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The Medial Prefrontal Cortex and the Emergence of Self-Conscious Emotion in Adolescence

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

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Abstract

The present study examined the relationship between developmental modulation of socioaffective brain systems and adolescents' preoccupation with social evaluation. Child, adolescent, and adult participants viewed cues indicating a camera was alternatingly off, warming up, and projecting their image viewable to a peer during the acquisition of behavioral, autonomic, and neural response (fMRI) data. Believing a peer was actively watching the participant was sufficient to induce self-conscious emotion that rose in magnitude from childhood to adolescence and partially subsided into adulthood. Autonomic arousal was uniquely heightened in adolescents. These behavioral patterns were paralleled by emergent engagement of the MPFC and striatal-MPFC connectivity during adolescence that are thought to promote adolescent motivated social behavior. These findings demonstrate that adolescents' self-consciousness is related to age-dependent sensitivity of brain systems critical to socioaffective processes. Further, unique interactions between the MPFC and striatum may provide a mechanism by which social evaluation contexts influence adolescent behavior.

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

Adolescence is a phase of the human lifecourse defined by immense social change. Given that adolescents spend more time with peers relative to children and adults (Brown, 2004), a unique feature of adolescent behavior is heightened attunement to, concern over, and reaction to perceived instances of peer evaluation. During adolescence, reported concern over social evaluation rises sharply from childhood (Westenberg, Drewes, Goedhart, Siebelink, & Treffers, 2004), reported daily self-consciousness peaks (Rankin, Lane, Gibbons, & Gerrard, 2004), and adolescents more frequently interpret themselves as being the target of social evaluation (e.g., *imaginary audience* behavior (Elkind & Bowen, 1979)).

An emerging viewpoint in neurodevelopmental research is that dynamic features of brain development are consequential to unique aspects of behavior that emerge over the lifecourse (Casey, Tottenham, Liston, & Durston, 2005; Somerville, Jones, & Casey, 2010). Despite the primary role of actual or perceived social evaluation in adolescents' daily lives and well-being, little is known about the biological mechanisms that accompany phenomenological shifts in adolescent social concern. The present study sought to test the hypothesis that experiential, autonomic, and socioaffective brain responses would change nonlinearly from pre-adolescence to post-adolescence, even under minimal conditions – simply being looked at by a peer.

The current study focused on developmental modulation of the response properties and connectivity of the medial prefrontal cortex (MPFC). The MPFC is commonly engaged by social and emotional processes (Amodio & Frith, 2006; Roy, Shohamy, & Wager, 2012), and is a key node in neuroscientific models of the development of the adolescent self-concept (Sebastian, Burnett, & Blakemore, 2008). Given that the MPFC shows dynamic structural and connectivity-based maturation throughout the adolescent years (Shaw et al., 2008), we sought to evaluate the

neurodevelopmental features of MPFC response and connectivity during instances of

experimentally induced social evaluation. Sixty-nine human participants ranging in age from 8 to

22.9 years completed self-report, autonomic arousal (galvanic skin response; GSR) and

functional brain imaging (fMRI) measures to test *a)* whether adolescents experience heightened

emotional and autonomic responses to instances of peer evaluation; *b)* whether these responses

extend to social anticipatory contexts; *c)* whether such a behavioral profile is paralleled by

distinct recruitment and connectivity patterns of the MPFC in adolescents; and *d)* whether such

potential effects subside or persist into early adulthood. Analyses utilized age as a continuous

variable to test for linear, quadratic (U or inverted-U shaped), and asymptotic (change during

childhood and adolescence stabilizing into adulthood) effects on responses to evaluation and

anticipation periods.

Methods

Participants

N=69 healthy participants 8.0-22.9 years of age completed fMRI scanning. Participant

volunteers were recruited from the New York City metropolitan area (for demographics, see

Table S1 available online). See Supplementary Materials for inclusion and exclusion criteria.

Participants provided informed written consent (parental consent and subject assent for minors)

approved by the Institutional Review Board of Weill Cornell Medical College.

Task

Participants were led to believe that a small, one-way video camera was embedded in the head coil of the fMRI scanner. They were instructed that this was a novel technology, and that the experimenters wished to test it during their experimental session by cycling through its settings (off, warming up, on) several times. Participants were instructed to passively view the screen and monitor the video camera's status. Cued by low-level changes in the screen display, the supposed video camera cycled between three phases (Figure 1a): "Off" (resting baseline condition), "Starting…" and would turn on at any moment (anticipation condition), or "On" and ostensibly project their image to be viewed by a peer (evaluation condition).

