Abstract

Poster Instructions

Title	EPILEPTIC ABSENCE SEIZURES STOPPED BY CLOSED-LOOP ACTIVATION OF CEREBELLAR OUTPUT Room: Poster Area - Session: C22 - Abstract Number: FENS-2760 - Poster Board Number: C060
Poster No:	C060
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Topic:	C.8 Epilepsy
Theme:	C. Disorders of the nervous system

Absence epilepsy is the most prevalent form of seizure disorders and has been characterized by generalized oscillatory activity in thalamo-cortical networks. Interruptions of thalamic (*e.g.*, Paz, J.T. et al.) and/or cortical activity (*e.g.*, Berenyi, A. et al) have been shown to be effective inhibitors of seizure activity. However, little is known about the impact of most of the afferent systems, like the cerebellum, during absence seizures. The cerebellar nuclei (CN) divergently connect mono-synaptically to a wide range of thalamic nuclei and therefore we hypothesized that CN activity plays a pivotal role in absence seizures. We first established that in awake *tottering Cacna1a*^{P601L} mice, a well-known animal model for epilepsy, CN neurons show phase-locked oscillatory activity during seizures. Next, we show that pharmacological blockade of CN activity by local application of the $GABA_A$-agonist muscimol significantly increases seizure occurrence, highlighting that the cerebellar output is of importance for seizure control. Indeed, when we optogenetically modulated (virally encoded AAV2-hSyn-ChR2(H134R)-EYFP vector) the CN activity with high temporal precision we were able to stop seizures within 150 ms. Importantly, unilateral activation of CN neurons was sufficient to completely deregulate and block bilateral seizure activity in the cortex. Moreover, we designed a closed-loop detection - stimulation interface that could reliably detect and stop seizures. Finally, we were able to repeat all outcomes of the experiments described above in another unrelated mouse model for absence epilepsy, the C3H/HeOuJ mouse, illustrating that blockage of absence seizures by manipulating cerebellar output can be generalized.

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