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Age-related changes in reappraisal of appetitive cravings during adolescence

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ABSTRACT

The ability to regulate temptation and manage appetitive cravings is an important aspect of healthy adolescent development, but the neural systems underlying this process are understudied. In the present study, 60 healthy females evenly distributed from 10 to 23 years of age used reappraisal to regulate the desire to consume personally-craved and not craved unhealthy foods. Reappraisal elicited activity in common self-regulation regions including the dorsal and ventral lateral prefrontal cortex (specifically superior and inferior frontal gyri), dorsal anterior cingulate cortex, and inferior parietal lobule. Viewing personally-craved foods (versus not craved foods) elicited activity in regions including the ventral striatum, as well as more rostral and ventral anterior cingulate cortex extending into the orbitofrontal cortex. Age positively correlated with regulation-related activity in the right inferior frontal gyrus, and negatively correlated with reactivity-related activity in the right superior and dorsolateral prefrontal cortices. Age-adjusted BMI negatively correlated with regulation-related activity in the predominantly left lateralized frontal and parietal regions. These results suggest that the age-related changes seen in the reappraisal of negative emotion may not be as pronounced in the reappraisal of food craving. Therefore, reappraisal of food craving in particular may be an effective way to teach teenagers to manage cravings for other temptations encountered in adolescence, including alcohol, drugs, and unhealthy food.

Adolescence presages dramatic increases in autonomy and exposure to temptations, such as unhealthy food, alcohol, and drugs. Learning how to manage appetitive cravings and resist these temptations is a vital aspect of healthy adolescent development (Davidson et al., 2000; Gross, 1998; Gross and Munoz, 1995). However, little is known about how the adolescent brain regulates these cravings. Recently, we and others have leveraged the considerable work done in the field of emotion regulation to better understand the cognitive regulation of craving. Like emotions, cravings are affective states that motivate behavior, in ways that are not always desirable or appropriate — and may thus benefit from being regulated.

One useful regulation strategy is reappraisal, the cognitive reinterpretation of an event or stimulus so as to change its affective meaning (Giuliani and Gross, 2009). Reappraisal can be used to significantly reduce cravings for personally-craved unhealthy foods by, for example, focusing on the negative consequences of indulging in that food (Giuliani et al., 2013). In adults, reappraisal of the craving for food stimuli recruits a network of brain regions quite similar to those recruited during the reappraisal of other affective states, including the dorsolateral prefrontal cortex (DLPFC), the inferior frontal gyrus (IFG), and the dorsal anterior cingulate cortex (dACC; Buhle et al., 2013; Giuliani et al., 2014; Hollmann et al., 2011). Recruitment of this network often modulates or overrides activity in regions like the ventral striatum (VS), whose activity often reflects the anticipation of reward (e.g. Buhle et al., 2013; Hare et al., 2009; Martin Braunstein et al., 2014).

The ability to use reappraisal to regulate affective states begins to emerge as early as age 5 (DeCicco et al., 2012). Increases in reappraisal ability and usage throughout adolescence have been noted in some samples (Garnefski et al., 2002; McRae et al., 2012; Silvers et al., 2012), but not all (Gullone et al., 2010; Silvers et al., 2014). Several studies have interrogated the neural correlates of emotion reappraisal in adolescence, using stimuli including sad pictures, disgusting pictures, negative pictures from the International Affective Picture System, and sad film clips (Belden et al., 2014; Lévesque et al., 2004; McRae et al., 2012; Pitskel et al., 2011). Across all of these studies, using reappraisal to reduce negative affect (measured by the difference in self-reported affect between passive viewing and reappraisal) commonly recruited aspects of lateral prefrontal cortex (PFC). However, only two of these studies investigated age-related effects on the behavioral and neural correlates of emotion reappraisal, and the findings were conflicting. Pitskel et al. (2011) found that age was associated with less reappraisal-related activity in the orbitofrontal cortex (OFC), medial PFC, left IFG, and left amygdala, and McRae et al. (2012) found that age had a positive linear relationship with reappraisal-related activity in the left IFG and a positive quadratic relationship with activity in the posterior cingulate cortex (PCC). Additional well-powered investigations of

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the neural correlates of reappraisal across adolescence may help to resolve this inconsistency.

While most of the extant work on reappraisal has focused on the reappraisal of negative affective states, other affective motivational states are also useful and important targets of cognitive regulation (e.g., Giuliani et al., 2008; Kober et al., 2010a; Parrott, 1993). In particular, reappraisal is an effective way of reducing cravings such as those elicited by cigarettes and junk food (Giuliani et al., 2013; Kober et al., 2010a). Although much of the work on reward and appetitive motivation in adolescence has focused on secondary rewards like money, some studies have begun to investigate how primary, non-monetary rewards like food are processed in the adolescent brain (e.g., Holsen et al., 2005; Luking et al., 2014; Silvers et al., 2014). This is an especially important question during this phase of development, when experimentation with rewarding appetitive substances like alcohol or drugs often begins (Eaton et al., 2012).

The transient peak in approach and exploratory behaviors during adolescence is thought to be adaptive, as it biases the adolescent to pursue experiences that are essential for developing adult independence (Luciana and Collins, 2012). However, adolescents encounter many situations in which regulation of these approach behaviors is preferable or even necessary for survival. Unfortunately, little work exists on the cognitive regulation of affective states beyond negative emotion (e.g., Giuliani et al., 2014; Hollmann et al., 2011; Kober et al., 2010b; Siep et al., 2012), and even less exists on the adolescent regulation of the desire for non-monetary rewards like food. One recent study investigated the neural bases of food craving reappraisal in adolescence, comparing reappraisals focusing on the costs of eating an unhealthy food with ones focusing on the benefits of not eating the unhealthy food. Both strategies elicited activity in the left medial superior frontal gyrus (SFG) and IFG, which was not moderated by body mass index (BMI; Yokum and Stice, 2013). However, this study ($N = 21$; M age $= 15.2$, $SD = 1.18$) did not investigate whether or how food craving reappraisal ability develops from childhood into adulthood. Another recent study of the neural bases of food craving reappraisal examined neural activity in participants across a much wider age range ($N = 105$, ages 6–23 years), and asked them to focus more or less on the appetizing features of unhealthy foods (Silvers et al., 2014). This study mentioned only one age effect specific to reappraisal strategy, in the putamen; it also found that leaner (age-adjusted BMI) individuals recruited left ventrolateral and parietal regions more during regulation trials, especially at younger ages. Taken together, it remains unclear from the limited literature whether activity in neural circuitry supporting appetitive reappraisal should increase, decrease, or remain stable across adolescence.

