synaptic cleft (Canli and Lesch 2007). Given that s carriers are vulnerable to depression and depressed individuals are characterized by negative self-schema, we hypothesize that

Imaging Parameters

Functional brain images were acquired using 3.0-Tesla Siemens Trio at the Beijing MRI Center for Brain Research. Blood oxygen-level–dependent (BOLD) gradient echo planar images were obtained using a 12-channel head coil (64 × 64 × 32 matrix with 3.44 × 3.44 × 5.0-mm spatial resolution, repetition time (TR) = 2000 ms, echo time (TE) = 30 ms, flip angle = 90°, field of view = 24 × 24 cm) while participants performed trait judgments. A high-resolution T_1-weighted structural image (256 × 256 × 144 matrix with a spatial resolution of 1 × 1 × 1.33 mm, TR = 2530 ms, TE = 3.37 ms, inversion time (TI) = 1100 ms, flip angle = 7°) was subsequently acquired.

Imaging Data Analysis

The functional image data were analyzed using the general linear model for event-related designs in the statistical parametric mapping (SPM) software (the Wellcome Trust Centre for Neuroimaging, London, UK). The functional images were corrected for differences in acquisition time between slices for each whole-brain volume and realigned within and across runs to correct for head movement. Six movement parameters (translation: , , and rotation: pitch, roll, yaw) were included in the statistical model. The anatomical image was coregistered with the mean realigned image and then normalized to the standard T1 Montreal Neurological Institute (MNI) template. The normalizing parameters were applied to the functional images, which were resampled to 2 mm of isotropic voxel size and spatially smoothed using an isotropic Gaussian kernel of 8-mm full-width half-maximum.

Trials during self-reflection were sorted into 4 conditions based on the valence of each trait adjective and participants' responses regard-

(6/30/26), SMA (3/18/57), and dmPFC (6/30/39; 0/36/42), and the AI/IF cluster included the bilateral IF (left: −45/21/30; right: 42/18/30) and bilateral AI (left: −33/21/−3; −36/15/−12; right: 33/21/−12; 42/21/−15). However, l/l genotype group did not show any significant activation during negative self-reflection.

To examine whether judging negative traits as high in self-relevance and judging positive traits as low in self-relevance similarly activated the dACC/dmPFC and the AI/IF in the s/s genotype group, we calculated the contrasts of $\text{Negative}_{(\text{high} - \text{low self-relevance})}$ and $\text{Positive}_{(\text{low} - \text{high self-relevance})}$, respectively. Both contrasts revealed significant activations in the dACC/dmPFC and AI/IF clusters in s/s genotype group ($\text{Negative}_{(\text{high} - \text{low self-relevance})}$: dACC/dmPFC (6/30/36; 0/42/39), left AI (−30/21/−18; −33/21/−6), left IF (−54/21/30; −45/18/39); right AI (42/27/−15; 33/24/−12); $\text{Positive}_{(\text{low} - \text{high self-relevance})}$: dACC/dmPFC (6/27/39; 0/36/42; 0/24/54), left AI/IF (−45/18/27; −36/21/3; −42/18/−15), right AI/IF (36/21/3; 48/18/−9, 42/12/36), Supplementary Fig. 4). A conjunction analysis of the 2 contrasts further confirmed that among s/s genotype participants, there were common dACC/dmPFC and bilateral AI/IF activations when judging negative traits as highly self-relevant and when judging positive traits as low in self-relevance (Fig. 1). Direct comparison of these 2 contrasts did not show any significant difference, suggesting comparable dACC/dmPFC and AI/IF activity linked to the acknowledgement of one's possession of negative traits and one's lack of positive traits. Similar conjunction analysis did not show any significant activation in l/l genotype group.

We next examined the relationship between subjective ratings and brain activity during negative self-reflection. A linear regression analysis showed a positive correlation between AI/IF activity and self-reported distress across all participants (right: $\beta = 0.422$, $P = 0.001$, Fig. 1 ; left: $\beta = 0.333$, $P = 0.009$). Individuals who felt more distressed when thinking about their negative traits activated the bilateral AI/IF more strongly during negative self-reflection. Separate regression analyses were also conducted for s/s and l/l genotype groups. We found that the relationship between AI/IF activity and self-reported distress was significant in the s/s genotype group (right: $\beta = 0.384$, $P = 0.036$, left: $\beta = 0.399$, $P = 0.029$) but not in the l/l genotype group (right: $\beta = 0.312$, $P = 0.093$, left: $\beta = 0.152$, $P = 0.423$).

We then conducted mediation analysis to test whether the type 0.309,

Experiment 2

Participants judged more positive traits as high in friend-relevance and more negative traits as low in friend-relevance ($F_{1,\ 38} = 30.646$, $P < 0.001$). A similar analysis on response speed did not show any significant effect (Ps > 0.2). Response ratio and RTs did not significantly differ between s/s and l/l genotype groups (Fs < 1, Supplementary Fig. 5).

fMRI data analysis focused on a 2-sample -test of the contrast of Negative$_{(\text{high} - \text{low friend-relevance})}$ minus Positive$_{(\text{high} - \text{low}}$

precuneus during self-referential processing (Northoff et al. 2006; Schmitz and Johnson 2007

negative self-schema. In contemporary societies, people are often confronted with negative social feedback and social comparisons in daily life, both of which may provoke negative self-view (Swallow and Kuiper 1988; Swann et al. 1992) and may in turn lead to the core symptom of depression—negative schema of the self (Kuiper and Olinger 1986; Haaga et al. 1991; McIntosh and Fischer 2000).

Our findings may have implications for treatment of depression. Established treatments for depression include medications and psychotherapy. Antidepressant medication