

To Accompany

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Medial prefrontal cortex and the emergence of self-conscious emotion in adolescence

Psychological Science

Supplementary Online Materials (SOM-R)

METHODS

Participant inclusion and exclusion

Participants were recruited from the greater New York City metropolitan area. All participants passed an initial screening to verify right-handedness (Denckla, 1985), no contraindication for MRI, the absence of psychiatric illnesses (structured diagnostic interviews SCID for adults (First, Spitzer, Williams, & Gibbon, 1995), K-SADs for minors (Birmaher et al., 2009)), and a score above 80 on estimated IQ (WASI (Wechsler, 1991, 1999)). Of the N=79 participants tested, seven were excluded for excessive head motion during MRI scanning, one was excluded for evidence of inattention, and two were excluded for technical issues, leaving a final sample of N=69 for fMRI and self-report samples (See Table S1 for sample characteristics).

Self-reported emotion analysis

Six self-reported emotion measures were obtained for anticipation and evaluation conditions: *Embarrassment*, *Happiness*, *Excitement*, *Worry*, *Fear*, and *Nervousness*. A factor analysis was conducted on all emotion ratings to assess the latent structure of the six self-report

measures. A Principal Components Analysis using Varimax orthogonalization yielded three latent variables exceeding an eigenvalue of one. *Nervousness* and *Worry* ratings loaded strongly on one variable, *Excitement* and *Happiness* ratings loaded strongly on a second variable, *Embarrassment* ratings uniquely loaded onto a third variable, and *Fear* ratings did not load strongly on any latent variable and thus were not analyzed further.

To reduce the number of independent tests conducted, *nervousness* and *worry* scores were averaged to create an *Anxiety* composite score, and *happiness* and *excitement* were averaged for a composite *Positive Arousal* score, and embarrassment ratings constituted the *Embarrassment* score as justified by the factor analysis. For these three emotion categories, a series of analysis of variance (ANOVA) tests assessed the effects of task phase (anticipation, evaluation) and age on self-reported emotion, with each of the three age models tested in separate ANOVAs. To adjust for separate, independent tests of *Anxiety*, *Positive Arousal*, and *Embarrassment* emotion scores, each statistical analysis is presented alongside an adjusted critical $\alpha=0.0167$ (accounting for three sets of self-reported emotion ratings). The peak age for significant age effects on emotion ratings was calculated using the fit-line that corresponds to the most significant age prediction (based on *p*-value).

Skin conductance analysis

Skin conductance was not recorded for N=7 of the final fMRI sample due to technical issues. Of the N=62 participants with GSR data, data from N=6 participants were deemed unusable (zero instances of biologically-driven responses 0.05 microsiemens or greater) leaving a usable sample of N=56 participants (see Table S1 for sample characteristics).

Linear regression slope estimates were calculated for each block within a time window of one-second lagged block onset to three seconds after block offset, and scaled to units of SCL change per minute for each task block. GSR averages were computed separately for anticipation and evaluation periods. The GSR average for rest blocks was incorporated into group analyses as a covariate of non-interest to control for baseline properties of the GSR signal that could vary across participants due to measurement quality, properties of skin on the fingers, and other potential nuisance variables unrelated to the task. Incorporating rest block GSR levels as a covariate ensured that any observed age differences in GSR for task blocks was not due to covarying baseline differences in GSR measurement properties. Significant effects were plotted for inspection of distribution, possible outliers, and directionality.

To assess whether any age group reliably differed in rest block GSR activity, follow-up analyses were conducted to assess whether rest block GSR reliably differed as a function of age. A series of linear regressions tested the significance of linear, quadratic, and asymptotic predictors of rest block GSR.

Neuroimaging acquisition

A high resolution, 3D magnetization prepared rapid acquisition gradient echo anatomical scan (MPRAGE) was acquired (256x256 in-plane resolution, FOV=240mm; 124 1.5mm sagittal slices). The task was conducted during a single 155 TR functional scan. Functional images were acquired with a spiral in and out sequence to optimize signal in the temporal and orbital frontal lobes (Glover & Thomason, 2004) (repetition time=2000ms, echo time=30, FOV=200mm, flip angle=90, interleaved with skip 0, 64x64 matrix). Twenty-nine 5-mm thick coronal slices per TR

(in-plane resolution: 3.125x3.125mm) acquired the entire brain except for much of the occipital lobe.

