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Disrupted network-activity profiles in cultured hippocampal neurons lacking GluR1

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How do the molecules central to synaptic physiology influence the emergent properties of living neuronal networks? We have established a platform to study directly the network electrophysiology of neurons carrying genetic deletions or modifications of key synaptic molecules. Here, we describe the effects of knock-out of the AMPA receptor subunit, GluR1, on the network-activity profiles of primary neuronal cultures. On multi-electrode arrays, we maintained primary cultures of hippocampal neurons from GluR1 knock-out and wild-type mouse embryos for up to a month. During that time, we recorded the spontaneous activity of each culture at different developmental time-points. From the spike train data, we derived a small number of parameters that describe network activity throughout the maturation of the cultures. Comparing wild-type and GluR1 knock-out cultures, both fired relatively few action potentials at a few days *in vitro* and these spikes showed little spatio-temporal pattern. In the second week, wild-type cultures underwent a steep growth phase in the number of spikes, and these became increasingly entrained into bursts, which showed progressively higher spatial correlation across the network. During this phase, GluR1 knock-out cultures also increased their overall output of spikes, but the entrainment of these into bursts was severely impaired, and only small portions of the network were active at any given time. From the third week onwards, wild-type cultures displayed network activity almost exclusively in the form of periods of synchronous bursting across most of the network. By contrast, GluR1 knock-out cultures retained a deficit in synchronous network-wide activation despite activity at individual sites occurring largely in bursts by this stage. Our results suggest a role for AMPA receptors in the expression of adaptive processes within neuronal networks during their development and stabilisation.