More generally, several models of adolescent neurobiological development have combined the literature on regulation and reactivity to better understand risk-taking behavior in adolescence. For example, dual-systems and imbalance models (e.g., Casey, 2015; Somerville and Casey, 2010; Steinberg, 2010) contrast non-linear patterns of incentive motivation and reward seeking (uniquely heightened in adolescence) with linear age-related increases in cognitive regulation to account for the transient peaks in approach behaviors and risk-taking seen during this time. These models have been generative and useful, but the existing neuroimaging evidence in human adolescents relies primarily upon affective faces and money to represent the vast array of stimuli motivating approach (or avoidance) behavior encountered in everyday life. It is presently unknown how well these models apply to other stimuli, and thereby represent the full complexity of the changes taking place (Bjork et al., 2012; Crone and Dahl, 2012; Pfeifer and Allen, 2012).

Therefore, in the present study, we sought to investigate the behavioral and neural correlates of food craving reappraisal and reactivity in a large sample of healthy adolescents across a wide age range. Specifically, we hypothesized that, across all subjects, cognitive reappraisal would effectively moderate the desire to consume personally-craved unhealthy foods. Neurally, our a priori regions of interest were based on the expectations that reappraisal of food cravings would elicit regulation-related activity in the DLPFC, IFG, and dACC, and food reactivity would elicit reward-related activity in the VS and OFC. We were also interested in whether and how individual differences in age, BMI, and self-reported reappraisal usage related to the behavioral and neural correlates of food reappraisal and reactivity. In light of the neurobiological imbalance models discussed above, it may be expected that reappraisal ability and related neural activity would exhibit a linear association with age in adolescence, whereas cravings and related neural activity would exhibit a nonlinear pattern (such as an adolescent-specific peak). However, due to the mixed findings in the literature thus far regarding the relationship between the neural correlates of reappraisal and age, we did not have an a priori hypothesis as to the predicted direction of the relationship (if any) between age and brain activity during reappraisal.

Methods

Participants

Participants were 60 females between the ages of 10 and 23 ($M = 16.66$, $SD = 3.68$, range 10.16–22.89 years) recruited from the Eugene, OR metropolitan area. The sample was distributed across the age range; in one-year increments, Ns ranged from 3 to 6 ($M = 4.62$, $SD = .77$). There was no overlap between this sample and those from previous studies using this task (Giuliani et al., 2013, 2014). Potential participants were excluded if they were left-handed, under 10 or over 23 years of age, non-native English speakers, had a current or past diagnosis of neurological or psychological disorder, had a history of head trauma, were pregnant, currently used psychoactive medication, or had any non-MRI compatible conditions (e.g., metal in body). All gave informed consent in accordance with the University of Oregon Institutional Review Board.

Task

Details of the task are outlined in our previous work (Giuliani et al., 2013) and shown in Fig. 1. Briefly, images of two types of palatable foods were included as stimuli: low energy density foods ("Neutral"), and energy-dense (ED) foods of the participants' choosing. The total stimulus set consisted of 14 pictures of low energy-density food (carrots, corn, cucumber, beans, broccoli, Brussels sprouts, eggplant, lettuce, squash, tomatoes; pre-tested desirability $M = 2.51$, $SD = .23$), and 28 pictures in each of the following categories of ED food (pre-tested desirability $Ms = 3.46–3.53$, $SDs = .16–.37$): chocolate, cookies, donuts, fries, ice cream, pasta, and pizza. Importantly, images were chosen such that the mean desirability ratings of the ED food categories were not significantly different from each other (all paired-samples p-values $> .2$), and that the mean of each ED food category was significantly greater than the mean of the Neutral stimuli (p-values $< .001$). All participants saw the same set of 14 Neutral stimuli. For the ED stimuli, participants chose from the above list of seven food types the one that they craved the most ("Craved") and the one they craved the least ("Not Craved"), and saw only images within those two categories in addition to the Neutral stimuli during the task. Craving was defined as the desire and tendency to consume the target food, even in the absence of hunger.

There were two types of instructions: Look or Regulate. The Look instruction directed participants to focus on the pictured food, imagine it was actually in front of them, and think about consuming it. The Regulate instruction directed participants to focus on the food, imagine it was in front of them, and think about the short- or long-term negative consequences of eating a large quantity of the food (e.g., stomachache, weight gain). Participants chose one specific strategy before the task and were directed to use that same strategy on every Regulate trial. For the rating period, we instructed participants to report their craving honestly at the end of each trial. To minimize the demand characteristics of the task regarding regulation success (i.e., reduced desire ratings

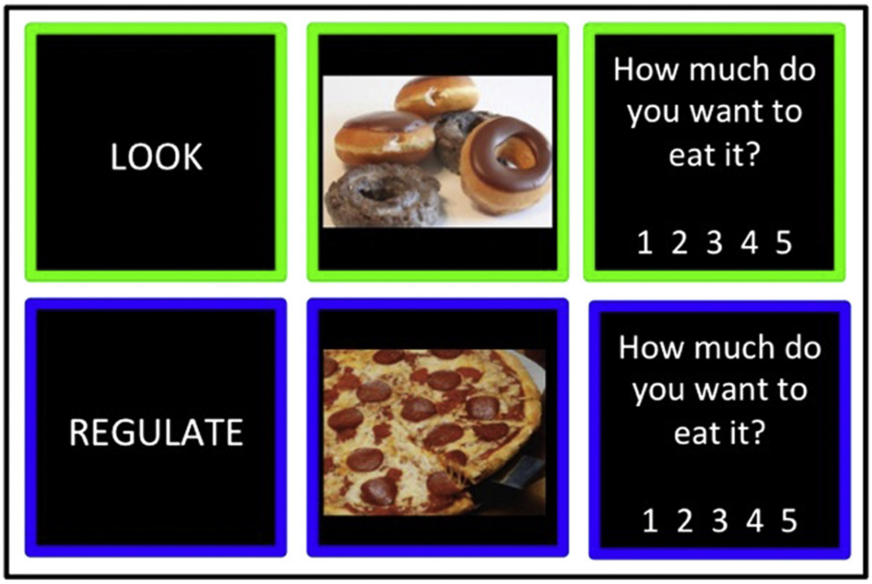

Fig. 1. Example Look and Regulate trials from the task.

on Regulate trials), we explicitly stated “we don't expect you to be able to do this on every picture, so please honestly rate how much you desire the food when all is said and done.” To minimize instruction contamination across trials, we instructed participants to view each trial as a fresh event, and to do their best to only look or only regulate according to the cue. The final event-related design included 5 trial types (Look Neutral, Look Craved, Look Not Craved, Regulate Craved, and Regulate Not Craved), with 13–14 trials for each condition totaling 67 trials, distributed across two approximately even runs with a brief break in between.