Participants were instructed that a same-sexed peer of similar age would monitor the video feed during the participant's scan, and could see the participant's face in real-time whenever the camera was "on". They were told the camera was a one-way projection, and thus should not expect to view a peer. Although there was, in fact, no camera, all participants had completed a separate peer interaction task immediately prior to this study (Jones et al., 2011) which conveniently made the cover story more believable. Though it cannot be ruled out that the prior task influenced the present findings, the two tasks were held consistent across all participants and each participant had a short break between the two studies.

The task was structured as a block design that pseudorandomly alternated between rest, anticipation, and evaluation conditions. Participants saw a total of 12 blocks, four of each condition (rest, anticipation, evaluation). To reduce predictability, block length varied in duration between 16 and 38 seconds. Across the task, participants spent an equal total duration viewing anticipation and evaluation conditions (total per condition: 92 seconds), and the mean duration of anticipation and evaluation blocks was matched (mean: 23 seconds). Participants viewed the

resting baseline "camera off" stimulus for a total of 126 seconds, in blocks averaging 31.5 seconds duration.

Measures

Emotion. Immediately following the task, participants were asked to rate the extent to which they experienced the following emotions: *Happiness, Excitement, Nervousness, Worry, Fear,* and *Embarrassment*. Participants rated each emotion category by bisecting a continuous line with anchors "Not at all" (far left) and "Extremely" (far right). Ratings were completed for anticipation and evaluation phases separately and were not acquired for the rest blocks when participants believed the camera was off.

Skin conductance. Skin conductance (GSR) was sampled simultaneously for N=62 of the participants, with usable data acquired from N=56 participants (see Supplementary Materials for exclusion criterion and Table S1 for demographics). An MRI compatible skin conductance recording system (SCR100C Biopac, Goleta, CA) together with AcqKnowledge 4.0 (Biopac; Goleta, CA) software continuously sampled skin conductance data at 100 Hertz.

Neuroimaging. Participants were scanned with a General Electric Signa 3.0 Tesla MRI scanner (General Electric, Milwaukee, WI) with a quadrature head coil. See Supplementary Materials for structural and functional acquisition sequences.

Data analysis

Age effects. Statistical analysis of each dependent variable (self-report, GSR, fMRI activity, fMRI connectivity) assessed the significance of three continuous age predictors, each assessing a distinct pattern of age-dependent change (Figure 1b-d): *a)* linear-age predictor with

increasing age was modeled as a mean-centered linear age variable; *b)* adolescent-specific

predictor to detect U- or inverted-U effects for which adolescents differ from both children and

adults, modeled as a quadratic function (calculated by squaring the linear-age predictor; the

quadratic peak fell at 15.94 years in the present sample); and *c)* adolescent-emergent predictor,

that shows rapid change throughout adolescence and persists in magnitude into adulthood, which

was modeled with a mean-centered asymptotic predictor calculated by generating a quadratic

function peaking at 18 years of age and asymptoting (retaining the maximum value) for adult

ages. The adolescent-emergent predictor closely mimicked a truncated cubic function for which

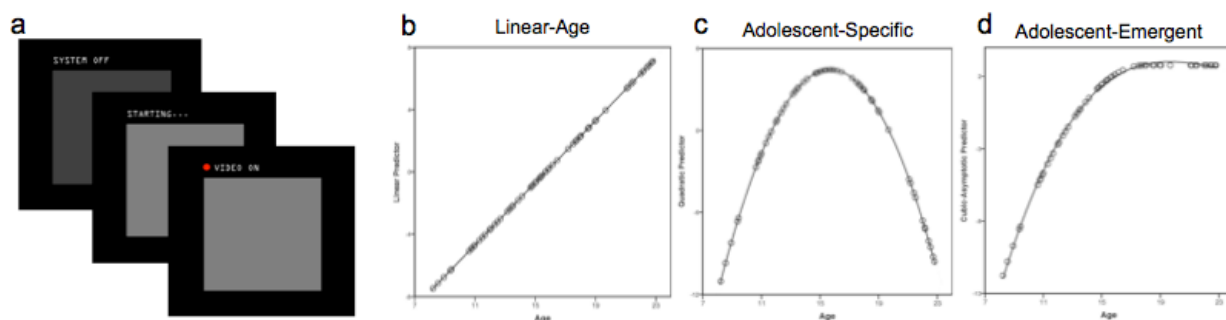the inflection point was fixed at 18 years of age.

