Supplementary Material

A pilot study on amygdala volumetric changes among young adults with childhood maltreatment histories after a mindfulness intervention

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Section 1: Negative association between PSS score changes and gray matter concentration changes

S1.1 Introduction and Methods

To directly compare with the previous study [1], we conducted Voxel based Morphometry (VBM) analysis using the same protocol as in the previous study [1] . For direct comparison with the previous study, an “un-modulated” version of the VBM protocol was used to estimate gray matter concentration as in the previous study. The VBM analysis was conducted using the CAT12 toolbox [2] and SPM12 [3]. The MPRAGE anatomical MRIs of each subject from all time points were segmented into gray matter, white matter and cerebrospinal fluid using the longitudinal model of CAT12. The mean MRI of all time points was created for each subject then segmented, which was used to estimate the normalization parameters for the MRI from each time point, which was then applied on the segmentation of MRIs from each time point. Then the segmentations were co-registered to the Montreal Neurological Institute (MNI) template without modulation and smoothed with Gaussian kernel of full width at half maximum 8 by 8 by 8 mm^3.

Multiple linear regression analysis was conducted in SPM12 with data from the mindfulness group with the difference (post minus pre-intervention) maps calculated from the smoothed gray matter volume estimates using the PSS score changes of each subject as the regressor. Statistical threshold was set at $p < 0.05$ uncorrected, no threshold was set on cluster size. Anatomical masks of bilateral amygdalae, obtained from the neuromorphometrics label template in SPM12 software, were imposed on the statistical maps to constrict our investigation within our regions of interest. We used the 3dClustSim function in the AFNI (afni.nimh.nih.gov) package to determine the appropriate threshold for multiple comparison corrections within bilateral amygdalae, which suggest a minimum of 74 continuous voxels that pass uncorrected *p*-threshold of $p < 0.05$ (out of a total of 375 voxels) for each amygdala to reach to reach a FDR corrected significance level of $p < 0.05$. For illustrative purposes, after we identified significant voxels, we used the MarsBar toolbox [4] of SPM12 to extract individual subject data of the average value of gray matter concentration change from significant clusters, and used for a scatter plot with PSS score change.

S1.2 Results

One cluster was identified in each side of the amygdala showing negative associations with PSS score changes, although only the cluster in the left amygdala passed the cluster size threshold for FDR corrected significance level of $p < 0.05$. Information about the clusters are displayed in Figure S1.A and Table S1.Scatter plots between the average gray matter concentration change and PSS score change are displayed in Figure S1.B and Figure S1.C. The strength of the associations was represented by Pearson correlations of $r = -0.75$ ($p < 0.01$) between left amygdala gray matter concentration change and PSS score change and $r = -0.64$ ($p < 0.01$) for that of the right amygdala.

Table S1

Clusters negatively associated with PSS score change within the mindfulness group on the difference (post minus pre-intervention) MRIs of unmodulated gray matter concentration within bilateral amygdalae. Clusters that pass the minimum size threshold of 73 voxels for FDR corrected significance level of $p < 0.05$ are highlighted in **bold**.

VBM Metric	Cluster size	t value	Z value	p-value uncorrected	side	Peak voxel MNI coordinates (x, y, z)		
Unmodulated Concentration	**148**	**3.749**	**3.032**	**0.001**	L	**-24**	**-4.5**	**-25.5**
	66	3.062	2.610	0.005	R	28.5	-3	-24

