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At risk of being risky: The relationship between "brain age" under emotional states and risk preference

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ABSTRACT

Developmental differences regarding decision making are often reported in the absence of emotional stimuli and without context, failing to explain why some individuals are more likely to have a greater inclination toward risk. The current study (N = 212; 10–25y) examined the influence of emotional context on underlying functional brain connectivity over development and its impact on risk preference. Using functional imaging data in a neutral brain-state we first identify the "brain age" of a given individual then validate it with an independent measure of cortical thickness. We then show, *on average*, that "brain age" across the group during the teen years has the propensity to look younger in emotional contexts. Further, we show this phenotype (i.e. a younger brain age in emotional contexts) relates to a group mean difference in risk perception – a pattern exemplified greatest in young-adults (ages 18–21). The results are suggestive of a specified functional brain phenotype that relates to being at "risk to be risky."

1. Introduction

Even before the earliest conceptions of a juvenile justice system, adolescents and young adults have presented unique challenges to policy-makers (Steinberg, 2009). Higher incidents of criminal activity, substance use disorders, and the emergence of psychopathologies are often reported during this sensitive time period amongst a range of potentially comorbid factors (Bava and Tapert, 2010; Cohen and Casey, 2014). Prominent aspects include an increase in risky behaviors, higher degrees of sensation seeking and impulsivity, greater sensitivity to rewards, and heightened reactivity to threat and punishment (Benthin et al., 1993; Brown et al., 2015; Dreyfuss et al., 2014).

A particular locus of concern pertains to the functional neuroanatomy of adolescent development and autonomy in decision-making from young, to full adulthood, particularly within and amongst socio-affective environments known to have a profound impact on cognition and behavior. Impeded decision-making abilities have been reported in response to emotionally charged-situations, peer influence, and paradigms assessing the salient nature of rewards and punishment (Brown et al., 2012a; Dreyfuss et al., 2014; Gardner and Steinberg, 2005; Ladouceur, 2012; Mueller, 2011; Somerville and Casey, 2010). Indeed, these matters are currently being debated at the intersection of law and neuroscience, where legal decisions regarding the criminal culpability of juveniles remain in flux (Cohen and Casey, 2014; Jones et al., 2014;

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Steinberg, 2008). Legal issues concerning the *age of majority* beg the question – *when should an adolescent be considered an adult* (Cohen et al., 2016)?

In all aspects of development, a great deal of heterogeneity exists amongst typically and non-typically developing populations (Fair et al., 2012b). Particular characteristics may predispose certain subgroups of individuals more than others with a greater inclination toward risk. Some of these characteristics may normalize over time, in part due to structural and functional brain maturation; but regardless of age, there is much uncertainty regarding which individuals are most at-risk. Simply stated, while on average the increased prevalence of risky behavior and irrational decision-making across the adolescent and young adult periods have been shown repeatedly, not all adolescents fit this behavioral profile (Steinberg, 2008).

This variation across individuals may explain why general hypotheses concerning mismatches in brain development (e.g. dual-process models, grey matter vs. white matter, subcortical vs cortical regions), cognitive control and emotional regulation (hot/cold, top-down/bottom-up, BIS/BAS, etc.) have difficulty accounting for the myriad of behaviors and heterogeneity reported in this timeframe (Cohen and Casey, 2014; Mills et al., 2014). Importantly, developmental differences are often reported in the absence of emotional stimuli and without context. A key advancement in the study of development with respect to atypical behavior lies in exploring these relationships while taking into consideration the "brain state" in which a decision is made.

1.1. Task-based & task-free imaging paradigms

Neuroimaging studies combining data from resting-state (rs-fcMRI; task-free) and task-based (fMRI; event-related) paradigms have mapped developmental changes in network dynamics, formation, and development (Fair et al., 2009, 2007a; Power et al., 2010). These studies and their antecedents have documented shared functional properties at both the regional and systems level (Fair et al., 2007b; Fox et al., 2006; Fox and Raichle, 2007). In essence, they cite a universality of intrinsically organized neural coherence; an underlying organization of functional brain connectivity that appears to be closely related to task-evoked neural responses (Cole et al., 2014; Fox et al., 2007). However, the nature of the intrinsic brain connectivity that lies beneath event-related task-activity is not static. Alterations in intrinsic activity under various conditions may yield important insights into the nature of decision making independent of the task evoked activity (Fair et al., 2007b).

1.2. Model-Based science, neuroimaging & prediction

With this framework in mind – recognizing the brain as a dynamic and complex biological system – a key direction for cognitive and behavioral neuroscience research is the acquisition and examination of large datasets employing multivariate analytical solutions and robust statistical validation procedures (Power et al., 2010). Such approaches applied to the study of brain and behavior in typically and atypically developing cohorts across the lifespan has already begun to show great promise and translational potential (Betzel et al., 2016, 2014; Cao et al., 2014; Chan et al., 2014; Dosenbach et al., 2010; Fair et al., 2012b; Helfinstein et al., 2014).

1.3. Purpose & goals

The current research examines the influence of sustained emotional contexts (neutral, negative, and positive) on residual patterns of functional connectivity (pseudo-resting state, RS)(Fair et al., 2007b). We test whether an individual's predicted functional "brain age" deviates under emotional influence (emotional brain age) and whether or not this deviation from one's true age in a given context is related to a propensity toward, or aversion to risk regardless of biological age.

2. Methods

2.1. Participants

As part of a large, ongoing study, 212 healthy right-handed 10–25 year olds (118 Females) with no history of mental illness, neurologic disorders, or use of psychotropic medications was recruited and included in the current report. Participants come from a diverse community sample in New York City (NY; N = 119) and Los Angeles (LA; N = 98) (all participants—M = 19.05, SD = 3.91; 11 children—6 female, ages 10–12 years, M = 11.55, SD = 0.89; 80 teens—45 female, ages 13–17 years, M = 15.77, SD = 1.44; 58 young adults—33 females, ages 18–21 years, M = 19.86, 1.11; 63 adults—34 females, ages 22–25 years, M = 23.7, SD = 1.03) self-identified as African American (23.6%), Asian (14.6%), Caucasian (34.4%), Hispanic (22.6%), or Other (4.7%), completed the Cognitive Control Under Emotion (CCUE) fMRI task (Cohen et al., 2016) and the Benthin Risk Assessment (Benthin et al., 1993; Steinberg, 2008). Nineteen participants were excluded for motion as described in more detail below. All participants provided informed written consent approved by the Institutional Review Boards at each site (see Supplemental Table S6 for more detail). A smaller subset of these data (N = 85; see discussion) has been used in previously published analyses cited within the current report (Cohen et al., 2016).

2.2. Behavioral risk assessment

As part of a larger behavioral (non-imaging) battery, participants completed a modified version of the Benthin Risk Perception Measure (BRPM)(Benthin et al., 1993; Gardner and Steinberg, 2005; Steinberg and Chein, 2015) to assess perception of, and preference for risk taking through self-report. Variables of interest used in the present report were graded on a 4-point scale and included risk perception (how risky is an activity), risk seriousness (how serious are the consequences for engaging in a risky behavior), risk cost (how much do costs outweigh the benefits), and risk preference (how much do the benefits outweigh the costs). A composite "risk assessment" index provided an overall measure of risk reflecting the mean score across risk perception, cost and seriousness. Except for risk preference, lower scores indicate less overall awareness and preference for risk.

2.3. fMRI task design & presentation

Participants completed a rapid event-related emotional go/nogo impulse control task to transient social cues under sustained negative (threat: anticipation of an aversive noise), positive (excitement: anticipation of a reward), and neutral (no anticipation of an aversive noise or reward) emotional contexts. The task featured a pseudo-random design with variable inter-stimulus time intervals for presentation of sustained emotional contexts and six transient social cue trial type pairings (fear/calm, calm/fear, fear/happy, happy/fear, calm/happy, and happy calm). During each emotional context, a participant was presented with the full-range of emotional and non-emotional faces and transient cue pairings. The potential for an emotional versus neutral event occurring was indicated by a colored background (Supplemental Fig. S4). A more detailed description of the novel CCUE task used in the present report, including effects concerning altered decision-making under the sustained emotional contexts can be found in previous reports (Cohen et al., 2016, 2015). Data were acquired during six 8-min and 2-s runs (for a total of 48 min and 12 s), allowing each emotional

expression (calm, fear, happy) to be used as a go or a nogo stimulus within runs counterbalanced for emotional context. For each trial, a face appeared for 500 ms, followed by a jittered intertrial interval (2–7 s). A total of 114 trials were presented in each run in a pseudorandomized order (84 go, 30 nogo across all cue types). In total, 60 nogo and 168 go trials, across all three cue types, were acquired for each emotional state. A portion of the participants (85 of 212) underwent a peer condition where a theoretical peer was present during task administration. Assessing individuals with and without peer influence separately produced results consistent with the primary findings described in the results section (see Supplemental Text). In brief, this manipulation *did not* have any statistically significant effects on the current findings.