Each trial began with a 2 s instructional cue (Look or Regulate), followed by a 5 s stimulus presentation, 4 s to rate the desirability of the stimulus, and a jittered inter-trial-interval averaging 1 s and following a gamma distribution. The stimuli assigned to each condition were counterbalanced across participants (e.g., if two participants chose donuts (either craved or not craved), the donut images assigned to the Look instruction for one participant would be assigned to the Regulate instruction for the next participant, and vice versa). The stimuli within each category did not vary between participants choosing that category. Desirability ratings (“How much do you desire to eat this food?”) were made on a 1-to-5 Likert scale, where 1 = “not at all” and 5 = “very much.” Within-run stimulus order was optimized to maximize contrast estimation efficiency using a genetic algorithm (Wager and Nichols, 2003). Run order was counterbalanced across subjects.

Strategy training

Prior to beginning the task, participants underwent a structured training session in which they received the strategy instructions described above and viewed a sample trial for each of the two instructions. Sample trials provided participants experience with using the cognitive reappraisal strategies while looking directly at pictures of foods not used during the experimental session. Participants then completed a 5 trial practice run with the experimenter to ensure comprehension of the task and reappraisal instructions. The experiment began when the training session was complete and the experimenter was confident that participants understood the directions and procedures.

Experimental procedure

After providing informed consent, height, and weight, participants completed the individual difference measures detailed below, and reported level of hunger on a 1 (“very hungry”) to 5 (“very full”) Likert scale. Next, participants were trained on the task. They were then asked to choose their most and least craved categories of ED stimuli and the regulation strategy they believed would be most effective for them during Regulate trials. Participants then practiced the task with the experimenter (N.G.). In the MRI, participants completed two runs of the eating regulation task, as well as another task not reported here. Following the completion of the task in the scanner, the experimenter interviewed each participant to ensure that they had indeed used the selected regulation strategy on the Regulate trials.

Behavioral data analysis

Self-reported ratings of desire for the ED foods were subjected to a 2 × 2 repeated-measures analysis of variance (RMANOVA) to determine main effects of stimulus and instruction and test for interaction effects. Pairwise *t*-tests between conditions were performed to decompose observed effects, as well as to investigate the differences between Look Neutral, Look Craved, and Look Not Craved. Regulation success was defined in two ways: 1) percent difference in self-reported desire to consume the pictured food between Regulate and Look (i.e., the main effect of regulation) and 2) percent difference in self-reported desire between Look Craved and Regulate Craved (i.e., the simple effect of regulation of personally-craved foods). Reactivity to food cues was also defined in two ways: 1) percent difference in self-reported desire to consume the pictured food between Look Neutral and Look Craved, and 2) percent difference in self-reported desire to consume the pictured food between Look Not Craved and Look Craved. The alpha level was set to .05 for all analyses. For behavioral data and individual difference measures described below, outliers were Winsorized at 3 standard deviations from the mean, and all significantly non-normal variables were transformed to improve normality when possible. All statistical analyses of behavioral data were performed in SPSS21.0 (IBM Corp., Armonk, NY).

Functional MRI data acquisition and analysis

Data were acquired using a 3.0 T Siemens Skyra scanner at the University of Oregon's Robert and Beverly Lewis Center for Neuroimaging. Blood oxygen-level dependent echo-planar images (BOLD-EPI) were acquired with a T2*-weighted gradient echo sequence (TR = 2000 ms, TE = 30 ms, flip angle = 90°, matrix size = 64 x 64, 33 contiguous axial slices with interleaved acquisition, field of view = 200 mm, slice thickness = 4 mm). For each participant, a high-resolution structural T1-weighted 3D MP-RAGE pulse sequence (TR = 2300 ms, TE = 2.1 ms, matrix size = 192 × 192, 160 contiguous axial slices, voxel size = 1 mm^3, slice thickness = 1 mm) was acquired coplanar with the functional images.

Before preprocessing, non-brain tissue was removed from the brain images using robust skull stripping with the Brain Extraction Tool (BET) in FMRIB's Software Library (FSL; http://www.fmrib.ox.ac.uk/fsl/). Image preprocessing was implemented in SPM12b (Wellcome Department of Cognitive Neurology, London, UK; http://www.fil.ion.ucl.ac.uk/spm/), which included realignment and co-registration of each subject's own high-resolution structural image to a mean of the functional images using a six-parameter rigid body transformation model, reorientation of all images to the plane containing the anterior and posterior commissures, segmentation of the structural image into six tissue priors, spatial normalization of all images into Montreal Neurological Institute (MNI) template space using the deformations resulting from segmentation, and smoothing using a 8 mm^3 full-width half-maximum Gaussian kernel.

Statistical analyses were implemented in SPM12b. For each subject, event-related condition effects were estimated according to the general linear model, using a canonical hemodynamic response function, high-pass filtering (128 s) and a first-order autoregressive error structure. At the subject level, BOLD signal was modeled in a fixed effects analysis with separate regressors modeling each condition of interest during the picture presentation period (5 s) and for the instruction and rating periods. Six-parameter motion regressors were calculated as deviations from the origin, and entered into single-subject models as covariates of non-interest. One additional participant was excluded from analyses due to excessive movement in the scanner that shifted her head outside of the field of view. Linear contrasts were created for each ED food condition versus rest (Look Craved, Look Not Craved, Regulate Craved, Regulate Not Craved) for each participant. These four contrasts were then imported to a group-level RMANOVA, where contrasts of interest (e.g., Regulate Craved > Look Craved) were modeled for inference to the population. The remaining contrast of interest (Look Craved > Look Neutral) was modeled separately for each participant, and was imported to group-level random effects analyses using a one-sample *t*-test.

Because the brain regions previously identified in reappraisal encompass several large cortical and subcortical regions, we investigated the neural correlates of food craving regulation using whole-brain analyses. For these whole-brain analyses, we applied a combined voxel-height and cluster-extent correction for multiple comparisons to guard against Type I error derived from AFNI's AlphaSim software (Cox, 1996). AlphaSim takes into account the size of the search space and the estimated smoothness of the data (using AFNI's 3dFWHMx) to generate probability estimates (using Monte-Carlo simulations) of a random field of noise producing a cluster of voxels of a given size for a set of voxels passing a given voxel-wise *p*-value threshold. In our data set, these simulations determined that a voxel-wise threshold of $p < .005$ combined with a spatial extent threshold of 62 voxels corresponded to a family-wise error (FWE) corrected false-positive probability of $p < .05$ across the whole brain for the RMANOVA, and 72 voxels for the Look Craved > Look Neutral two-sample *t*-test. Because one of our a priori ROIs, the VS, is a small structure, activity localized there is not expected to survive a volume correction of 62–72 voxels. Therefore, to investigate task-related activity in the VS, we relaxed the cluster threshold to 20.

