Supplementary Information (SI) Appendix

Participants

Individuals in the present experiment were recruited from a larger study of 161 people who had participated in a previous study when they were children (1). Participants were assessed with the Youth Life Stress Interview (YLSI; Rudolph & Flynn, 2007), when they were 9-13 years old (mean = 11.2 years). We re-contacted participants from the highest and lowest quintiles of childhood stress scores a decade later, when participants were entering early adulthood. These individuals had either high YLSI scores (4.0 or above) or relatively low scores reflecting normative levels of childhood stress exposure (2.5 or below). Participants were recruited from the highest and lowest quintiles in order increase the range of early life stress (YLSI scores). Fifty-four individuals ranging in age from 19.0 years to 23.7 years (mean=20.5 years) participated in the current study. Within this group of 54 participants, 29 individuals (17 female) were assessed as having had high levels of stress during early childhood, and 25 individuals (11 female) were assessed as having relatively low levels of childhood stress. In addition to those who agreed to participate, 12 individuals we contacted declined participation: 9 were currently living out of state and could not travel back to the lab, 1 declined because she was pregnant and could not undergo scanning, 1 did not wish to undergo the neuroimaging component, and 1 individual was currently in prison. Of those who declined, 7 were from the low stress group and 5 were from the high stress group; these individuals did not differ on any childhood or demographic measures from those who did participate.

Current (adult) life stress was assessed in these participants using the UCLA Life Stress Interview (see below), when they returned to our laboratory as young adults.

Participants had a wide range of stress scores both from the early time point (childhood stress) and the current time point (adult stress). Some individuals who experienced high childhood stress experienced high current stress, but some did not; similarly, some individuals with low stress childhoods were experiencing stressful periods of adult life (see Figure S13).

The current study was approved by the University of Wisconsin Institutional Review Board and all participants provided informed consent. A number of participants had to be excluded from the data analysis: 2 participants agreed to participate but could not undergo MRI scanning because of claustrophobia; 7 participants (4 low stress, 3 high stress) were excluded from fMRI analyses because of excessive head motion (> 5mm movement during either run of the MID task); 1 participant was excluded due to a structural brain abnormality (significantly enlarged ventricles); and 1 participant was excluded due to significant mental health issues (suspected active psychosis). Two additional participants (1 low stress, 1 high stress) were excluded from the analyses because they failed to hit the target on all loss trials. This resulted in a final group of 42 participants (19 low stress, 23 high stress) for fMRI analysis. There were no significant differences between groups on the depression sub-scale of the Symptom Checklist 90revised, SCL-90-R (2). Participants from the high childhood stress group scored a M =6.78 (SD = 5.87) and those from the low childhood stress group scored M = 5.59 (SD = 7.83), p > .6.

Procedures

Participants had their life stress measured in our laboratory when they were children (mean age 10.2 years), and were re-contacted approximately 10 years later. They returned to our laboratory as young adults (mean age 20.6 years), and underwent an MRI scan during which they performed a reward processing (monetary incentive delay, MID) task. Following the MRI scan, participants had their current life stress reevaluated, completed a battery of neuropsychological tests including the Cambridge Gambling Task, and reported their current risk-taking behaviors. These measures are described in greater detail below.

Measures:

Childhood Stress Exposure

The Youth Life Stress Interview (YLSI) assesses the child's exposure to severe negative life events and circumstances. Trained interviewers used semi-structured questions to assess the context of the event (e.g., timing, duration, objective consequences). Data from these interviews were then evaluated by an independent team of three to seven raters who provided a consensual rating on a 10-point scale reflecting an overall level of cumulative life stress. The following examples illustrate the kinds of experiences children in this study described that were associated with each score. A life stress score of 1 was given to a child whose pet was hit by a car, but the pet was not seriously injured. A score of 5 was given to a child who was placed in foster care early in life and then experienced multiple placements between families; during this

time the child's biological parent, with whom the child maintained a relationship, died. A score of 7.5 was given to a child whose parent and sibling both had serious, chronic medical and mental health problems; long-term instability in parental employment; severe inter-parental marital conflict resulting in parental separation; and extensive incarceration of one of the child's parents. A score of 10 was given to a child who was homeless; had several close family members die unexpectedly; and had physically violent parents, resulting in separation of the child from the family. This rating system has high reliability and validity (3). The sample of 42 participants had a mean YLSI score of 4.2, with a standard deviation of 2.7 and range 1-10.

