A Simultaneous NIRS-EEG Study of Seizure in the Mouse Brain

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Abstract: We measured hemodynamic responses of seizure in the mouse brain using frequency-domain near infrared spectroscopy (NIRS) and electroencephalogram (EEG). We adapted microfabricated optical holder for consistent contact of the optical fiber to the mouse brain. Our results show that the cerebral oxygenation and hemodynamics of mice can be stably monitored with EEG in the mouse brain.

Background and Purpose. Genetically engineered mice are tremendously powerful tools in understanding the cellular and molecular origin of human diseases. In particular, the uses of specific gene knock-out or knock-in mice have untangled the complicated phenomenon occurring in the brain which is the most complex system in nature. In addition, the innovative imaging techniques of the mouse brain have accelerated the growth of the neuroscience community by visualizing from the cell level to the network level [1]. However, the functional brain imaging of an intact mouse brain has remained as a challenging problem. The limited size and fragility of the mouse brain require micro-fabricated brain-sensor interface which is absolutely tickler more than handwork [2, 3]. The neurovascular coupling has been demonstrated in rat study [4, 5] but not in mouse model. In this study, we caused the biggest brain activation pharmacologically to monitor the corresponding hemodynamic events.

Methods. Eight channel frequency domain NIR spectroscopy (ISS, Urbana, IL) was applied to monitor the cerebral hemodynamics and cerebral oxygenation of the mouse brain. Each channel contains two wavelengths (690 and 830 *nm*) and each laser diode was turned on and off sequentially under time-based multiplexing. Two optical fibers carrying different wavelength were carefully co-localized on one point with help of micro-fabricated optical holder. The skin of the mouse head was removed. The detector was located at center of the brain (middle point of bregma and the lambda point) [6]. Each channel was located around the brain at olfactory, right frontal, right temporal, dorsal right temporal, occipital, dorsal left temporal, left temporal, left frontal, in sequence. Monopolar EEG electrode was implanted in left frontal area and the ground electrode was implanted on occipital area [7]. Mice (B6 no genotype, male, 30 *gram*) were anesthetized by urethane (1.3g/kg) and the seizure was pharmacologically driven by administering 4-AP (10 *mg/kg*). Animal care and handling followed the institutional guidelines of KIST.

Results. Basal cerebral oxygenation and oxy- and deoxyhemoglobin concentrations did not alter significantly after the administration of 4-AP. Also, the hemodynamic responses during the epileptic waves were insignificant. However, a high regional synchronization during urethane anesthesia in the NIR channels was observed (CCF = 0.80 ± 0.13). Whereas, the regional synchronization between NIR channels was reduced significantly (p-*value* = 0.0001) after the administration of 4-AP ($CCF = 0.43 \pm 0.19$).

Conclusions. Microfabricated optical holder plays a critical role in simultaneous NIRS and EEG recording in the mouse brain by maintaining consistent contact of the optical fibers to the mouse brain. Although the hemodynamic changes during the epileptic events were not noticed, the stable and robust recording modality of the optical and electrical signals of the mouse brain may provide comparable information of functional brain imaging in the transgenic mice

References

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