Neuroimaging preprocessing and first-level modeling

Images were slice-time corrected and realigned to the first volume using 6-plane rigid body transformation. Given the developmental sample, analyses minimized the influence of participant motion on fMRI signal. Functional volumes were flagged for excessive motion if associated with head movement exceeding 1.5 mm in any plane relative to the volume before it. If more than 10% of volumes were flagged for a given participant, that participant was excluded (N=7). If between 0 and 10% of TRs were flagged, participants were deemed usable, with flagged TRs censored during first-level GLM analysis. Of the N=69 usable participants, N=58 had no timepoints that met criteria for censoring. N=11 participants had between 1.9 and 10% of functional volumes censored (mean=4.64%, standard deviation=3.12%).

Anatomical and functional datasets were spatially coregistered. Both sets of images were warped to Talairach and Tournoux (Talairach & Tournoux, 1988) coordinate space by applying the warping parameters obtained from the transformation of each subject's high-resolution anatomical scan using a 12-parameter affine transformation to a template volume (TT_N27). Talairach transformed functional images were smoothed with an isotropic 6mm Gaussian kernel and resampled to a resolution of 3x3x3mm.

A general linear model (GLM) was performed for each participant to compute parameter estimates representing task effects at each voxel. Task regressors were created for each stimulus type (anticipation, evaluation) by convolving a boxcar function representing task block timings with a gamma-variate hemodynamic response function. Linear and quadratic trends and motion

parameters were modeled as regressors of non-interest to account for correlated drift and residual motion effects.

Neuroimaging Psychophysiological Interaction (PPI) analysis preprocessing and first-level modeling

The seed timecourse was extracted from a 6mm spherical region of interest about the peak MPFC activation (xyz= -13,53,6; see main text). The PPI analysis was carried out using standard processing steps (Friston et al., 1997) by extracting the functional timecourse within the MPFC seed ROI, removing sources of noise and artifact, deconvolving the neural signal, and convolving the time-course data with evaluation block timings and the canonical hemodynamic response function (as specified in Gitelman, Penny, Ashburner, & Friston, 2003).

Neuroimaging control analyses evaluating age-data quality confounds

Additional analyses were conducted to verify that reported developmental effects remained significant when accounting for differences in motion and signal to noise ratio (SNR) across participants. For each participant, the plane of maximum displacement was identified for each TR and cross-TR motion values were averaged to obtain a single metric of motion. SNR for each participant was computed as the ratio between the mean baseline estimate from first-level general linear modeling and the standard deviation of the residual time series (Johnstone et al., 2005; Murphy, Bodurka, & Bandettini, 2007; Somerville, Hare, & Casey, 2011). Two SNR values were calculated for each participant: one extracted from the MPFC only (6mm spherical ROI), and one within a mask containing each participant's in-brain functional acquisition space (whole brain except the posterior aspect of the occipital lobe). Partial correlation analyses tested

whether age effects on MPFC response (e.g., Fig. 3) and connectivity (e.g., Fig 4) remained significant when controlling for motion and SNR.

Analysis of sex differences

Each dependent variable that showed significant age effects (embarrassment, GSR, MPFC activity, MPFC-caudate connectivity) was tested for additional modulation of response by participant sex (main effect of sex, sex by task phase interaction).

RESULTS

Emotion ratings

Embarrassment (supplement to main text). As reported in the Main Text, there was a trend-level adolescent-specific main effect of age on embarrassment ratings ($F(1,67)=5.52$, $p=0.02$, Bonferroni-adjusted critical $\alpha=0.0167$) and a significant adolescent-emergent main effect of age on embarrassment ratings ($F(1,67)=6.07$, $p=0.016$; Bonferroni-adjusted critical $\alpha=0.0167$; Figure 2). There was not a main effect of linear age on embarrassment ratings ($F(1,67)=1.61$, $p=0.21$). There were no task phase by age interactions on embarrassment ratings for any age predictor (p 's > 0.5).

