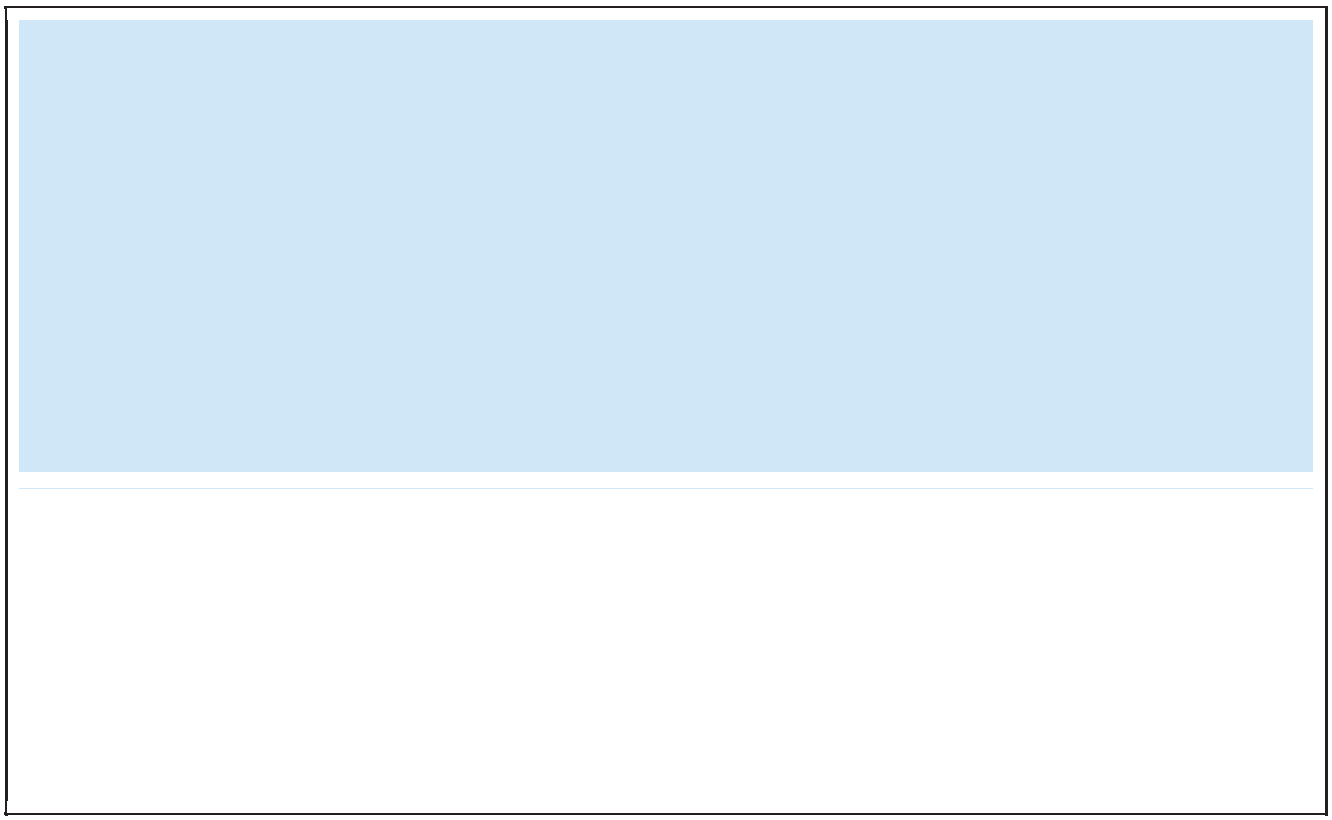
G C e I b e Se P ce a d e



excitement, and stress, thereby calling for control of the autonomic responses to the low-level physiological challenge [16]. The rostral part of the cingulate cortex has been consistently implicated in emotion regulation [18–21]. Thus, it is conceivable that the ACC integrates afferent information received from, for example the insula, signaling the presence of a stressor (e.g., unpleasant temperature or a state of hypoglycemia), and prepares the organism for the potential challenge [9]. Indeed, several studies have reported the co-activation or increased functional connectivity between the AI and the ACC in participants facing stress-

for the left STS and the left AI. Clearly, the noise-induced activation was significantly attenuated in the Chew condition as compared with in the NoChew condition.