Figure 1. a. Participants were led to believe that a one-way video camera was embedded in the head coil of the fMRI scanner. During different blocks of the experiment, participants believed that a camera was projecting an image of their face in real-time ('evaluation' condition, right), 'starting' while evaluation was absent yet imminent ('anticipation' condition, middle), or off (left). *b-d.* Linear (b), quadratic (c), and asymptotic (d) age patterns under investigation. Plots of predictor variables, with each dot representing a participant.

Because the three predictors naturally share variance, group analyses consisting of a

single 'competing' statistical model incorporating all age predictors are statistically invalid.

Given that the objective of the present study was to assess age influences on self-conscious

emotion and associated neural activity, every dependent variable was submitted to a triad of

group statistical tests, each incorporating one continuous age predictor. From the triad

of analyses, every age predictor that reached statistical significance is reported in the main

Results section, and is represented by a fit-line in Figures. Full analysis of variance (ANOVA)

results for every age predictor are reported in Supplementary Materials. This approach mitigates

model instability caused by multicollinearity, and the need to engage in potentially biased

experimenter choices regarding the importance of the three age predictors (e.g., choosing a

testing order in stepwise group regressions, or choosing to orthogonalize one predictor with

respect to another). Though this approach does not permit direct quantitative comparison of the

three age patterns, we believe it provides the most efficacious and unbiased method of

identifying the age predictor(s) that explain variance in the variables of interest.

Emotion. Self-reported emotion ratings were scored by recording the distance from the

far left anchor at which the participant bisected the line, with a greater value indicating greater

endorsement of the emotion category. Raw scores were proportionalized by dividing each score

by the total line length and by the sum of all measurements for that participant.

Statistical analyses were conducted in IBM SPSS Statistics 19.0. A factor analysis

indicated three latent variables evident in the self-report ratings corresponding to *Anxiety*,

Positive Arousal, and *Embarrassment* (see SOM-R). For each of the three emotion variables, a

group ANOVA tested for effects of task phase (anticipation, evaluation) and each of the three

age predictors on self-reported emotion. If age effects but no significant effects of task phase

were observed, data were averaged across task phases for post-hoc analyses that evaluated the

specificity of age effects to the Anticipation and/or Evaluation phases. Significant age effects

were plotted for inspection of distribution, possible outliers, and directionality. Given the focus

of the present manuscript on developmental differences in task-evoked emotion, findings for the

embarrassment ratings that yielded significant developmental differences are reported in the

main text. Results for emotion ratings that did not show significant developmental differences are reported in Supplementary Materials for completeness. To account for independent tests of the three emotion variables (*Anxiety, Positive Arousal, and Embarrassment)*, each statistical test is interpreted using an adjusted critical $\alpha=0.0167$ ($\alpha=0.05$ Bonferroni corrected for three tests).

Skin conductance analysis. Skin conductance analysis in N=56 usable participants was performed using AcqKnowledge 4.0 software and IBM SPSS Statistics 19.0. Skin conductance analyses focused on changes in response slope, or skin conductance level (SCL) per block. This standard analysis for block design data (Dawson, Schell, & Filion, 2001) measures the signal habituation rate during a task block, such that larger value corresponds to less habituation, indicative of autonomic arousal maintenance throughout the block. See Supplementary Materials for slope calculation methods.

Group analyses tested for effects of task phase (anticipation, evaluation) and age on GSR and included baseline GSR as a covariate of no interest to account for task-independent variance in GSR reactivity across participants. Group analyses were conducted as described above, with task time (first half of the experiment, second half of the experiment) additionally included as a within-subjects factor given the strong tendency for GSR effects to habituate over time (Andreassi, 2006; Dawson et al., 2001).

Neuroimaging. Functional imaging data were preprocessed using Analysis of Functional NeuroImages (AFNI) software (Cox, 1996). See Supplemental Materials for details on preprocessing and first-level task-based general linear modeling (GLM). Following GLM estimation for each participant, random effects group analysis consisted of a triad of linear mixed effects group models with regressors representing dummy-coded variables representing task phase (anticipation, evaluation), participant, and each age predictor (Fig.1b-d). Results yielded

group statistical maps representing the main effect of task phase (anticipation vs. evaluation), the main effect of each age predictor, and interactions of task phase by age predictor. Given the present focus on brain-behavior parallels, the present manuscript retains focus on age effects that persist for both anticipation and evaluation conditions as observed for embarrassment and GSR findings. However, a number of brain regions demonstrated significant age by task phase interactions indicating differential age modulation for anticipation and evaluation conditions. These regions and descriptions of age patterns are reported in Supplementary Table 2.

