# "Challenge the Brain, Change the Future"

August 30 (Wed)-31 (Thu), 2017
Grand Hilton, Seoul

The 20th Annual Meeting of
the Korean Society for Brain and Neural Science
Co-organized by the Korean Society for Neurodegenerative Disease


**HOSTED BY** · The Korean Society for Brain and Neural Science  The Korean Society for Neurodegenerative Disease

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## Dopamine receptor D1 agonism and antagonism using a field-effect transistor assay

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The field-effect transistor (FET) has been used in the development of diagnostic tools for several decades, leading to high-performance biosensors. Therefore, the FET platform can provide the foundation for the next generation of analytical methods. A major role of G-protein-coupled receptors (GPCRs) is in the transfer of external signals into the cell and promoting human body functions; thus, their principle application is in the screening of new drugs.
The research community uses efficient systems to screen potential GPCR drugs;nevertheless, the need to develop GPCR-conjugated analytical devices remains for next-generation new drug screening. In this study, we proposed an approach for studying receptor agonism and antagonism by combining the roles of FETs and GPCRs in a dopamine receptor D1 (DRD1)-conjugated FET system, which is a suitable substitute for conventional cell-based receptor assays. DRD1 was reconstituted and purified to mimic native binding pockets that have highly discriminative interactions with DRD1 agonists/antagonists. The real-time responses from the DRD1-nanohybrid FET were highly sensitive and selective for dopamine agonists/antagonists, and their maximal response levels were clearly different depending on their DRD1 affinities. Moreover, the quilibrium constants (K) were estimated by fitting the response levels. Each K value indicates the variation in the affinity between DRD1 and the agonists/antagonists; a greater Kvalue corresponds to a stronger DRD1 affinity in agonism, whereas a lower K value in antagonism indicates a stronger dopamine-blocking effect.

**Key Words:** Dopamine, Dopamine receptor, Agonist, Antagonist, FET

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## Quantification of in vivo 1H Spectrum using an experimentally measured basis-set at 9.4T

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Proton magnetic resonance spectroscopy (1H-MRS) is a non-invasive technique that allows quantifying brain metabolites. Our purpose is to measure experimentally basis-set of brain metabolites using 1H-MRS and quantify in vivo 1H spectrum in a mouse brain based on the basis-set. We made phantoms of 17 brain metabolites maintaining the condition that were in the physiological pH (7.0-7.2) and low temperature (0-4°). All spectra of the phantoms were acquired at 9.4T MRI scanner (Agilent) using point resolved spectroscopy (PRESS) sequence with following acquisition parameters: repetition time (TR): 10000 ms, echo time (TE): 15 ms, the number of scans (NS): 128, volume of interest (VOI): 27 μL. The measured spectra of brain metabolites were used to make the basis-set using LCModel. We used the basis-set to fit in vivo 1H spectrum in a C57BL/6 mouse brain. We set the VOI of 3.6μL in hippocampus of the mouse brain. In vivo 1H spectrum was also measured at same scanner using PRESS sequence (TR: 6000 ms, TE: 15 ms, NS: 384). We experimentally measured basis-set of the 17 brain metabolites and quantified 12 brain metabolites in hippocampus of the mouse brain. In this study, we attempted to make basis-set from phantom spectra and then quantified in vivo 1H spectrum of brain metabolites in a mouse. We determined the basis-set of the brain metabolites. From these basis-set, we quantified 12 brain metabolites in the mouse. In our future study, we could quantify the change of the brain metabolites, which may result from the brain disease, and be periodically monitored.

**Key Words:** 9.4T, Proton magnetic resonance spectroscopy, Brain metabolites, Mouse, Basis-set

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## Preliminary study report of Alzheimer's disease stage monitoring technology based on multimodal neurophysiological measurement

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Due to the rapid growing of the aging population, the demand for low-cost analytical monitoring technology for Alzheimer's patients is rapidly increasing. Simultaneous measurement of Electroencephalography (EEG) and functional near-infrared spectroscopy (fNIRS) is emerging technology for low-cost multimodal neurophysiological measurement and it can provide the complementary electrical and metabolic changes of local cortical area. To classify the Alzheimer's patients from mild cognitive impairment (MCI) to late stage, we are analyzing multimodal brain signals through experiments associated with cognitive function (visual oddball task), working memory capacity (1-back task), and language processing (verbal fluency task). Totally 57 elderly subjects, including 32 normal controls, 20 patient with MCI, and 5 patients with AD, participated in this study and all subjects performed three paradigms in consecutive order. The dataset was simultaneously recorded using the 32-channel wireless EEG and 4-channel customized fNIRS devices and resting state was also measured for 1 minute before first paradigm. In data analysis, we are investigating the feature signals such as event-related potentials (ERPs), event-related desynchronization/synchronization (ERD/S) and the oxy- and deoxy-hemoglobin concentration changes for each paradigm dataset. We are also developing the hybrid brain monitoring system capable of acquiring high resolution, multi-channel, and fully synchronized EEG and NIRS signals for out-of-lab applications. In this preliminary study, we will briefly report the analysis results and development progress.

**Key Words:** EEG, fNIRS, Alzheimer's disease, Multimodal, Portable system

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## Approaches for modulation of glial functions by GPCR signaling regulation

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Neuronal functions are closely regulated by glia cells. Because glia hardly express voltage-sensitive channels, lots of modulations are mediated by glial GPCR. We are intended to develop methods for glia-selective functional modulation, and its impact on neuronal functions by examining synaptic plasticity and animal behavior control effect. To this end, we will develop synaptic transmission and synaptic plasticity control techniques by regulating glia activity using GPCR modulations (DREADD etc.). We will also study GPCR-Ca2+ signaling and TLR-GPCR interaction using a behavioral abnormality analysis and behavior improvement evaluation technique for animal models of brain diseases. Finally we will develop a platform for evaluating the efficacy of glia-specific regulatory methods that integrate these analytical techniques. We expected to obtain fundamental answers to the development of the glia-related drug sing the animal model of various glia-related brain diseases. It is expected that the research system to be established through the this detailed research will be useful in studying the pathogenesis of other brain diseases including neurodegenerative diseases.

**Key Words:** Glia, GPCR, Brain, Neuronal, Modulation