

5-HTTLPR polymorphism modulates neural mechanisms of negative self-reflection

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Supplementary Results

Do the dACC and AI encode arousal during negative self-reflection?

A possible account of the differential dACC/dmPFC and AI activity related to negative self-reflection between the s/s and l/l genotype groups is that the activity in these brain regions might arise from encoding of different levels of arousal associated with negative vs. positive trait adjectives. To test this, we first assessed genotype differences by asking participants to rate their arousal level induced by negative and positive trait adjectives used during self-reflection on a 7-point Likert scale (0 = not aroused at all, 6 = extremely aroused). A 2 (valence: positive vs. negative) x 2 (self-relevance: high vs. low) ANOVA of arousal rating scores did not show significant difference in arousal between positive and negative traits ($F(1,58)=1.6$, $p=0.212$). The main effect of self-relevance did not reach significance ($F(1,58)=1.8$, $p=0.183$), suggesting comparable arousal induced by self-relevant and self-irrelevant items. There was a significant interaction of valence and self-relevance ($F(1,58)=38.3$, $p<0.001$), suggesting higher arousal to positive trait adjectives that were high vs. low in self-relevance but lower arousal in response to negative traits that were rated as high vs. low in self-relevance. However, none of these effects were significantly different between the s/s and l/l genotype groups ($F_s<1$, $p_s>0.464$, Fig. S6).

Next we performed a whole-brain analysis to assess whether differences in arousal in response to negative and positive trait adjectives also led to increased dACC/dmPFC and AI activity. We first sorted trials into four conditions based on the valence and arousal ratings of trait adjectives. For each participant, the positive and negative trait adjectives were subdivided into categories of low and high arousal. We then calculated the contrast of $\text{Negative}_{(\text{high} - \text{low arousal})}$ minus $\text{Positive}_{(\text{high} - \text{low arousal})}$ to identify brain activations associated with differential arousal evoked by negative vs. positive trait adjectives. This contrast did not show any significant activation in either genotype group. Moreover, a whole-brain two sample t-test of this contrast did not show any significant difference in neural activity between the s/s and l/l genotype groups either. Thus the two genotype groups did not differ significantly in neural responses to arousal related to negative and positive trait words and the dACC/dmPFC and AI activity observed during self-reflection was specific to encoding of the self-relevance of negative vs. positive personality traits.

Table S1. Brain activations observed in s/s genotype participants in Experiment 1 (p<0.05, topological FDR corrected)

Region	x/y/z (MNI)	t-value	cluster size
Negative (high - low self-relevance) minus Positive (high - low self-relevance)			
Frontoinsular cortex (L)			
Anterior insula (L)	-33/21/-3	10.34	1268
Inferior frontal (L)	-45/21/30	8.40	
Medial prefrontal cortex			
Anterior Cingulate	6/30/39	9.78	878
SMA	3/18/57	8.30	
Frontoinsular cortex (R)			
Anterior insula (R)	33/21/-12	8.67	916
Inferior frontal (R)	45/18/33	5.47	
Positive (high - low self-relevance) minus Negative (high - low self-relevance)			
Precuneus	9/-36/51	6.73	523
Lingual Gyrus(R)	21/-57/-9	4.59	89
Negative (high - low self-relevance)			
Anterior insula (L)	-33/21/-6	6.04	288
Anterior insula (R)	42/27/-15	5.45	229
Anterior Cingulate	6/30/36	6.23	629
Inferior frontal (L)	-54/21/30	4.98	106
Positive (high - low self-relevance)			
<i>None significant brain regions</i>			
Positive (low - high self-relevance)			
Frontoinsular cortex (L)			903
Anterior insula (L)	-36/21/3	5.98	
Inferior frontal (L)	-45/18/27	6.24	
Anterior insula (R)	36/21/3	6.87	462
Medial prefrontal cortex			
Anterior Cingulate	6/27/39	5.39	444
Supplementary Motor Area	0/24/54	6.08	
Positive - Negative			
Dorsal medial prefrontal	-3/57/42	5.29	153
Negative - Positive			
<i>No significant activation</i>			
High - Low self-relevance			
<i>No significant activation</i>			

