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Title: Development of spontaneous activity patterns in dysplastic cortical networks

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The basis for hyperexcitability in cortical malformations and the role that heterotopic clusters of neurons play in the development of seizure susceptibility is unknown. Describing the development of both intrinsic neuronal and organizational network properties is important for understanding the emergence of aberrant activity in cortical malformations. Here we utilize network-level two-photon calcium imaging and whole-cell recordings to describe the development of spontaneous activity patterns in a doublecortin RNAi model of subcortical band heterotopia. In neonatal animals, levels of early spontaneous activity were similar in both heterotopic and normotopic networks. These immature network activities in heterotopic, normotopic, and control neocortex consisted mainly of intrinsic activities including synchronous nonsynaptic calcium plateaus. However, a marked difference in levels of spontaneous activity was seen in heterotopic networks with respect to normotopic and control networks by the end of the first postnatal week. At this time, normotopic and control neocortex exhibited synaptically driven activities with periods of robust population synchrony, whereas heterotopic neurons continued to exhibit immature network patterns. These results demonstrate profound similarities and differences in spontaneous activity patterns between developing heterotopic and normal cortical networks. Further extension of this work will elucidate the acquisition of aberrant activity patterns in cortical malformations and may provide valuable insight into the development of spontaneous activity in neocortical networks.

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