$GABA_A$ receptors play roles in acquisition and retention of mouse eyeblink conditioning in the cerebellar nuclei

（小脳核GABA受容体はマウス瞬目反射条件づけの獲得と保持に重要な役割を持つ。）

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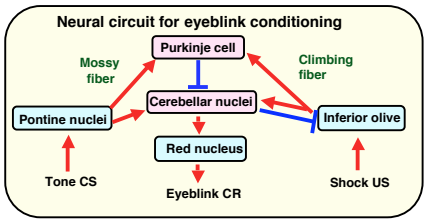
Abstract

Neural circuits for eyeblink conditioning in rabbits has been studied in detail, however, the basic knowledge on eyeblink conditioning in mice remains limited. In the present study, we examined the role of $GABA_A$ receptors in the mice deep cerebellar nuclei (DCN) for delay eyeblink conditioning. Bilateral injection of Muscimol (MSC) and Picrotoxin (PTX) significantly impaired learned eyeblink responses (LER) in an acquisition test. MSC-injected mice could not acquire LER, however, PTX-injected may have acquired LER, suggesting the distinctive effect of these drugs in DCN. Bilateral injection of MSC and PTX also impaired the retention of acquired LER in a 7-day retention test. Furthermore, ipsilateral injections of MSC and PTX impaired the acquired LER as much as bilateral injection of them. Contralateral MSC injections also impaired the expression of LER, but contralateral PTX injections only partially impaired eyeblink conditioning. These results reveal that $GABA_A$ receptors in DCN play essential roles in both the acquisition and the expression of mouse eyeblink conditioning.

Introduction



Basic knowledge for neural circuits on mouse eyeblink conditioning remains limited.

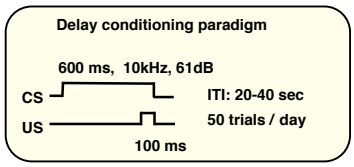
The role of bilateral and unilateral deep cerebellar nuclei in acquisition and retention of mouse eyeblink conditioning was examined.

Methods

Animals: Male C57BL/6 mice 8–9 weeks old.

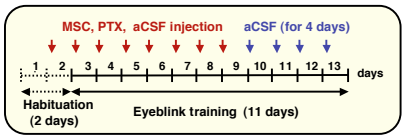
Surgery:
(1) Drug injection into the cerebellar nuclei bilaterally (AP = -6.05, ML = ±1.80, DV = -2.25 mm).
(2) Electromyogram (EMG) recording for eyeblink responses; Stainless wires were implanted under the left upper eyelid.

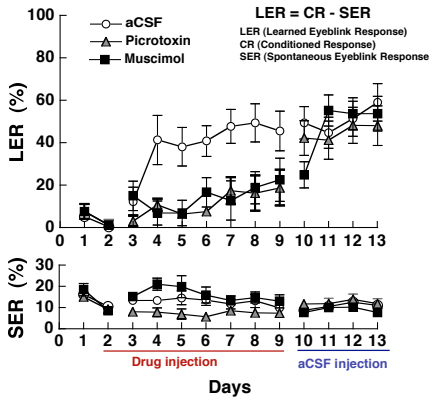
Drug injection: 0.2 μl of 10 mM muscimol, 200μM picrotoxin, aCSF (artificial cerebrospinal fluid) (0.15 μl / min)



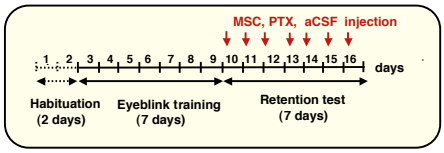
Results

(1) Acquisition test

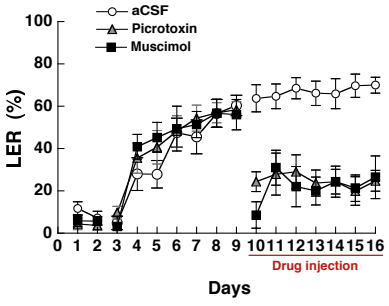




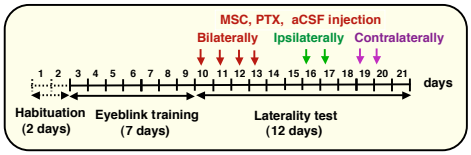
(2) Retention test



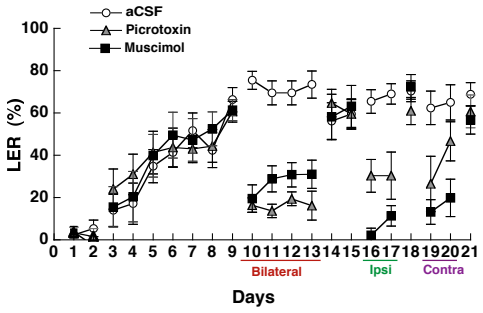
Injection of MSC and PTX impaired retention of eyeblink learning



(3) Laterality test

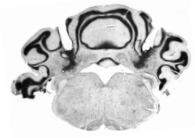


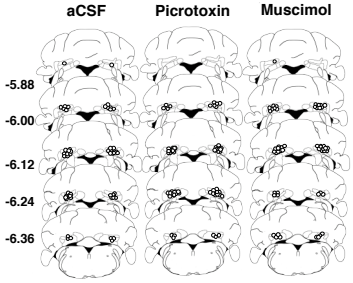
Unilateral injection of MSC and PTX also impaired retention of eyeblink learning



(4) Histology

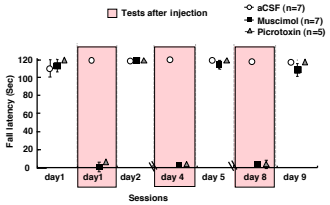
Tips of internal cannulae were positioned in the cerebellar nuclei





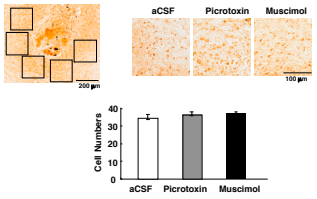
(5) Rotor-rod test

MSC and PTX impaired performance of rotor rod tests



(6) Numbers of cells around injection sites

No significant differences in the average number of Hu-immunopositive neurons in MSC-, PTX-, and aCSF-injected mice



Summary

1. Bilateral Muscimol-injected mice could not acquire learned eyeblink responses, however, Picrotoxin-injected mice may have acquired them.
2. Bilateral injection of Muscimol and Picrotoxin impaired the retention of acquired learned eyeblink responses.
3. Both ipsilateral and contralateral injection of of Muscimol and Picrotoxin impaired expression of learned eyeblink responses.

Conclusions

$GABA_A$ receptors in cerebellar nuclei play essential roles in both the acquisition and the expression of mouse eyeblink conditioning.

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