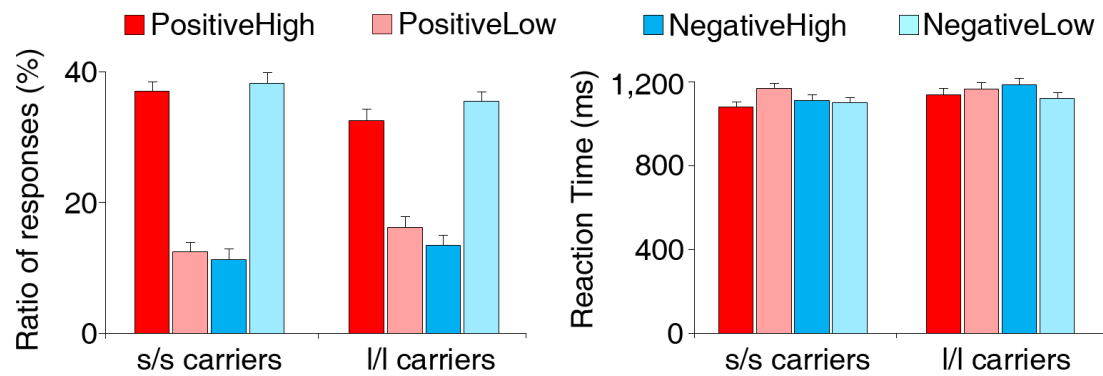


Figure S1. Behavioral Performance during Scanning in Experiment 1. Participants judged more positive traits as high in self-relevance (rated with 3 or 4) and more negative traits as low in self-relevance (rated with 1 or 2) ($F(1, 58)=133.8, p<0.001$). Participants took longer time to acknowledge their negative traits but shorter time to admit their positive traits ($F(1, 58)=11.0, p=0.002$). However, the patterns of response ratio and RTs did not significantly differ between s/s and l/l genotype groups (Response ratio: $F(1, 58)=2.8, p=0.098$; RTs: $F(1, 58)=0.04, p=0.841$).

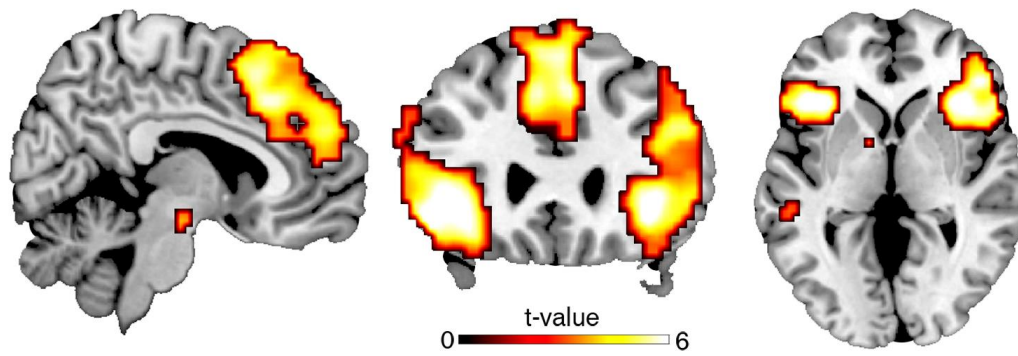


Figure S2. Results of Whole Brain Analyses in Experiment 1 across All Participants. The contrast of Negative_(high - low self-relevance) minus Positive_(high - low self-relevance) across all participants showed significant activations in the bilateral frontoinsula cortex (FI) (left FI: -33/21/-6; -45/21/27; right FI: 48/27/-6, 42/24/3) and a cluster in the midline cortical structure including the dACC, dmPFC, and SMA (-3/21/54, -3/33/42).