Positive arousal. Though positive arousal ratings were greater during the anticipation condition than the evaluation condition, this difference was not statistically reliable ($F(1,67)=3.04$, $p=0.09$, Bonferroni-adjusted critical $\alpha=0.0167$, see SOM-R). There was not a main effect of linear age on positive arousal ratings ($F(1,67)=1.02$, $p=.32$), and possible trends toward an adolescent-specific decrease in positive arousal ratings ($F(1,67)=2.76$, $p=0.10$), and an

adolescent-emergent decrease in positive arousal (with lesser endorsement of positive arousal with increasing age asymptoting into adulthood; $F(1,67)=3.23, p=0.077$) should be interpreted with caution given the Bonferroni-adjusted critical $\alpha=0.0167$. There were no task phase by age interactions on positive arousal ratings for any age predictor ($p's>0.5$).

Anxiety ratings. Analysis of anxiety ratings yielded no significant effects of task phase, age (for any of the three predictors) and no task phase by age interactions.

Skin conductance (GSR)

Results (supplement to main text). The main of time (first half, second half) was significant ($F(1,53)=5.27, p=0.026, \eta^2_{\text{partial}}=0.09$), consistent with the expected pattern of habituation on GSR signal. GSR was not significantly explained by the linear-age predictor ($F(1,53)=1.92, p=0.17$) or the adolescent-emergent predictor ($F(1,53)=0.027, p=0.87$). The linear-age predictor trended toward a significant interaction with task phase ($F(1,53)=3.91, p=0.054$) such that GSR responses to the anticipation period showed a stronger increasing linear trend than the evaluation period. No other age predictors showed an interaction with trial phase ($p's>0.1$).

GSR baseline analysis. To address the possibility that adolescents (or another age group) demonstrated a nonspecifically heightened GSR response to the entire task - rather than modulated responding as a function of anticipation and evaluation blocks - a control analysis assessed possible age differences in GSR response during rest blocks. None of the three age predictors explained a significant proportion of variance in rest block GSR activity ($p's>0.18$). Thus, it is unlikely that global GSR differences could explain adolescent-specific GSR effects.

Analysis of sex differences

We observed no main effects of sex, and no significant sex by task interactions for any of the dependent measures listed above (embarrassment: p 's > 0.5; GSR: p 's > 0.2; MPFC parameter estimates: p 's > 0.3; MPFC-caudate connectivity p > 0.9). It is worth noting that the present study might be underpowered in detecting sex differences. The slightly uneven age split (42 females, 27 males), combined with reduced statistical power due to additional between-subjects factors (e.g., age) might have rendered this study's design fairly insensitive to age effects.

Supplementary fMRI Results

For completeness and to aid meta-analytic endeavors, we present findings that surpassed whole-brain corrected thresholding which demonstrated an interaction between task phase and any age regressor (p < 0.05, corrected). See Table S2 for coordinates and qualitative descriptions of the interaction pattern in each region. Due to space constraints, regions of the brain demonstrating effects of task phase (anticipation, evaluation) that are not modulated by age will be reported elsewhere.

Neuroimaging control analyses evaluating age-data quality confounds

When simultaneously controlling for MPFC SNR, whole-brain SNR, and average TR-to-TR motion, the quadratic relationship between MPFC activity and age ($r(63) = 0.284$, $p = 0.022$), the asymptotic relationship between age and MPFC ($r(63) = 0.440$, $p < 0.001$), and the asymptotic relationship between age and PPI values in the caudate remained significant ($r(63) = 0.40$, $p = 0.001$). Thus, the observed age effects on neural response are unlikely to be an artifact of signal quality or motion variation across participants.

Relation among variables

There was substantial commonality in the age predictors that explained significant proportions of variance in embarrassment ratings (adolescent-emergent and trend-level adolescent-specific), GSR (adolescent-specific), and MPFC fMRI results (adolescent-specific and adolescent-emergent). Analyses were conducted to determine the degree of shared variance between embarrassment, GSR, and fMRI data. Because task phase (anticipation versus evaluation) did not explain significant variance in any of the dependent variables, we collapsed across task phase and conducted a series of bivariate correlations on embarrassment, first-half GSR, MPFC activity, and MPFC-striatum connectivity. All correlations were positive in directionality, but not significant (p 's > 0.2).

