The menopause may be associated with hippocampal volume reduction

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[Introduction]

Many studies report the neuroprotective effects of estrogen and describe the relation between estrogen therapy and hippocampal volume [1], the association between hippocampal glucose metabolism and cerebrospinal fluid 17β-estradiol concentration in postmenopausal women [2]. These previous studies suggest a significant correlation between estrogen and hippocampal volume; therefore, menopause may affect hippocampal volume atrophy. To the best of our knowledge, no study has reported a correlation between age at menopause and hippocampal volume. The aim of the present study is to investigate hippocampal volume change in normal adult women divided into the premenopausal group and postmenopausal group using high spatial resolution T1-weighted images obtained using 3.0-T scanners and voxel-based morphometry (VBM) [3].

[Materials and Methods]

Subjects with a Mini-Mental State Examination [4] score of 26 or lower were excluded from this study. The age at menopause was interviewed from all subjects. Subjects with the following findings were excluded from the study: brain tumors, infarctions, hemorrhage, and white matter lesions graded higher than grade 2 of Fazekas's classification [5]. We then divided the remaining 171 subjects. On a 3.0-T scanner (Signa EXCITE HDx, GE Medical Systems, Waukesha, WI, USA), MRI data were obtained with 8-channel brain phased-array coil. Three-dimensional fast spoiled-gradient recalled acquisition in the steady state (3D-FSPGR) was used to obtain 180 contiguous sagittal T1-weighted images with a slice thickness of 1.0 mm (TR / TE = 5.3 / 1.8 ms; inversion time = 450 ms; flip angle = 15°; field of view = 24 cm; number of excitations = 0.5; 256 × 256 pixel matrix). An acceleration factor of R = 2.0 was employed for parallel imaging using the Array Spatial Sensitivity Encoding Technique. We used Statistical Parametric Mapping 5 [6]. The 3D-FSPGR images in native space were bias-corrected, spatially normalized, and segmented into gray matter, white matter, and cerebrospinal fluid images [3]; the voxel sizes of the normalized images were 2 × 2 × 2 mm. The affine regularization space template from the International Consortium for Brain Mapping was changed from the European to the East Asian brain template. During the modulation step, the voxel values of the normalized gray and white matter images were multiplied by a measure of the relative volumes of the warped and unwarped structures derived from the nonlinear step of spatial normalization (Jacobian determinant). The resulting gray matter images were smoothed with a Gaussian kernel of 6 mm full width at half maximum. Statistical significance for gray matter volume between the premenopausal group and postmenopausal group was tested with age and the total intracranial volumes were included as confounding covariates. To test hypotheses with respect to regionally specific group effects, the estimates were compared with two linear contrasts (increased or decreased gray matter volume). The significance of each region was estimated by distributional approximations from the theory of random Gaussian fields. A *P* value of less than 0.05 corrected with false discovery rate in voxel difference and a cluster size greater than 30 voxels was considered to be statistically significant.

[Results]

Gray matter volume of the group of premenopausal women was compared with that of postmenopausal women using VBM analysis. Significant hippocampal volume reduction was found bilaterally in the postmenopausal group compared with the premenopausal group (Figure). MNI coordinates of peak voxel were 26, –26, –18; max *T* value = 4.51, max *P* value = 0.031 for right hippocampus, and –30, –18, –24; max *T* value = 3.59, max *P* value = 0.043 for left hippocampus.

[Discussions and Conclusion]

Lord et al. studied the relation between estrogen therapy and hippocampal volume in estrogen therapy users, past users, never users, and men, and suggested a positive association between estrogen and hippocampal volume [1]. In the present study, a significant decrease in gray matter volume was found in the hippocampus bilaterally in the postmenopausal group compared with the premenopausal group. The results of the current study suggest that the decreased release of estrogen in menopausal women may be associated with hippocampal volume reduction. Figure

[Reference]

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