Current Life Stress

The UCLA Life Stress Interview (UCLA LSI; (4) measures current life stress in adult participants. This interview was developed for use with adolescents and adults and queries ten domains including close friendships, social life, romantic relationship, family relationships, relationship with child/children, academic experiences, work, finances, health, and other (i.e., bereavement, moves, natural disasters, victimization, and legal issues). All items are open-ended. Sample items include:

1. Do you have a steady romantic partner or are you married? How long have you been together? What is your relationship like (probe: duration, stability, emotional supportiveness, reciprocity, trust, communication)? How often do you and your partner fight? What are the fights like, what are they about, how do you and your partner deal with them?

2. Are you currently in school? Are you a full or part-time student? Where are you attending? What type of coursework are you studying? How have things been going at school? What grades are you receiving? Have you failed any subjects or tests? Have you received any awards? Do you receive any special help with your learning? A trained interviewer conducted all interviews. The interviewer did not score the interview, only recorded the participants' verbatim responses. The responses were then scored by a trained team of three researchers, who never met the participants and were unaware of the identity or background of those whose responses they are rating. The interviews were coded by this team of researchers using a scale of 1-10, with 10 being extreme stress. High inter-rater reliability on scoring of domains and types of events, and good validity has been reported (5). Our sample of 42 participants had a mean LSI score of 4.2, with a standard deviation of 2.7 and range 1-9.

Laboratory test of reward-motivated decision-making:

Neuropsychological functioning in reward processing was assessed through the Cambridge Gambling Task (CGT), a subtest of the Cambridge Neuropsychological Test Automated Battery (CANTAB; Cambridge Cognition Ltd., Cambridge, United Kingdom). This test was administered using a touch screen computer in a 1-1 setting with a trained researcher. The CGT assesses impulse control and risk-taking in decision-making. In this task, the participant is presented with a row of ten red and blue boxes. A yellow token is hidden behind a random square. The ratio of red to blue boxes varies for each trial (9/1, 8/2, 7/3, 6/4, 4/6, 3/7, 2/8, or 1/9), and the participant must guess whether a

yellow token is hidden in a red box or a blue box. Participants then select a proportion of their points to gamble on their confidence in the location of the yellow token. A number indicating a fraction of the participant's total points is displayed in either ascending or descending order (i.e. either counting up or down), and the participant is instructed to press the button when the number reaches the desired bet amount. The CGT has traditionally been designed to distinguish risk-taking from impulsivity because in the ascending bet condition, a participant who wants to make a risky bet must wait patiently for it to appear. We focused in particular on four key behavioral summaries from the CGT: deliberation time, delay aversion (measuring impulsivity), risk adjustment, and quality of decision-making. "Deliberation time" is the mean time taken to decide the color to bet on. "Delay Aversion" is the difference in the percentage bet in the ascending versus descending bet conditions. "Risk adjustment" is the extent to which the bet amount varies with the likelihood of winning. "Quality of Decision Making" is defined as the fraction of time that the participant chose the most likely outcome (e.g. betting on red when 6 red squares and 4 blue squares are shown).

Maladaptive Risk-Taking

To measure actual maladaptive risky behaviors in participants daily lives, participants completed a modified version of the Youth Risk Behavior Survey (YRBS; (6) developed and used by the U.S. Centers for Disease Control and Prevention. This 52 question instrument (see Appendix) queried risky behavior in areas including driving, weapons, tobacco, alcohol, drugs, sex, health, and crime. Each answer to each question was attached to a certain number of points, with risky behaviors weighted more heavily than

non-risky behaviors. For example, "How many times have you intentionally tried to hurt yourself? (Consider such actions as attempted suicide, poisoning, overdose, and cutting.)" 0 times=0; 1 time=1; 2 or 3 times=2; 4 or 5 times=3; 6 or more times=4. Scores were then created for each of 10 risky behaviors (see Table S3). The scored points were then summed to create a total score of risky behavior.

fMRI Tasks:

Brain activation related to reward processing was assessed using a monetary incentive delay (MID) task (7, 8). This task allows separate measurement of both the anticipation of reward or loss as well as response to the receipt of reward/loss. Subjects were first trained on the task on a computer outside the MRI scanner immediately prior to the MRI scan. The MID task consists of 90 trials. In each trial, participants were first presented with a 2s cue indicating a possible win (+\$1, +\$5), loss (-\$1, -\$5), or no gain/loss (+\$0, -\$0). After a variable delay of 2-2.5s,a target appeared, and participants were instructed to press a button as quickly as possible while the target is on the screen. If the button was pressed during the target, the participant either won or avoided losing money; a press too early or late resulted in no win or a loss. Feedback (win/loss) was provided 1.5-2s after the response, which was then followed by a variable inter-trial interval of 2-6s. The duration of the target was dynamically adjusted for each trial based on the performance of prior trials to achieve a success (hit) rate of 67% for each cue. The initial value of this target duration was determined during the training session, and was typically around 250ms. Total duration of the task was 18 minutes, split into two runs (8

minutes, and 10 minutes). A schematic of the paradigm is presented in Figure 1. This task has been shown to reliably activate reward-processing regions (ventral striatum, insula, thalamus, medial PFC), and allows the dissociation of reward anticipation and outcome. Participants were told that any money that they gained during the task would be added onto their payment for the study. However, unbeknownst to the participants, we heavily "rounded up" and paid everyone the same amount at the end of the study.