2.4. Data acquisition

Whole brain fMRI data were acquired using Siemens Magnetom Trio 3.0 T scanners located at the Citigroup Biomedical Imaging Center at Weill Cornell Medical College (WCMC) or at the Staglin Center for Cognitive Neuroscience at the University of California, Los Angeles (UCLA). Scanning parameters were identical across data collection sites and each site acquired imaging data across the range of ages included in the current sample. A high resolution, T1 weighted magnetization-prepared rapid-acquisition gradient echo (MPRAGE) sequence scan was acquired using BIRN optimized sequences (repetition time [TR] of 2170 ms, echo time [TE] of 4.33 ms, 256-mm field of view [FOV], 160 slices x 1.2-mm sagittal slices). Functional images were acquired using T2*-sensitive echo planar pulse sequences covering the full brain. Thirty-eight 4-mm thick axial slices were acquired per 2500 ms TR (TE = 30 ms; FOV = 200-mm; Flip angle = 90°, 3.1 × 3.1 × 4.0 mm voxels).

2.5. Data pre-processing

Preprocessing of functional data, including preparation of fMRI data for connectivity analyses, was performed in-house at the Oregon Health & Science University (OHSU) using methods described previously to reduce artifacts, register subjects to a target atlas and resample data (Miezin et al., 2000). Steps included: (1) removal of a central spike caused by MR signal offset, (2) correction of odd vs. even slice intensity differences attributable to interleaved acquisition without gaps (differences in acquisition time), (3) correction for head movement within and across runs (Power et al., 2012) and (4) within-run intensity normalization to every voxel using a whole brain mode value of 1000. Atlas transformation of the functional data was computed for each individual via the MPRAGE scan. Each run then was resampled in atlas space (Talairach and Tournoux, 1988), using a target T1-weighted template (711-2B), on an isotropic 3 mm grid, combining movement correction and atlas transformation in one interpolation (Lancaster et al., 1995). All subsequent operations were performed on the atlas-transformed volumetric time series (Fair et al., 2012b).

2.6. Pseudo-resting state (pseudo-RS)

To examine functional connectivity under emotional influence independent of task performance and deterministic task-related events, task-related BOLD responses were modeled using the general linear model (GLM) and removed by regression prior to functional connectivity preprocessing on a voxel-by-voxel basis (Fair et al., 2007b; Fox et al., 2007, 2006; Miezin et al., 2000). Similar to Fair et al., 2007a,b; the GLM design included time as a seven level factor (7 frames following stimulus presentation) and the BOLD response was modeled over a period of ~17.5 s (7 frames, 2.5 s per MR frame), including two additional regressors coded in the GLM for baseline signal and linear drift. Importantly, given issues with parameter estimation across brain regions and timescales, a canonical hemodynamic impulse response function/shape was not assumed (Boynton et al., 2012; Fair et al., 2007b).

2.7. Connectivity pre-processing

Additional preprocessing steps were employed to reduce spurious variance stemming from non-neuronal activity (Fox et al., 2005; Fox and Raichle, 2007). Steps included: 1) regression of six parameters (head re-alignment estimates) obtained by rigid body head motion correction, 2) regression of the whole brain signal (Power et al., 2014a; Power et al., 2014b; See limitaions within the discussion), 3) regression of ventricular signal averaged from ventricular regions-of-interest (ROI), 4) regression of white matter signal averaged from white matter ROI, 5) regression of first order derivative terms for whole brain, ventricular, and white matter signals (to account for variance between regressors), and 6) temporal bandpass filtering ($0.009\,Hz < f < 0.08\,Hz$)(Fair et al., 2012b, 2009, 2008, 2007b). As described in the steps above, nuisance regression was applied prior to bandpass filtering to circumvent the potential for reintroducing unfiltered noise (i.e. previously filtered frequencies) back into the data (Hallquist et al., 2013). In addition, and in light of research demonstrating the profound impacts of in-scanner movement on connectivity estimates, motion was censored on a frame-by-frame basis via framewise displacement (FD)(Fair et al., 2012b; Power et al., 2012). Frames (or volumes), including adjacent frames (1 prior to and 2 following a censored frame) associated with greater than 0.3 mm displacement (translation and rotation) were removed from a time series prior to analyses (Minutes remaining: M = 33.94 min, SD = 10.08; Percent Frames Remaining: M = 71.78%, SD = 21.23). Nineteen participants were excluded from analyses for having less than 10 min or 20% of frames remaining across all runs (Laumann et al., 2015; Van Dijk et al., 2010).

2.8. Pseudo-RS connectivity pre-processing & ROI definition

To assess the discrete effects of sustained emotional contexts on underlying connectivity, all analyses were performed on motion-corrected residual timeseries (after removal of modeled task-specific effects as described in the previous section) for a given emotional context. This step is accomplished on a subject by condition basis whereby a binary vector representing the total number of frames (accounting for excluded frames due to motion) is further modified in order to ensure successful separation of adjacent epochs of fMRI data. Specifically, the aim is to eliminate any interaction between emotional conditions and to remove potential confounds induced by hemodynamic delay and response patterns (Fair et al., 2007b; Logothetis and Wandell, 2004). Supplemental Fig. S5 depicts a generalization of this process: steady-state is assumed after the first four frames, then the two frames preceding a block of sustained emotional valence (neutral, negative, and positive) are removed and six frames after a contextual block are included to account for the delay in the hemodynamic response. Frames removed are censored by setting the values of those frames to zero, whereas frames included are set to one.

From there, for each participant, blocks specific to a given emotional context are concatenated together, providing 3 vectors (neutral context, negative context, and positive context). Connection matrices were generated for each emotional context by taking the pairwise cross-correlation of valid time points between a set of 264 regions of interest (ROIs; 10 mm spheres) derived from a prior meta-analyses of task fMRI data and resting-state activity mapped onto a cortical surface (Dosenbach et al., 2010; Power et al., 2011, 2010). This process results in a 264 × 264 × 212 correlation matrix comprising 34,716 unique connections for a given context.

2.9. Partial least squares regression (PLSR)

Given the high-dimensional space (number of features) and covariance structure in the connectivity data, we chose to use PLSR to assess a participant's predicted age. PLSR is a multivariate technique similar to Principle Components Analysis (PCA) that models a response by reducing a large set of correlated features into orthogonal (uncorrelated) components. However, unlike PCA which focuses solely on the input (x; the independent variables, or predictors), PLSR takes the output (y; dependent variable) into consideration by limiting the relationship (amount of covariance) between the predictor variables and maximizing covariance (prediction) between x and y via singular-value decomposition (SVD)(Abdi and Williams, 2013). For further details and insightful schematics depicting this process we refer the reader to (Krishnan et al., 2011).

2.9.1. Applying PLSR to residual connectivity matrices

Here, (x) represents a 212 (participant) x 34,716 (connection) two-dimensional input matrix for a given context and (y), a 212×1 vector containing ages for each participant. We used 10-fold cross-validation on the entire sample in the neutral (baseline) context to identify the optimal number of components used to predict age. Cross-validation is an iterative process whereby a sample dataset is randomly partitioned in order to train and test sets used to assess a model's robustness, prevent overfitting, and increase generalizability to unseen data (Abdi and Williams, 2013; Fair et al., 2012b; Gabrieli et al., 2015; Krishnan et al., 2011). This approach identified four components capable of providing the best overall fit while simultaneously reducing the mean-squared error (MSE) and explaining the greatest variance in y (Fig. 1).

2.10. Predicting age

Counter to traditional correlation-based methods utilizing known outcomes/relationships, prediction is herein formalized as a model-based approach to predicting some outcome/response variable in a subset of unseen data from parameters generated within a larger dataset (Gabrieli et al., 2015).

2.10.1. Constructing the model

In order to avoid selection bias and maximize generalizability within our dataset, (using a fixed *number of four components* as described above) PLSR models are generated and tested on randomly selected groups using a cross-validation process repeated over 4000 iterations. Specifically, on each round of cross-validation, participants were randomly partitioned using a 30% holdout procedure resulting in 70% training (148) and 30% test (64) sets. Training of a model is based exclusively on functional connectivity data (in a Training set) from the neutral condition given no external stimulus was present. That is to say, participants are presented with the range of cues and faces across all contexts (neutral, negative and positive), however only the neutral context is absent of external manipulation (presentation/anticipation of noise or reward), and therefore serves as a baseline condition to derive predicted "brain ages". From here, in order to assess differences in connectivity under emotional influence (across contexts) within subject, we identified a test case with the best out-of-sample (test) fit between true and predicted ages in the neutral condition. As described below, this approach also allows us to test hypotheses regarding the association between alterations in functional connectivity under emotional influence and risk.