Given dynamic changes in MPFC morphology and connectivity (Shaw et al., 2008), and motivated social behavior (Steinberg, 2004) from childhood to adulthood, group connectivity analyses sought to assess putative age modulation of coupling between the MPFC and systems of the brain critical to motivated behavior, such as the striatum (Robbins & Everitt, 1996). A whole-brain psychophysiological interaction (PPI) analyses (Friston et al., 1997) was carried out to identify selective MPFC task-based functional coupling that could be subsequently queried for age effects. See Supplementary Materials for first-level PPI modeling methods. Random effects group analysis regressed voxelwise PPI parameter estimates against each of the three age patterns of interest (e.g., Fig 1b-d). Resultant maps identified regions of the brain whose MPFC signal coupling during evaluation contexts fit each of the three age patterns.

All brain imaging findings considered statistically significant exceeded correction for multiple comparisons to preserve $\alpha \leq 0.05$ by using a p-value/cluster size combination stipulated by Monte Carlo simulations run in the Clustsim subroutine. The search space of the simulation constituted the spatial coverage obtained for functional images (42,341 voxels in mask; whole-brain coverage minus much of the occipital lobe). Thus, all imaging findings achieve $p < 0.05$, corrected thresholding for the full acquisition space.

Significant age effects were plotted for inspection of distribution, possible outliers, and directionality by extracting parameter estimates for each participant from a 6mm spherical ROI about the cluster peak. These parameter estimates were also used for analyses to test possible sex differences, the relationship between dependent measures, and were used to rule out potential age confounds in signal-to-noise ratio and motion (see Supplementary Materials).

Relationship between variables. Bivariate correlational analyses were conducted to quantify the degree of shared variance between self-reported embarrassment, GSR, and fMRI measures. Partial correlation analyses controlling for embarrassment and GSR assessed whether reported age effects in neural response remain significant when controlling for experiential measures. Results of this analysis (see Supplementary Materials) verified that the observed age differences could not be solely explained by covarying experiential differences across participants.

Results

The social evaluation task elicited self-conscious emotion (e.g., increased ratings of embarrassment) (Keltner & Haidt, 1999) and physiological arousal in adolescents. Repeated ANOVAs including task phase (anticipation, evaluation) and each age predictor indicated that the adolescent-emergent age predictor yielded a significant main effect on embarrassment ratings (asymptotic: $F(1,67)=6.07$, $p=0.0163$; η^2partial=0.083; Bonferroni-adjusted critical $\alpha=0.0167$, see SOM-R; Figure 2), with the adolescent-specific age predictor yielding trend-level prediction of embarrassment ratings (quadratic: $F(1,67)=5.52$, $p=0.022$; η^2partial=0.076; Bonferroni-

adjusted critical α=0.0167, see SOM-R). The estimated age of peak embarrassment ratings is

17.2 years.

Given the significant adolescent-emergent effects, embarrassment ratings were further

queried for modulation by task phase. The adolescent-emergent age predictor yielded a trend-

level effect for the anticipation condition ($F_{(1,67)}$=3.57, p=0.063; η^2partial=0.051) and a

significant effect for the evaluation condition ($F_{(1,67)}$=7.14, p=0.009; η^2partial=0.096),

suggesting consistency in age effects on embarrassment in both conditions but a more robust age

difference during the evaluation phase. There was no main effect of task phase on

