Assessment to anti-epilepsy drugs in human iPSC-derived neural network

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Anti-epileptic drugs (AEDs) have different mechanisms of action depending on the generation. For example, the old generation AEDs are mainly Na+ channel inhibitory and GABA receptor agonists. On the other hand, a new generation of AEDs has a mechanism of action different from that of the previous generation, such as those that act on AMPA-type glutamate receptors and act on multiple channels and receptors. In addition, drugs with unknown mechanism of action such as Levetiracetam are also widely used as AEDs. We have developed the assay using microelectrode array (MEA) combined with hiPSC-derived neurons and have detected the responses to a lot of convulsants. In this study, it was attempted to administer AEDs to the hiPSC-derived neurons that caused seizures with convulsants, and to detect differences in the effects of old and new generation AEDs. HiPSC-derived neurons were cultured on MEA Plate, seizure-like activities (SLAs) were induced by 4-aminopyridine (4-AP), bicuculline, kainic acid, respectively, and then 6 types of AEDs were administered. Old generation AEDs were effective in case of only SLAs induced by 4-AP. On the other hand, the new generation AEDs were also effective in SLAs induced by bicucullin and kainic acid. This result suggests that MEA measurement of hiPSC-derived neurons are effective for AEDs screening.