Individual difference measures

We investigated the relationship between the behavioral and neural correlates of appetitive reappraisal and reactivity and several individual difference measures, including age, BMI, hunger at time of scan, and self-reported emotion regulation usage. We modeled age as both a linear and quadratic (mean-centered, squared) variable. Hunger was included as a covariate using the 1 (“very hungry”) to 5 (“very full”) rating made before the scan. Because BMI percentile (i.e., BMI relative to same-age, same-sex peers) more accurately represents body composition during childhood and adolescence than raw BMI scores (Mei et al., 2002), we calculated BMI percentile for the 46 individuals under 20 years of age using the Center for Disease Control's BMI-for-age growth chart as implemented at http://nccd.cdc.gov/dnpabmi/Calculator.aspx. Age-adjustments to BMI are not available for individuals over the age of 20, so the remaining 14 participants in this category were excluded from analyses examining BMI. Self-reported emotion regulation was assessed using the reappraisal subscale of the Emotion Regulation Questionnaire for Children and Adolescents (ERQ-CA; Gullone and Taffe, 2012) for participants aged 10–17 and the reappraisal subscale of the Emotion Regulation Questionnaire (ERQ; Gross and John, 2003) for participants aged 18–22. Scores on the ERQ-CA were linearly transformed to a 1-to-7 Likert scale and combined with ERQ scores to create one composite reappraisal variable for all participants.

To investigate whether there was a significant relationship between appetitive reappraisal or reactivity and these individual difference measures at the behavioral level, we ran Pearson's correlations in SPSS. To investigate the relationship between age and appetitive reappraisal or reactivity at the neural level, we created one-sample *t*-test contrasts for the regulation and reactivity simple effect contrasts (Regulate Craved > Look Craved, Look Craved > Look Not Craved) at the single-subject level, brought them up to the group level, and included age as a regressor. We also examined correlations between other individual difference measures (reappraisal strategy or age-adjusted BMI) and activity in clusters resulting from the whole brain analyses (specifically in the contrasts of Regulate Craved > Look Craved, Look Craved > Look Not Craved). Self-reported hunger at the time of the scan was included as a covariate of non-interest in all models, but did not significantly change the results.

Results

Behavioral

Replicating our two previous studies with this task (Giuliani et al., 2013, 2014), we observed significant main effects of Stimulus (Craved $M = 3.16$, $SD = .43$; Not Craved $M = 1.97$, $SD = .53$; $F_{(1,59)} = 191.4$, $p < .001$) and Instruction (Look $M = 3.06$, $SD = .43$; Regulate $M = 2.07$, $SD = .39$; $F_{(1,59)} = 340.4$, $p < .001$) on self-reported desire to consume the depicted food. As shown in Fig. 2, reappraisal successfully reduced self-reported desire to consume both the Craved (Look $M = 3.83$, $SD = .51$; Regulate $M = 2.49$, $SD = .52$; $t_{(59)} = 19.07$, $p < .001$) and Not Craved foods (Look $M = 2.28$, $SD = .69$; Regulate $M = 1.65$, $SD = .48$; $t_{(49)} = 9.04$, $p < .001$) as compared to passive viewing. This was qualified by a Stimulus by Instruction interaction ($F_{(1,59)} = 61.74$, $p < .001$), indicating that the magnitude of regulation success (reduction in self-reported desire) was greater for Craved than Not Craved foods. Regulation success was not significantly related to age ($p = .81$), which demonstrates that reappraisal strategy training was equally effective across subjects of all ages. Regulation success was not significantly related to self-reported hunger ($p = .18$) or reappraisal usage from the ERQ and ERQ-CA ($p = .99$).

Paired samples *t*-tests revealed that reactivity was greater than zero under both definitions (Look Neutral to Look Craved, Look Not Craved to Look Craved). Look Craved foods were rated as significantly more desirable than Look Neutral ($M = 2.65$, $SD = .89$; $t_{(59)} = 9.12$, $p < .001$) and Look Not Craved foods ($t_{(59)} = 13.91$, $p < .001$), and Look Neutral foods were rated significantly more desirable than Look Not Craved foods ($t_{(59)} = 2.56$, $p = .013$). Reactivity defined as the percent change from Look Neutral to Look Craved was significantly related to age ($r_{(58)} = -.26$, $p = .042$), but the percent change from Look Neutral to Look Not Craved was not ($p = .22$). This indicates that the magnitude

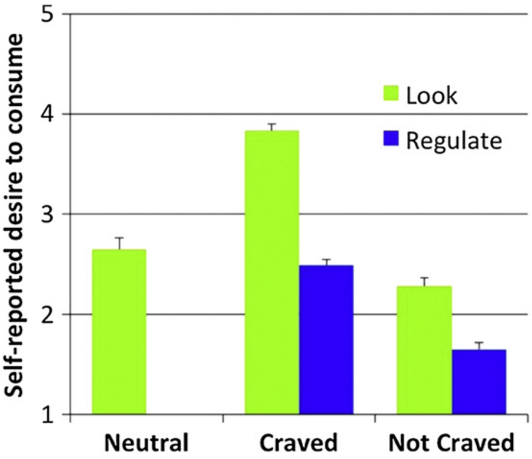

Fig. 2. Self-reported mean desire to consume pictured food in the five conditions: look neutral, look craved, look not craved, regulate craved, regulate not craved. Error bars represent standard error of measurement (SEM).

Table 1
Regions, MNI coordinates, cluster sizes and peak *t*-values for the Regulate > Look and Look > Regulate main effects ($p < .005$, $k = 62$ threshold used for all contrasts).

Contrast and Region	MNI coordinates (x, y, z)	Cluster size	Peak *t*
Regulate (Craved + Not Craved) > Look (Craved + Not Craved) ($p < .005$, $k = 62$)			
Left supramarginal gyrus	(−57, −49, 29)	1224	11.19
Left IPL	(−54, −49, 44)		10.38
Left middle temporal gyrus	(−54, −34, −7)		7.05
Left DLPFC/dACC	(−39, 5, 47)	4096	9.56
Left SFG	(−9, 14, 59)		8.79
Left IFG	(−51, 23, −7)		7.57
Left anterior insula	(−42, 11, −4)		7.21
Left cuneus	(−12, −79, 8)	509	7.07
Right cuneus	(15, −67, 8)		5.36
Right IPL	(60, −46, 41)	326	6.7
Right IFG	(54, 23, 1)	458	6.5
Right anterior insula	(45, 14, −4)		6.45
Left anterior PCC	(−3, −19, 32)	297	6.5
Left precuneus	(−9, −67, 35)	230	5.67
Right superior temporal gyrus	(48, −28, −7)	183	5.32
Right caudate	(18, 8, 11)	415	4.74
Look (Craved + Not Craved) > Regulate (Craved + Not Craved) ($p < .005$, $k = 62$)			
Right superior parietal lobe	(33, −70, −50)	630	6.11
Right precuneus	(33, −73, 32)		4.64
Left precentral gyrus	(−39, −22, 62)	250	5.56
Left postcentral gyrus	(−39, −28, 50)		5.36
Right MFG	(48, 35, 14)	102	4.67
Right IFG	(42, 8, 23)	120	4.24
Right anterior insula	(42, 2, 14)		3.85
Right DLPFC	(21, 29, 38)	114	3.94
Right SFG	(30, 17, 53)		3.82
Left fusiform gyrus	(−30, −49, −13)	200	3.76
Left posterior insula	(−42, −4, 11)	80	3.65

