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Cortical Spreading Depolarizations Occur in the Presence of Surgical Field Blood in a Mouse Model of Neurosurgery

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Introduction

Cortical spreading depolarization (CSD) occurs in traumatic brain injury, malignant stroke, and subarachnoid hemorrhage and is associated with poor clinical outcomes. Electrocautery during neurosurgical procedures can also evoke CSD waves in the brain. It is unknown whether blood contacting the cortical surface during surgical bleeding affects the frequency of CSD. Using a mouse neurosurgical model, we tested the hypotheses that (1) electrocautery induces CSD waves; (2) surgical site blood is associated with increased numbers of CSD's; (3) CSD is reliably observed by monitoring fluorescence of GCaMP6f expressed in neurons.

Methods

CSD waves were monitored by using confocal microscopy to detect fluorescence increases in the cortex in mice expressing GCaMP6f in CamKII-expressing neurons. The cortical surface was cauterized through an adjacent burr hole. Surgical site blood was simulated by applying tail vein blood to the brain through the burr hole.

Results

CSD waves are readily detected in GCaMP6f-expressing mice. Monitoring fluorescence of GCaMP6f provides good sensitivity and spatial resolution. Electrocautery evokes CSD waves. On average, 0.67 ± 0.08 CSD events are generated per cautery episode, and multiple CSD waves can be induced the same mouse by repeated cauterization (average, 7.9 ± 1.3 events; maximum events in one animal was 13). In the presence of surgical site blood, significantly more spontaneous CSD's are generated (0.021 ± 0.004 events per minute vs 0.002 ± 0.001, p=0.002, n=8 mice per group). Ketamine effectively decreases the frequency of spontaneous CSD waves (0.021 ± 0.004 CSD waves/min to 0.006 ± 0.003 CSD waves/min, p=0.016) and cautery-stimulated CSD waves (0.80 ± 0.05 CSD waves/cautery to 0.18 ± 0.07 CSD waves/cautery, p =0.00001).

Conclusions

Electrocautery reliably evokes CSD waves, and spontaneous CSD waves occur more frequently when blood is applied to the cortical surface. These experimental conditions recapitulate common neurosurgical operating room scenarios. Ketamine can block stimulated and spontaneous CSD's. More research is required to understand the clinical importance of intraoperative CSD.

Learning Objectives

By the conclusion of this talk, participants should be able to:
(1) Explain the significance of CSD in acute brain injury;
(2) Describe the intraoperative conditions in which CSD is triggered in a mouse model;
(3) Discuss why and how CSD should potentially be limited during neurosurgery.

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