2.10.2. Applying the model

Here, we use the established 'optimal' model to predict a participant's age within the test case under varying emotional contexts by re-applying the model parameters (beta weights) generated exclusively from the training set in the neutral context to connectivity data from the test case for the negative and positive contexts.

2.11. Emotional brain age & group comparisons on risk

In order to assess the relationship between altered intrinsic functional connectivity in an emotional context and risk, we generated an adjusted emotional brain age for participants within the test case. Emotional brain age is herein defined as the difference between an individual participant's predicted age in the neutral context, from their predicted ages in the negative and positive emotional contexts (see Methods). This approach provides a zero-mean index such that those predicted to be younger in emotional contexts relative to the neutral condition fall below zero, and above zero if predicted to be older. Predicted emotional brain age within a given emotional context was used to split the test set into participants predicted as younger or older, and to test for group differences on risk metrics using standard univariate analyses (Fig. 2). Seven participants could not be included due to missing data on risk metrics. Additional independent *t*-tests were used to ensure predicted group status, and differences observed on risk metrics, were not due to a variety of factors including movement as discussed further below.

Data smoothing procedures (Fair et al., 2012b, 2007a, 2006) were applied to the predicted emotional brain ages using locally weighted sum of squares (loess). Such tests require no assumptions regarding the structure of data, and help zero in on appropriate model fits (Cleveland et al., 1988). Polynomial functions were also fit to the data permitting a qualitative comparison between a participant's biological and predicted emotional brain age (Fig. 2). Additional tests were performed to assess group differences within and between predicted groups by gender and peer group status (see Supplementary Material).

2.12. Structural data

Cortical thickness measurements, extracted from 244 cortical nodes mapped to the cortical surface (Gordon et al., 2014) within the 264 ROI set were used to generate a new PLSR model to predict age within the cross-validated training and test sets (Note: subcortical regions from the 264 region set were not used for the validation as they cannot be mapped for cortical thickness measurements). This procedure permitted additional validation of predicted ages derived from functional activation within the baseline neutral context. Thirteen participants within the training set and three within the test set could not be included in the current analysis. Two-participants were excluded due to bad image segmentations and 11 had not completed proper quality assurance at the time of the analysis, leaving 127 of 148 training participants and 61 of 64 test participants. Cortical reconstruction and volumetric segmentation was performed with the Freesurfer image analysis suite, which is documented and freely available for download online (http://surfer.nmr.mgh.harvard.edu).

2.13. Predictive features

Correlation matrices for the neutral, negative, and positive conditions represented 34,716 unique functional connections between 264 ROIs used as features in the PLSR model to predict age. The beta weights obtained, signifying the importance of a particular connection between ROIs in the model, were ranked and summed by their absolute values. ROIs were then plotted on a standardized brain surface using Caret 5 (University of Washington, St. Louis) scaled proportionally by their absolute beta weights.

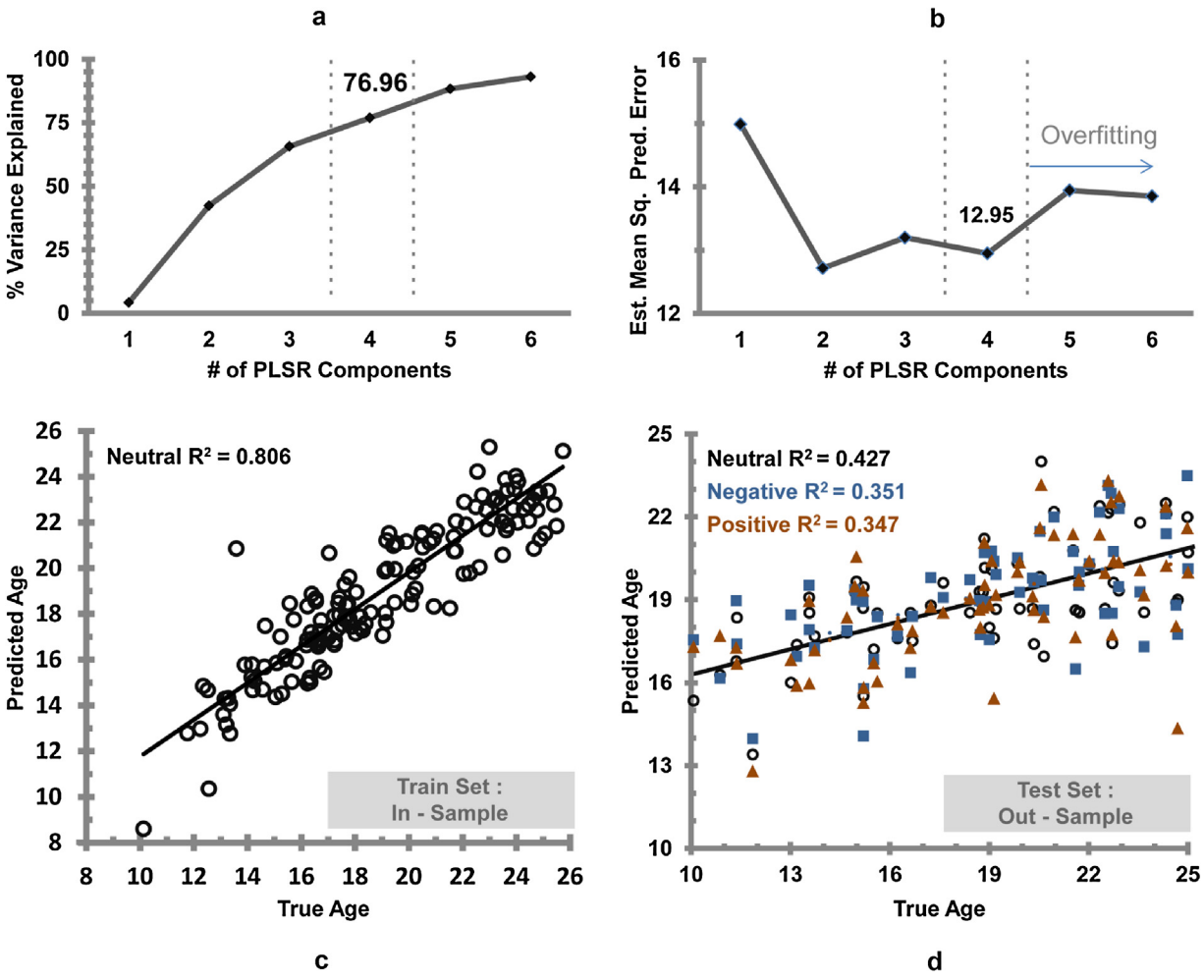

Fig. 1. Partial least squares regression (PLSR) & age prediction. 10-fold cross-validation identifies the optimal number of components able to predict age in the current sample. Four components were selected (a) minimizing the mean-squared prediction error and (b) maximizing the amount of explained variance in the predicted variable (age). Linear fits illustrate the predictive quality for age (exact age at scan) in the (c) training group for 148 randomly selected participants (70% Holdout; 83 Females, 65 Males) and (d) testing sets (64 Participants; 35 Females, 29 Males) in the NEUTRAL training condition after 4000 repetitions.

3. Results

3.1. Age prediction

We begin by examining the ability for our models to predict age in a given individual within a neutral baseline condition (see Methods). Age prediction was highly accurate over each round of cross-validation (Mean $r = 0.3846$; $SD = 0.0988$; $p <= 0.00001$). The optimal model was also highly significant (Fig. 1), and importantly well matched in demographic characteristics between train and test sets. The strength of prediction for the training set for this model is high as expected, as these data are used to generate the model itself (see Methods). However, the model significantly predicted age in the novel test sample with high accuracy as well (Fig. 1; Train r^2 0.810, $r^{2-adjusted}$ 0.808, *RMSE* 1.503; Test r^2 0.421, $r^{2-adjusted}$ 0.412, *RMSE* 1.591). In sum, these findings are consistent with prior work using alternative models with resting-state functional connectivity (Dosenbach et al., 2010; Fair et al., 2012b).

