Supplemental Material

Todd et al. Neurogenetic variations in norepinephrine availability enhance perceptual vividness

Supplemental Results

Memory analyses

Two participants failed to complete the recognition memory task one week later. We thus analyzed memory data from 19 deletion carriers and 18 non-carriers.

Because our primary interest was in potential genetic influences on the relation between perceptual and mnemonic vividness, we first conducted item analyses to examine the influence of emotionally enhanced vividness (EEV) and rated arousal on memory vividness for each image, averaged across participants, in *ADRA2b* deletion carriers and non-carriers separately. Hierarchical multiple regressions were performed on memory vividness for each group with measures of objective salience for each image (hue, scene complexity and visual salience) entered at the first level and EEV for each image entered at the second level. EEV did not predict memory vividness in either group, *p*s > 0.37. In contrast, arousal predicted memory vividness in both groups - at least at trend level, deletion carriers: $R^2\Delta = 0.04$, $p = 0.07$; non-carriers: $R^2\Delta = 0.08$, $p = 0.01$.

In order to directly compare the influence of genotype on subsequent memory vividness and recognition memory accuracy for emotionally arousing and neutral images one week later, we next conducted repeated measures ANOVAs with emotion category (negative, neutral, positive) as the within-subject factor and *ADRA2b* genotype (Deletion, No Deletion) as the between-subject factor. For recognition memory accuracy (proportion of hits, or correctly remembered images) there was a main effect of emotion category, $F(2, 70) = 12.38$, $p < 0.001$, $\eta_\rho^2 = 0.26$, with negative images most vividly remembered. There was no main effect of *ADRA2b* genotype and no interaction between *ADRA2b* genotype and emotion category, *p*s > 0.69. For memory vividness (for correctly recalled images) we observed a similar pattern of results. There was again a main effect of emotion category, $F(2, 70) = 8.83$, $p < 0.001$, $\eta_\rho^2 = 0.20$, with negative images being more vividly remembered than neutral or positive images. And again, there was no main effect of *ADRA2b* genotype and no interaction between *ADRA2b* genotype and emotion category, *p*s > 0.40. Although we found no effect of *ADRA2b* on emotional modulation of memory, it should be noted that effects of *ADRA2b* on emotional enhancement of memory have been found in behavioral studies with substantially larger sample sizes. In contrast, previous smaller-N imaging studies have similarly failed to find effects of *ADRA2b* on emotional enhancement of memory.

Path analyses

In addition to models described in the main text, a number of additional models were tested. The role of the amygdala and the left lateral occipital complex (LLOC) has been demonstrated before (Todd et al., 2012). The parametric analysis led to models investigating how and if EEV modulates activity in ventromedial prefrontal cortex (VMPFC) and a right parietal region.

Model 1 (Fig. S1) is similar to the complex model described in the main paper extended by an indirect path from VMPFC via LLOC to EEV. The data of deletion carriers do not fit the model well ($X^2(2) = 2.99$, $p = 0.05$, SRMR = 0.023, PGFI = 0.199, AICc = 62.85), but model fit is decent for non-carriers ($X^2(2) = 2.2$, $p = 0.11$, SRMR = 0.035, PGFI = 0.199, AICc = 61.28). It further demonstrates that in deletion carriers EEV does not modulate VMPFC activity by an indirect path via LLOC ($b = 0.06$, $p = 0.192$), whereas for non-carriers the direct path from VMPFC to EEV is not significant ($b = -0.01$, $p = 0.677$) (Tab.1).

Model 2 (Fig. S2) supports the assumption that EEV does not modulate VMPFC activity via an indirect pathway in deletion carriers (b = 0.06, p = 0.154). Hence, model fit is poor for deletion carriers ($X^2(2)$ = 4.66, p = 0.01, SRMR = 0.035, PGFI = 0.198, AICc = 66.19) but good for non-carriers ($X^2(2)$ = 0.18, p = 0.84, SRMR = 0.007, PGFI = 0.2, AICc = 57.22) (Tab.1).

