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17 β-Estradiol Valerate Reduces Protein Disulfide Isomerase through Neurodamage of Ischemic Rat Brain

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Neuronal death seems to play crucial roles in the cognitive deficits of neurodegenerative diseases. Cellular homeostatic adaptation to cerebral ischemia is complex and contains changes in gene expression and signaling pathways. More recently, it has become increasingly clear that 17 β-estradiol valerate(EV) plays neuroprotective effects when administered before an ischemic insult. Protein disulfide isomerase(PDI) is a multi-functional protein mainly located in the endoplasmic reticulum(ER). PDI could be a target for unfolding protein response-induced gene expression. Recent studies have reported that over expressed PDI has a neuroprotective effect against hypoxia in neuronal cells. The present study was conducted to evaluate the effect of estrogen on the brain damage and on the transcriptional levels of PDI gene known to play a role in antioxidant systems after transient focal ischemia in rat brain. Focal ischemia was induced in rats by middle cerebral artery occlusion (MCAO). Group I was untreated. Group II received EV(200㎍/kg), Group III received EV and Phenylarsine oxide, known to PDI antagonist (100㎍/kg), and Group IV received ICI 118,551, known to EV receptor antagonist (100㎍/kg) i.p. beginning 3 days prior to MCAO. Twenty-four hours after reperfusion, the brain was taken and sectioned in coronal slices. The slices were stained with TTC or total RNA was extracted for the analysis of gene expression. Histopathological analysis revealed a significant ($P<0.05$) decrease in infarct size in the ipsilateral brain on group II compared with group I . The infarct sizes of group II was 37 ± 2% in the EV pretreamed animals

compared to 82 ± 4% in untreated group Ⅰ, respectively. In constract, infarct size of group Ⅲ was 57 ± 3% in the PAO pretreated animals to 37 ± 2% in EV treated group Ⅱ. Moreover, the levels of PDI transcription was significantly increased in EV group versus untreated group and ICI 118,551 treated group Ⅳ ($P<0.05$).

These finding suggest that PDI and EV may play a critical role in resistance to ischemic damage and that the elevation of levels of this antioxidant gene expression in the brain may have benificial effects against brain stroke.

Key words) *17β-estradiol valerate, ischemia, MCAO, neuroprotection, PDI, Phenylarsine oxide*