3.2. Predicted ages with structural connectivity

Generating a model within the training and test sets using an independent brain measure (i.e., structural, as opposed to functional data) provided an additional layer of support for predicted ages derived from pseudo-RS connectivity data in the neutral condition, despite predicting the same outcome measure (i.e. age). Cortical thickness measurements from 244 cortical nodes used for the functional predictions (see Methods) significantly predicted age (Fig. 2), consistent with prior work (Brown et al., 2012b). Importantly, predicted ages derived from cortical thickness estimates and pseudo-RS data in the neutral context were highly correlated and not significantly different. A paired samples *t*-test was used to test for differences between the predicted ages ($t_{(60)} = -1.211$, $p = 0.2667$). Panel c (Fig. 2) displays the significant relationship between both sets of predicted ages. For the current report we define "brain age" as ones predicted age based on brain measurements relative to their true age. Along with the functional data in the neutral state, these data provide evidence for a baseline "brain age" for a given individual (see Methods).

3.3. Predicted emotional brain age & risk

Given the ability of the models to predict age within the neutral context for both the training and test sets, and validation of predicted ages using structural data, we sought to assess the impact of sustained emotional context on connectivity and predict age under emotional influence in the negative and positive contexts relative to the neutral condition (*a comparison, of note, that cannot be conducted with anatomical data alone*). Applying the validated model (derived from the neutral baseline context in the training

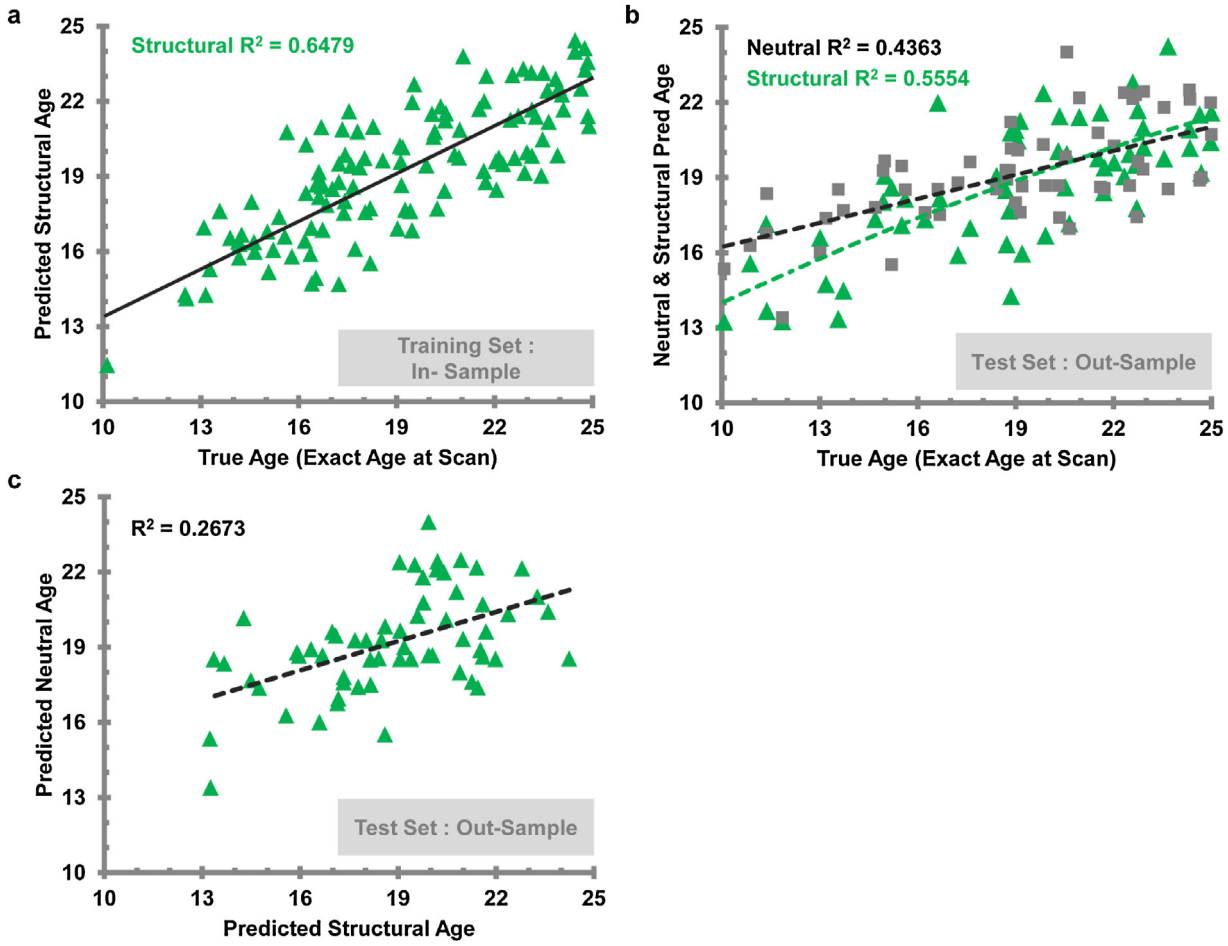

Fig. 2. PLSR-structural & age prediction. Using cortical thickness measurements from 244 nodes within the 264 node set, PLSR significantly predicted age in both the (a) in-sample (train; N = 127) and (b) out-of-sample (test; N = 61) data. Structural x Neutral predicted ages (c) were not significantly different and correlated at $r = 0.517$.

set exclusively) to connectivity data from the test sample in both the negative and positive emotional contexts yielded significant age predictions (Fig. 1; Negative r^2 0.349, $r^{2-adjusted}$ 0.338, *RMSE* 1.688, Positive r^2 0.333, $r^{2-adjusted}$ 0.323, *RMSE* 1.708). Although the slopes of these predictions were not statistically different (neutral vs. negative: p = 0.589; neutral vs. positive: p = 0.518), we next tested for any non-systematic differences within participants in predicted age between emotional contexts relative to neutral.

Predicted emotional brain ages (i.e. the difference between an individual's age predicted in the neutral baseline condition versus a given emotional condition) were plotted against a participant's true age and fit with LOESS curves (Fig. 3) to identify trends within the data. In sum, this analysis highlighted participants who tended to be predicted as relatively younger or older in an emotional context when compared to the neutral context. Adolescents (teens) showed a greater inflection overall toward being predicted younger on average (this particular result was further explored using a 3° polynomial for the negative and positive contexts, see Fig. 3; Negative $r^2 = 0.089$, *norm-R* = 10.139, $p = 0.131$; Positive $r^2 = 0.205$, *norm-R* = 0.897, $p = 0.003$). However, across all ages there were many participants who were predicted as being "older" in the emotional contexts as opposed to others who were predicted as "younger." Further, we acknowledge and discuss some potential limitations with regard to over-interpreting the adolescent specific results (see Discussion). The predicted ages between the negative and positive contexts were highly correlated (r = 0.823, r2 = 0.677, p = 0.000) and 15 of 64 (23.43%) participants switched predicted groups amongst the emotional contexts. In other words, for most participants, but not all, the phenotype (i.e. predicted younger vs. predicted older) cut across both emotional conditions.

We then set out to determine whether this phenotype (i.e. predicted "older" or "younger" under emotional contexts) related to differences on risk preference and risk perception across these groups of participants (regardless of various developmental and environmental factors). Within the final test set of 64 participants, 7 did not have risk data resulting in 57 participants used in all subsequent analyses assessing the relationship between predicted emotional brain age and risk.

Differences on risk metrics were assessed between predicted phenotypes (i.e. two levels: predicted younger versus predicted older) using a multivariate analysis of variance (MANOVA) for risk perception, cost, and seriousness for a given context (i.e. negative and positive). Results were just above significance at trend level in the negative context ($F_{(3.53)} = 2.684$, $p = 0.056$, $\eta p^2 = 0.132$) and significant in the positive context ($F_{(3.53)} = 3.433$, $p = 0.023$, $\eta p^2 = 0.163$). A univariate ANOVA was run separately for risk assessment (given it is a composite score of risk perception, risk cost, and risk seriousness; see Methods), and was significant in both the negative ($F_{(1.55)} = 4.000$, $p = 0.051$) and positive ($F_{(1.55)} = 8.020$, $p = 0.006$) context. Risk preference was assessed separately (different scale; see Methods) using an independent *t*-test and was significant at p < = 0.05 in the negative context ($t_{(55)} = 2.31$, $p = 0.024$) with the predicted younger group having a greater preference for risk. Differences on risk preference was trend level at p < = 0.10 in the positive context ($t_{(55)} = 1.72$, $p = 0.092$), again with the predicted younger group having a greater preference for risk.

