Convergence of emotion processing on the right ventrolateral prefrontal cortex: Parametric mediation analysis of fMRI

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Introduction

Numerous fMRI studies have observed activity in two key regions of the central circuitry of emotion: the amygdala and prefrontal cortex. However, it remains poorly understood whether emotional responses involved a direct or an indirect pathway between these two regions. To clarify the cortical-sub-cortical interactions underlying emotional processing, we investigated how activity in different regions of the brain is related to emotional valence. This relationship could be direct without mediation through other regions, or be mediated indirectly via activity in other regions. We used parametric mediation analysis [1] to identify multiple brain mediators.

Materials and Methods

Ten healthy subjects participated in the study (3 males, 7 females; ranging in age from 23 to 45 years) with no history of neurological or psychiatric illness. Before each study, written informed consent was obtained from all of the participants. The ethics committee of the Tokyo Metropolitan Institute of Medical Science approved the study. All subjects completed six separate sessions on a Philips 1.5T whole-body magnetic resonance unit equipped with an 8-channel head coil. A 3-dimensional T1-weighted anatomical scan was obtained for structure reference. Functional time series were acquired with a gradient echo single-shot echo-planar sequence. The following acquisition parameters were used in the fMRI protocol: TR = 2000 ms, TE = 60 ms, FOV = 20 cm, and acquisition matrix = 64 × 64. We accordingly acquired 24 axial-oblique slices (5 mm thickness, 1-mm gap between slices, and 3.2 × 3.2 mm in-plane resolution), aligned in a plane along the axis connecting the anterior-posterior commissure plane. Stimuli were presented in a blocked design (total of 90 pictures). The pool of 90 pictures was divided into six sets of 15 pictures, which were randomly presented to six study blocks to minimize possible intensity carryover effects. After the fMRI experiments, the subjects rated their valence for each of the 90 pictures as experienced at the time of the initial presentation in the scanner on scales ranging from unpleasant (1) to pleasant (9) using a Self-Assessment Manikin. The functional imaging data were analyzed using BrainVoyager QX software. Voxel-wise t-scores for the group analysis were calculated and thresholded using $P < 0.01$ (FDR), followed by 135-voxel cluster size thresholding. The valence for each subject was normalized to full valence range (i.e., 1 to 9). The fMRI signals were averaged for the same valence for each subject and were excluded if there were less than two pictures for a valence. A total of 72 data points for the 10 subjects was used for analysis. For the mediation model, we selected as a predictor, a cortical or subcortical region that was significantly activated based on the above criteria, and then searched the brain for a mediator of the relationship between emotion-induced brain activity and the valences. Firstly, we identified the significant activated regions related to the emotional pictures. Then, using standard statistical parametric analysis, we identified the regions significantly correlated with emotional valence as predictors. Finally, the identified correlation regions, i.e., the predictors, were searched using parametric mediation analysis to identify correlations with each of the other regions.

Results and Discussion

Unpleasant pictures (subject's valence 1 to 3) positively activated the bilateral inferior and superior frontal gyri, precentral gyrus, middle and occipital gyri, fusiform gyrus, and right middle and inferior frontal gyri (e.g., Figure 1A). Positive signals were also detected in the thalamus, caudate, putamen, and amygdala. Conversely, negative fMRI signals were detected in the paracentral lobule and posterior cingulate of both hemispheres, and in the left supramarginal gyrus and precuneus. For these regions, we analyzed correlations with the valence (Figure 1B), and then parametric mediation analysis was used to identify the regions significantly correlated with valence. Figure 2 shows whether a predictor contains mediator regions. Areas of the visual cortex have mediators in the prefrontal cortices and amygdala; however, these areas were not mediators for other predictors. Interestingly, although the ventrolateral prefrontal cortex (VLPFC), BA47, contained no mediator of valence, the region was a mediator for all other predictors, indicating that emotion processing converges on the right VLPFC from other cortical and sub-cortical regions. Since the VLPFC shows activity during non-linguistic emotion [2,3] and lesion of the VLPFC causes difficulty in comprehending emotional body and facial gesturing [4], the VLPFC might be important in non-linguistic meaning and communication of emotional information.

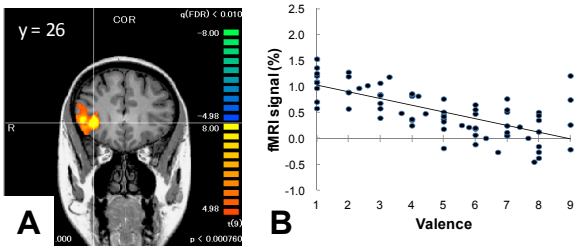

Fig. 1 (A) Coronal slice of a t-statistic map, showing parts of the prefrontal cortex. (B) Relationship between the signal in the inferior prefrontal cortex, BA47, and the valences.

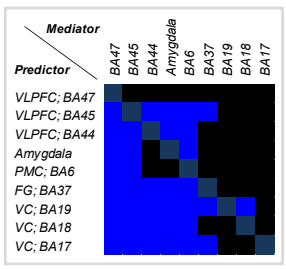

Fig. 2 Regional matrix of the right hemisphere obtained using mediation analysis. Blue cells show that the predictor has regions that are mediators of the valence (i.e., indirect pathway), whereas the black cells indicate that the predictor has no mediator regions (i.e., direct pathway). VLPFC: ventrolateral prefrontal cortex, PMC: premotor cortex, FG: fusiform gyrus, VC: visual cortex.

Conclusion

Parametric mediation analysis of fMRI revealed the convergence of emotion processing on the right VLPFC via the amygdala and other cortical regions.

References

[1] Wager et al., *Neuron* 59:1037-50, 2008; [2] Hariri et al., *Biol Psychiatry* 53:494-501, 2003; [3] Liberman et al., *Psychol Sci* 18:421-8, 2007; [4] Hornak et al., *Neuropsychologia* 34:247-61, 1996