Deep learning for the prediction of seizure liability and MoA of drugs based on the electrophysiological activities in hiPS cell-derived neurons

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Human iPSC-derived neurons are expected to be applied to toxicity evaluations in nonclinical studies and drug screening. Microelectrode array (MEA) measurement system is suitable to evaluate the neuronal electrophysiological responses to drugs. We have previously reported the electrophysiological responses to convulsants using MEA in cultured hiPSC-derived neurons. In this study, we aimed to develop an analytical method enabling the evaluation of toxicity and the classification of MoA of convulsants using multivariate analysis and deep learning. hiPSC-derived cerebral cortical neurons were cultured on Micro-electrode array (MEA) plate, and the pharmacological responses over 10 drugs in spontaneous firings were obtained. We firstly constructed the raster plots of spontaneous firing and the divided image data. The 4096 feature vectors of the divvied image data in raster plots were extracted by pre-trained model. Next, CNN model was trained with feature vectors each drug name. Using this trained CNN model, we have succeeded in separating the responses between non-convulsive drugs and convulsants, and classifying the MoA of convulsants. This deep learning methods are useful for the prediction of seizure liability and the classification of MoA of new drugs.