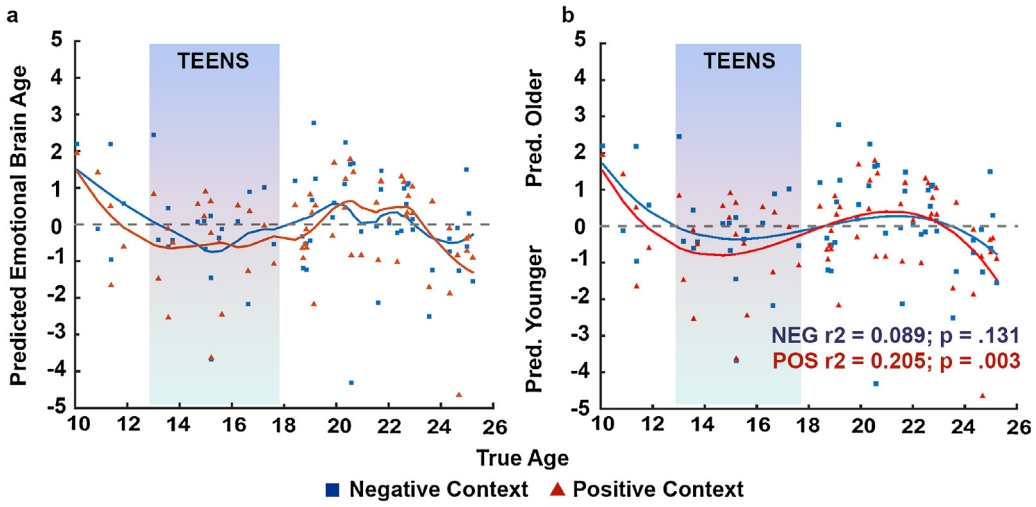

Fig. 3. Smoothing curves (LOESS) & Polynomial Fits. Qualitative visualization of trends present within predicted emotional brain age groups for negative (Younger N = 33; Older N = 31) and positive (Younger N = 33; Older N = 31) emotional contexts. Data (true age x predicted emotional brain age) is fit with a) LOESS curves sensitive to outliers (40% of the data). The sharpest inflection occurs about mid-adolescent to young-adult range. The decline occurs around mid-adolescence stabilizing somewhat by the late young-adulthood. In panel b) a polynomial fit is used (Negative $r^2 = 0.089$, *norm-R* = 10.139, $p = 0.131$; Positive $r^2 = 0.205$, *norm-R* = 0.897, $p = 0.003$).

Post-hoc independent *t*-tests in the positive context were significant for risk perception and risk seriousness at $p <= 0.05$, and trend level for risk cost at $p <= 0.10$ in that the predicted younger phenotype showed a decreased risk perception and greater inclination toward risk (see Fig. 4; Supplemental Table S2). Post-hoc independent *t*-tests for the negative context were significant for all but one measure (Fig. 4; Supplemental Table S2).

We note several important considerations here: 1) Although adolescents tended to show a greater overall trend toward being predicted as younger during emotional contexts, there were no differences in the predicted ages between the contexts (see Methods), 2) the predicted groups (i.e., predicted 'older' versus 'younger') did not differ on measures of pubertal development, site of scan acquisition, IQ, socioeconomic status (SES), race, task performance, or movement (percent frames remaining or remaining mean FD; Supplemental Table S1), this was true for both the negative and positive contexts. Motion is discussed further within the supplemental material in relation to age, predicted outcomes and metrics assessed here.

Overall, the results suggest that regardless of context, age, or gender (in addition to the additional post-hoc group comparisons described above), the phenotype of being predicted younger in emotional contexts is associated with greater risk preference and lower risk perception (Fig. 4; Supplemental Table S2, although see caveats in Supplemental Table S2). Importantly, a participant's predicted "brain age" in an emotional context (as opposed to the predicted emotional brain age defined as the difference of 'brain age' in neutral and emotional contexts) did not predict scores on risk metrics (Supplemental Fig. S1). Further, simply taking the difference between predicted ages in the neutral context and a participants true age, does not result in observed differences between predicted groups on any of the risk metrics assessed; risk perception ($t(55) = -1.531$, $p = 0.132$), risk cost ($t(55) = -0.778$, $p = 0.440$), risk seriousness ($t(55) = 0.550$, $p = 0.585$), risk assessment ($t(55) = -0.768$, $p = 0.446$), risk preference ($t(55) = -0.778$, $p = 0.440$). This result further supports the relationship between predicted emotional brain age as defined in the current study and the risky behavioral phenotype. Small, but significant relationships

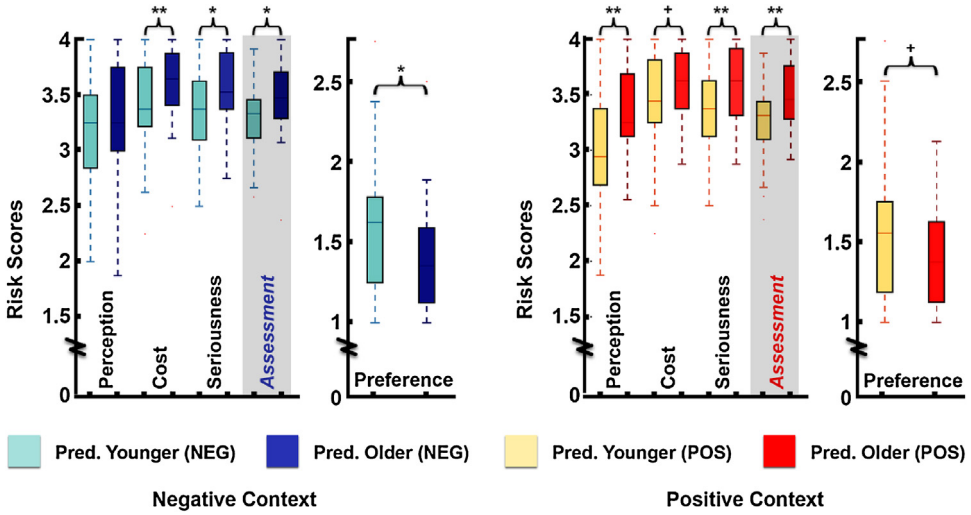

Fig. 4. Predicted emotional brain age group comparisons on risk metrics. Post-hoc independent *t*-tests were performed between individuals predicted as younger or older in both the negative (Younger N = 29; Older N = 28) and positive (Younger N = 28; Older N = 29) emotional contexts relative to the neutral condition on metrics assessing awareness of and preference for risky behavior. * $p <= 0.05$, ** $p <= 0.01$, + trend at $p <= 0.10$.

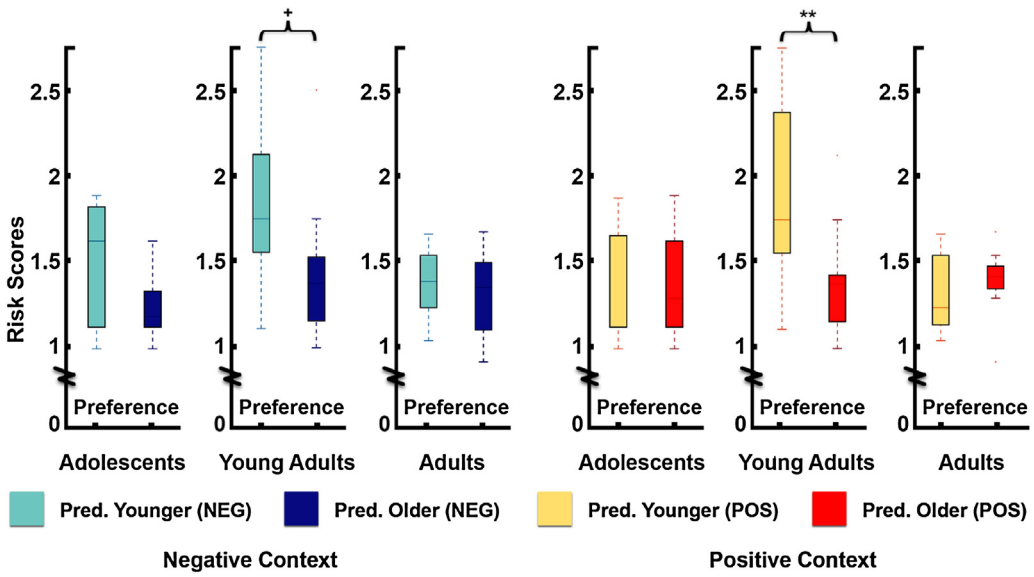

Fig. 5. Predicted emotional brain age & risk preference by age cohort. Significant differences were observed for risk preference only in young adults. No significant differences were observed for adolescents or adults on risk preference in the negative or positive context. *p < = 0.05, ** p < = 0.01, + trend at p < = 0.10. See supplementary material for predicted emotional brain age and other risk measures as a function of age cohort.

with risk metrics were observed for a participant's biological age, predicted age in the neutral context (Supplemental Fig. S1), and predicted emotional "brain ages" for both emotional contexts.

