

Multi-electrode Array (MEA) Profiling of Disease and Drug-response Network Dysfunction in Human iPSC-derived Cerebral Organoid Models of Neurodegeneration

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Patient-derived cerebral organoids from familial and sporadic Alzheimer's disease, frontotemporal dementia and control iPSC lines were recorded repeatedly on 96-well multi-electrode array (MEA) plates. Well-level metrics (firing rate, bursting, synchrony) were combined with custom raster-level spike-train analysis and rank-based non-parametric statistics; calcium-imaging readouts provided complementary validation. Organoid networks showed a stable, disease-specific activity hierarchy: hyperexcitable, burst-rich networks in sporadic AD, elevated but progressively fragmenting activity in familial AD, and relative hypoactivity in FTD and controls, with significant group differences and large effect sizes. The phenotype was stable across weeks of recording. MEA-based functional readouts reproducibly capture disease-specific network pathology in human organoids, establishing a robust platform for neurodegeneration modelling and drug screening.

Keywords: cerebral organoids; MEA; network bursting; hyperexcitability; iPSC; Alzheimer's disease; drug screening

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