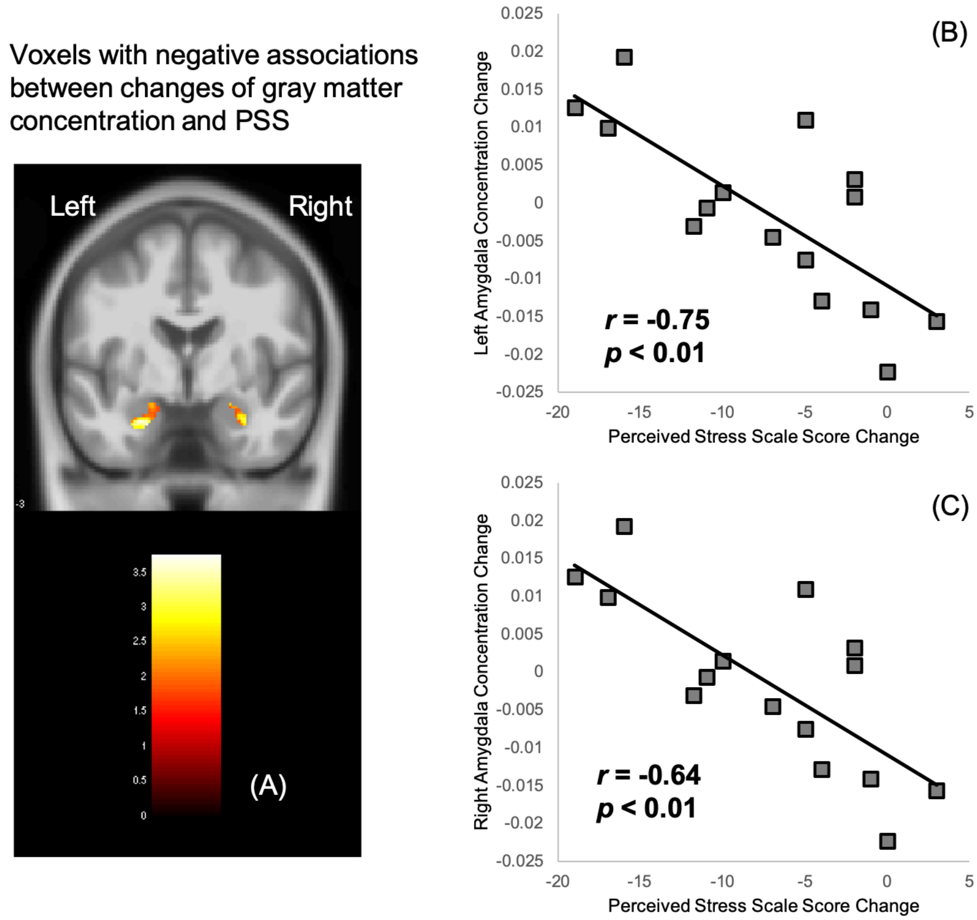

Figure S1: (A) Clusters in bilateral amygdalae showing significant correlations with PSS score changes. (B) Scatter plot between average gray matter concentration change in the left (B) and right (C) amygdala and PSS score changes.

S1.3 Discussion

Results from this additional VBM analysis which identified a significant cluster in the left amygdala with negative correlation with PSS score changes are very similar with the results from Freesurfer estimate in the main paper These results are contrary from the positive associations between PSS score change and changes of right amygdala gray matter concentration reported in the previous study [1]; such contradiction has been discussed in detail in the Discussion section of the main paper, with regard to multiple differences between the present study and the previous study, particularly the much less amount of home practice which could have contributed to the different neural changes, similar to the contradictory neural changes in response to different level of motor skill practice in previous studies [5,6].

Section 2: Correlation with hippocampal volumetric changes
Exploratory analyses were conducted to investigate whether there were any significant associations between volumetric changes of the amygdala and the hippocampus. Pearson correlation was used to calculate the pairwise correlation between left and right amygdala and hippocampal volumetric changes (post- minus pre- intervention volumes) within the mindfulness group. Results showed significant correlation between the volumetric changes of the right amygdala and right hippocampus (r = 0.704, p = 0.003, Figure S2, Table S2). This preliminary finding highlights the importance for investigating the relationship between the amygdala and hippocampal changes in response to the mindfulness intervention in future studies.

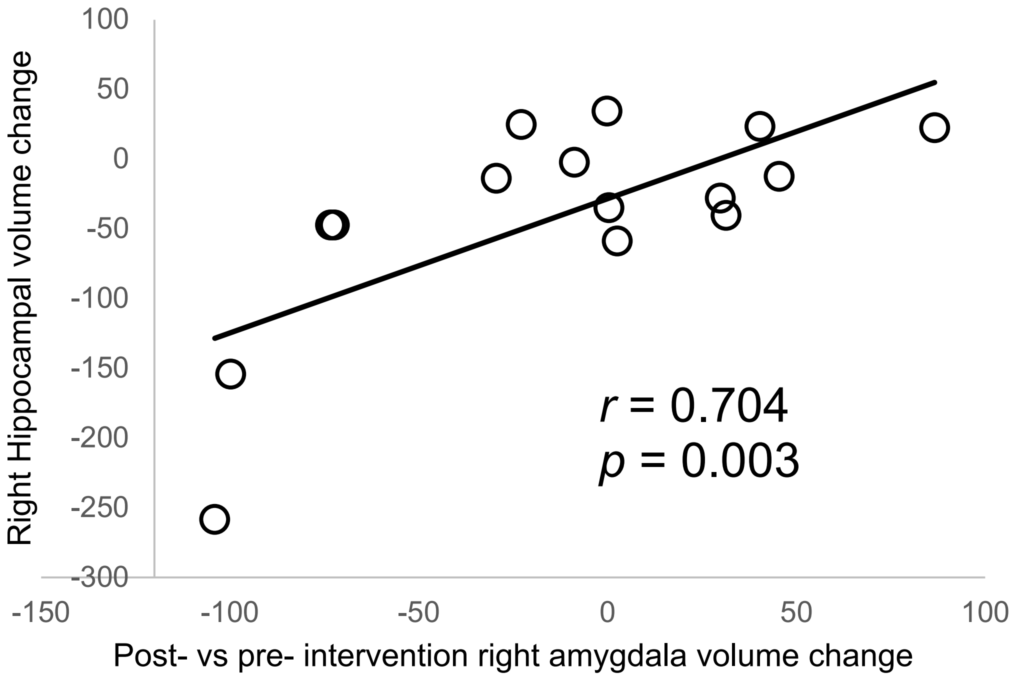

Figure S2: Correlation between volumetric changes of the right amygdala and right hippocampus.

Table S2
Pairwise correlation coefficients between the volumetric changes of left and right amygdala and hippocampus. (*: $p < 0.01$, $^\#$: p =0.06)

	Left Hippocampus	**Right Hippocampus**
Left Amygdala	0.329	0.211
Right Amygdala	0.490$^\#$	0.704*