Supporting Information

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SI Text

Derivation of OKR Gain and Related Learning Rules

First, we simplified equations as follows:

$$\begin{aligned}\mathrm{PC}(t)&=w(t)\mathrm{GR}(t)-\mathrm{MLI}(t)+\mathrm{PC}_0\\&=w(t)\mathrm{MF}(t)-w_{\mathrm{MLI}}\mathrm{MF}(t)+\mathrm{PC}_0\\&=\mathrm{MF}(t)\left(w(t)-w_{\mathrm{MLI}}\right)+\mathrm{PC}_0,\end{aligned}\qquad\textbf{[S1]}$$

$$\begin{aligned}\mathrm{VN}(t)&=v(t)\mathrm{MF}(t)-w(t)\mathrm{MF}(t)+w_{\mathrm{MLI}}\mathrm{MF}(t)-\mathrm{PC}_0+\mathrm{VN}_0\\&=\mathrm{MF}(t)\left(v(t)-w(t)+w_{\mathrm{MLI}}\right)-\mathrm{PC}_0+\mathrm{VN}_0,\end{aligned}\qquad\textbf{[S2]}$$

$$\tau_w\frac{dw}{dt}=-w(t)+\langle\mathrm{MF}(t)\rangle-\langle\mathrm{MF}(t)\mathrm{CF}(t)\rangle,\qquad\textbf{[S3]}$$

$$\begin{aligned}\tau_v\frac{dv}{dt}&=-\langle\mathrm{MF}(t)\rangle v(t)+\langle\mathrm{MF}(t)(\mathrm{VN}(t)-\theta(t))\rangle\\&=-\langle\mathrm{MF}(t)\rangle v(t)+\langle\mathrm{MF}(t)\left(\mathrm{MF}(t)\left(v(t)-w(t)+w_{\mathrm{MLI}}\right)\right.\\&\qquad\left.-\mathrm{PC}_0+\mathrm{VN}_0-\theta(t)\right)\rangle.\end{aligned}\qquad\textbf{[S4]}$$

We decomposed $\mathrm{MF}(t)=\overline{\mathrm{MF}}+\delta\mathrm{MF}(t)$, where $\overline{\mathrm{MF}}$ and $\delta\mathrm{MF}(t)$ are the mean and the fluctuation around the mean, respectively. We also decomposed $\mathrm{CF}(t)$ in a similar way. We attempted to take a temporal average over a long enough time span to yield $\langle\delta\mathrm{MF}(t)\rangle=\langle\delta\mathrm{CF}(t)\rangle=0$ during and after training but short enough to yield $\langle w(t)\rangle=w(t)$ and $\langle v(t)\rangle=v(t)$, because $w(t)$ and $v(t)$ change slowly over time. Thus, we obtained the following:

$$\begin{aligned}\tau_w\frac{dw}{dt}&=-w(t)+\langle\overline{\mathrm{MF}}+\delta\mathrm{MF}(t)\rangle-\langle(\overline{\mathrm{MF}}+\delta\overline{\mathrm{MF}}(t))(\overline{\mathrm{CF}}+\delta\overline{\mathrm{CF}}(t))\rangle\\&=-w(t)+\overline{\mathrm{MF}}+\langle\delta\mathrm{MF}(t)\rangle-\overline{\mathrm{MF}}\;\overline{\mathrm{CF}}-\langle\delta\mathrm{MF}(t)\delta\mathrm{CF}(t)\rangle\\&\quad-\overline{\mathrm{MF}}\langle\delta\mathrm{CF}(t)\rangle-\overline{\mathrm{CF}}\langle\delta\mathrm{MF}(t)\rangle\\&=-w(t)+\overline{\mathrm{MF}}-\overline{\mathrm{MF}}\;\overline{\mathrm{CF}}-\langle\delta\mathrm{MF}(t)\delta\mathrm{CF}(t)\rangle\\&=-w(t)+w_0-\langle\delta\mathrm{MF}(t)\delta\mathrm{CF}(t)\rangle,\end{aligned}\qquad\textbf{[S5]}$$