Note: IPL = inferior parietal lobe; MFG = middle frontal gyrus; DLPFC = dorsolateral prefrontal cortex; SFG = superior frontal gyrus; IFG = inferior frontal gyrus; dACC = dorsal anterior cingulate gyrus; PCC = posterior cingulate cortex.

of reactivity between low-energy density and personally-craved ED foods decreases with age, but differences between personally-craved and not craved ED foods does not; this pattern extends results from prior studies finding decreased reactivity with age to ED foods (presented with no distinction between those personally craved or not) (Silvers et al., 2014). Reactivity was not significantly related to self-reported hunger or reappraisal usage (p-values > .1), but the difference between Look Craved and Look Not Craved was significantly related to age-adjusted BMI ($r_{(45)} = -.31$, $p < .05$), driven almost entirely by associations between age-adjusted BMI and Look Not Craved ($r_{(45)} = .34$, $p < .05$) rather than Look Craved ($r_{(45)} = -.09$, $p = .55$), suggesting that leaner females experienced a greater differential in reactivity to personally-craved ED foods.

Across all participants, 32 chose to use the short-term negative consequences reappraisal strategy, 27 chose the long-term negative consequences strategy, and one reported using both. Neither reactivity nor regulation success (percent difference in self-reported desire between Look Craved and Regulate Craved) differed significantly by strategy used (p-values > .33), nor was there a significant effect of age or BMI on strategy choice (p-values > .29).

fMRI

Regulation

As shown in Table 1, the main effect of Regulate > Look across both picture types (Craved, Not Craved) produced a large cluster of activity encompassing the left and right superior frontal gyrus, left DLPFC, left IFG, left anterior insula, and bilateral dACC. Other clusters included the left inferior parietal lobule (IPL) and supramarginal gyrus, left and right cuneus, right IPL, right IFG and anterior insula, left PCC, left precuneus, right superior temporal gyrus, and the caudate body.

A whole-brain investigation of the voxels significantly more active in the Regulate Craved > Look Craved contrast as compared to the Regulate Not Craved > Look Not Craved contrast was conducted to formally test for the Stimulus by Instruction interaction (Table 2). This contrast revealed clusters encompassing the left and right precuneus and right IPL. The reverse contrast revealed significant clusters in the left and right posterior insula, left precentral and postcentral gyri, right parahippocampus and fusiform gyrus, left dACC and paracentral lobule, left IFG, left medial frontal gyrus extending into the caudate body and dACC, left fusiform gyrus, and left PCC. To further understand the nature of this interaction, we conducted post-hoc analyses that individually interrogated the simple effects of Regulate Craved > Look Craved and Regulate Craved > Regulate Not Craved. As shown in Fig. 3a, the whole-brain contrast of Regulate Craved > Look Craved revealed significant clusters of activity in the left IPL and supramarginal gyrus, left DLPFC, left posterior medial and superior frontal gyri, right IPL, left precuneus, left PCC, left middle temporal gyrus, right IFG, left anterior superior and middle frontal gyri, left cuneus, and right superior and middle frontal gyri. The whole-brain contrast of Regulate Craved > Regulate Not Craved revealed significant clusters of activity in the right precuneus and IPL.

Reactivity

The whole-brain contrast of Look > Regulate across both picture types produced significant clusters of activity in the right superior parietal lobe (SPL) and precuneus, left precentral and postcentral gyri, right middle frontal gyrus (MFG), right IFG extending into the anterior insula, right DLPFC, left fusiform gyrus, and left posterior insula (Table 1). The whole-brain contrast of Look Craved > Look Not Craved revealed significant clusters in the left precentral cortex, bilateral perigenual ACC extending rostrally from the OFC and subgenual ACC around the genu into the left dACC, and left superior and middle temporal gyri. Relaxing the voxel extent threshold to investigate the small a priori region of interest for this contrast, the VS, revealed a 29 voxel cluster with significantly more activity in Look Craved versus Look Not Craved (Fig. 4a, Table 3). The one-sample t-test contrast of Look Craved > Look Neutral revealed significant clusters in the right lingual gyrus extending into the right SPL and middle temporal gyrus, left parahippocampal and middle occipital gyri, and left precuneus and middle temporal gyrus (Table 3). Relaxing the voxel extent threshold did not reveal any VS activity in this contrast.

Correlations with age

To investigate whether regulation- or reactivity-related activity was significantly related to age, we entered age as linear and quadratic regressors (mean-centered age and age^2) in the whole-brain simple contrasts of Regulate Craved > Look Craved and Look Craved > Look Not

Table 2
Regions, MNI coordinates, cluster sizes and peak *t*-values for the Stimulus x Instruction, Regulate Craved > Look Craved, and Regulate Craved > Regulate Not Craved contrasts ($p < .005$, k = 62 threshold used for all contrasts).