Due to the finding that a right parietal region was associated with EEV in deletion carriers, we tested two models including this region. Model 3 (Fig. S3) includes a direct path from VMPFC to EEV, indirect pathways via left amygdala and left LOC and additionally tests an indirect modulation of right parietal activity by EEV. The data of both groups do not fit the model (deletion carriers: $X^2(3)$ = 3.5, p = 0.02, SRMR = 0.035, PGFI = 0.198, AICc = 95.8; non-carriers: $X^2(3)$ = 5.88, p = 0.84, SRMR = 0.007, PGFI = 0.2, AICc = 102.95) (Tab. 1). The finding of a non-significant path from VMPFC to the right parietal region in non-carriers (b = -0.04, p = 0.432) is in line with the results from the parametric analysis.

In Model 4, VMPFC, left amygdala and the right parietal region are covariates mediating the influence of left LOC activity on EEV (Fig S4). This model does not adequately represent data of deletion carriers ($X^2(3)$ = 3.61, p = 0.01, SRMR = 0.031, PGFI = 0.198, AICc = 96.13). Model fit for non-carriers is fine ($X^2(3)$ = 0.82, p = 0.49, SRMR = 0.017, PGFI = 0.198, AICc = 87.76) (Tab.1).

In conclusion, unlike the models discussed in the main text, none of the alternative models tested fit the data of deletion carriers well.

Table 1. Fit indices for assessing model fit of four different path models in deletion carriers and non-carriers.

	Chi-square	Df	Chi/Df	p	SRMR	CFI	PGFI	AICc
deletion carriers								
Model 1	5.977	2	2.989	0.05	0.023	0.987	0.199	62.851
Model 2	9.316	2	4.658	0.01	0.035	0.977	0.198	66.190
Model 3	10.481	3	3.494	0.02	0.035	0.978	0.198	95.792
Model 4	10.823	3	3.608	0.01	0.031	0.977	0.198	96.134
non-carriers								
Model 1	4.405	2	2.203	0.11	0.035	0.985	0.199	61.279
Model 2	0.350	2	0.175	0.84	0.007	1.000	0.200	57.224
Model 3	17.636	3	5.879	0.00	0.052	0.926	0.197	102.947
Model 4	2.448	3	0.816	0.49	0.017	1.000	0.200	87.759

p > 0.05 indicates good fit (Barrett, 2007)

Df=degrees of freedom; SRMR= standardised root mean square residual, CFI=comparative fit index, PGFI=parsimony goodness-of-fit index, AICc=corrected Akaike information criterion