where the term $(\overline{\mathrm{MF}}-\overline{\mathrm{MF}}\;\overline{\mathrm{CF}})$ is denoted by w_0. Here, the terms $\overline{\mathrm{MF}}$ and $-\overline{\mathrm{MF}}\;\overline{\mathrm{CF}}$ represent PF-LTP and PF-LTD, respectively, induced by spontaneous activity of PFs and CF. Therefore, we call them spontaneous PF-LTP and PF-LTD, respectively. We regard w_0 as the baseline weight of w, at which spontaneous PF-LTP and PF-LTD are balanced. During OKR adaptation training, $\delta\mathrm{MF}(t)$ and $\delta\mathrm{CF}(t)$ are correlated in time (1), so the value of $w(t)$ decreases by PF-LTD, which we call specifically training-induced PF-LTD. At resting states, $\delta\mathrm{MF}(t)$ and $\delta\mathrm{CF}(t)$ are independent, so $w(t)$ returns to the baseline level w_0. Electrophysiological studies have demonstrated that induction of PF-LTD or PF-LTP occurs quickly within 5 min and reaches its plateau within 30 min, and the recovery from the induction takes more than 24 h (2, 3). To simulate the asymmetry of the time necessary for induction and recovery, we used two equations for $w(t)$, one for during training and the other for after training, with different time constants:

$$\frac{dw}{dt}=\begin{cases}\dfrac{1}{\tau_{\mathrm{learn}}}(-w(t)+w_0-c_{\mathrm{OKR}}) & \text{(During training)}\\[2mm]\dfrac{1}{\tau_{\mathrm{recov}}}(-w(t)+w_0), & \text{(After training)}\end{cases},\qquad\textbf{[S6]}$$

where $\tau_{\mathrm{learn}}\ll\tau_{\mathrm{recov}}$, and $c_{\mathrm{OKR}}=\langle\delta\mathrm{MF}(t)\delta\mathrm{CF}(t)\rangle$.

Similarly, we obtained the following:

$$\begin{aligned}\tau_v\frac{dv}{dt}&=-\langle\overline{\mathrm{MF}}+\delta\mathrm{MF}(t)\rangle v(t)\\&\quad+\langle(\overline{\mathrm{MF}}+\delta\mathrm{MF}(t))\left((\overline{\mathrm{MF}}+\delta\mathrm{MF}(t))\left(v(t)-w(t)+w_{\mathrm{MLI}}\right)\right.\\&\qquad\left.-\mathrm{PC}_0+\mathrm{VN}_0-\theta(t)\right)\rangle.\end{aligned}\qquad\textbf{[S7]}$$

Because $\theta(t)$ is a running average of $\mathrm{VN}(t)$, we obtained the following:

$$\theta(t)\approx\overline{\mathrm{MF}}(v(t)-w(t)+w_{\mathrm{MLI}})-\mathrm{PC}_0+\mathrm{VN}_0,\qquad\textbf{[S8]}$$

and thereby

$$\begin{aligned}\tau_v\frac{dv}{dt}&=-\langle\overline{\mathrm{MF}}+\delta\mathrm{MF}(t)\rangle v(t)\\&\quad+\langle(\overline{\mathrm{MF}}+\delta\mathrm{MF}(t))\left(\delta\mathrm{MF}(t)\left(v(t)-w(t)+w_{\mathrm{MLI}}\right)\right)\rangle\\&=-\overline{\mathrm{MF}}v(t)+\langle\delta\mathrm{MF}(t)\delta\mathrm{MF}(t)\rangle\left(v(t)-w(t)+w_{\mathrm{MLI}}\right)\\&=-(\overline{\mathrm{MF}}-\langle\delta\mathrm{MF}(t)\delta\mathrm{MF}(t)\rangle)v(t)\\&\quad+\langle\delta\mathrm{MF}(t)\delta\mathrm{MF}(t)\rangle\left(-w(t)+w_{\mathrm{MLI}}\right).\end{aligned}\qquad\textbf{[S9]}$$

Here, we carefully examined the value of $\langle\delta\mathrm{MF}(t)\delta\mathrm{MF}(t)\rangle$. In the following, we assumed that MFs discharge spikes under the Poisson distribution (4), which means that the mean firing rate is given, whereas the detailed spike timing varies. Let $f_{\mathrm{MF}}(t)$ be the instantaneous firing rate of a MF at time t. Electrophysiological studies have shown that MF activity correlates with the optokinetic stimulus, i.e., screen velocity, and its peak modulation amplitude is as large as its mean amplitude (5). Therefore, $f_{\mathrm{MF}}(t)$ is given by the following:

$$f_{\mathrm{MF}}(t)=\begin{cases}\overline{\mathrm{MF}}+\overline{\mathrm{MF}}\sin\left(\dfrac{2\pi}{T}t\right) & \text{(During training)}\\[2mm]\overline{\mathrm{MF}} & \text{(After training)}\end{cases},\qquad\textbf{[S10]}$$

where T is the period of sinusoidal screen oscillation, for example, 6 s (6–8). Under the assumption of a Poisson distribution, the probability of which MFs make n spikes in 1 s, denoted by $P(n)$, is given by the following:

$$P(n)=\frac{f^n_{\mathrm{MF}}(t)}{n!}e^{-f_{\mathrm{MF}}(t)}.\qquad\textbf{[S11]}$$

