Title:

Rodent model of fetal EEG development reveals a thalamic locus for the developmental acquisition of continuous, state-dependent cortical activity

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Abstract

Background

Electroencephalograms (EEG) of human pre-term infants show that cortical activity patterns change drastically as the neonate approaches term age. During late second and third-trimester, long-lasting silent periods are prevalent and the most prominent activity consists of a large-amplitude oscillation called the 'delta-brush' which is pronounced in central, temporal and occipital areas. Delta-brushes disappear around term age, and cortical activity becomes continuous and state-dependent; i.e., silences become rare and cortex begins to consistently exhibit distinct patterns of activity associated with specific behavior states. While the acquisition of this continuous activity and state-dependent modulation is one of the major hallmarks of human brain development and critical for good prognosis of babies born preterm or suffering brain damage caused by ischemia or hypoxia, the circuit mechanisms of this maturation are poorly understood.

Objective

Here we test the hypothesis that acquisition of continuous EEG activity and its modulation by arousal state is due to the maturation of thalamic, not cortical, circuits.

Design/Methods

We use the rodent visual system as a model to understand the circuit mechanisms of brain activity maturation in human fetuses and neonates. Prior work has shown that rodents have similar cortical activity changes as human preterm infants during the first two post-natal weeks, which allows us to experimentally test our hypotheses. We simultaneously recorded activity in visual thalamus (the

dorsal lateral geniculate nucleus (LGN)), and visual cortex (VC) of awake head-fixed rats throughout development using multi-electrode arrays with pharmacological manipulations.

Results

We found that the neuronal activity in LGN changes from discontinuous to continuous between P11 and P13 (just before eye-opening), contemporaneously with VC. Furthermore, movement begins to increase spike rates in both structures at this age. To determine if LGN is required for continuous activity in cortex we pharmacologically silenced LGN and measured the effect on cortex. LGN silencing causes the cortex to become discontinuous and causes movement to suppress, rather than increase, cortical activity. On the other hand, silencing cortex after its acquisition of continuity did not affect LGN activity or movement-dependence.

Conclusions

These results demonstrate that maturation of LGN circuitry, not intracortical connections, plays a determinative role in the maturation of the infant EEG near term. Our results have implications for understanding EEG abnormalities and locus of brain injuries following perinatal insults in term and preterm infants.