embarrassment ratings ($F_{(1,67)}$=0.093, p=0.76; Bonferroni-adjusted critical α=0.0167).
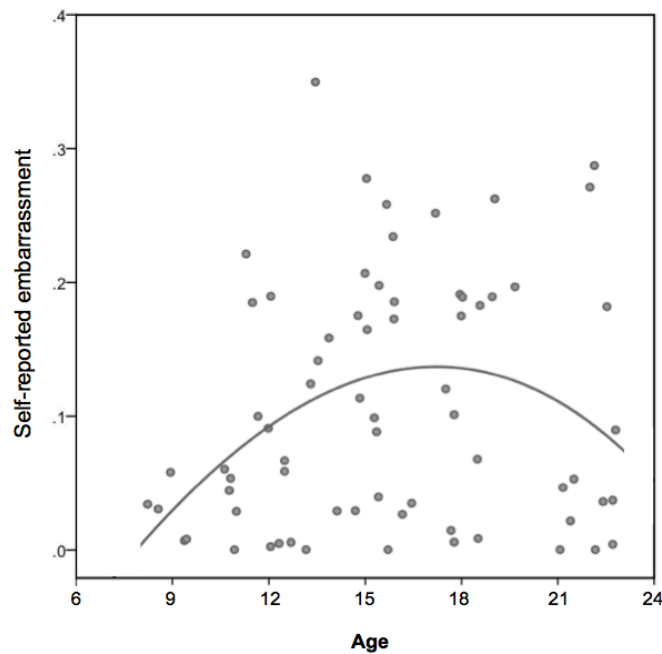

Figure 2. Scatterplot of embarrassment ratings response to evaluation and anticipation
conditions(collapsed) by age. The fit line was derived from the adolescent-emergent predictor.

Skin conductance data yielded a quadratic age by time interaction ($F_{(1,53)}$=10.34,

p=0.002; η^2partial=0.163). Post-hoc analyses isolating the first half of the experiment indicated

an adolescent-specific age effect which can be described as greater autonomic arousal (less

habituation of slope) rising into adolescence and subsiding into adulthood (F(1,53)=9.40,

p=0.003; η^2partial=0.151; Supplementary Figure 1). The estimated age of peak GSR response

was 14.38 years. There were no significant effects of task phase or age during the second half of

the experiment (p's>0.2). Significant adolescent-specific age effects during the first half were

evident for anticipation and evaluation phases when tested separately (anticipation: F(1,53)=4.77,

p=0.033; η^2partial=0.083), evaluation: (F(1,53)=6.95, p=0.011; η^2partial=0.12). These results

suggest that minimal social evaluative contexts are sufficient to induce heightened self-conscious

emotion and physiological arousal that peaks in mid-adolescence.

A triad of a voxelwise whole-brain mixed model ANOVAs were conducted with the

repeated factor of task phase (anticipation, evaluation) and each age predictor serving as a

continuous covariate of interest. Guided by the behavioral findings, fMRI analyses focused on

revealing neural activations that were similarly engaged by anticipation and evaluation phases,

and differentially active as a function of the age predictors (Figure 1b-d). A single region of the

brain located in the medial prefrontal cortex (xyz=-13,53,6; 72 3x3x3mm voxels; Brodmann area

32/10; mean cluster statistic F(1,67)=11.84; p<0.05 corrected; Figure 3a) was significantly

related to the adolescent-emergent age predictor. The estimated age of peak in MPFC activity

was 15.25 years. The identical, single region was also identified in an analysis of adolescent-

specific age effects at p<0.05, corrected thresholding, albeit smaller in size (mean cluster statistic

F(1,67)=10.38, 30 voxels). No regions demonstrated significant linear-age effects at whole-brain

corrected thresholding. To summarize, mirroring the levels of experienced embarrassment and

arousal, the MPFC demonstrated an elevated response in adolescents both during anticipation

and evaluation conditions that partially retained its activity strength into young adulthood. Age