3.4. Age group comparisons

The results demonstrate that regardless of biological age, emotional situations influence underlying physiology and relate to "risky" phenotypes. However, to test whether the strength of this effect is dependent on age or more prominent within a particular age range we ran additional analyses. That is, to assess the differential effects of emotional context on a particular age range and risk phenotype, we re-ran analyses, and examined differences between and within predicted emotional age groups in three of the four predefined age-cohorts (Adolescents 13–17; Young Adults 18–21; Adults 22 +). Children were excluded from these analyses given that only 5 of 7 children in the test sample had risk data, as well as concerns with validity and reliability of self-reporting on the risk assessment (also see Supplemental Text). Importantly, the primary analyses testing for differences on risk metrics between predicted age groups on this subsample showed that the initial results survived largely unaltered (Supplemental Fig. S2, Supplemental Table S3).

Results from a two-way analysis of variance (ANOVA) using predicted emotional group (i.e. two levels: predicted younger versus older) and age cohort (i.e. three levels: teens, young adults, and adults) as factors revealed both significant and trend-level interaction effects within in the positive context. An age x group interaction was identified for risk cost ($F_{(2.52)} = 4.365$, $p = 0.018$), and risk preference ($F_{(2.52)} = 4.365$, $p = 0.018$). Post hoc analyses showed this finding was largely driven by decreased risk cost and increased risk preference for those predicted younger within the young-adult cohort (risk cost ($t_{(19)} = -2.798$, $p = 0.0115$) and risk preference ($t_{(19)} = 2.798$, $p = 0.0112$); Fig. 5, Supplemental Fig. S3, and Supplemental Table S4). This finding demonstrates a decreased awareness of and a greater preference for risk respectively for those predicted younger within the young-adult cohort. An age x group interaction for risk seriousness ($F_{(2.52)} = 2.714$, $p = 0.077$) and risk assessment ($F_{(2.52)} = 3.084$, $p = 0.055$) were trend-level at p < = 0.10. Results were again driven by decreased risk seriousness ($t_{(19)} = -2.434$, $p = 0.0250$) and risk assessment ($t_{(19)} = -2.921$, $p = 0.009$) for those predicted younger within the young-adult cohort (Supplemental Fig. S3, and Supplemental Table S4), likely representing a decreased awareness of risk.

Importantly, the overall trend for being predicted younger and at greater risk was evident across age groups and context, but not necessarily for all measures, as direct comparisons failed to reach significance in the negative context. This result is of particular interest as it suggests that although teens may be slightly more likely to have the younger "brain age" phenotype in emotional contexts, the tendency for this phenotype (relative to the older "brain age" phenotype) to elicit increased risk preference and decreased risk perception is greater during the young-adult period.

3.5. Supplementary material

Though not a primary aim of the current paper, we explored the relationship between gender and risk, as well as the potential influence of peer presence amongst predicted brain age groups and risk. No significant effects were found with regard to peer influence. While not significant, trends were identified within the gender comparisons. In addition, we assessed whether or not puberty, scan site, race, and task performance had any influence on predicted brain age groups (i.e. predicted younger vs. older) and risk. No effects were found for scan site, puberty or race. For task performance, no differences were found between groups on the number of false-alarms (FA; go-nogo errors) in either context. However trend-level mean-differences were found in the positive context for FA, though these results had no effect on differences found between predicted groups on the risk metrics assessed. Results and discussion are provided within the supplemental information.

3.6. Functional neuroanatomy associated with the age prediction models

Correlation matrices for the neutral, negative and positive conditions represented 34,716 unique pseudo-RS functional connections between 264 ROIs used as features in the PLSR model to predict age. The beta weights obtained, signifying the importance of a particular connection between ROIs in the model, were

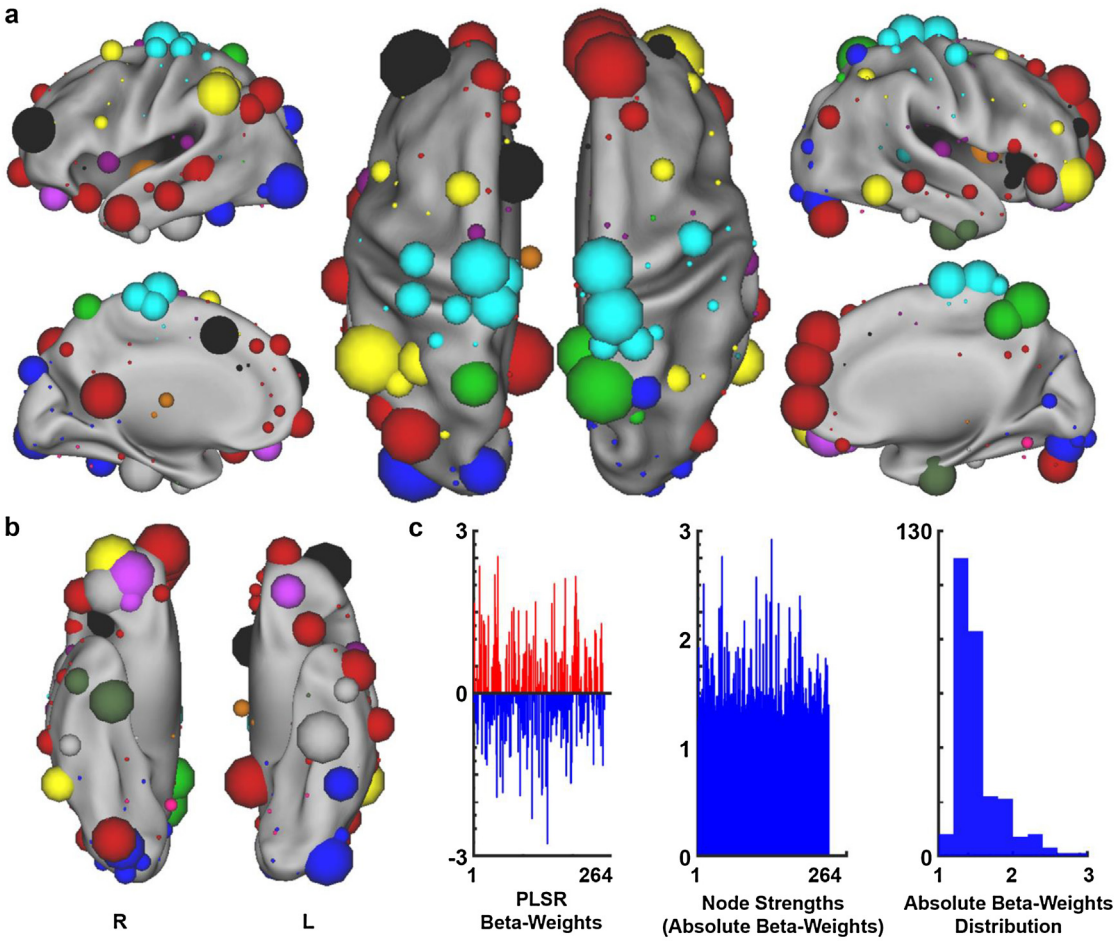

Fig. 6. Predictive features. 264 regions of interest visualized on a standardized brain surface representing pre-established networks (Default Mode (Red), Dorsal Attention (Green), Frontoparietal (Yellow), Salience (Black), Cingulo-opercular (Purple), Visual (Blue), Subcortical (Orange), Ventral Attention (Teal), etc.) as described in Power et al., 2011. Nodes are scaled proportionally according to their degree of importance (sum of absolute beta weights for each connection to an ROI) in predicting age using PLSR. Panel a) provides dorsal, lateral and medial views of the brain, while panel b) shows the ventral surface. Panel c) depicts the relative (left-most graph) and absolute beta-weight distributions for all 264 regions. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

ranked and summed by their absolute values for each ROI (Fair et al., 2012a). ROIs were then plotted on a standardized brain surface using Caret 5 (University of Washington, St. Louis) scaled proportionally by their absolute beta weights (Fig. 6). The histogram in Fig. 6 shows a distribution of weights for each ROI. Of the 264 nodes used in the current study, 27 represent the top 10% (90th percentile), 14 the top 5%, and 4 ROIs in total had beta weights greater than 2.5. Interestingly, the top 5% included key nodes consisting of developmentally important hubs within large-scale networks identified in rs-fcMRI studies and regions cited throughout the fMRI literature as important for the integration of affective stimuli and socioemotional processing (Fig. 6, Supplemental Table S5a). For example, important cognitive control hubs included regions within the default mode (DFM; posterior cingulate [PCC]), dorsal attention (DAN; superior parietal [sPAR]), frontoparietal (FP; inferior lateral parietal [IPL], ventrolateral prefrontal [vlPFC]) and salience (SAL; dorsal anterior cingulate [dACC]) networks. Regions within large-scale networks with task-specific functional properties included three medial prefrontal areas (ventral [vmPFC], medial [mPFC], dorsal [dmPFC]) within the DFM, a primary visual node (V1) and the dorsomedial thalamic nuclei (dmTHAL) as part of a subcortical network. The remaining nodes within the top 5% consisted of two inferior temporal regions (ventral anterior [vaTEMP], ventral medial [vmTEMP]) and one within the orbitofrontal (OFC) region. Although all 34,716 connections are considered within the model, we have provided the top 20 pairwise connections between ROIs (Supplemental Table 5b). We have also included the full list of ROIs used as a supplementary document. Additionally, in order to highlight topology related to the predictive features (connections) we have provided the absolute beta weights in matrix format sorted by network (Fig. 7).