MRI Data Acquisition

A series of structural and functional brain images were acquired on a 3T General Electric (GE) MR750 MRI scanner using an 8-channel receive-only RF head coil (General Electric Medical Systems, Waukesha, WI). Structural anatomical brain data was acquired using a T1-weighted BRAVO pulse sequence (TI:600ms, TR/TE/flip:9ms/1.8ms/10°, matrix:256x192x134, FOV:240mm, slice thick:1mm). Functional data was acquired using a series of sagittal T2*-weighted echo-planar images (263 image volumes in the first run, 300 image volumes in the second run, sagittal slices, resolution: 3.5mm x 3.5mm x 3.5mm, FOV: 22.4cm, TR: 2000ms, TE: 25ms, flip angle: 70 degrees).

fMRI Task Analyses

All MRI data analyses were performed using the Analysis of Functional NeuroImages (AFNI) analysis package (9), unless otherwise specified. Echo-planar MR images acquired during the task were first corrected for subject motion using a rigid body volumetric realignment (3dvolreg). The first 3 image volumes were discarded to allow

magnetization to reach steady state. Data were then corrected for slice-timing differences (3dTshift), aligned to the T1-weighted anatomical image (align_epi_anat.py), and spatially smoothed by Gaussian kernel with a full-width at half maximum (FWHM) of 4mm (3dmerge).

Brain activation during the task was estimated using multiple linear regression (3dDeconvolve) with 12 regressors of interest. The first 6 regressors modeled the gain/loss anticipation period as a 4s block beginning at the start of the cue for +\$5, +1\$, +0\$, -0\$, -1\$, and -\$5. (This 4s block encompasses the period of time between the onset of the cue and the target.) The other 6 regressors modeled the success or failure of pushing the button during the target as a 3s block, beginning at the time of the target, for potential gains (+\$1, +\$5), losses (-\$1, -\$5), or no gain (+\$0, -\$0). That is, the 6 regressors used to model the response to reward or loss were: 1) successfully pressing the button during the target ("hits") for gain trials (+\$1 and +\$5); 2) hits during loss trials (-\$1 and -\$5); 3) hits during no-gain trials (+\$0 and -\$0); 4) failing to press the button during the target ("misses") for gain trials; 5) misses during loss trials; and 6) misses during no-gain trials. The 6 estimated motion realignment parameters, as well as constant and linear trend, were used as additional nuisance regressors. To further reduce the influence of head motion, time points where the sum squared difference (SSD) of the 6 motion parameters to the preceding time point exceeded 0.25 mm were excluded from the analysis (i.e. these time points were given a weight of zero in the multiple regression analysis). Supplementary Figure S11 shows the distribution of the fraction of time points censored in each subject.

The period of time between the cue and the motor response to the button press, modeled as the "anticipation of reward or loss" described above, likely includes both the anticipation of a potential reward or loss as well as the motor preparation for the button press. Therefore, we construct general linear tests to contrast the anticipation of a large reward (+\$5) versus no reward (+\$0), or large loss (-\$5) vs. no loss (-\$0). All of these trials involve the preparation of a motor response, and by contrasting a large compares to no reward or loss, we can isolate the activation specific to the magnitude of the reward or loss. Therefore, general linear tests of the regressors described above were constructed to compute 1) the difference in the anticipation of potential rewards vs. no rewards (+\$5 vs. +\$0); 2) the difference in the anticipation of potential losses vs. no loss (-\$5 vs. -\$0); 3) the response to successfully hitting the target on a gain trial vs. no-gain trial, Hit(+) vs. Hit(0); 4) the response to missing on a potential gain trial vs. no-gain trial, Miss(+) vs. Miss(0); 5) the response to successfully avoiding a loss, Hit(-) vs. Hit(0); and 6) the response to missing on a loss vs. no-loss trial, Miss(-) vs. Miss(0).