differences in MPFC activity are plotted in Figure 3b for descriptive purposes.
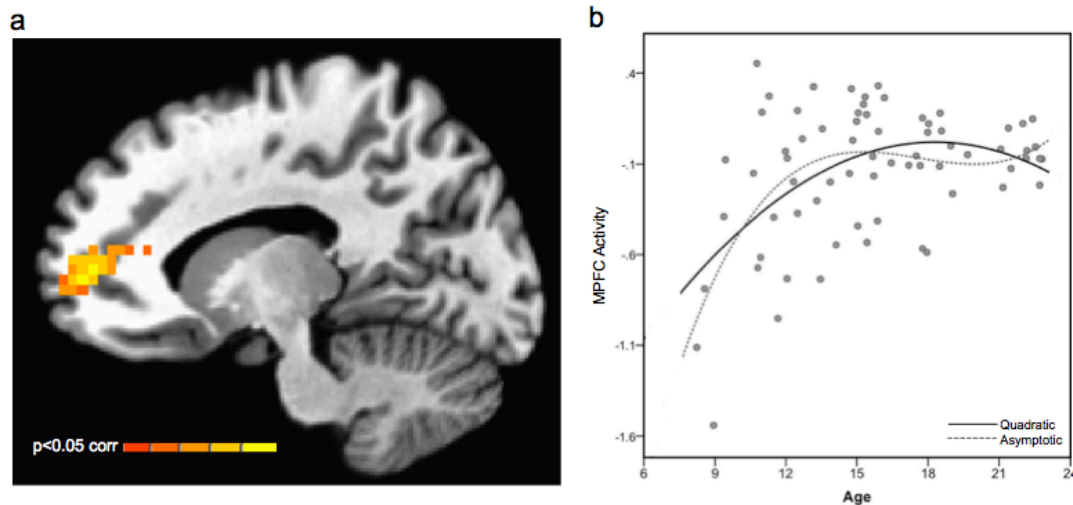
Figure 3. a. Statistical map of the main effect of adolescent-emergent age predictor revealed heightened engagement of the medial prefrontal cortex (MPFC) during adolescence that persists into adulthood. Image threshold $p<0.05$, corrected for acquisition space. *b*. Scatterplot of MPFC response to evaluation and anticipation conditions (collapsed) by age, for descriptive purposes.

Given the powerful influence of social evaluation on motivated and affective behaviors in adolescence (Steinberg, 2008), psychophysiological interaction analyses tested the extent to which the MPFC demonstrates differentially selective connectivity during evaluation periods as a function of age (see Supplementary Materials for methodological details). Resultant statistical maps revealed MPFC coupling with the dorsal striatum that significantly fits an asymptotic age pattern (left caudate xyz=-8,20,6; 35 3x3x3 voxels; mean cluster statistic F(1,67)=10.24; $p<0.05$, corrected; Figure 4). No other activations were observed for this analysis. No regions demonstrated significant linear-age or adolescent-specific (quadratic) effects at whole-brain corrected thresholding. Thus, the transition from childhood through adolescence predicts the emergence of MPFC-striatal coupling during evaluation contexts, a pattern that persists into adulthood.
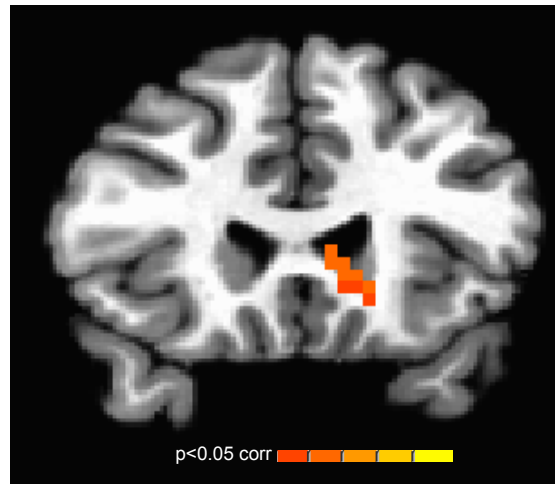
Figure 4. Striatum-MPFC functional coupling during evaluation fits an adolescent-emergent pattern of age modulation. Image threshold *p*<0.05, corrected for acquisition space.

Discussion

Using a simulated a social evaluation task, we observed that being watched by a peer was sufficient to generate nonlinear changes from childhood to young adulthood in self-conscious emotion and related physiological indices of emotional arousal. The nonlinear pattern of embarrassment and skin conductance findings support the hypothesis that even subtle social-evaluative contexts - and anticipation of them - lead to heightened self-conscious emotion and arousal during adolescence. Self-conscious emotion rose during adolescence and stabilized into adulthood, while arousal (skin conductance) levels showed maximal levels during adolescence.

There are numerous factors that are thought to converge during adolescence and contribute to the central role of social evaluation in adolescents' everyday experience. On one hand, the transition to adolescence typically marks a rise in the frequency and intensity of peer interaction that has been documented in humans and animals (Cairns, Leung, Buchanan, & Cairns, 1995; Primus & Kellogg, 1989) and reflected high rates of digital communication (Wang,

Iannotti, & Nansel, 2009). Such a shift in investment likely reflects a heightened motivation for peer acceptance, rendering social evaluation contexts increasingly salient to adolescents.

The present study evaluated whether adolescents instantiate unique neural response patterns to instances of social evaluation by peers that parallel phenomenological shifts in social sensitivity. We observed that behavioral shifts in adolescent social sensitivity are accompanied by nonlinear changes in MPFC response magnitude and selective MPFC-striatal connectivity, which sharply rise from late childhood into adolescence and partially subside into early adulthood.

