Development of neuronal network connectivity in cultured cerebral cortex neurons

Kampert E, Van Aken A, Reis S*, Oostra BA*, Ramakers GJA
Neurons and Networks, Netherlands Institute for Brain Research, Amsterdam, *Department of Clinical Genetics, Erasmus Medical Center, Rotterdam

The brain is a highly complicated network of neurons, whose function it is to process information. The functional properties of neuronal networks are dependent on the intrinsic properties of the neurons and their synaptic connectivity. Alterations in network connectivity can result in disorders such as mental retardation or epilepsy. We used primary cultures of dissociated fetal rat/mouse cerebral cortex neurons to investigate the cellular mechanisms that regulate neuronal network formation, and the outcome of developmental and experimental alterations in network structure on the functional properties of the network. Structural network development was analyzed quantitatively upon fluorescent labeling of individual neurons in combination with immunocytochemical staining for neurotransmitters. Functional network activity was continuously monitored for weeks by extracellular recording of up to 60 neurons simultaneously, through microelectrodes etched in the bottom of the culture dish. The morphological development of neurons proceeded in several distinct phases. Axons grew out from the start and showed more or less continuous elongation and branching up to at least the end of the second week. Highly unstable dendrites remained very short until about seven days, when they showed a rapid phase of elongation and branching. GABAergic and non-GABAergic (excitatory) neurons showed distinct outgrowth patterns from the start as well as differences in final morphology. This indicated that the morphological differentiation of specific neuronal cell types is primarily under control of intrinsic factors. When network structure was altered by culturing neurons from FMR1 knock-out mice, functional properties of spontaneous firing activity were also changed. Conversely, when epileptiform activity was induced, dendritic outgrowth was enhanced through increased branching. Our observations show that structural network properties are regulated by both intrinsic (genetic) and environmental factors, and in turn affect the functional properties of the network. Modeling studies should help to further clarify the relationship between network structure and function.
Supported by the Hersenstichting Nederland and the National Epilepsy Fund- 'The Power of the Small' project number 20-06

Ger JA Ramakers, Neurons and Networks, Netherlands Institute for Brain Research, Meibergdreef 33, 1105 AZ Amsterdam ZO, t 020-5668967, e-mail g.ramakers@nih.knaw.nl

Poster session of choice: Neuroscience 1