Group and Individual differences in activation were estimated by first converting the estimated activation amplitudes (beta weights) to percent signal change, aligning the T1-weighted anatomical volume to Talairach space using a 12-parameter affine transformation, and then applying this transform to the activation maps. Differences in activation as a function of ELS were assessed on a voxel-wise level using a t-test (3dttest++) with the LSI-score as a covariate. More specifically, we ran 2 analyses, where we included either 1) the YLSI scores from the interview administered when the

participants were children, or 2) the LSI scores from the interview conducted in young adulthood on the same day as the scanning session. Voxel-wise t-tests were corrected for multiple comparisons by estimating the spatial autocorrelation function from the preprocessed fMRI data (3dFWHMx), and setting a minimum cluster size threshold based on a Monte Carlo simulation that incorporates this estimated autocorrelation function (3dClustSim) (10, 11).

Figures 2-5 show the brain activation during the MID task that is correlated with childhood stress (the YLSI score), when the YLSI score is used as a continuous measure in the analysis. Figures S3-S6 show the main effect of the MID task across the whole group (all 42 participants). These figures show that the anticipation of potential rewards vs. no-rewards is associated with increased activation in the basal ganglia, and the anticipation of potential loss vs. no-loss is associated with increased activation in the insula, consistent with prior studies (7, 8).

Figures S7-S10 show the group differences (High Stress – Low Stress) in activation, and the activation in each group (Low Stress, High Stress) separately, when we repeat the analysis using a two-group design, based on the childhood stress (High Stress, Low Stress) rather than treating childhood stress as a continuous measure. We present these results in order to help the interpretation of the findings in Figures 2-5.

Mediation analysis

We used a standard multivariate analytic framework (12) to test whether the relationship

between ELS and both laboratory measures of risk-taking (as measured with the CGT) and real-life measures of risk-taking (as measured with the YRBS) is statistically mediated by the brain's activation during either the anticipation or receipt of rewards and losses, as measured by the MID task. Brain activations during the MID task were extracted from those regions that showed significant group differences (high vs. low childhood stress), p<0.05, corrected for multiple comparisons. Significance of mediation was assessed using the 'Causal Mediation Analysis' package in R, using a nonparametric bootstrap resampling with 5000 iterations.

Figures

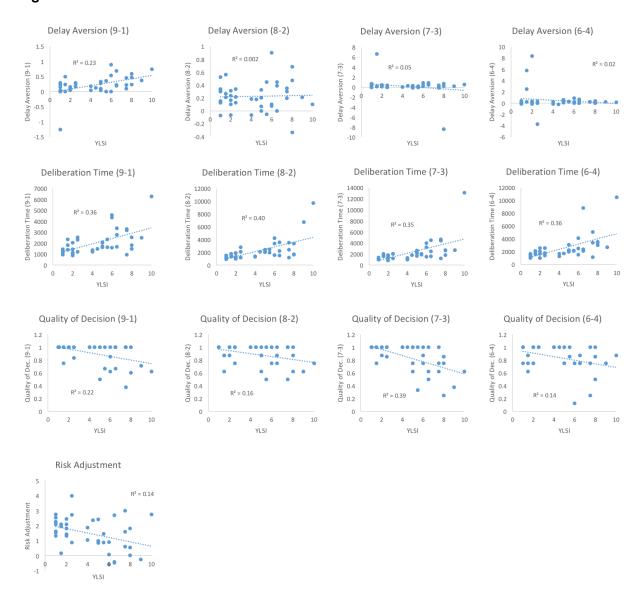


Figure S1: Scatter plots showing the behavioral measures derived from the Cambridge Gambling Task (CGT) compared to childhood stress, as assessed by the Youth Life Stress Interview (YLSI). "Deliberation time" is the mean time taken to decide the color to bet on. "Delay Aversion" is the difference in the percentage bet in the ascending versus descending bet conditions. "Risk adjustment" is the extent to which the bet amount varies with the likelihood of winning. "Quality of Decision Making" is defined as the fraction of time that the participant chose the most likely outcome (e.g. betting on red when 6 red squares and 4 blue squares are shown). The numbers following the labels indicate the proportion of red/blue squares. Note that some participants with higher childhood stress bet on the less likely outcome (e.g. the one with only a 10% chance of winning, in the 9-1 condition) over half of the time (a "Quality of Decision Making" score less than 0.5).