We considered the ensemble average of the events, that is, the average firing rate with respect to many epochs of 1 s Let $\mu(t)$ be the average, which is calculated by the following:

$$\mu(t)=\sum_{n=0}^{\infty}nP(n)=f_{\mathrm{MF}}(t).\qquad\textbf{[S12]}$$

We can see that $\overline{\mathrm{MF}}$, the mean firing rate of MFs with respect to time, can be obtained by taking the temporal average of $\mu(t)$:

$$\langle \mu(t) \rangle = \langle f_{\mathrm{MF}}(t) \rangle = \overline{\mathrm{MF}}. \quad \textbf{[S13]}$$

Similarly, we calculate the variance of the events, i.e., the variance of the firing rate with respect to many epochs of 1 s. Let $\sigma^2(t)$ be the variance. Because the variance equals to the average in the Poisson distribution (9), we obtain the following:

$$\sigma^2(t) = \mu(t). \quad \textbf{[S14]}$$

Now, we regard this as the variance of temporal modulation of MF signals, namely, $\langle \delta\mathrm{MF}(t)\delta\mathrm{MF}(t) \rangle$, because the temporal average over a long time would be interchangeable with the ensemble average of many epochs of 1 s, if we split the long time period for the temporal averaging into these epochs. Thus, by taking a temporal average of them, we can obtain the following:

$$\langle \delta\mathrm{MF}(t)\delta\mathrm{MF}(t) \rangle = \left\langle \sigma^2(t) \right\rangle = \langle \mu(t) \rangle = \overline{\mathrm{MF}}. \quad \textbf{[S15]}$$

Therefore, $v(t)$ is updated by the following:

$$\tau_v \frac{dv}{dt} = \overline{\mathrm{MF}}(-w(t) + w_{\mathrm{MLI}}). \quad \textbf{[S16]}$$

We also considered the activities of PCs and VN:

$$\begin{aligned} \mathrm{PC}(t) &= \left(\overline{\mathrm{MF}} + \delta\mathrm{MF}(t)\right)(w(t) - w_{\mathrm{MLI}}) + \mathrm{PC}_0 \\ &= \left(\overline{\mathrm{MF}}(w(t) - w_{\mathrm{MLI}}) + \mathrm{PC}_0\right) + \delta\mathrm{MF}(t)(w(t) - w_{\mathrm{MLI}}), \end{aligned} \quad \textbf{[S17]}$$

$$\begin{aligned} \mathrm{VN}(t) &= \left(\overline{\mathrm{MF}} + \delta\mathrm{MF}(t)\right)v(t) - \mathrm{PC}(t) + \mathrm{VN}_0 \\ &= \overline{\mathrm{MF}}v(t) + \mathrm{VN}_0 + \delta\mathrm{MF}(t)v(t) - \left(\mathrm{MF}(w(t) - w_{\mathrm{MLI}}) + \mathrm{PC}_0\right) \\ &\quad - \delta\mathrm{MF}(t)\left(w(t) - w_{\mathrm{MLI}}\right) \\ &= \left(\overline{\mathrm{MF}}(v(t) - w(t) + w_{\mathrm{MLI}}) - \mathrm{PC}_0 + \mathrm{VN}_0\right) \\ &\quad + \delta\mathrm{MF}(t)\left(v(t) - w(t) + w_{\mathrm{MLI}}\right). \end{aligned} \quad \textbf{[S18]}$$

Moreover, we defined eye movement in proportion to the modulatory activity of the VN in response to the sinusoidally oscillating screen. We thereby omitted all of the constant terms from VN(t) to obtain the following:

$$\mathrm{EYE}(t) = g_{\mathrm{EYE}}\delta\mathrm{MF}(t)\left(v(t) - w(t) + w_{\mathrm{MLI}}\right), \quad \textbf{[S19]}$$

where g_{EYE} is a constant to translate the neuronal activity to eye movement. Then, OKR gain was defined as the maximum amplitude of the eye movement with respect to the screen oscillation. We denote OKR gain as follows:

$$\begin{aligned} \mathrm{OKR}(t) &= g_{\mathrm{EYE}} 2|\delta\mathrm{MF}(t)|(v(t) - w(t) + w_{\mathrm{MLI}}) \\ &= g_{\mathrm{OKR}}(v(t) - w(t) + w_{\mathrm{MLI}}), \end{aligned} \quad \textbf{[S20]}$$

where $|\delta\mathrm{MF}(t)|$ is the max of $\delta\mathrm{MF}(t)$, and $g_{\mathrm{OKR}} = g_{\mathrm{EYE}} 2|\delta\mathrm{MF}(t)|$. We normalized the screen oscillation amplitude to 1 without loss of generality.