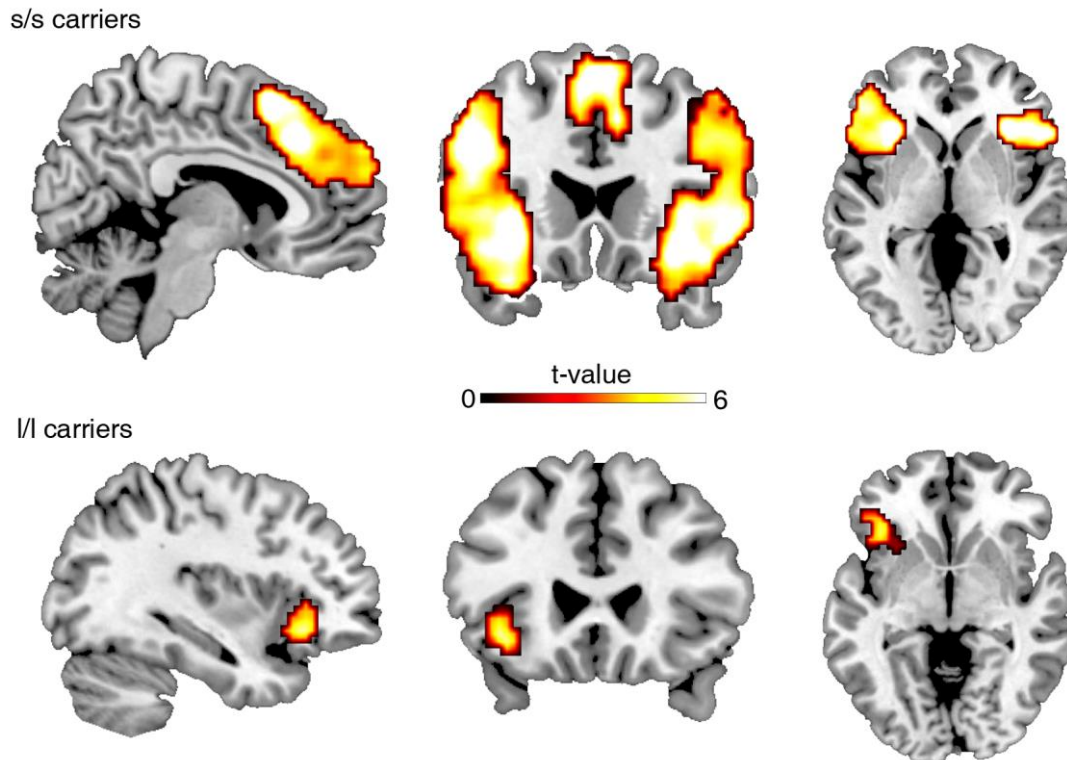
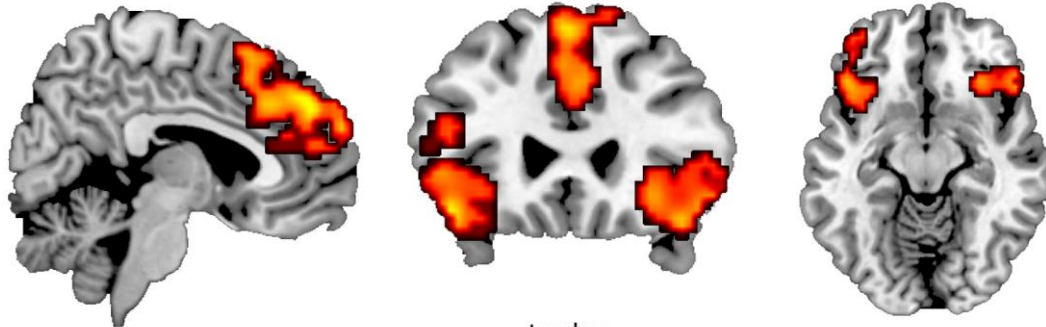


Figure S3. Results of Whole Brain Analyses in Experiment 1 for the s/s and l/l genotype groups. The contrast of Negative (high - low self-relevance) minus Positive (high - low self-relevance) showed stronger activations in the dACC (6/30/39; 3/18/57; 6/30/26), left AI (-33/21/-3; -36/15/-12); right AI (33/21/-12) at the threshold of $p < 0.05$ (topological FDR corrected) in the s/s genotype participants. This contrast in l/l genotype group did not show any significant activation at the threshold of $p < 0.05$ (topological FDR corrected). The left AI activation (-36/24/-9) observed in l/l genotype participants was significant at the threshold of $p < 0.001$, uncorrected.

NegativeHigh vs. NegativeLow



PositiveLow vs. PositiveHigh

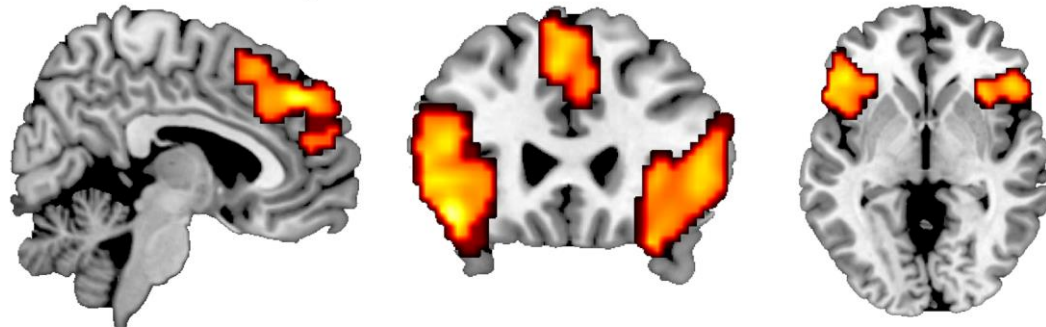


Figure S4. Results of Whole Brain Analyses in Experiment 1. The contrast of Negative (high - low self-relevance) resulted in stronger activation in the dACC (0/42/39), the left AI (-45/27/-15; -33/21/-21) and the right AI (42/27/-18; 30/27/-9) in s/s genotype participants. The contrast of Positive (low - high self-relevance) showed stronger activations in the dACC (3/42/39), the left AI (-45/27/-12; -33/21/-24), and the right AI (30/24/-24; 33/21/0; 48/21/3) in s/s genotype participants.