4. Discussion

4.1. Functional connectivity under emotional contexts and risk

The dimensional data-driven approach taken in the present study permitted the mutual investigation into both similarities and differences in brain connectivity across development based on affective states within an individual and across groups. Utilizing a robust multivariate methodology and two distinct MRI measurements (i.e. function and structure) we replicate, and add to, previous findings that highlight the ability to identify a "brain age" in individuals (Brown et al., 2012b; Dosenbach et al., 2010). Adding to previous work, based on pseudo rs-fcMRI, we demonstrate the ability to predict age across emotional contexts in a sizeable training set using cross-validation (as we have previously shown)(Dosenbach et al., 2010; Fair et al., 2012b) as well as in a completely separate test set (which understandably had slightly lower fit statistics (Combrisson and Jerbi, 2015)). We further show

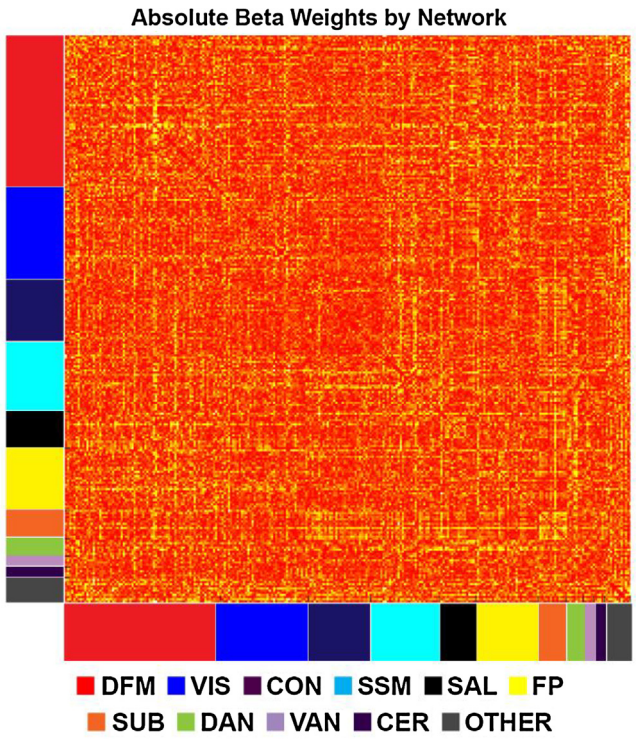

Fig. 7. Absolute beta weights sorted by network. 264 regions of interest visualized as a matrix and sorted according to the pre-established networks (Default Mode (Red), Visual (Blue), Cingulo-opercular (Purple), Sensorimotor (Cyan), Salience (Black), Frontoparietal (Yellow), Subcortical (Orange), Dorsal Attention (Green), Ventral Attention (Teal), Cerebellum (Dark Blue), and nodes not part of a large-scale network (Grey) as described in Power et al., 2011). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

that both positive and negative contexts can alter an individual's "brain age" based on changes in functional connectivity patterns. This finding is not to say there are no differences in functional neuroanatomy between contexts (e.g., see Cohen et al., 2016) — rather similar patterns are identified with pseudo rs-fcMRI. Importantly, two distinct phenotypes (i.e., a subgroup of participants whose emotional brain age was predicted 'older' versus a subgroup whose was predicted 'younger') were related to risk perception and preference.

As noted above, across the range of ages examined in the present study, we identified a subgroup of participants who had a phenotype whereby their brain organization was predicted as younger in an emotional context, while another subgroup had a phenotype whereby they were predicted as being older. *While not all participants that were predicted as being younger had a more "risky" phenotype (i.e. lower risk perception and higher risk preference), on average they did*. In essence, based on alterations in functional connectivity in an emotional context, our data suggest that the subgroup of participants whose functional brain patterns reverted back to patterns of a younger age in an emotional context were at "risk for being risky." That is, the predicted age under emotional (negative or positive) contexts, relative to the neutral context, was related to increased risk preference and lower risk perception as measured via the Benthin Risk Perception Measure. Importantly, we do not argue that these phenotypes are predicting future behaviors, which by necessity would require a longitudinal design. Rather, we are highlighting that these phenotypes relate to current risk perception and preference of the participants.

Of note, while on average all participants who had the "predicted younger" phenotype regardless of biological age, were at "risk to be risky," the propensity to be "predicted younger" was slightly more evident during the adolescent time period (see Fig. 3 and 1). Specifically, this trend occurs around mid-adolescence and stabilized somewhat by the late young adult period. This finding is consistent with the literature that shows that adolescence and early young-adulthood is a particularly vulnerable period for higher incidence of risky behaviors, higher degrees of sensation seeking and impulsivity, greater sensitivity to rewards, heightened reactivity to threat and punishment, increased criminal activity and substance use disorders, as well as, the emergence of psychopathologies (Bava and Tapert, 2010; Benthin et al., 1993; Brown et al., 2015; Dreyfuss et al., 2014; Steinberg, 2009; Sweeten et al., 2013) — a vulnerability that may not be captured in controlled research settings per se. While we did not observe a difference in pubertal status in those predicted younger or older during emotional contexts, this "dip" during adolescence and early young-adulthood might be related to pubertal development, which we plan to explore further (also see Supplemental Text).

Interestingly, while the adolescent period was the period of time that individuals were more likely to have the "predicted younger" phenotype on average, it was individuals in the young adult period (i.e. ages 18–21) who were at the greatest *risk to be risky* for the "predicted younger" versus "predicted older" phenotype. In other words, the results suggest that this period of development is an important transition where one might be less likely to be "predicted as younger" relative to the adolescent period, but if they are, they are even more inclined to be risky relative to the "predictive older" phenotype. Post hoc comparisons within the young adult cohort (predicted younger vs. predicted older; Fig. 4 and Supplemental Fig. S3) were trend-level in the negative context, while all comparisons were significant or trend level within the positive context, a result not seen within any of the other age group comparisons. By adulthood (ages 22+), many of these findings were reduced or limited, but present to a degree. Such results support and extend previous studies assessing young adults (within the age-range defined here), documenting developmental and behavioral differences aligning their behavior more closely to adolescents than fully matured adults (Cohen et al., 2016). Previous studies examining age-dependent differences on risk taking and risky behavior through measures of self-report are consistent with our overall findings (Steinberg, 2009, 2008). Such studies posit that adolescents and young adults are not less capable of making proper or logical decisions, per se, from their adult counterparts, but rather inconsistencies in behavior emanate from a variety of environmental, psychological, sociological and biological factors. In our case, a charged emotional context *may* change state physiology (i.e. functional connectivity) in *some individuals*, such that decisions are made more impulsively relative to what the individual is capable of doing outside of that context. Such hypotheses are likely to be an important area of investigation in future work.

The idea that not all adolescents or young adults are poor executive decision-makers is not a new concept. As indicated by Gardner and Steinberg (2005), such findings lend support to concepts like group polarization theory. The general idea is that those with risky predispositions, especially during adolescence and young-adulthood, are more likely to make risky-decisions and engage in risky behavior under emotionally salient situations and/or in response to the influence of peers. With that said, it is important to note that, while to a lesser extent than adolescents and young adulthood, even individuals in the adult cohort that were "predicted younger" were slightly more at *risk to be risky* for some measures (e.g. decreased risk perception, etc.) — suggesting that while on average adults are not known to be risky, the phenotype (predicted as younger in emotional contexts) in subpopulations of

adults might lead to impulsive, risky decisions (who are often in a position of authority) as well.