Contrast and region	MNI coordinates (x, y, z)	Cluster size	Peak *t*
Stimulus × Instruction (RC > LC) > (RNC > LNC) ($p < .005$, k = 62)			
Left precuneus	(0, −70, 41)	82	3.55
Right precuneus	(12, −67, 56)		3.1
Right IPL	(51, −49, 56)	114	3.2
Stimulus × Instruction (RNC > LNC) > (RC > LC) ($p < .005$, k = 62)			
Right posterior insula	(51, −19, 14)	885	4.98
Left posterior insula	(−45, −1, −1)	1205	4.76
Left IPL	(−60, −28, 35)		3.91
Left precentral gyrus	(−33, −22, 65)	359	4.74
Left MFG	(−21, −16, 68)		4.24
Left postcentral gyrus	(−24, −37, 68)		3.48
Right parahippocampal gyrus	(27, −34, −22)	642	4.62
Right fusiform gyrus	(39, −37, −13)		3.88
Left dACC	(0, 2, 41)	376	4.34
Left paracentral lobule	(−9, −22, 50)		3.28
Left IFG	(−42, 32, 5)	65	3.52
Left medial frontal gyrus	(−6, 41, −16)	192	3.48
Left caudate body	(−9, 26, 8)		3.31
Left dACC	(0, 35, 2)		3.26
Left fusiform gyrus	(−42, −46, −16)	64	3.42
Left PCC	(−9, −55, 11)	62	3.23
Regulate Craved > Look Craved ($p < .005$, k = 62)			
Left IPL	(−54, −52, 41)	575	8.01
Left supramarginal gyrus	(−57, −52, 32)		7.73
Left DLPFC	(−39, 5, 47)	866	6.57
Left medial frontal gyrus/dACC	(−6, 17, 50)	745	5.96
Left SFG	(−12, 20, 59)		5.33
Right IPL	(57, −46, 44)	314	5.86
Left precuneus	(−6, −70, 38)	173	5.21
Left PCC	(0, −19, 29)	173	5.16
Left middle temporal gyrus	(−60, −37, −4)	178	5.07
Right IFG	(57, 20, 2)	217	4.79
Left SFG	(−24, 50, 26)	232	4.66
Left MFG	(−33, 59, 2)		3.18
Left cuneus	(−12, −82, 8)	82	4.06
Right SFG	(24, 53, 26)	64	3.42
Right MFG	(39, 44, 26)		2.87
Regulate Craved > Regulate Not Craved ($p < .005$, k = 62)			
Right precuneus	(12, −67, 56)	63	4.29
Right IPL	(54, −64, 47)	95	3.2

Note: IPL = inferior parietal lobe; MFG = middle frontal gyrus; dACC = dorsal anterior cingulate gyrus; IFG = inferior frontal gyrus; PCC = posterior cingulate cortex; SFG = superior frontal gyrus.

Craved. For regulation, the linear effect of age was significantly positively related to Regulate Craved > Look Craved activity in a cluster in the right IFG (peak at 57, 20, 11; $p < .005$, k = 20; Fig. 5a), such that older participants displayed more activity in this region than younger participants. The quadratic effect of age was not significantly related to regulation-related activity.

To see whether the linear age-related effect in right IFG was due to increases in Regulate Craved-related activity or decreases in Look Craved-related activity, we conducted post-hoc analyses to interrogate the simple effects of Regulate Craved > rest and Look Craved > rest. Regulate Craved > rest produced positive age-related clusters of activity in regions including the right SFG, left and right MFG and IFG, and right IPL. Look Craved > rest produced no negative age-related clusters of activity. In addition, we extracted mean parameter estimates of activity during Regulate Craved > rest and Look Craved > rest, from the right IFG cluster resulting from the Regulate Craved > Look Craved contrast in the whole brain RMANOVA. We averaged Regulate Craved > Look Craved values across three age group bins (pre/early adolescence, ages 10-13; middle adolescence, ages 14–17; and late adolescence, ages 18–23), and also displayed individual participant datapoints for each condition (see Fig. 5b). When taken together, these analyses suggest that reappraisal-related right IFG activity resulted primarily from increases in Regulate Craved-related activity with age.

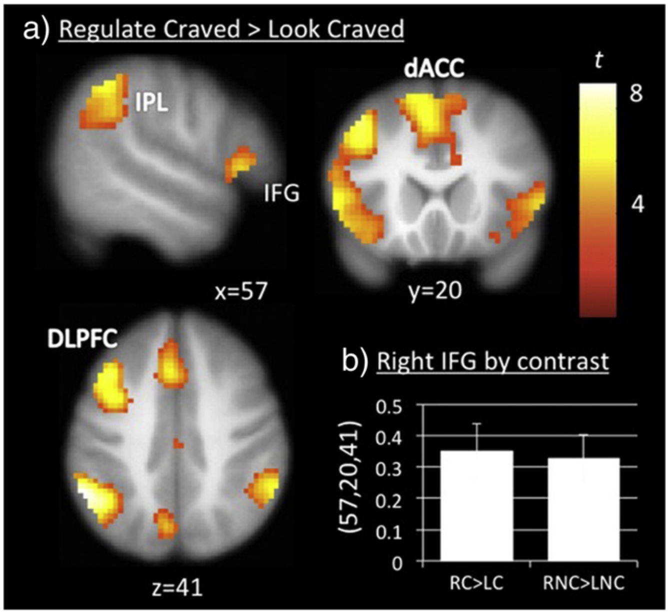

Fig. 3. a) Regulate Craved > Look Craved ($p < .005$, k = 62), and b) bar graphs illustrating the magnitude of activity in the right IFG by regulation contrast (RC = Regulate Craved; LC = Look Craved; RNC = Regulate Not Craved; LNC = Look Not Craved).

For reactivity, the linear effect of age was significantly positively related to Look Craved > Look Not Craved activity in the left occipital (peak at −3, −91, −10; k = 223) and right parietal lobes (peak at 33, −34, 29; k −227), and negatively related to activity in the right SFG (peak at 14, 20, 56; k = 238) and DLPFC (peak at 36, 29, 38; k = 127). The quadratic effect of age was not significantly related to reactivity-related activity. To see whether the linear age-related effects were due to decreases in Look Craved-related activity or increases in Look Not Craved-related activity, we interrogated the simple effects of Look Craved > rest and Look Not Craved > rest. As mentioned above, Look Craved > rest produced no age-related clusters of activity, and Look Not Craved > rest produced several positive age-related clusters in regions including the left and right IFG, DLPFC, SFG, and IPL. This right IFG cluster from Look Not Craved > rest overlaps with the positive age-related cluster from the Regulate Craved > rest contrast, which suggests that older participants may be engaging in more implicit regulation of their craved foods.

Correlations with other individual differences

Regulation-related activity from the Regulate Craved > Look Craved contrast was not significantly related to self-reported reappraisal usage from the ERQ and ERQ-CA. However, it was significantly related to age-adjusted BMI. Leaner females displayed less activity in left supramarginal gyrus, left middle temporal gyrus, left MFG, and right IPL ($rs_{(46)} = .399, .413, .337$, and $.315$, $ps = .007, .005, .024$, and $.035$, respectively). Reactivity-related activity from the Look Craved > Look Not Craved contrast was not significantly related to either age-adjusted BMI or self-reported reappraisal usage from the ERQ and ERQ-CA.