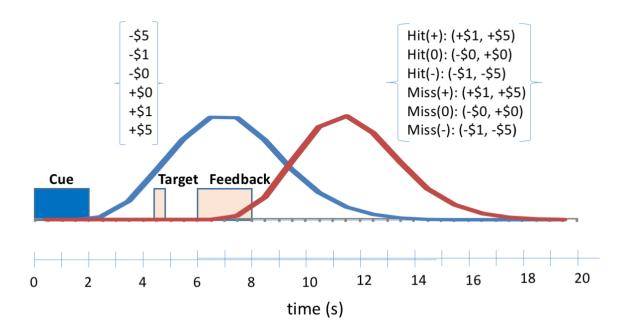


Figure S2: Regressors used to model the activation during the MID task. Six regressors modeled the fMRI response to the cue (blue curve) for the 6 different potential rewards (+\$5, +\$1), losses (-\$5, -\$1) or no gain/loss (+\$0, -\$0). Six additional regressors modeled the fMRI response to the target and feedback (red curve) for 6 different outcomes: 1) hitting the target on a win (+\$1, +\$5) trial, Hit(+); 2) hitting the target on a loss (-\$1, -\$5) trial, Hit(-); or 3) hitting the target on a no gain/loss (+\$0,-\$0) trial, Hit(0); 4-6) missing the target for each of these trials, Miss(+), Miss(-), Miss(0). Note, as shown in Figure 1, that there is a variable inter-trial interval after the feedback before the begin of the next trial.

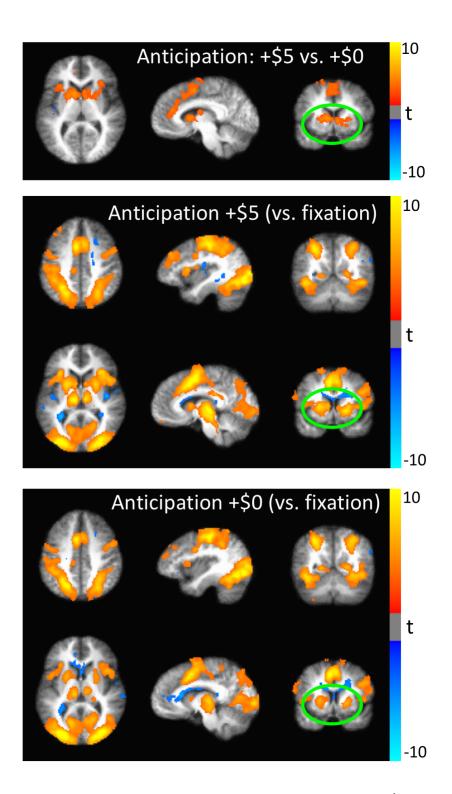


Figure S3: Main Effect - Anticipation of potential reward (+\$5) vs. no-reward (+\$0) for the entire group of 42 participants. Significant activation for the anticipation period vs. fixation baseline is seen in visual cortex, bilateral insula, parietal cortex, cingulate, thalamus, and putamen. Anticipation of potential large rewards (+\$5) compared to no-rewards (+\$0) is associated with greater activation in anterior and mid-cingulate and putamen (green circle).

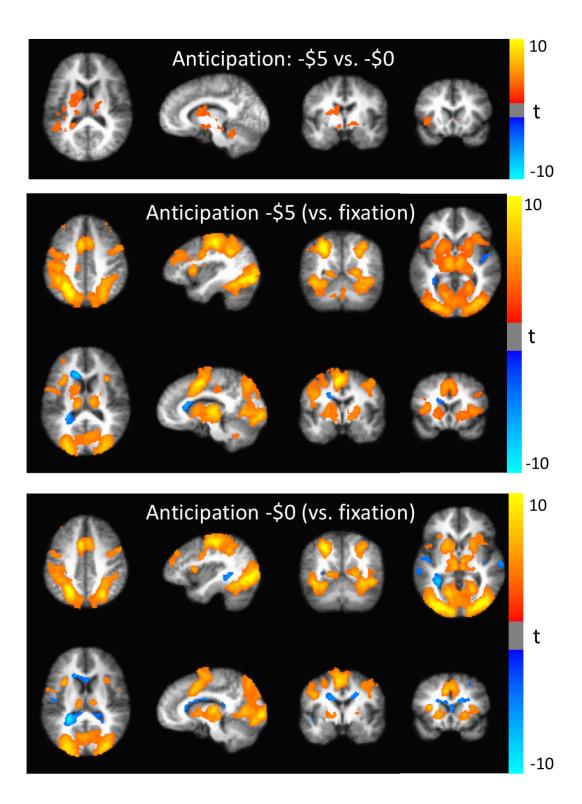


Figure S4: Main Effect - Anticipation of potential loss (-\$5) vs. no-loss (-\$0) for the entire group of 42 participants. Significant activation for the anticipation period vs. fixation baseline is seen in visual cortex, bilateral insula, parietal cortex, cingulate, thalamus, and putamen. Anticipation of potential large losses (-\$5) compared to no-loss (-\$0) is associated with greater activation in the left putamen and left insula.

