Electroconvulsive shock (ECS) for treatment of many psychiatric diseases is known to induce immediate early genes (IEGs) in rat brain. To elucidate the intracellular signaling processes involved in the induction of c-fos after ECS in vivo, I investigated the effects of non-competitive NMDA antagonist, MK-801, on the induction of c-fos and on the phosphorylation of mitogen-activated protein kinases (MAPKs: ERK, JNK, and p38) after ECS in various rat brain regions. Following treatment of ECS, MK-801, or ECS with MK-801 pretreatment, I analyzed the amount of c-Fos and the phosphorylation of MAPKs and MAPK kinases (MEK1, SEK1, and MKK3/6) by immunoblotting.

ECS increased the expression of c-Fos in the cerebral cortex, hippocampus and cerebellum. MK-801 (1 mg/kg) definitely increased the expression of c-Fos in the cerebral cortex and hippocampus, but not in the cerebellum. Pretreatment of MK-801 dose dependently attenuated the increases of c-Fos by ECS. MK-801 (1 mg/kg) increased the phosphorylation of 42 kDa ERK only in the hippocampus, but did not affect the phosphorylation of 46 kDa JNK and p38 in all of the observed regions. ECS increased the phosphorylation of 42, 44 kDa ERK in all of the observed brain regions. Pretreatment of MK-801 (1 mg/kg) partially attenuated the phosphorylation of ERK and MEK1 by...
ECS in the cerebral cortex and cerebellum. In the hippocampus, however, phosphorylation of these kinase was attenuated by relatively high dosage of MK-801 (2 mg/kg). In all of the observed regions, MK-801 did not attenuate the phosphorylation of ERK and MEK1 any more at an extreme dosage (8 mg/kg). ECS increased the phosphorylation of 46 kDa JNK and SEK1 in the cerebral cortex and hippocampus. In the cerebellum, ECS only increased the phosphorylation of SEK1. Pretreatment of MK-801 attenuated the phosphorylation of 46 kDa JNK only in the cerebral cortex, and increased that of SEK1 only in the hippocampus after ECS. ECS increased the phosphorylation of p38 and MKK6 but MK-801 pretreatment blocked an increase in the phosphorylation of p38 induced by ECS almost completely in all of the observed brain regions. This attenuation of the phosphorylation of p38 was dependent upon the dosage of MK-801.

These findings indicate that NMDA receptor activation is partially involved in the ECS-induced c-Fos expression in all of the observed brain regions. I suggest that both activation of MAPK after ECS and involvement of NMDA receptor in MAPKs activation are different among various brain regions and MAPKs.

Key Words : ECS, rat brain, NMDA receptor antagonist, MAPK

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