traits might be more susceptible to depression or anxiety disorders.

Regional brain volume in amygdala showed no significant correlation with the score of HA in the current study sample, which is consistent with previous studies reviewed below. For example, Hariri et al. (2002) reported no significant association between amygdala responsivity/morphology and individual differences in HA, although they reported genetic contribution (5-HTTLPR) to amygdala responsivity to fearful stimulus (Hariri et al. 2002; Pezawas et al. 2005). Similarly, Omura et al. (2005) found no significant correlation between amygdala volume and neuroticism using VBM in 41 healthy individuals, although they reported a significant association between gray matter concentration and neuroticism without intensity modulation. In addition, Wright et al. (2006) found no correlation between amygdala volume and neuroticism in 28 healthy subjects. Previous studies, most of which reported smaller-than-normal hippocampus, have consistently revealed no volumetric abnormality involving the amygdala in patients with PTSD (reviewed in Rauch et al. 2006), although one study reported small amygdala volume in cancer survivors with intrusive recollections compared with those without such symptom (Matsuoka et al. 2003). However, the reasons for a consistent lack of association with HA in the amygdala in these studies including ours, and of structural MRI reports of reduction in amygdala volume in PTSD, remain unclear. In consistent with the current results, recent lesion studies suggested that the human amygdala may be recruited during phenomenal affective states in the intact brain but is not necessary for the production of these states (Anderson and Phelps 2002). Thus, the failure of amygdala size to relate to anxiety trait scores in our study may fit well with the hypothesis that human amygdala may not be critical for emotion per se. Another possibility may be that the functional heterogeneity of the amygdala, which is divided into functionally distinctive subnuclei, might obscure the association. This speculation may be supported by our finding of a subthreshold association between HA and the left amygdala of 4-mm FWHM smoothed images of female subjects. To clarify this issue, therefore, studies with larger sample sizes for both genders are necessary.

Here we address the methodological considerations and limitations of the current study. First, cross-sectional study design cannot access the etiology of the neuroanatomical correlates of anxiety-related traits, although the current study design minimized aging and pathological effects on regional brain volume. Second, the number of male subjects was disproportionally larger than that of females. Thus, the ability to identify female-specific correlation might be weaker than that to find male-specific correlation, although in fact the present analysis revealed a female-specific correlation. Third, gender differences in age and SES were observed in the current study sample, although statistical analyses controlling these effects preserved a significant interaction with gender on the association between HA and regional volume in anterior prefrontal cortex. Fourth, the specificity of current hippocampus findings for HA was limited in the current study because a significant positive correlation between the regional gray matter volume in right hippocampus and the score of reward dependence of TCI in the combined subjects ([34, -30, -8], FWE-corrected $P = 0.002$ with 3.5 ml SV, $z = 3.79$) was found with no significant gender difference in the correlation.

In conclusion, the present study provides evidence that smaller right hippocampal volume contributes to higher anxiety-related traits in human individuals. These results are consistent with a previous study reporting small right hippocampal volume as predisposing factor to develop stress-related disorders. Together with the female-specific relationship between left anterior prefrontal cortical volume and HA, the present findings may at least partly explain individual and gender differences in the susceptibility to develop anxiety and depressive disorders.

## Notes

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