Discussion

This study examined the behavioral and neural correlates of craving reappraisal in a sample of healthy 10–22 year old females. In support of our hypotheses, reappraisal of the craving for personally-craved unhealthy foods effectively decreased self-reported desire for the food and elicited activity in regions including the left DLPFC, left IFG extending into anterior insula, SFG extending into dACC, and IPL. Viewing one's craved foods as compared to similarly unhealthy but not craved foods elicited activity in the VS, perigenual ACC (more rostral and ventral

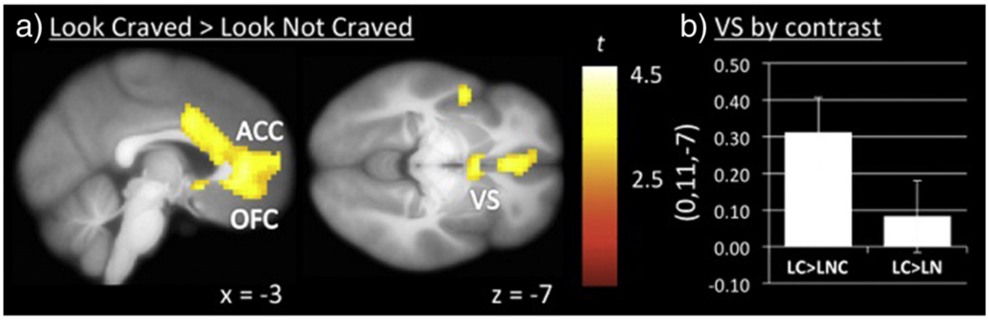

Fig. 4. a) Look Craved > Look Not Craved ($p < .005$, k = 20), and b) bar graphs illustrating the magnitude of activity in the VS by reactivity contrast (LC = Look Craved; LNC = Look Not Craved; LN = Look Neutral).

regions of ACC than observed in reappraisal, but extending inferiorly into subgenual ACC and OFC as well as superiorly into left dACC), left superior and middle temporal gyri, and precentral gyrus. Developmentally, age exhibited positive linear correlations with regulation-related right IFG activity and negative linear correlations with reactivity-related right SFG and DLPFC activity. In contrast, leaner individuals (as indicated by age-adjusted BMI) displayed less activity in several regulation-related regions during reappraisal.

Neural correlates of appetitive reappraisal and reactivity throughout adolescence

The clusters of activity revealed by the regulation and reactivity contrasts in the present study are very similar to those observed in a completely non-overlapping sample of male and female adults performing this task (Giuliani et al., 2014). In both samples, reappraisal of craved food elicited activity in a large swath of the prefrontal and anterior cingulate cortices, more lateralized to the left hemisphere. While the two sets of results were gathered on different scanners and analyzed in different versions of SPM, qualitative inspection of them suggests the present, younger, entirely female sample seems to have more significant clusters of activity in the right hemisphere (including right IPL, cuneus, and caudate). In the adult mixed-gender sample, neither whole-brain reactivity contrast (Look Craved > Look Not Craved, or Look Craved > Look Neutral) elicited activity in the VS or OFC, whereas the Look Craved > Look Not Craved contrast in the present adolescent female sample revealed activity in both VS and OFC. The prior study needed to use an anatomical region of interest to interrogate task-related activity in the nucleus accumbens, a region of the ventral striatum, to reveal significant differences in activity between the Look Craved and Look Not Craved conditions (Giuliani et al., 2014). Furthermore, the fact that we saw reactivity-related VS activity in both samples while participants viewed their craved foods compared to their not craved foods, but not compared to looking at neutral foods, highlights the importance of using an appropriate baseline condition. Interestingly, Silvers et al. (2014) found a positive linear correlation between age and VS activity to unhealthy foods regardless of reappraisal strategy.

Table 3
Regions, MNI coordinates, cluster sizes and peak t-values for the Look Craved > Look Neutral and Look Craved > Look Not Craved contrasts ($p < .005$, k = 62 threshold used for Look Craved > Look Not Craved; $p < .005$, k = 72 threshold used for Look Craved > Look Neutral).

Contrast and region	Coordinates (x, y, z)	Cluster size	Peak t
Look Craved > Look Not Craved ($p < .005$, k = 62)			
Left precentral gyrus	(−39, −25, 62)	85	4.64
Perigenual ACC	(0, 38, 2)	703	3.93
dACC	(0, 5, 35)		3.78
Left perigenual ACC	(−12, 47, 5)		3.48
Subgenual ACC/OFC	(0, 41, −10)		3.21
Left STG	(−48, 2, −4)	73	3.5
Left MTG	(−57, −1, −13)		2.94
[a]Ventral striatum	(0, 11, −7)	29	3.7
Look Craved > Look Neutral (from one-sample t-test; $p < .005$; k = 72)			
Right lingual gyrus	(12, −76, −1)	1615	6.2
Right SPL	(24, −70, 53)		5.41
Right MTG	(36, −82, 26)		5.09
Right precuneus	(15, −73, 50)		4.81
Right parahippocampal gyrus	(27, −55, −7)		3.6
Left parahippocampal gyrus	(−15, −46, −4)	281	3.78
Left middle occipital gyrus	(−39, −61, −7)		3.28
Left precuneus	(−15, −79, 47)	475	4.75
Left MTG	(−36, −82, 26)		4.08

Note: ACC = anterior cingulate cortex; dACC = dorsal anterior cingulate cortex; OFC = orbitofrontal cortex; STG = superior temporal gyrus; MTG = middle temporal gyrus; SPL = superior parietal lobe.

[a] A priori region with relaxed cluster extent threshold.

The present group-level findings are in alignment with other investigations of reappraisal during adolescence, in which reappraisal of negative emotional stimuli was associated with activity in the dorsal and ventral extents of the left lateral PFC (Belden et al., 2014; Lévesque et al., 2004; McRae et al., 2012; Pitskel et al., 2011; Yokum and Stice, 2013). As in previous studies specifically investigating the reappraisal of food craving in this age range, we also found regulation-related activity in dorsal and ventral lateral PFC (particularly in the left hemisphere), medial SFG extending into dACC, and bilateral IPL (Silvers et al., 2014; Yokum and Stice, 2013). These regions are very similar to those underlying reappraisal in adults (Buhle et al., 2013), which suggests that, when it is engaged, reappraisal in adolescence may be not fundamentally different than in adulthood. Therefore, teaching reappraisal may be an effective way to help children and adolescents to manage their appetitive desires.

Age-related changes in appetitive reappraisal and reactivity

To investigate whether there were age-related changes in the behavioral or neural correlates of food craving reappraisal or reactivity within this sample, we modeled the linear and quadratic effect of age at the behavioral and whole-brain levels. Behaviorally, past research has found both linear and quadratic effects of age in reappraisal success (e.g., McRae et al., 2012), but not reactivity. Interestingly, we found no significant relationship between age and task performance, in either reappraisal success (Look Craved minus Regulate Craved) or reactivity (Look Craved minus Look Not Craved), despite the fact that self-reported reappraisal usage (scores on the ERQ and ERQ-CA) increased with age ($r_{(58)} = .41$, $p = .002$). The lack of age-related changes in reappraisal success are most likely due to the extensive training participants completed before beginning the task in the MRI. We worked hard to ensure that, despite individual differences in reappraisal usage, all participants understood the task. As such, we may have reduced any pre-existing individual differences in reappraisal ability.