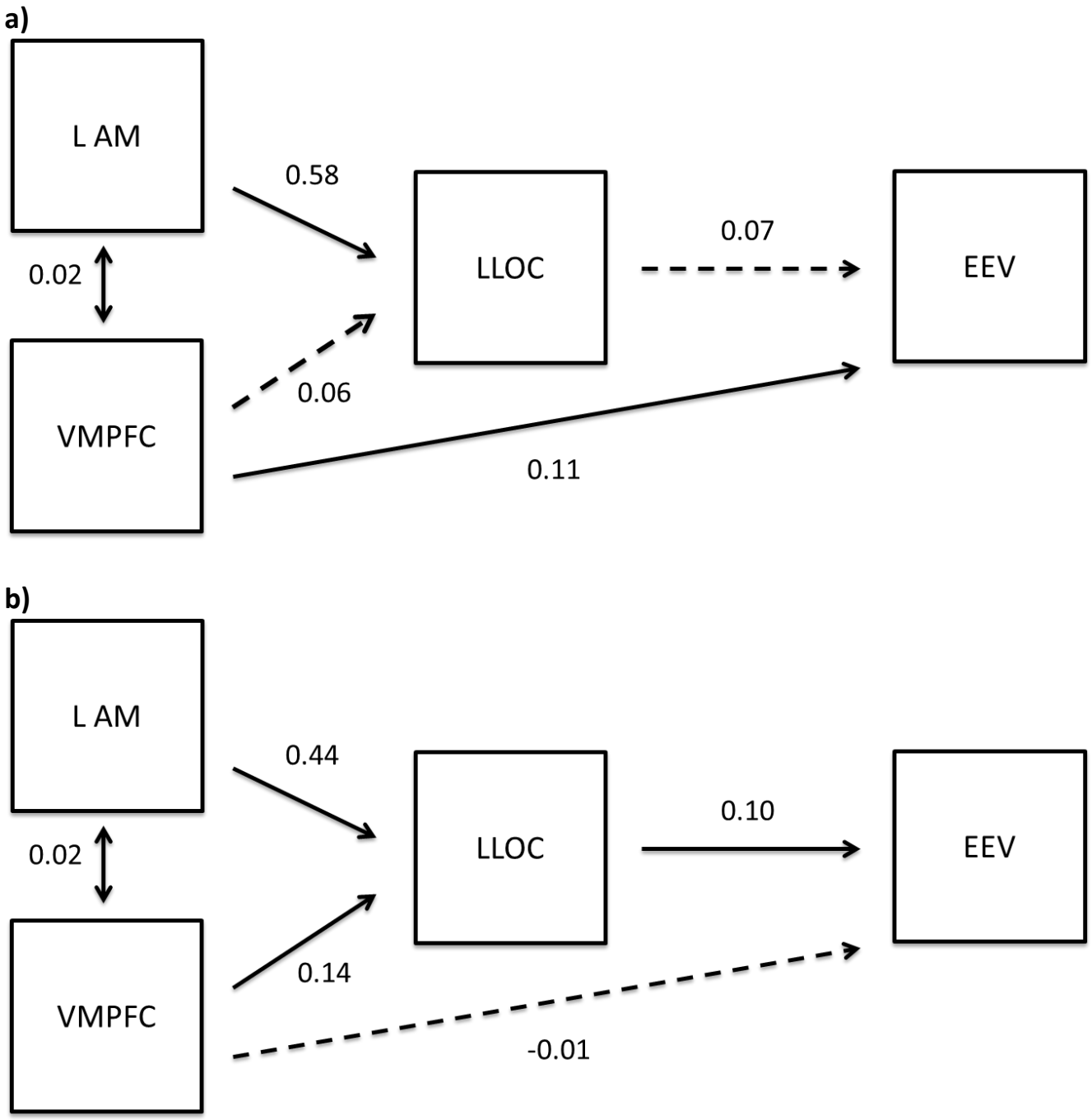

Figure S1. Model 1 tests whether emotionally enhanced vividness (EEV) is predicted by ventromedial prefrontal cortex (VMPFC) and left lateral occipital complex (LLOC) activity and if the left LOC is mediated by both left amygdala (L AM) and VMPFC activity. a) In deletion carriers VMPFC activity does not mediate the influence of LLOC on EEV. b) VMPFC activity is not directly modulated by EEV in non-carriers. Beta estimates for each path are shown. Significant paths are indicated by solid lines, dashed lines indicate non-significance.