Finally, we arbitrarily set $\overline{\mathrm{MF}} = \mathrm{PC}_0 = \mathrm{VN}_0 = w_0 = w_{\mathrm{MLI}} = 1$ for simplicity. Summarizing, we obtained the following set of equations as a model of long-term OKR adaptation:
OKR gain:

$$\mathrm{OKR}(t) = g_{\mathrm{OKR}}(v(t) - w(t) + w_{\mathrm{MLI}}). \quad \textbf{[S21]}$$

Updating rule of the synaptic weights:

$$\frac{dw}{dt} = \begin{cases} \frac{1}{\tau_{\mathrm{learn}}}(-w(t) + w_0 - c_{\mathrm{OKR}}) & \text{(During training)} \\ \frac{1}{\tau_{\mathrm{recov}}}(-w(t) + w_0) & \text{(After training)} \end{cases}, \quad \textbf{[S22]}$$

$$\frac{dv}{dt} = \frac{1}{\tau_v}(-w(t) + w_{\mathrm{MLI}}). \quad \textbf{[S23]}$$

Parameters are $w(0) = v(0) = 1$, $c_{\mathrm{OKR}} = 0.3$, $\tau_{\mathrm{learn}} = 20$ min, $\tau_{\mathrm{recov}} = 2.5$ h, $\tau_v = 5.5$ h, and $g_{\mathrm{OKR}} = 0.3$. These values were chosen to fit simulation results with experimental data (6).

Simulation of Cortical Shutdown and Muscimol Infusion

The cortical shutdown by injection of lidocaine (6) was simulated by setting the activity of PCs at 0 immediately after training. A calculation yields the following set of equations:
OKR gain:

$$\mathrm{OKR}(t) = \begin{cases} g_{\mathrm{OKR}}\left(v(t) - w(t) + w_{\mathrm{MLI}}\right) & \text{(During training)} \\ g_{\mathrm{OKR}}\left(v(t)\right) & \text{(After training)} \end{cases}. \quad \textbf{[S24]}$$

Updating rule of the synaptic weights:

$$\frac{dw}{dt} = \begin{cases} \frac{1}{\tau_{\mathrm{learn}}}(-w(t) + w_0 - c_{\mathrm{OKR}}) & \text{(During training)} \\ \frac{1}{\tau_{\mathrm{recov}}}(-w(t) + w_0) & \text{(After training)} \end{cases}, \quad \textbf{[S25]}$$

$$\frac{dv}{dt} = \begin{cases} \frac{1}{\tau_v}(-w(t) + w_{\mathrm{MLI}}) & \text{(During training)} \\ 0 & \text{(After training)} \end{cases}. \quad \textbf{[S26]}$$

Infusion of muscimol into the cerebellar cortex (7) was also simulated by the same equations after training with a certain delay but not immediately after training.

Simulation of Gene-Manipulated Animals

We also considered the case of deficits of either PF-LTP or PF-LTD at PF–PC synapses (10, 11). We introduced nonlinearity explicitly to maintain positive synaptic weights and neural activity, namely $w(t) \ge 0, v(t) \ge 0, \mathrm{PC}(t) \ge 0, \mathrm{VN}(t) \ge 0$. In normal circumstances, these conditions hold naturally. In the update rule of the synapses (Eq. **S5**), the baseline value of PF–PC synaptic weight is determined by the balance of spontaneous PF-LTP and PF-LTD ($w_0 = \overline{\mathrm{MF}} - \overline{\mathrm{MF}}\ \overline{\mathrm{CF}}$).

First, we considered the case of a deficit in PF-LTP. If PF-LTP is impaired, the synaptic weight decreases toward $-\overline{\mathrm{MF}}\ \overline{\mathrm{CF}}$ but stops at 0. Thus, all synapses vanish, that is, $w(t) = 0$ for any t. Under this condition, a calculation yields the following set of equations:
OKR gain:

$$\mathrm{OKR}(t) = g_{\mathrm{OKR}}(v(t)). \quad \textbf{[S27]}$$

Synaptic weights:

$$w(t) = 0 \quad \text{for any } t. \quad \textbf{[S28]}$$

$$v(t) = v(0) \quad \text{for any } t. \quad \textbf{[S29]}$$

Apparently, OKR gain is a constant $g_{\mathrm{OKR}}v(0)$.