Psychophysiological interaction (PPI)

We conducted PPI analysis to find brain regions in which functional connectivity (''Noise > NoNoise'') with the left AI was modulated by gum chewing (see Methods, fMRI data analysis). The contrast in functional connectivity between NoChew and Chew

enhance the connectivity from the STS to the AI, the Chew_Noise inhibits that connectivity.

Discussion

In this study, we investigated the neural effects that gum chewing, as a stress reducer, on noise-induced stress. The participants' rating of stress during fMRI scanning showed that the noise stimuli were effective in inducing stress and that gum chewing was able to reduce the level of this noise-induced stress. In a separate experiment with the same experimental conditions as this study, we recorded participants' skin conductance level (SCL), which is a valid physiological index of stress [32,33]. The noise

states'' [42]. Consistent with this view, we found that the functional connectivity between the dACC and the left AI was increased in the NoChew_Noise condition, as compared with the NoChew_NoNoise condition, reflecting an increased demand for the control of the autonomic responses to the noise.

It is important to note that although gum chewing by itself increased the functional connectivity between the dACC and the

sign during the whole experiment except during the chewing phase of a trial in the Chew condition (Figure 1). For each trial, the participant saw first this instruction and the fixation sign for 4 s. To measure the participant's baseline stress level, a computer version of the SVAS scale, a horizontal line with a moving cursor on it, was presented at the onset of the 5th second at the center of the screen, replacing the fixation sign (i.e., the SVAS-5). Participants rated their stress level from 0 to 100 by stopping a moving cursor on a horizontal scale; the initial direction of the cursor's movement was balanced across conditions to remove any effect of sensorimotor confounds. The SVAS scale was presented for 3 s, followed by the fixation sign for 12 s. During this period, a written instruction was presented with the fixation sign; for the Chew conditions, the instruction was ''Keep chewing,'' which prompted the participant to continue chewing as long as the instruction remained on the screen; for the NoChew conditions, the instruction was ''No chewing''; for the Noise conditions, in addition to the visual instruction, a noise stimulus was presented for 10 s from the beginning of the 10th second. For all the conditions, at the beginning of the 20th second, another SVAS scale was presented and the participants were asked to indicate their current level of stress (i.e., the SVAS-20) within 3 s. Finally, the fixation sign and the instruction of ''No chewing'' were presented again for 7 to 9 seconds. Each full trial lasted for 29 to 31 seconds and the participant was asked to fixate on the fixation sign throughout the trial. The scanning session contained 64 trials (16 per condition) and lasted about 32 minutes. Participants viewed the screen through an angled mirror on the head-coil. Auditory stimuli were presented via an MRI-compatible headphone.

fMRI data acquisition and analysis

A Siemens 3T Trio scanner with a standard head coil at the Beijing MRI Center for Brain Research was used to obtain T2*-weighted echo-planar images (EPI) with blood oxygenation level-dependent (BOLD) contrast (matrix, 64×64, in-plane resolution, 3 mm$\times$3 mm). Thirty-seven transversal slices of that covered the whole brain were acquired according to an interleaved order with a 0.4 mm gap (repetition time: 2200 ms, echo time: 30 ms, field of view: 220 mm * 220 mm, flip angle: 90°, matrix size: 64*64, voxel size: 3.4 mm * 3.4 mm * 3.5 mm).

The obtained fMRI data were preprocessed and analyzed using Statistical Parametric Mapping software SPM8 (Wellcome Trust Department of Cognitive Neurology, London, UK). The first five volumes of each session were discarded to allow stabilization of magnetization. Preprocessing was done with SPM8 default settings. All images were transformed into standard MNI space and re-sampled to $2\times2\times2$ mm^3 isotropic voxel. The data were then smoothed with a Gaussian kernel of 8 mm full-width half-maximum to accommodate inter-subject anatomical variability.

Analyses on BOLD activation

Statistical analyses based on GLM were performed first at the participant level and then at the group level. Each trial was

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