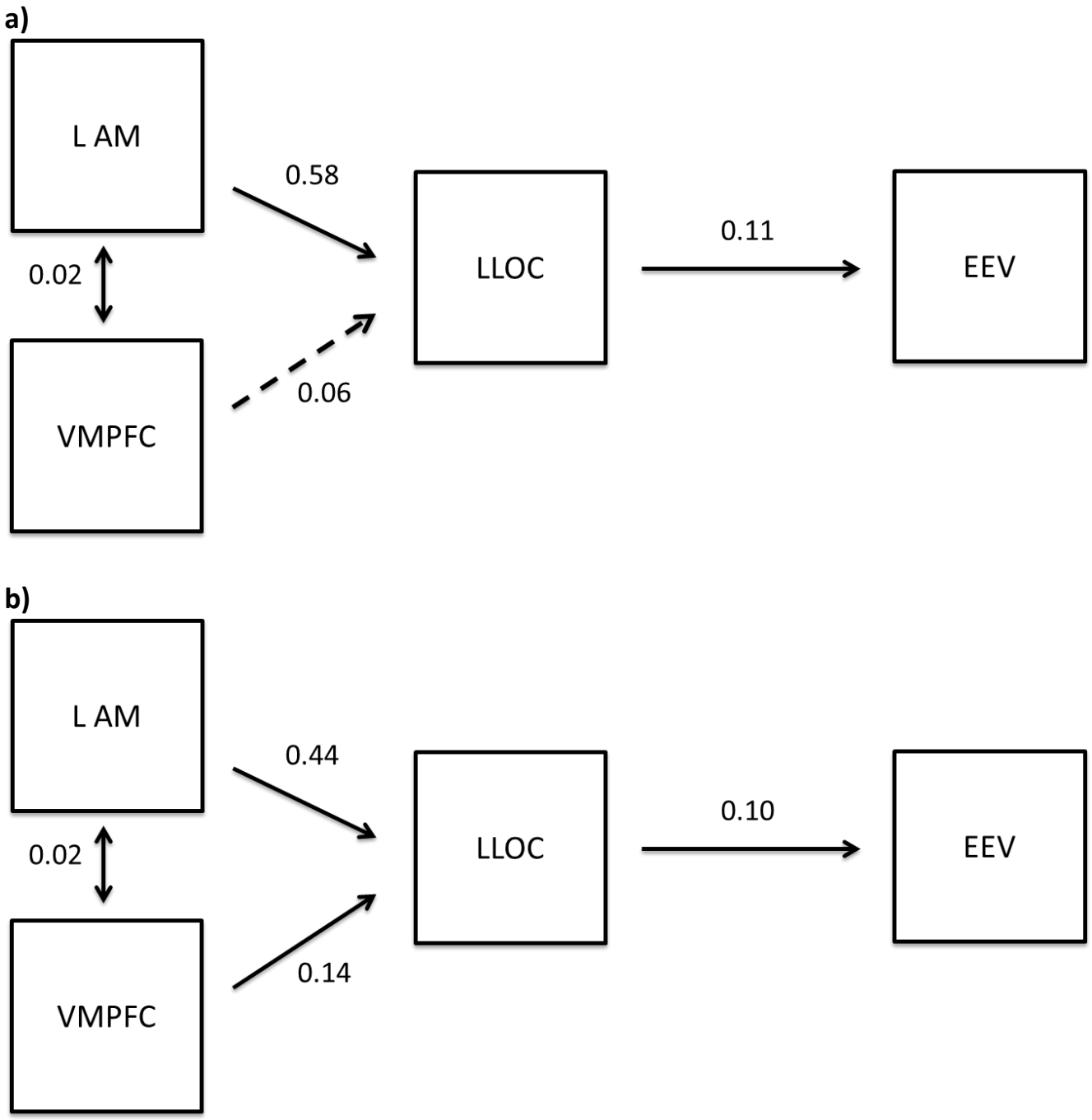

Figure S2. Model 2 assumes that left amygdala (L AM) and ventromedial prefrontal cortex (VMPFC) activity mediate the relationship of left lateral occipital complex (LLOC) and emotionally enhanced vividness (EEV). In deletion carriers VMPFC activity does not directly influence left lateral occipital complex LLOC activity (a), but does so in non-carriers (b). Beta estimates for each path are shown. Significant paths are indicated by solid lines, dashed lines indicate non-significance.

