大学院特別講義

新潟脳神経研究会特別例会
オンラインセミナーの御案内

日　　時：令和３年２月３日(水) 14:00～

開催方法：Zoom による配信

オンデマンド脳活動介入による てんかん発作制御とその応用
On-demand intervention of epileptic seizures and beyond

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Approximately 1% of world population have epilepsy and more than 30% of them are drug-resistant; therefore, a new therapeutic approach is desired. We have previously developed a closed-loop transcranial electrical stimulation (TES) technique to control absence (petit mal) seizures using rats[1]. Non-invasive and time-targeting natures of the closed-loop TES technique will diminish risks associated with intracranial electrode implantations and disturbance of normal brain functions. We have also developed another technique for controlling secondary generalized, grand-mal seizures of temporal lobe epilepsy (TLE) using a 'proxy' intervention strategy[2]. As seizure generator network of TLE is often distributed over bilateral hippocampi and para-hippocampal gyri, direct intervention on these structures is not technically feasible. Thus, we stimulated the medial septum (MS) to modulate highly synchronous hippocampal oscillations in seizures of TLE harnessing the MS's diffuse bilateral connections to the hippocampi and para-hippocampal structures, which govern oscillatory activities there. We found that closed-loop MS electrical stimulation effectively terminated electrographic and motor seizures of hippocampally-kindled rats whereas open-loop MS stimulation did not. Cell-type specific optogenetic stimulation of MS neurons revealed that precisely timed activation of MS GABAergic neurons could underlie the MS-mediated seizure terminating effects. To translate these findings into clinical practice, we have then developed a new TES technology to spatially target brain regions: Intersectional Short Pulse stimulation[3]. To focus intensity of electrical stimulation to an intracranial region, we placed multiple pairs of stimulus electrodes over the head of rats, human cadavers, and healthy volunteers. We found that the focused electrical stimulation could successfully modulate neural activities and oscillatory brain activities in the focused region. Our seizure intervention techniques with non-invasive, time-, spatial-, and proxy-targeting natures would be useful to control refractory epilepsy. In addition, I'm going to discuss possible

applications of our technique to other neurological and psychiatric disorders[4].

1. Berényi A, Belluscio M, Mao D, Buzsáki G, Closed-loop control of epilepsy by transcranial electrical stimulation. Science 337: 735–737, 2012.
2. Takeuchi Y, Harangozó M, Pedraza L, Földi T, Kozák G, Li Q, Berényi A, Closed-loop stimulation of the medial septum terminates epileptic seizures, Brain, in press.
3. Vöröslakos M, Takeuchi Y, Brinyiczki K, Zombori T, Oliva A, Fernández-Ruiz A, Kozák G, Kincses ZT, Iványi B, Buzsáki G, Berényi A, Direct effects of transcranial electric stimulation on brain circuits in rats and humans. Nat Commun 9: 483, 2018.
4. Takeuchi Y, Berényi A, Oscillotherapeutics – Time-targeted interventions in epilepsy and beyond. Neurosci Res 152: 87-107, 2020.

どうぞ奮ってご参加ください。

担当：システム脳病態学分野／田井中研究室