Second, we considered the PF-LTD–deficient case. There are two PF-LTD terms in Eq. **S5**: one is spontaneous PF-LTD ($-\overline{\mathrm{MF}}\ \overline{\mathrm{CF}}$) and the other is training-induced PF-LTD ($-c_{\mathrm{OKR}} = -\langle \delta\mathrm{MF}(t)\delta\mathrm{CF}(t)\rangle$). The conventional PF-LTD induction protocol, which uses paired stimulation of PFs at 1 Hz and CF at 1 Hz in slice experiments, corresponds to the spontaneous PF-LTD. Impairment of PF-LTD was confirmed by this protocol (11). Training-induced PF-LTD has never been tested to date. We assume that PF-LTD–deficient mice (11) lack only spontaneous PF-LTD. Thus, we removed the term from Eq. **S5** and defined $w_0 = \overline{\mathrm{MF}}$. Under this condition, PF–PC synaptic weight is so large that $\mathrm{VN}(t) = 0$. It follows $v(t) = 0$ at the resting state from Eq. **S9**. Moreover, from Eq. **S9**, plasticity at MF–VN synapses works only when $v(t) - w(t) + w_{\mathrm{MLI}} \geq 0$. After a calculation, we obtain the following set of equations:

OKR gain:

$$\mathrm{OKR}(t) = \begin{cases} g_{\mathrm{OKR}}(v(t) - w(t) + w_{\mathrm{MLI}}) & \text{when } v(t) - w(t) + w_{\mathrm{MLI}} \geq 0, \\ 0 & \text{otherwise.} \end{cases} \quad \textbf{[S30]}$$

Updating rule of the synaptic weights:

$$\frac{dw}{dt} = \begin{cases} \dfrac{1}{\tau_{\mathrm{learn}}}(-w(t) + w_0 - c_{\mathrm{OKR}}) & \text{(During training)} \\ \dfrac{1}{\tau_{\mathrm{recov}}}(-w(t) + w_0) & \text{(After training)} \end{cases}, \quad \textbf{[S31]}$$

$$\frac{dv}{dt} = \begin{cases} \dfrac{1}{\tau_v}(-w(t) + w_{\mathrm{MLI}}) & \text{when } v(t) - w(t) + w_{\mathrm{MLI}} \geq 0, \\ 0 & \text{otherwise.} \end{cases} \quad \textbf{[S32]}$$

To demonstrate that normal motor learning can occur under PF-LTD knockout in a certain condition, we changed values of three parameters, which could be mediated by some compensation mechanisms in gene-manipulated animals. We set $g_{\mathrm{OKR}} = 1.0$, which was set at 0.3 in normal condition, and $v(0) = 0$ and $w(0) = w_0 = 1.1$, which were set at 1 in the normal condition. Other parameters were identical to the normal condition. Training was made for 8 d to observe the success or failure of memory transfer clearly.

Furthermore, we consider the case of selective depletion of GABA receptors on PCs (12). We deleted the inhibition term from PCs. This was made equivalently by setting $w_{\mathrm{MLI}} = 0$. This manipulation strengthens the inhibition from PCs to VN, thereby making the OKR gain totally negative. To compensate for this, we added a constant $c_{\mathrm{compensate}}$ to $\mathrm{OKR}(t)$. A calculation yields the following set of equations:

OKR gain:

$$\mathrm{OKR}(t) = g_{\mathrm{OKR}}(v(t) - w(t)) + c_{\mathrm{compensate}}. \quad \textbf{[S33]}$$

Updating rule of the synaptic weights:

$$\frac{dw}{dt} = \begin{cases} \dfrac{1}{\tau_{\mathrm{learn}}}(-w(t) + w_0 - c_{\mathrm{OKR}}) & \text{(During training)} \\ \dfrac{1}{\tau_{\mathrm{recov}}}(-w(t) + w_0) & \text{(After training)} \end{cases}, \quad \textbf{[S34]}$$

$$\frac{dv}{dt} = \frac{1}{\tau_v}(-w(t)), \quad \textbf{[S35]}$$

where $c_{\mathrm{compensate}} = 1.0$, $v(0) = 0.0$. Other parameters were identical to the normal case.

Simulated Training Paradigms

A typical simulated training was 1 h of daily training followed by 23 h of rest for 4 or 5 consecutive days. Simulated OKR gain was calculated while $w(t)$ and $v(t)$ were updated. Specifically, during the training and afterward, $w(t)$ was updated by interleaving two equations "during training" and "after training," respectively. Some simulations used much shorter daily trainings of 15 or 7.5 min. Simulation programs were written in C language. Differential equations were solved numerically by the forward Euler method with a time step of 1 min.

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