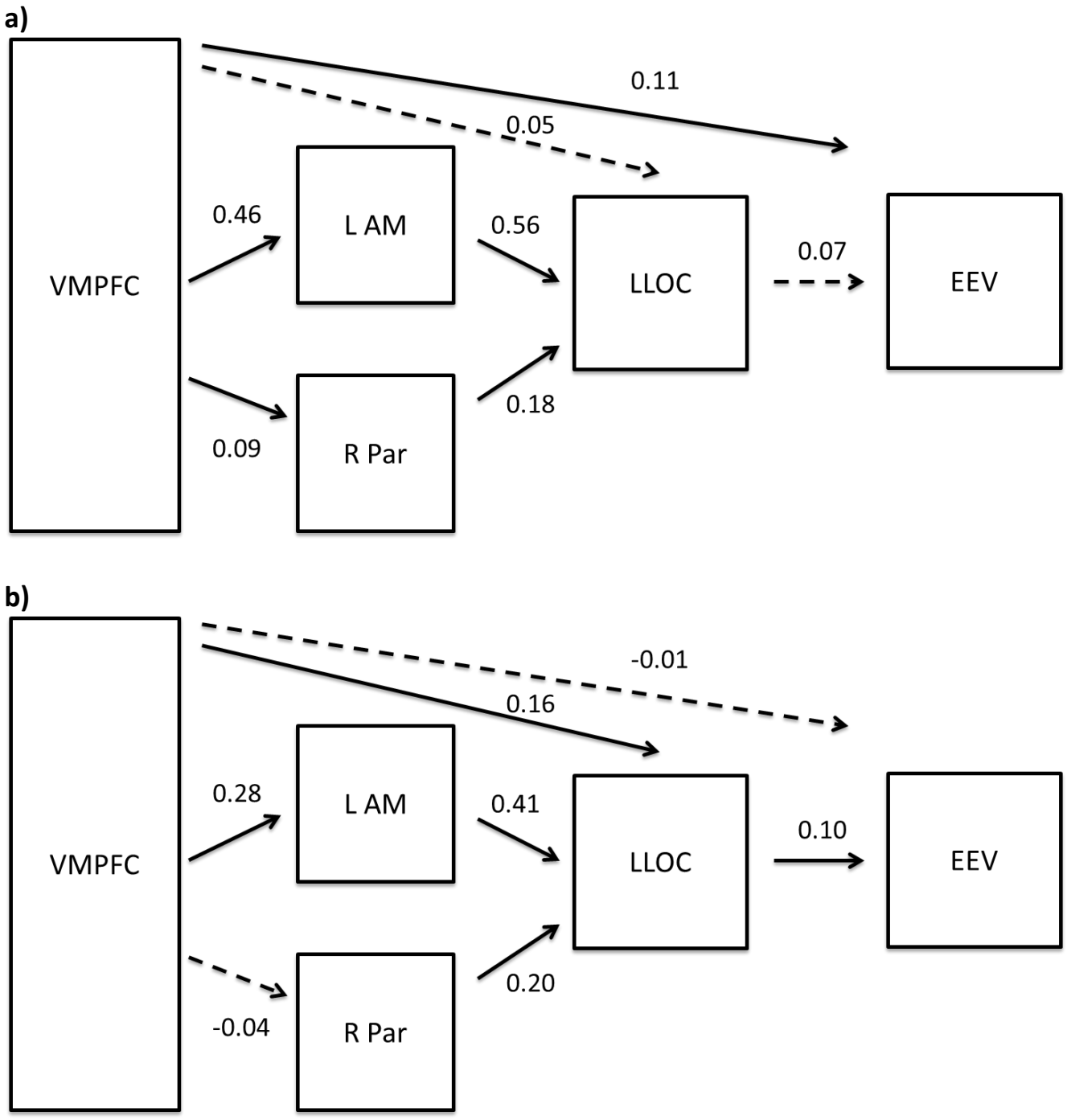

Figure S3. Model 3 suggests that emotionally enhanced vividness (EEV) is directly predicted by ventromedial prefrontal cortex (VMPFC) and left lateral occipital complex (LLOC) activity and that in turn LLOC activity is predicted by VMPFC, left amygdala (L AM) and right parietal (R Par) activity. a) The analysis revealed that EEV is not predicted by an indirect VMPFC pathway in deletion carriers. b) In non-carriers EEV does not directly modulate VMPFC activity. VMPFC and right parietal activation are not associated. Beta estimates for each path are shown. Significant paths are indicated by solid lines, dashed lines indicate non-significance.