4.2. Documenting developmental differences

Results described above, stemming from differences in pseudo-resting state connectivity, may extend and bridge prior research utilizing task-free and task-based studies alike to document developmental differences during this sensitive time period. Specifically, in a related study, Cohen et al. found that under negative emotional contexts young adults (18–21) appeared to perform more like their younger (teen) than older (adult) counterparts both in measures assessing task performance and task-related neural activation (within a subset of the participants used here; see Methods). Both teens and young adults show decreased task performance and activity (percent signal change) in cognitive control regions such as the dorsolateral prefrontal cortex (dlPFC) and dorsal anterior cingulate (dACC) in response to emotional stimuli, particularly fearful cues. In parallel, greater activity was recorded with decreasing performance in the ventromedial prefrontal cortex (vmPFC), a region implicated in affective processing. The authors suggest this imbalance between top-down and bottom-up control, as previously reported in adolescents (Galvan et al., 2007; Somerville and Casey, 2010) is present within young adults when emotional context is taken into account. However, the authors point out that more studies are needed in order to assess the differential impact emotional states may have on cognitive control across individuals. Our results lend further support and suggest considering developmental differences regarding decision making under salient conditions, particularly during adolescence and young-adulthood, an important direction for future research. We add to this prior work showing that while teens may on average be affected greater than older cohorts, both young adults and adults are susceptible to large-scale alterations in FC under emotional contexts. Importantly, our results are also distinct, in that we are considering the overall affect emotional context has on underlying functional topology and demonstrate that such properties are capable of distinguishing and predicting individuals more likely to be at risk across the age spectrum, particularly in young adults.

4.3. Comparison across studies

As previously stated (see methods), a portion of the total participants (N = 85; 32 with a hypothetical peer) used in the Cohen et al. study were included in our analyses. Of these participants, 66 (28 with a hypothetical peer) belonged to the final training set, and 19 (4 with a hypothetical peer) within the final test set. Differences between samples and methodologies make comparing results between these and other studies complex, and interpretations are likely not straightforward. Task activations in response to an external stimulus are not the same as changes in intrinsic connectivity during emotional states. While limitations are discussed further below, and caution is warranted, we hope our findings A) highlight this complex interaction between intrinsic and task evoked activity that is in need for further study, and B) highlight the importance of considering individual differences and heterogeneity across development in both typical and atypical populations (Fair et al., 2012a; Gates et al., 2014; Karalunas et al., 2014).

Across studies, differences in brain maturation (Casey and Jones, 2010; Shaw et al., 2008; Somerville and Casey, 2010), functional network development and organization (Fair et al., 2007a; Power et al., 2010), differences in socio-emotional development (Dreyfuss et al., 2014; Somerville and Casey, 2010), and other such developmental factors may all have implications for why some teens and young adults are more likely than others to engage is risky behaviors. Such correspondence across investigations may infer the existence of a biological phenotype further aiding to explain such behavior. While the speed at which neuroscience is being used in the courtroom to adjudicate law may be premature (e.g., see limitations below)(Cohen and Casey, 2014; Jones et al., 2013) (Roper v. Simmons, 2005; Graham v. Florida, 2010; Miller v. Alabama and Jackson v. Hobbs, 2012), future advances that consider brain development and contextual information may provide additional insight into these complex decisions.

4.4. Limitations & considerations

4.4.1. Regarding developmental trajectories

Several limitations within the present study should be taken into consideration and are discussed here and within the provided supplemental information. While care was taken in the current cohort to obtain a nationally representative sample, as a cross-sectional study, inferences cannot be made at the individual or group level as to whether patterns regarding individual predicted ages and the relation to risky decision making reported are developmental or purely situational in nature. Longitudinal samples will be needed in order to assess the true developmental characteristics of the identified risk brain phenotypes. With regard to the age cohorts used, age distribution was lower at both tails. Specifically, the number of children in the study was negligible, and concerns regarding comprehension within the risk assessment cannot be eliminated. However, excluding children from post-hoc analyses had no significant effect on differences in risk between groups predicted as younger or older. In addition, the adult age-range is constrained at 22–25 years of age and may not give an adequate representation of the population at a biological and or psychological level.

4.4.2. Regarding risk assessment

Given current and/or past propensities toward and experiences with risk, differing contingencies amongst age groups present another potential concern with respect to validity of the self-report measure used in general. Presumably, without such limitations the ability to discern between the predicted groups would only improve. Further, how risk is defined, operationalized, and assessed in clinical and behavioral studies may deserve attention. Methodological differences and interpretations may account for inconsistencies noted elsewhere regarding perception and preference at any age. While in the present report, we were simply interested in the existence of a relationship between risk and connectivity under emotional influence, studies in the future will likely benefit from refined methodologies to tease apart developmental differences.

4.4.3. Regarding the fMRI paradigm

The novel CCUE task designed to assess the effects of emotional context on cognitive capacity and brain activity is a positive step forward for developmental science. However, the paradigm does not likely mimic real-world situations and therefore direct extrapolations to legal matters are unwarranted at this time. Further the task design may present a few methodological challenges. Most obvious, is the ability to discern effects attributed solely to cues presented from trial-to-trial and in relation to a particular sustained emotional context in which the cues are presented (Ollinger et al., 2001). Further, whether or not an individual is experiencing or feeling a change in overall mood versus simply being emotionally excited during anticipation of reward and/or punishment is unknown. Though several recommended steps were taken to enhance the detectability of discrete neural events from trial-to-trial (Fair et al., 2007b; Fox et al., 2007; Huettel, 2012), and ensure no overlap between emotional contexts existed (Supplemental Fig. S5), the complexity and lack of any true rest periods between a given emotional context may pose an issue with such detection

and interpretation (Petersen and Dubis, 2012). In the present report we tested the influence of emotional context on task-residual activation in an attempt to circumvent such concerns, and in light of research citing the complex interplay between intrinsic resting-state fluctuations and task-induced BOLD activity (Fox et al., 2006, 2005; Mennes et al., 2010). In the future, studies assessing the influence of contextual information may benefit from the use of more advanced methods to design task fMRI paradigms (Kao et al., 2009; Wager and Nichols, 2003).

4.4.4. Regarding motion artifact

As outlined in the methods section (and discussed further within the supplementary material), we have attempted to robustly correct for motion related confounds to the best of our abilities guided by the most recent literature. Of note, global signal regression (GSR) is used within the current analyses following several insightful reports noting its merits in reducing global artifacts and robustly dealing with in-scanner movement especially when used in combination with motion scrubbing (i.e. framewise displacement)(Burgess et al., 2016; Power et al., 2012, 2014a,b; Power et al., 2016, 2015; Satterthwaite et al., 2013, 2012; Siegel et al., 2016, 2014). As discussed elsewhere, while GSR has been criticized for inducing negative correlations (by shifting the distribution of r values for observed connections) and causing distortions in the data (Saad et al., 2012), motion has been shown to skew the distribution in the opposite direction and quite remarkably so (Burgess et al., 2016; Power et al., 2015, 2012; Satterthwaite et al., 2012; Siegel et al., 2016, 2014) – distortions that GSR correct. As shown in the cited literature, these confounds correlate highly with behavioral results and often lead to false-positives across studies (Burgess et al., 2016; Siegel et al., 2016). Thus, while individual studies need to take their own data into account, we feel in the context of the current study the use of GSR is important. In addendum, though we feel confident in our approach toward ameliorating such confounds using this approach; we acknowledge more work is warranted in order to identify the optimal solutions to remove artifacts biasing developmental findings.

4.5. Conclusions

In the present study we demonstrate the ability to predict age derived from pseudo-RS connectivity in emotional contexts and categorize individuals into predicted emotional brain age groups. Further, we show that differences in individuals predicted age under such influence related to certain metrics assessing awareness of and preference for risky behavior. Results suggest that regardless of biological age contextual settings have an impact on underlying functional neurophysiology, in this case an individual's "predicted emotional brain age," and that some individuals are more at-risk than others, particularly from the teen years through the transitional period of young-adulthood (as defined within the present study), but also within some adults depending on how risk is assessed.

Author contributions

M. D. Rudolph and D. A. Fair drafted the manuscript and designed analyses. M. D. Rudolph managed data and performed data analysis under supervision of D. A. Fair and O. Miranda-Dominguez. B. J. Casey, A. Galván, and L. Steinberg developed the study concept for collection of behavioral and task fmri data. A. O. Cohen, K. Breiner, and D. V. Dellarco collected and distributed the data. J. Chein and K.C. Fettich provided measurements of cortical thickness. L. Steinberg, R.J. Bonnie, E.S. Scott, K. Taylor-Thompson and J.A. Richeson provided legal interpretations. All authors provided critical revisions and approved the final version of the manuscript for submission.

Competing financial interests

Network members (Casey & Steinberg) acknowledge receipt of consulting fees and research funding from the MacArthur Foundation. No other competing financial interests are reported.

Conflict of interest

None.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.dcn.2017.01.010.

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