at every stimulus speed, and represents the complete dynamic motor command for ocular-following response.

6. Neural mediation of ocular-following: the parieto–ponto cerebellar pathway

As discussed in the previous sections, the cortical MST area represents selective aspects of retinal error, and VPFL of the cerebellum represents the dynamic motor command for ocular-following. How is the visual information transformed into the motor commands that produce eye movement? Glickstein (1997, 2000), suggested that the parieto–ponto cerebellar pathway has an important role in visuomotor coordination. In the neural circuitry for ocular-following, DLPN receives projections from MST and then projects to VPFL. Neurons in DLPN also show strong directional preferences, and the population of preferred directions extends over a wide range of directions. Their response properties during ocular-following are very similar to those of MST neurons. Furthermore, the temporal characteristics of DLPN neurons are very close to those of MST neurons, and no clear differences are observed between MST and DLPN neurons—DLPN firing patterns do not yet represent the dynamic component of a motor command but locally encode the dynamic properties of the retinal error within a limited range. However, MST neurons have receptive fields of various sizes, whereas DLPN neurons have large receptive fields (Thier et al., 1988; Suzuki et al., 1990). There might be spatial integration of visual information (receptive field) in MST and/or DLPN, and further spatial and temporal integration (temporal firing pattern) between the mossy fibers and a VPFL P-cell. A simple spike results from the synaptic action of granule cell axon terminals (Ito, 1984). In the cerebellum, granule cells receive mossy fiber inputs from the brain stem and send their axons up to the molecular layer, where they bifurcate and traverse as parallel fibers, making numerous serial contacts with P-cell dendrites (Ito, 1984). Thus, a possible explanation for temporal integration is that every single P-cell receives a large number of inputs with various time delays, and these inputs are summed together to produce the P-cell firing pattern. The firing pattern of P-cells coincidentally represents limited visual information and the complete dynamic motor command independent of the stimulus speed, suggesting that VPFL P-cell is the major site of the sensory-to-motor trans-
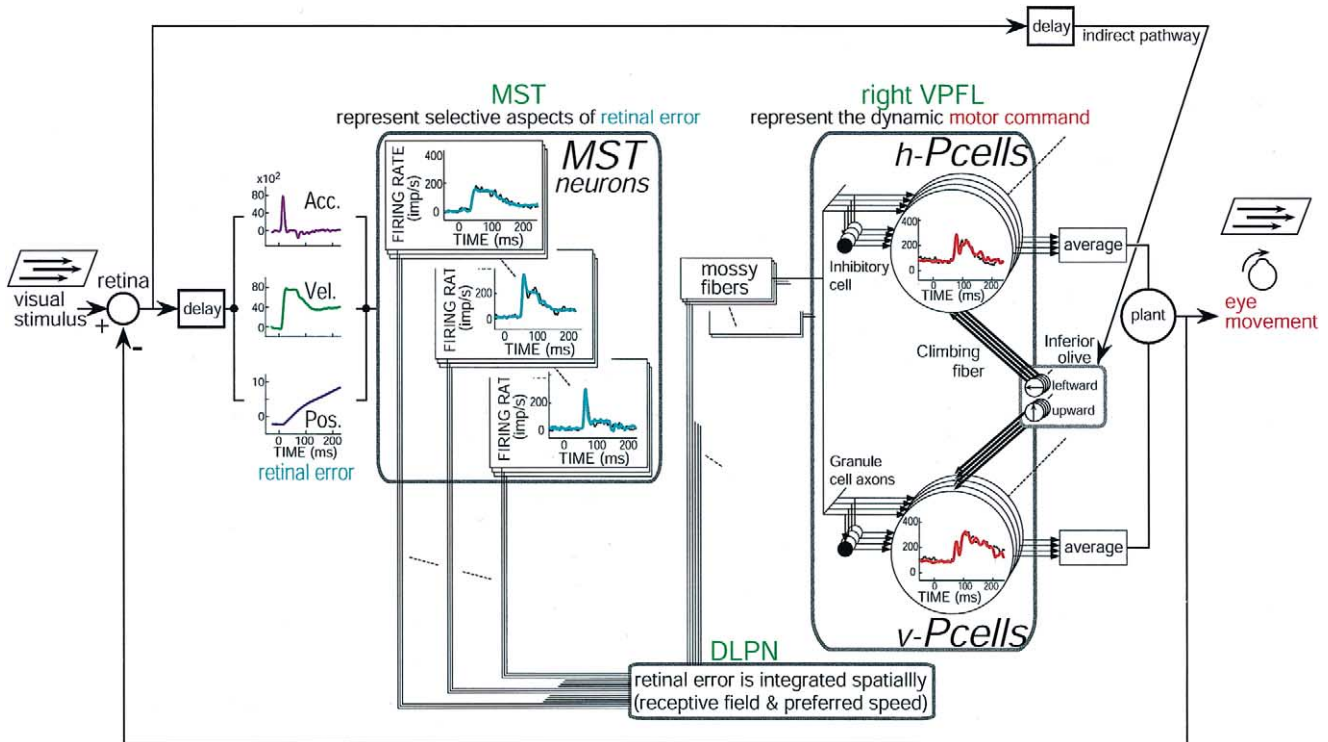
Fig. 2. The hypothetical scheme of the spatio-temporal and sensory-to-motor transformation involved in ocular-following. MST firing is reconstructed using retinal error acceleration, velocity, and position. DLPN neurons receive projections from MST and integrate the visual information spatially (size of the receptive field). A large number of granule cell axons and inhibitory cells have excitatory and inhibitory synapses with individual weights. Many inputs with various time delays are summed together to produce the P-cell firing patterns. The output from VPFL is the dynamic motor command for ocular-following.

formation for ocular-following. Fig. 2 shows a hypothetical scheme for the spatio-temporal and sensory-to-motor transformations for ocular-following.

A recent computational study of ocular-following by Yamamoto et al. (2002) suggests that acquisition and adaptation of the ocular-following responses arise from cerebellar plasticity. Their model included MST, VPFL, climbing fiber system, brain-stem oculomotor network and oculomotor plant, according to our research (Kawano et al., 1994; Takemura et al., 2001). They selected three typical MST neurons (acceleration-dominant cells, velocity-dominant cells and intermediate cells), which are shown in MST portion of Fig. 2, and divided P-cells into two groups (horizontal and vertical P-cells, shown in the right VPFL portion of Fig. 2) in both the hemispheres. To build the cerebellar synaptic plasticity into their model, each P-cell in the model received three synaptic inputs from a vast array of granule cells, multiple inhibitory cells and a single climbing fiber. When the synaptic weights were computed using models for long-term depression and long-term potentiation of the excitatory synapses from granule cell axons, and rebound potentiation of inhibitory synapses, the response properties of P-cells were acquired. The results suggest that, as a result of synaptic plasticity, the cerebellum acquires narrow response

ranges, and that the temporal characteristics of cell firing of various MST/DLPN neurons are markedly changed to a typical temporal characteristic of VPFL P-cells' firing.

The computational study strongly supports our hypothesis that VPFL P-cell is the major site of the spatio-temporal and sensory-to-motor transformation for ocular-following. The drastic change in the information encoded at the level of individual cells from MST/DLPN to VPFL during ocular-following is evidence of the transition of the neuronal representation from the population coding in the MST/DLPN to the firing-rate coding of simple spikes in the VPFL.

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