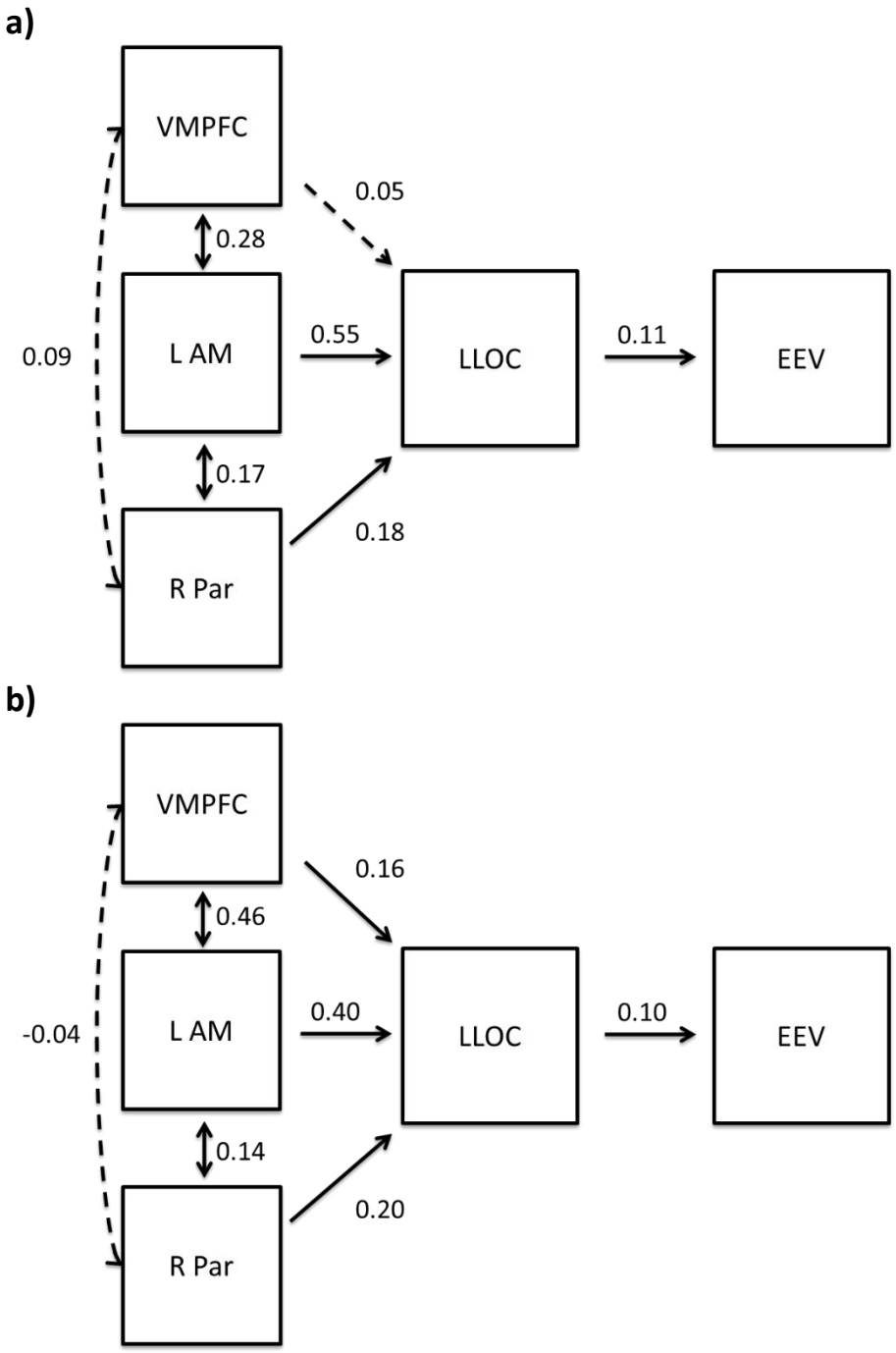

Figure S4. Model 4 hypothesizes that ventromedial prefrontal cortex (VMPFC), left amygdala (L AM) and right parietal (R Par) cortex are covariates mediating the influence of left lateral occipital complex (LLOC) activity on emotionally enhanced vividness (EEV). VMPFC and right parietal activation are neither in deletion carriers (a) nor in non-carriers (b) related. Model 4 shows that VMPFC activity does not mediate the influence of the LLOC in deletion carriers (a). Beta estimates for each path are shown. Significant paths are indicated by solid lines, dashed lines indicate non-significance.