Glucocorticoid receptor regulates gene expression of voltage gated calcium channels in rat hippocampal CA1 neurons

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The stress hormone corticosterone modulates voltage gated ion channels through activation of the low affinity glucocorticoid receptor (GR) in addition to the high affinity mineralocorticoid receptor (MR) in the rat hippocampus. As a transcription factor the activated GR translocates to the nucleus where it regulates the transcription of responsive genes that promote alterations of cellular function. In CA1 neurons, activation of the GR both suppresses firing rates by enhancing the slow afterhyper-polarization (sAHP) involving calcium dependent potassium channels (SKs) and increases calcium currents through voltage dependent calcium channels (VDCCs). We hypothesised that these functional changes after GR activation are caused by transcriptional regulation of the associated ionchannels. To test our hypothesis, GR was activated by a brief exposure of rat hippocampal slices to 100nM corticosterone. The CA1 area was dissected out 1 or 3 hours later for subsequent examination of expression by real-time quantitative PCR. We showed that expression of the α1C and β4 subunits of the VDCC and to a lesser extent the SK2 subunit were upregulated one hour after GR activation. The enhanced expressions were normalized to the vehicle level three hours after GR activation. Expression of ligand-gated ionchannel subunits was not affected. We furthermore showed that new protein synthesis was not involved in the upregulation of the VDCC α1C subunit mRNA, suggesting that VDCC α1C subunit gene is a direct target of GR. We conclude that upregulation of VDCC subunits and perhaps also of the SK2 channel may indeed contribute to the enhanced calcium currents and increased sAHP observed with electrophysiological methods in rat hippocampal CA1 neurons.

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