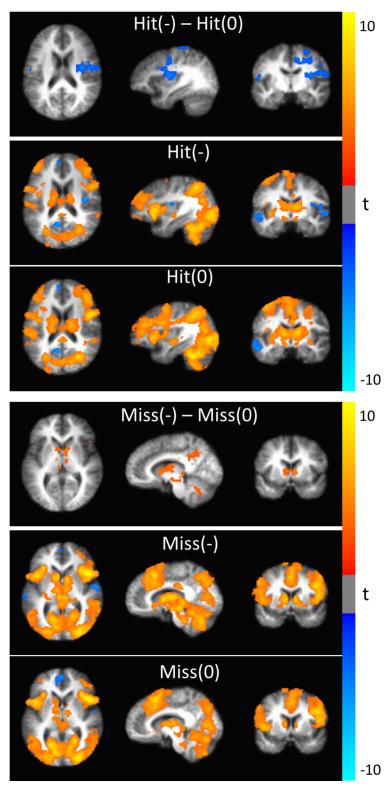


Figure S5: **Top**: Main effect of the response to successfully avoiding a loss, Hit(-) vs.no-loss, Hit(0), across the entire group. **Bottom**: Main effect of the response to missing on a loss trial, Miss(-),no-loss trial Miss(0), and the difference between the two: Miss(-) – Miss(0).

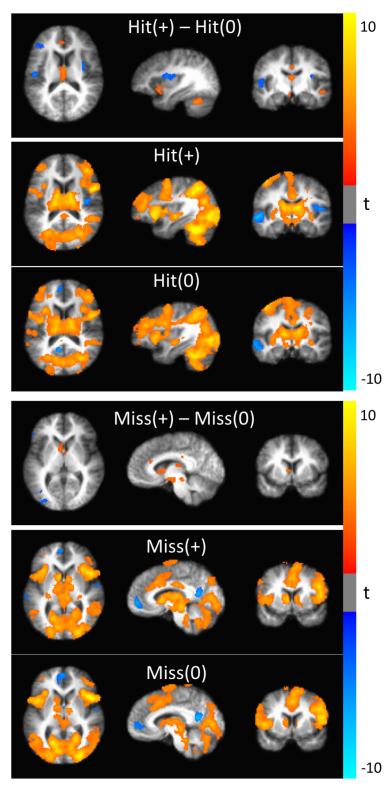


Figure S6: **Top**: Main Effect of the response to successfully hitting the target on a gain trial, Hit(+) vs.no-gain, Hit(0), and the difference between the two: Hit(+) - Hit(0), across the entire group. **Bottom**: Main effect of the response to missing the target on a gain trial, Miss(+) vs. nogain trial, Miss(0).

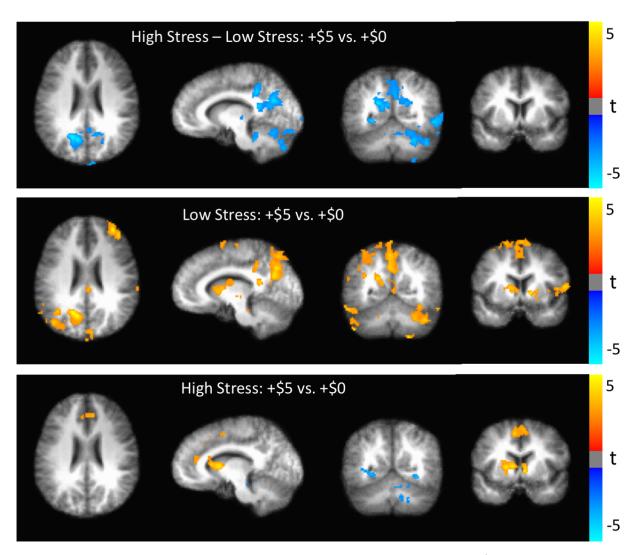


Figure S7: Activation during the anticipation of potential large rewards (+\$5) or no-rewards (+\$0) in participants with high vs. low childhood stress.

