Complex Oscillatory Waves Emerging from Cortical Organoids Model Early Human Brain Network Development.

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Public Summary:
Brain organoids are important tools to understand the formation of the human brain. However, up to now, these 3D self-assemble structures were similar to the developing human brain, from molecular (gene expression, epigenetic marks) and anatomical level. This publication reports the emergence of sophisticated neuronal networks using a novel brain organoid protocol. These networks mature over time and develop on oscillatory brain waves. Using machine learning, we compare these brain waves to electroencephalogram (EEGs) from preterm babies' brains and showed that the maturation trajectory follows the same direction as the human brain. The work pave the way for better disease modeling and also reframe the ethical discussions about this methodology.

Scientific Abstract:
Structural and transcriptional changes during early brain maturation follow fixed developmental programs defined by genetics. However, whether this is true for functional network activity remains unknown, primarily due to experimental inaccessibility of the initial stages of the living human brain. Here, we developed human cortical organoids that dynamically change cellular populations during maturation and exhibited consistent increases in electrical activity over the span of several months. The spontaneous network formation displayed periodic and regular oscillatory events that were dependent on glutamatergic and GABAergic signaling. The oscillatory activity transitioned to more spatiotemporally irregular patterns, and synchronous network events resembled features similar to those observed in preterm human electroencephalography. These results show that the development of structured network activity in a human neocortex model may follow stable genetic programming. Our approach provides opportunities for investigating and manipulating the role of network activity in the developing human cortex.