A series of partial correlation analyses were conducted to determine the extent to which experiential or autonomic differences across participants could explain the age differences observed in fMRI activity. For instance, if the MPFC age effects would fail to reach significance when controlling for GSR ratings, it would suggest that variability GSR – rather than age – would hold more explanatory power in predicting MPFC activity.

Despite the reduction in degrees of freedom, all age effects largely retained their statistical significance when controlling for the other factors. These findings suggest that amongst the variables examined, age predictors hold the greatest degree of explanatory power, and significant age effects are not a byproduct of a more powerful but covarying factor within the data tested. The age effects on MPFC fMRI activity remained significant while simultaneously controlling for embarrassment and GSR (adolescent-specific: $r(52)=0.33$, $p=0.015$; adolescent-emergent: $r(52)=0.56$, $p<0.001$). Adolescent-emergent age effects on

MPFC-striatum connectivity remained significant while simultaneously controlling for embarrassment and GSR ($r(52)=0.42, p=0.001$).

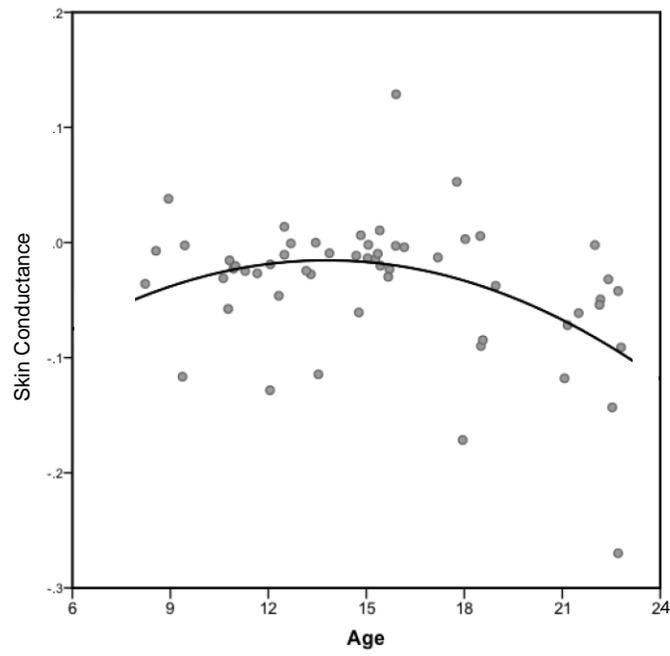


Figure S1. Quadratic relationship between age and skin conductance during the first half of the experiment. Skin conductance scores are composite of anticipation and evaluation phases.

Table S1.

Age and gender demographics of participants with usable fMRI data (left) and usable skin conductance data (right).

Sample	fMRI sample		GSR sample	
	N	Sex (# female)	N	Sex (# female)
8-12 years	20	14	18	12
13-17 years	30	16	22	10
18-22 years	19	12	16	9

Table S2.

Brain regions demonstrating significant Task Phase (Anticipation, Evaluation) by age interaction and qualitative description of interaction pattern.

Region	x	y	z	F statistic	k (mm ³)	Interaction Pattern
Cerebellum	17	-50	-49	23.13	999	Anticipation: Linear decreasing Evaluation: No age difference
Subgenual Anterior Cingulate	9	12	-12	20.68	1,161	Anticipation: Quadratic adolescent-peaking Evaluation: Asymptotic decreasing
Superior Temporal Gyrus	-36	-3	-15	18.66	1,377	Anticipation: No age difference Evaluation: Asymptotic decreasing
Brainstem/PAG	3	-9	-9	17.00	837	Anticipation: Asymptotic increasing Evaluation: Quadratic adolescent troughing
Insular Cortex	39	3	3	15.75	2,079	Anticipation: No age difference Evaluation: Asymptotic decreasing
Inferior Temporal Gyrus	-48	-39	-12	15.61	945	Anticipation: Asymptotic decreasing Evaluation: Quadratic adolescent-peaking
Putamen	-18	-9	12	15.33	2,268	Anticipation: Asymptotic increasing Evaluation: No age difference
Dorsal Anterior Cingulate	5	14	24	13.81	1,242	Anticipation: No age difference Evaluation: Asymptotic decreasing

Note: Threshold $p < 0.05$, corrected for acquisition space. XYZ coordinates in Talairach & Tournoux atlas space.