At the neural level, we found a positive linear relationship between age and regulation-related activity in the right IFG, which was driven by age-related increases in activity during the reappraisal of craved

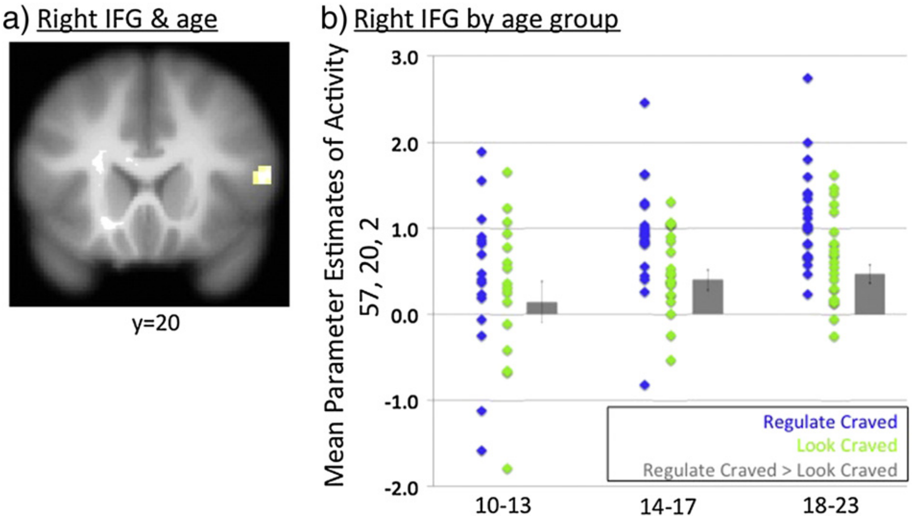

Fig. 5. a) The cluster of Regulate Craved > Look Craved activity in right IFG that positively correlates with age ($p < .005$, k = 20), and b) mean parameter estimates of activity during Regulate Craved > rest and Look Craved > rest, extracted from the right IFG cluster resulting from the Regulate Craved > Look Craved contrast in the whole brain RMANOVA. Gray bars represent averages within age group for Regulate Craved > Look Craved values. Blue dots represent individual datapoints for Regulate Craved > rest. Green dots represent individual datapoints for Look Craved > rest.

foods (Regulate Craved) versus rest. This is in line with the positive linear correlation with age found by McRae et al. (2012), but in the opposite hemisphere. The only other age-related effect found in the present data set was the negative linear correlations with activity in the right SFG and DLPFC during the viewing of personally not craved foods (Look Not Craved) versus rest, including the left and right IFG, DLPFC, SFG, and IPL. The right IFG clusters seen in these two contrasts, Regulate Craved > rest and Look Not Craved > rest, overlap, which suggests that older participants may be engaging this inhibitory region to a greater degree than younger participants while consciously reappraising their food cravings and perhaps implicitly or habitually engaging it while viewing their not craved foods.

The positive correlation between age and regulation-related right IFG activity combined with a lack of age-related changes in reappraisal success presents an interesting discrepancy. It may be that, while individuals of all ages are able to successfully reappraise their cravings for desired foods, older individuals must work harder to inhibit their desires for unhealthy food. Diet quality decreases during the transition from adolescence into adulthood (Demory-Luce et al., 2004; Niemeier et al., 2006), which may result in part from greater indulgence in cravings for these sorts of foods, and greater abilities to make personal choices about which foods one consumes. Furthermore, leaner individuals displayed less regulation-related activity in multiple lateral frontal–parietal regions. Overall, these mixed and more nuanced findings suggest that imbalance models of adolescent risk-taking, which predict significant age-related linear improvements in regulation contrasting with curvilinear changes in incentive motivation (peaking by mid-adolescence), may not apply as well to the development of food craving reappraisal between ages 10 and 23. One possibility is that reactivity to this primary reward stimulus may be fully in place by age 10, but this warrants further investigation.

Limitations and future directions

There were several limitations of the present study. First, we limited our sample to females, to try and minimize gender differences in adolescent development, particularly those related to brain development, puberty, and emotion regulation. Future work should investigate if and how the reappraisal of food craving differs between adolescent males and females. Second, personally craved and not craved stimuli were identified at the category but not stimulus level. We made this design decision in order to equate the categories on normative ratings, but it is possible that the observed differences between craved and not craved foods would have been even more pronounced if participants were able to identify each image as idiosyncratically craved or not (e.g., if someone craves pizza in general, but dislikes some pizza toppings, or only craves pizza with specific toppings). Third, participants' reappraisal success was measured using self-reported craving, not food choice behavior. This was done to adhere to previous work using this experimental design; future research on food craving reappraisal should investigate how reappraisal affects behavior (e.g., Hare et al., 2011). Future research may also benefit from the addition of an additional control condition that is better matched with the regulate instructions in terms of the level of abstraction (such as to think about where this food was purchased or grown), as our look instructions may have skewed towards processes that would enhance concrete attention to the stimulus. Lastly, we did not find a relationship between task-based neural or behavioral indices of reappraisal success and self-reported reappraisal usage as measured by the ERQ and ERQ-CA. This uncoupling of the ability to use reappraisal when taught and cued and the frequency with which reappraisal is applied to manage emotion in everyday life is not particularly surprising, as it has been documented in the adult literature (see McRae, 2013). The present findings add a developmental component to research observing this effect.

Conclusions

In the present study, we investigated the reappraisal of craving for personally-desired unhealthy foods across adolescence. While this work adds to the growing body of research on reappraisal (predominantly of negative affective stimuli) in adolescence, it is important to note that the mechanisms of craving reappraisal may differ from that of negative affective stimuli. For example, craving reappraisal may work by engaging specific negative emotions (e.g., disgust) associated with indulging in that craving. However, the specific target of reappraisal in this study may provide a useful model for the regulation of other appetitive temptations encountered in adolescence. Adolescence is a time hallmarked by exploration and individuation, when individuals encounter large numbers of novel, tempting stimuli and situations. While the desire for many of these is adaptive (e.g., investigating different job opportunities and activities that may shape career interests), the desire for others may be maladaptive or dangerous (e.g., drugs, alcohol). Our findings indicate that the ability to use reappraisal to regulate craving is firmly in place as early as age 10, and may be an effective tool to strengthen (particularly in high-risk samples) as adolescents navigate through a variety of temptations. Finally, studying reappraisal of food cravings can provide a useful reminder that the presence or absence of an appetitive desire is not necessarily problematic; desires that are unchecked or otherwise managed inappropriately may be the real concern. It is our hope that the present findings will inform future research on how craving reappraisal may affect food choice and other health behaviors in adolescence, including the degree to which reappraisal may be a useful technique to improve effective management of various appetitive desires throughout the lifespan.

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