

Integrating network activity with transcriptomic profiling in hiPSCs-derived neuronal networks to understand the molecular drivers of functional heterogeneity in the context of neurodevelopmental disorders

S Puvogel^{1,2}, U Ciptasari^{1,2}, E.J.H van Hugte^{1,2}, S Wang³, N Scheefhals^{1,2}, A Oudakker¹, H van Bokhoven^{1,2}, D Schubert^{2,4}, N Nadif Kasri^{1,2,4}

- 1) Department of Human Genetics, Radboudumc, Nijmegen, The Netherlands
- 2) Donders Institute for Brain, Cognition and Behaviour, Nijmegen, The Netherlands
- 3) Department of Biomedical Sciences, Universite de Lausanne, Zurich, Suisse
- 4) Department of Cognitive Neurosciences, Radboudumc, Nijmegen, The Netherlands

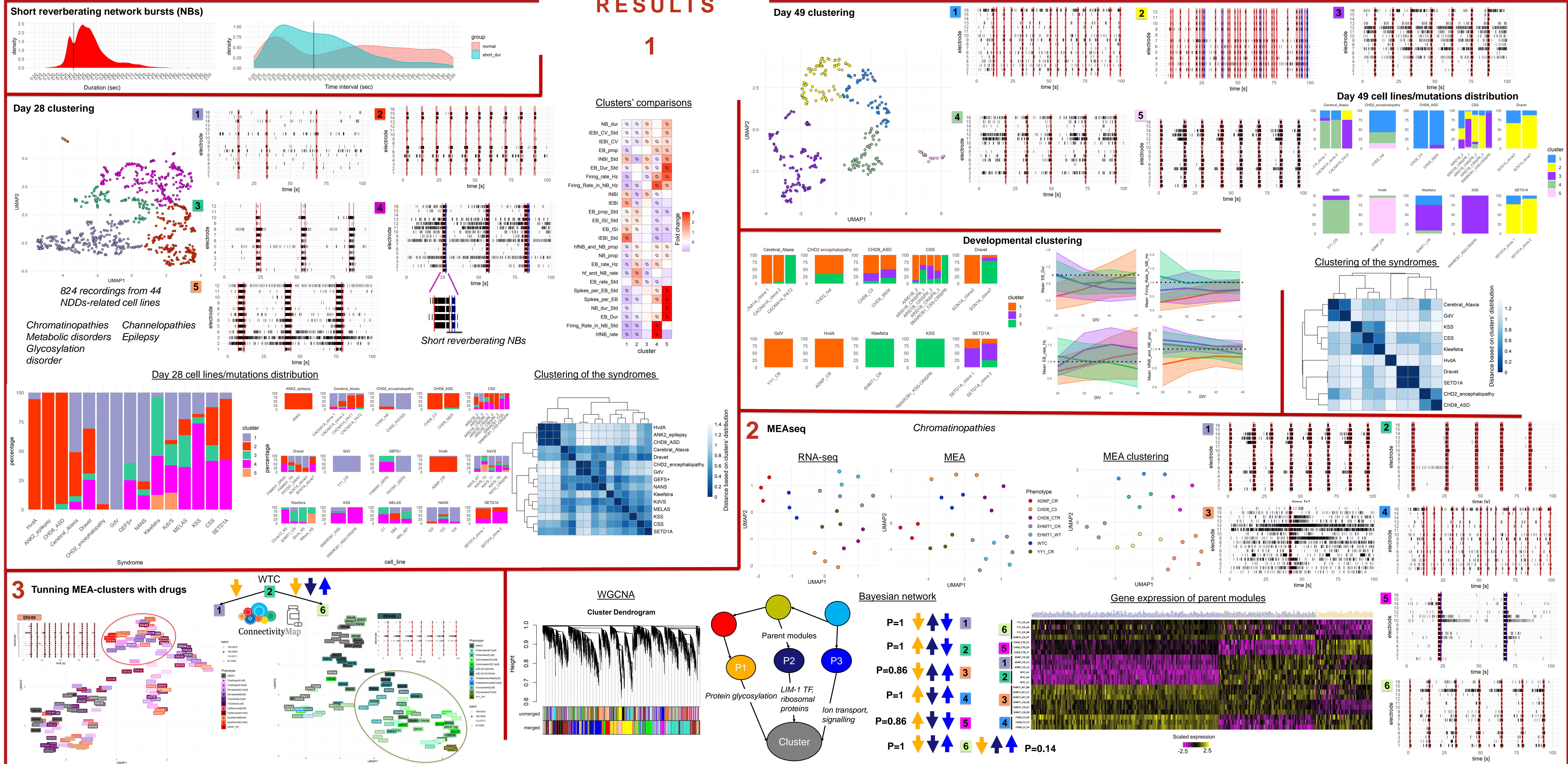
QUESTION

What are the molecular drivers of the heterogeneity in neuronal activity patterns in the context of neurodevelopmental disorders (NDDs)?

STRATEGY

1. **Characterize the phenotypic landscape of hiPSCs-derived network activity in NDDs:** Perform multivariate clustering analysis to investigate potential functional convergence and divergence of hiPSCs-derived networks carrying mutations associated with NDDs, cultured on micro-electrode arrays (MEA). Data from two MEA machines, the Maestro Pro MEA system (Axion BioSystems) and Multichannel Systems, were integrated.
2. **MEaseq:** Integrate RNA-sequencing and MEA data using Weighted Gene Correlation Analysis (WGCNA) and Bayesian Network analysis to identify core gene sets potentially driving the different activity clusters.
3. **Tuning network activity:** Computationally identify drugs likely capable of inducing the gene expression profile corresponding to target activity clusters and experimentally assess their effect on network activity.

RESULTS



*Correspondence: s.puvogellutjens@radboudumc.nl & nael.nadifkasri@radboudumc.nl

EB=Electrode burst, Dur=duration, hFNB=high frequency network burst (or short reverberating NBs), Prop=proportion, IEBI= inter electrode burst interval, CV= coefficient of variation, Std=standard deviation, ISI=inter spike interval, INBI=inter network burst interval.