Title: Suppressing neuronal seizure-like activity in vitro

Authors:

Siiri Sihvonen[1], Oskari Kulta[1], Lotta Isosaari[1], Andrey Vinogradov[1], Taina Viheriäl[2], Pasi Kallio[2] and Susanna Narkilahti[1]

[1]NeuroGroup, Faculty of Medicine and Health Technology, Tampere University, Tampere, Finland

[2]Micro- and Nanosytems Research Group, Medicine and Health Technology, Tampere University, Tampere, Finland

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Abstract

Epilepsy is one of the most common neurological diseases globally affecting 60 million people. Anti-epileptic drugs (AEDs) are ineffective in one third of the patients and can cause adverse drug reactions (ADR). PRIME project aims to establish a software design tool for preventing epileptic seizures.

This research uses commercially available human induced pluripotent stem cell (hiPSC, AICS0012 TUBA1B) derived cortical neurons to study glial cell line-derived neurotrophic factor's (GDNF) effects on suppressing seizure-like activity in vitro. The seizure -like activity is induced with kainic acid (KA, 30 µM) and the activity changes are studied with microelectrode array (MEA) measurements. For treatment, ARPE-19 epithelial cells engineered to secrete GDNF are embedded into polyethersulfone (PES) tubes on top of transwell membranes. GDNF secretion is measured from media with ELISA assay. Neuron's ability to response to GDNF is validated with gene expression analysis of GFRα1 express in neurons with qPCR.

The MEA data exhibits robust network bursting activity in cortical neuron networks. KA exposure is performed at three-week time point on neurons on MEA, followed by acute and long-term follow-ups. ARPE-19 tubes are administrated to neurons immediately after KA exposure. KA introduces typical activity alterations in neuronal network however, GDNF does not alleviate these changes.
Previously, GDNF was shown to reduce seizures in vivo, although the mechanisms of actions are unknown. This highlights the relevance to studying further the GDNF's effects on seizure-like activities in vitro.