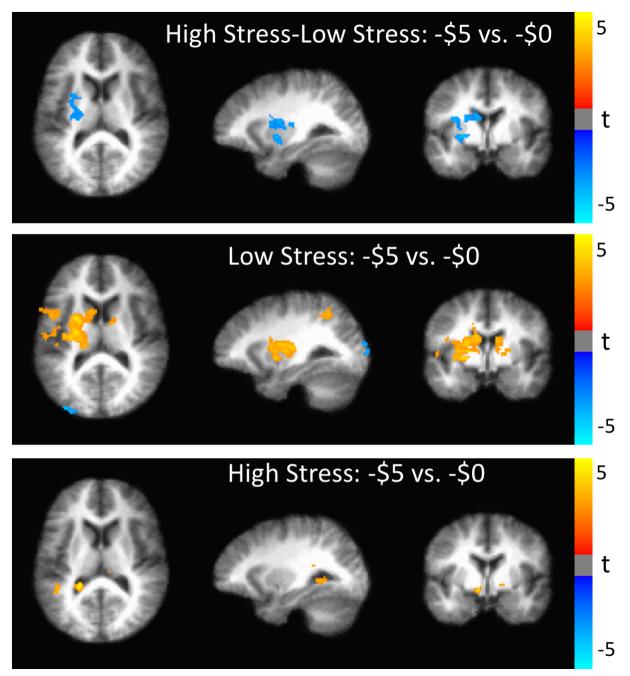


Figure S8: Differences in the anticipation of potential losses in participants with high vs. low childhood stress. Participants with low childhood stress show significantly greater activation in basal ganglia during the anticipation of potential losses, while subjects with high childhood stress show no such modulation. (p<0.05). Further examination of this regions showed that individuals with higher childhood stress had lower activation during the anticipation period of both loss (-\$5) and no-loss (-\$0) trials.

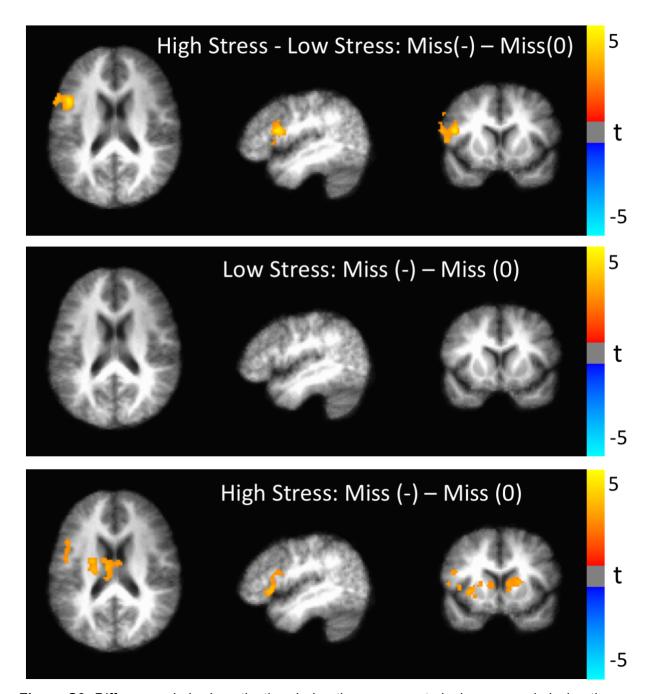


Figure S9: Differences in brain activation during the response to losing money (missing the target on a loss trial, Miss(-), compared to a no-loss trial, Miss(0)) in participants with high vs. low childhood stress. Participants with high childhood stress show significantly greater activation in the left inferior frontal gyrus in response to losing money (p<0.05).

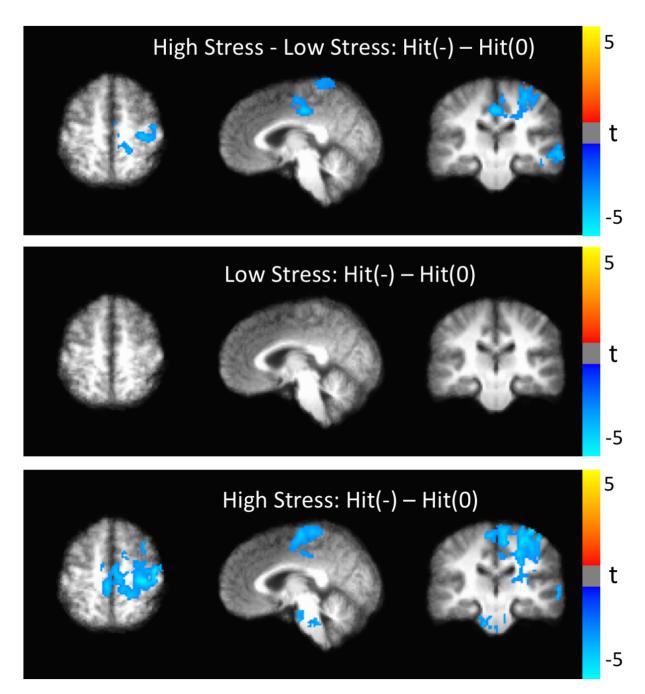


Figure S10: Differences in brain activation during the response to avoiding losing money (successfully pressing the button during a potential loss trial, Hit(-) vs. no-loss trial, Hit(0)) in participants with high vs. low childhood stress.