Though the present study was optimized to detect such age differences across the whole brain (except for the occipital lobe), nonlinear age effects were highly circumscribed to the MPFC. The specificity of effects to the MPFC converges with widely supported theories of the MPFC's key role in social cognition and emotional valuation processes (Amodio & Frith, 2006; Blakemore, 2008). These findings extend existing accounts of MPFC function to suggest that it maintains persistent representation in even the most minimal of social evaluative contexts – being looked at.

Although the MPFC is frequently conceptualized as specialized for social cognition, emerging theoretical viewpoints have noted common recruitment of the MPFC during contexts that draw on affective valuation and assessment of significance to the self (Krienen, Tu, & Buckner, 2010; Roy et al., 2012) – which are often, but not exclusively, 'social'. Indeed, the nonlinear age differences we observed were also evident in anticipatory situations during which participants believed they were not being viewed would be imminently, indicating that explicit evaluation was not necessary to invoke adolescent self-consciousness and its neural correlates. Based on this view, we propose that MPFC activity in the present study serves to incorporate

salient contextual cues (in this case, imminent or perceived social evaluation) with emotional valuation processes. Thus, emergent heightened magnitude of MPFC activity in adolescence could result in assignment of heightened emotional value and self-relevance to instances of supposed social evaluation. This conceptualization is consistent with prior findings indicating that MPFC response to positive and negative social feedback is exaggerated in individuals for whom social feedback is particularly salient, i.e., individuals with low self-esteem (Somerville, Kelley, & Heatherton, 2010).

Robust MPFC signaling paired with increasing connectivity between MPFC and striatal regions could provide a mechanism by which peer evaluation contexts come to increasingly modulate adolescent motivated behavior. Not only does social concern serve as a motivating force that drives adolescents to seek out social bonds (Steinberg & Morris, 2001), adolescents are more prone to engage in suboptimal choice behaviors when with peers (e.g., risky driving; (Gardner & Steinberg, 2005). The striatum serves a key role in incorporating motivational, control, and contextual signals to facilitate context-dependent learning and behavior (Alexander, DeLong, & Strick, 1986). Though tentative, the observed pattern of MPFC-striatal connectivity might selectively upregulate motivational signaling, effectively compelling adolescent behavior toward action or approach when being evaluated by peers. While consistent with extant models of peer influence on adolescent decision-making (Lenhart, Ling, Campbell, & Purcell, 2010; Somerville & Casey, 2010; Steinberg, 2008), the current study illuminates a key role played by the MPFC in maintaining a representation of peer evaluation and its emotional qualities, while selective connectivity with the caudate may provide a means for integrating signals relevant to social context with motivational systems that govern goal-directed behavior.

It should be noted that the age effects observed for behavioral measures (embarrassment and GSR) partially correspond with the age-related changes observed for the brain imaging measures. All measures showed a robust influx of response from childhood into adolescence, but measures diverged into young adulthood: GSR levels also showed declining magnitude into early adulthood, whereas the other measures demonstrate a partial no decline from adolescence to adulthood. Future research with a broader age range is warranted to determine whether the divergence of age patterns into early adulthood is reliable.

A second feature of the reported findings is that physiological, MPFC, and self-conscious emotion demonstrate common maximal responding during adolescence, as indicated by analyses solving for the peak age of response using fit-line equations. Future research may assess whether the particular convergence of measures during adolescence plays a functionally significant role in promoting social sensitivity. There are also subtle and intriguing differences between the peak ages for GSR (14.38 years), MPFC activity (15.25 years), and self-reported embarrassment (17.2 years). Each measure contains its own profile of measurement error, so comparing the particular timing differences between variables should be interpreted cautiously. However, these findings provoke speculation that social sensitivity resonates in physiological and neural indices at an earlier age than when these emotions are most strongly labeled as self-conscious per se. Though even young children are capable of understanding embarrassment (Seidner, Stipek, & Feshbach, 1988), the current findings suggest that the process of attributing such physiological patterns as 'embarrassment' might not manifest to later in adolescence, perhaps due to perspective taking skills that continue to improve throughout adolescence ((Crone & Dahl, 2012; Dumontheil, Apperly, & Blakemore, 2010)) that may scaffold simulation of negative consequences of potential social transgressions that serve as a foundation of embarrassment (Keltner & Haidt,

1999). A complementary explanation is that though social evaluations are arousing and across different stages of adolescence, they might be experienced as less specifically embarrassing in early and mid-adolescence relative to late adolescence. Comprehensive studies with broader emotion measures will be needed to address these possibilities.

