Abstract
Humans and animals are constantly exposed to environmental stress. The hypothalamic-pituitary-adrenal (HPA) axis responds to stress, followed by glucocorticoid secretion from the adrenal glands. This response serves to maintain homeostasis in the living body through energy mobilization or to restore it. The brain is an important target for glucocorticoids. The hippocampus participates in the regulation of the HPA axis. Stress activates glutamatergic neurons in the hippocampus, and serious stress induces dyshomeostasis of extracellular glutamate. This dyshomeostasis, which is potentiated by glucocorticoids, modifies cognitive and emotional behavior. On the other hand, zinc is necessary for glucocorticoid signaling and is released from glutamatergic (zincergic) neurons to modulate synaptic glutamate signaling. Stress also induces dyshomeostasis of extracellular zinc, which may be linked to dyshomeostasis of extracellular glutamate. Thus, glucocorticoid signaling might also contribute to dyshomeostasis of extracellular zinc. It is likely that zinc signaling participates in cognitive and emotional behavior through glucocorticoid and glutamate signaling under stressful circumstances. This Mini-Review analyzes the relationship among signals of glucocorticoid, glutamate, and zinc under stressful circumstances to elucidate the significance of the zinc signaling in response to stress.