Synergistic effects of corticosterone and kainic acid on neurite outgrowth in axotomized dorsal root ganglion

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摘要

Abstract

Corticosterone is the main adrenal glucocorticoids induced by stress in rats. Therapeutic use of high concentration of synthetic glucocorticoids in clinical treatment of spinal cord injury suggests that pharmacological action of glucocorticoids mightbe beneficial for nerve repair. In this article we cultured axotomized rat dorsal root ganglion neurons to investigate the effects of corticosterone and a glutamate receptor agonist kainic acid on neurite outgrowth. Our results revealed a synergistic effect of corticosterone and kainic acid in promoting neurite outgrowth when applied as early as one and two days in vitro, but not effective at three and four days in vitro. In addition, applied corticosterone and kainic acid were neurotoxic at three and four days in vitro but not at one and two days in vitro. The minimal concentrations of corticosterone and kainic acid to be effective were 10 &mgr;M and 1 mM, respectively. The neurotrophic effect of corticosterone and kainic acid was attenuated by the receptor tyrosine kinase A (TrkA) inhibitor AG-879. Western blot analysis and immunocytochemical studies revealed an increase of expressions of both TrkA and growth-associated protein GAP-43 in dorsal root ganglion neurons with combined treatment of corticosterone and kainic acid. Immunocytochemistry showed that corticosterone+kainic acid increase nerve growth factor immunoreactivity in dorsal root ganglion neurites and enhance GAP-43 immunointensity in dorsal root ganglion neurons. These results suggest that the neurotrophic effect of glucocorticoids on axonal regeneration might require facilitation of excitatory stimulation at an early stage of nerve injury, and nerve growth factor may mediate a growth signaling to accomplish the effect.