Estradiol Does Not Protect Against Cerebral Ischemic Injury After a Prolonged Intervening Period of Ovarian Hormonal Loss.

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Many studies support the belief that hormone therapy (HT) of postmenopausal women decreases the risk for stroke. However, the results from the Women's Health initiative (WHI) reported that HT afforded no such benefit or increased risk. Since the majority of WHI subjects had not had normal ovarian function for many years prior to the initiation of HT, we hypothesized that a prolonged absence of circulating ovarian hormones after the menopause would affect the ability of estradiol to exert protective actions in stroke injury. We (1) ovariectomized (OVX) adult C57BL/6 mice, implanted 10 weeks later with capsules containing either oil or 17 -estradiol (E_2) for 1 week; (2) OVX adult mice of equivalent age, implanted immediately with oil or E_2 capsules for 1 week (controls). Mice then underwent experimental ischemia by permanent occlusion of the middle cerebral artery. Cortical, striatal and total infarct volumes were measured using 2,3,5-triphenyltetrazolium chloride staining at 24 h after the onset of ischemic injury. We report that E_2 exerts powerful protection in the age-matched control animals. In marked contrast, E_2 does not reduce the infarct volume in either the cortex or the striatum when treatment is initiated after a prolonged period of hormonal loss. These data parallel the results of the WHI showing that women who are postmenopausal for a decade prior to the initiation of HT are not protected against stroke. Such findings point to the importance of initiating HT at the time of menopause, in preference to taking HT after a prolonged postmenopausal period.

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