Abstract:

Most synapses impinging onto an individual pyramidal cell (PC) in the neocortex originate from nearby excitatory cells, signifying the importance of recurrent excitatory connections in cortical circuits. We hypothesized that the density of recurrent connectivity directly correlates with the amount of network activity. To test this hypothesis, we used a mouse model in which the genetic ablation of the mitogen-activated protein kinase ERK2 within the dorsal telencephalon during embryonic development using the Emx1-cre system resulted in reduced density of mature PCs within cortical layers 2/3. Consequently, the reduction in the laminar density of PCs corresponds to a decrease in the amount of recurrent connections within layer 2/3. These effects are consistent with the critical role of ERK2 in the spatiotemporal organization of the cortex during development. We employed whole-cell patch clamp methods to record network activity in the form of high-conductance (~10 nS) synaptic events in layer 2/3 PCs from acute slices of somatosensory cortex in wild-type and conditional ERK2 knock-out (ERK2 cKO mice). Network activity was facilitated by bath-applying 5 uM gabazine. Using the number of network events as a measure of network activity, we observed reduced cortical excitability in ERK2 cKO mice compared to their wild-type (WT) littermates (see Figure). In addition, we quantified the recurrent synaptic activity (R) of the network mediated via excitatory feedback by taking the difference between the mean EPSP count two seconds before and after burst onset. ERK2 cKO mice have a reduced recurrent EPSP component...
compared to WTs (RWT = 14, RKO = 12; 14% decrease relative to WT).
The change in network excitability cannot be attributed to inhibitory
interneurons, since ERK2 in the neocortex was selectively suppressed in
pyramidal cells. Therefore, decreased network activity in cKO mice
resulted from defects in laminar distribution of PCs alone. Our study is the
first to quantify network excitability in mice lacking ERK2 and to
demonstrate that these animals have diminished cortical activity
accompanied by a decrease in recurrent excitation. These results emphasize
the importance of recurrent excitatory feedback in regulating cortical
network activity.

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