In conclusion, waiting to be looked at and believing one is being looked at were sufficient to induce nonlinear changes in self-conscious emotion and related physiological indices from childhood to young adulthood. Nonlinear differences in response in the MPFC, and MPFC-caudate connectivity, parallel this behavioral shift, and are proposed to influence adolescent social sensitivity. The functional properties of the MPFC are likely to be influenced by continued structural maturation (Shaw et al., 2008) and subcortical and cortical connections (e.g., (Asato, Terwilliger, Woo, & Luna, 2010) during adolescence. That said, future work will be needed to identify biological and experiential mechanisms that give rise to the functional differences illuminated by the present study. Together with other findings, this study bridges examinations of psychosocial development and neurodevelopmental science to inform how the emergent features of the adolescent social life can exert such a powerful influence over motivation, emotion, and well-being.

Figure Legends

Figure 1. a. Participants were led to believe that a one-way video camera was embedded in the head coil of the fMRI scanner. During different blocks of the experiment, participants believed that a camera was projecting an image of their face in real-time ('evaluation' condition, right), 'starting' while evaluation was absent yet imminent ('anticipation' condition, middle), or off (left). *b-d.* Linear (b), quadratic (c), and asymptotic (d) age patterns under investigation. Plots of predictor variables, with each dot representing a participant.

Figure 2. Scatterplot of embarrassment ratings response to evaluation and anticipation conditions (collapsed) by age. The fit line was derived from the adolescent-emergent predictor.

Figure 3. a. Statistical map of the main effect of adolescent-emergent age predictor revealed heightened engagement of the medial prefrontal cortex (MPFC) during adolescence that persists into adulthood. Image threshold $p<0.05$, corrected for acquisition space. *b*. Scatterplot of MPFC response to evaluation and anticipation conditions (collapsed) by age, for descriptive purposes.

Figure 4. Striatum-MPFC functional coupling during evaluation fits an adolescent-emergent pattern of age modulation. Image threshold $p<0.05$, corrected for acquisition space.

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To Accompany

Somerville, Jones, Ruberry, Dyke, Glover, & Casey

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 Supplementary Table 1 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 $\propto=0.0167$ (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 Supplementary Table 1 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 3×3×3mm.

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 statistical 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 ($F(1,53)=5.27$, $p=0.026$, η^2partial$=0.09$), 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 Supplementary Table 2 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).
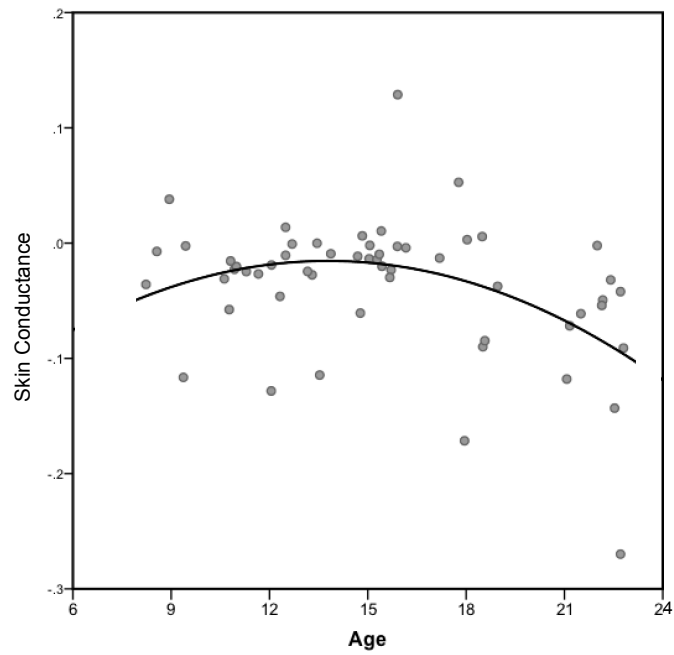
Supplementary Figure 1. Quadratic relationship between age and skin conductance during the

first half of the experiment. Skin conductance scores are composite of anticipation and

evaluation phases.

Supplementary Table 1.

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

Sample	fMRI sample		GSR sample	
Age	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

Supplementary Table 2.

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.