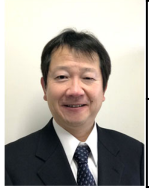
【Grant-in-Aid for Scientific Research (S)】

Mechanisms for updating behavioral strategies through cerebellar-cortical interactions



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Project Information	Project Number : 24H00064 Keywords : error-related potentials, adaptive behavioral control, cerebrocerebellar linkage, cortico-striatal pathway, nonhuman primate	Project Period (FY) : 2024-2028

Purpose and Background of the Research

●Outline of the Research

The cerebellum is thought to be involved in motor planning as well as motor execution. When we encounter difficult tasks, we deal with them carefully and slowly. Such adaptive behavioral control requires a series of processes: 1) detecting/predicting behavioral errors, 2) switching strategies, and 3) carefully selecting optimal behavior. We have previously shown that in monkeys performing eye movement tasks, neurons in the cerebellum exhibit increased activity during difficult task and immediately after failure. Because pharmacological inactivation of cerebellar neurons increases failure and shortens reaction time, these signals may be involved in updating behavioral strategies and subsequent behavioral control. This study will test the hypothesis that the cerebellum calculates error probabilities based on predictions of behavioral outcomes and sends this information to the frontal cortex to update behavioral strategies, which in turn changes the functional coupling of the cortical-striatal pathway to enable deliberate control. We aim to elucidate the mechanism of adaptive behavioral control by a large-scale network including the cerebellum.

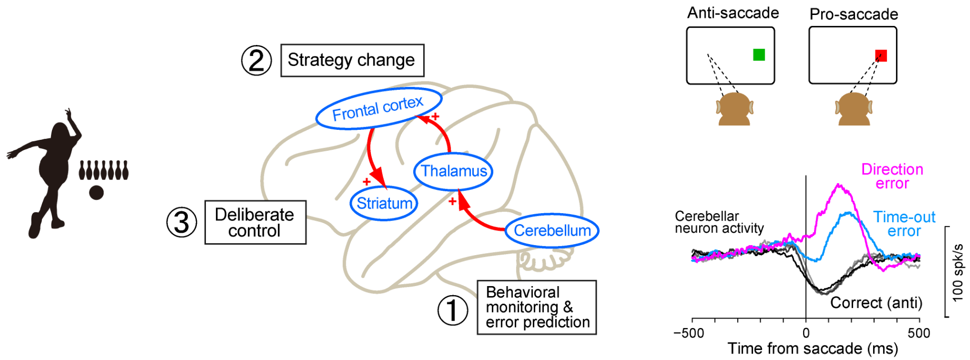

Figure 1. Research outline and neuronal activity in the cerebellum

●Behavioral monitoring and error-related potentials

Error-related potentials, EEG components recorded in the frontal cortex, occur immediately after an erroneous behavior, and their magnitude correlates with the degree to which reaction time is prolonged on the next trial. This potential is known to be markedly reduced in cerebellar damage. We have recently found that neurons in the dentate nucleus, the output node of the cerebellar hemisphere, are active immediately after an error, and that electrical stimulation of the same region produces short latency responses in the frontal cortex.

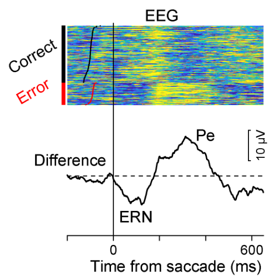

Figure 2. Error-related potentials

●Computation in cerebellar circuits

The cerebellum is divided into cortex and nuclei. The sole output of the cerebellar cortex is the large, inhibitory Purkinje cells, which generate two types of spikes with different shapes. Their timing is thought to be important for the plasticity of cerebellar circuits and may be involved in learning to predict error probabilities from one's own behavior.

●Optogenetic manipulation of neuronal activity

Normally, neurons themselves do not respond to light, but gene transfer using viral vectors can cause certain neurons to express light-sensitive molecules. Various applications are possible, for example, excitation of Purkinje cells in the cerebellar cortex by light stimulation to inhibit cerebellar nuclei, or activation of nerves projecting to the striatum to transiently increase dopamine during behavioral tasks.

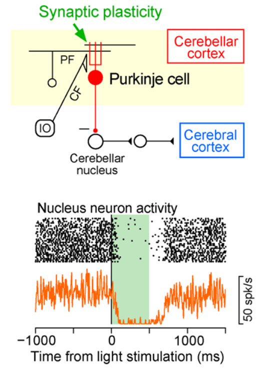

Figure 3. Cerebellar circuit

Expected Research Achievements

●Elucidation of the generation mechanism of error-related potentials

We will examine the information carried by neurons in the cerebellar nuclei and clarify the cortical layers that receive inputs from the cerebellum. Manipulation of neuronal activity in the cerebellum will determine its effects on behavioral strategies and the generation of error-related cortical potentials.

●Neural mechanisms that predict error probability from one's own behavior

Analysis of Purkinje cell activity, which is known to be important for synaptic plasticity, will elucidate the mechanisms for adaptively predicting behavioral errors.

●Mechanisms that alter functional connectivity of the cortical-striatal pathway

We recently found that the response of striatal neurons to electrical stimulation in the cortex is altered during difficult tasks. The relationship between functional connectivity and local EEG rhythms will be investigated and the role of dopamine, which is abundant in the striatum, will be explored.

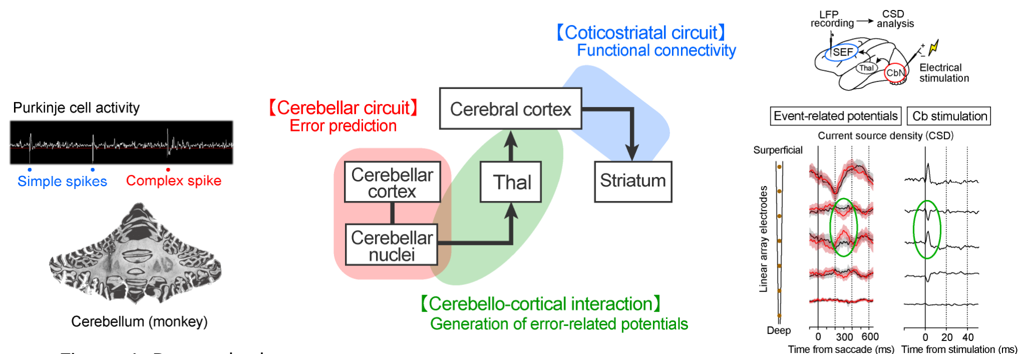

Figure 4. Research plan

●Significance and expected outcomes

This study will greatly advance conventional physiological studies of the cerebellum. The results will help us understand the pathophysiology of various neuropsychiatric disorders that impair adaptive behavioral control and increase impulsivity.

Homepage Address, etc.	https://niseiri.med.hokudai.ac.jp/en/ (Lab website)