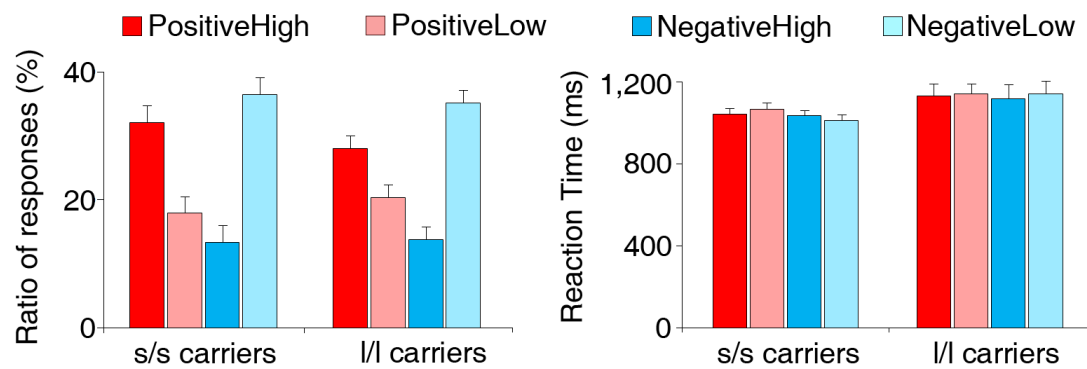


Figure S5. Behavioral Performances during Scanning in Experiment 2. Participants judged more positive traits as high in friend-relevance and more negative traits as low in friend-relevance ($F(1, 38)=30.6, p<0.001$). Similar analysis was conducted on RTs but did not show any significant effect ($p>0.2$). Moreover, behavioral performances did not significantly differ between the s/s and l/l genotype groups (Response ratio: $F(1, 38)=0.5, p=0.488$; RTs: $F(1, 38)=1.0, p=0.332$).

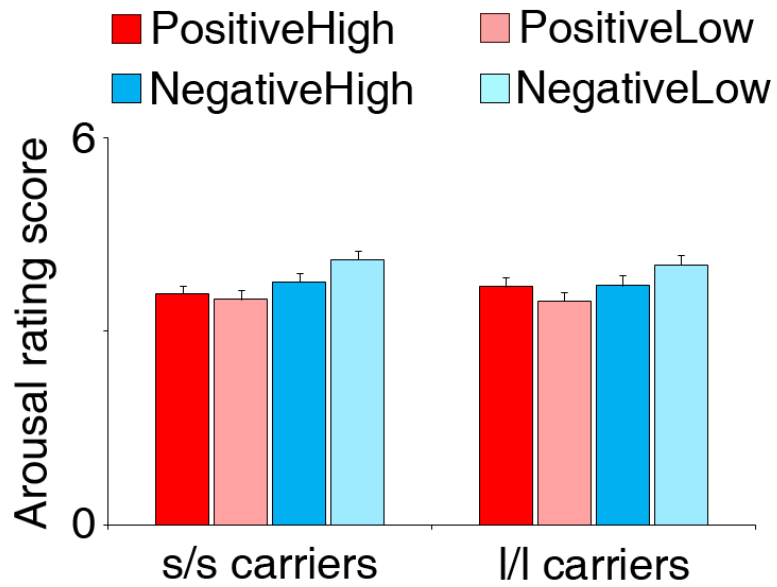


Figure S6 Rating Scores of Arousal in Experiment 1. There was a significant interaction of Valence (positive vs. negative) x Self-relevance (high vs. low) on arousal rating scores ($F(1, 58)=38.3, p<0.001$), suggesting higher arousal to positive trait adjectives that were rated high vs. low in self-relevance but lower arousal in response to negative traits that were rated high vs. low in self-relevance. Moreover, the pattern of arousal ratings did not differ between the s/s and l/l genotype groups ($F(1, 58)=0.5, p=0.464$).