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POSTER PRESENTATION

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Corticosterone enhances CSD susceptibility via glucocorticoid receptor activation in familial hemiplegic migraine 1 *Cacna1a* knock-in mice

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Introduction

FHM1 mutant mice carrying the R192Q gain-of-function mutation in CaV2.1 (P/Q-type) calcium channels display enhanced glutamatergic transmission and increased propensity for cortical spreading depression (CSD;1,2). Corticosteroids released after stress also enhance glutamatergic transmission but the relationship between stress and migraine is not well understood.

Objectives

We aimed to investigate the acute effects of corticosterone and the role of GR activation on CSD susceptibility in FHM1 R192Q knock-in mice.

Methods

Corticosterone (20 mg/kg) or vehicle was injected subcutaneously 4 hours before CSD frequency recordings were carried out in FHM1 R192Q mice. A subgroup of mice was injected with the glucocorticoid receptor antagonist mifepristone 50 minutes before corticosterone/vehicle injection.

Results

Corticosterone injection increased CSD frequency in FHM1 mice compared to vehicle-injected controls but not in wild-types. Pretreatment with mifepristone reduced CSD frequency to the level of vehicle-injected controls. Baseline corticosterone plasma levels were similar in WT and FHM1 mice, while 3 hours after corticosterone administration corticosterone plasma levels were strongly

elevated to comparable levels in both WT and FHM1 mice.

Conclusion

These data suggest that combined effects of glucocorticoid receptor activation and the FHM1 R192Q CaV2.1 gain-of-function mutation on excitatory neurotransmission may play a role in proposed effects of stress on migraine attacks.

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