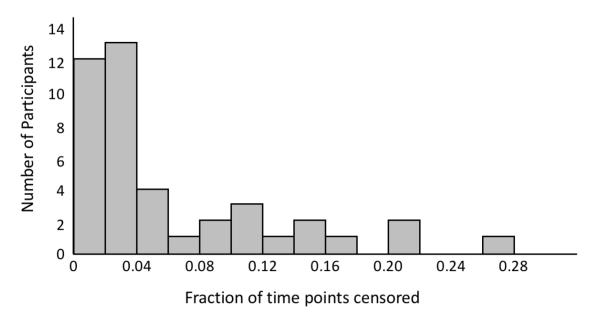


Figure S11: Histogram of the fraction of time points censored (out of 563 time points) due to high motion for the runs included in this study.

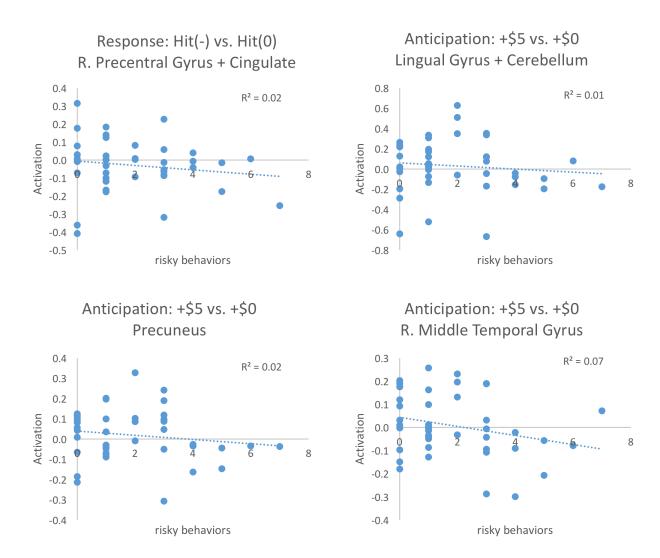


Figure S12: No significant correlations were found between the activation during the response to successfully avoiding losses, and the anticipation of potential rewards, versus real-life risk-taking behaviors.

Childhood vs. Current (Young Adult) Stress

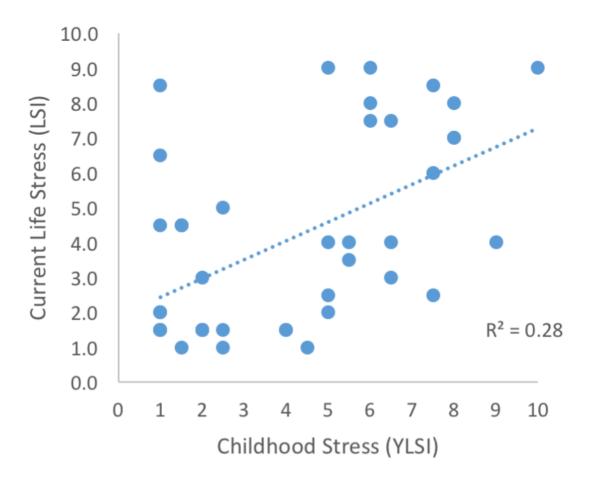


Figure S13: Current life stress (LSI) is slightly correlated with measures of early life stress (YLSI) (R^2 =0.28), but the two measures are differentially associated with brain activity to reward and loss.

Contrast	Cluster	Volume (mm³)	MNI coordinate (peak t)	
Anticipation: +\$5 vs. +\$0	Precuneus	38264	(-18, -61, 21)	
	Lingual Gyrus / Cerebellum	37888	(28, -76, -12)	
	Left Precentral Gyrus	4512	(-36, -14, 30)	
	Right Middle Temporal Gyrus	4184	(59, -45, -3)	
	Left Middle Temporal Gyrus	3408	(-38, -76, 26)	
	Right Middle Frontal Gyrus	3168	(30, 20, 49)	
Anticipation: -\$5 vs\$0	Putamen / Insula	2856	(-34, -3, 17)	
Response: Hit(-) vs. Hit(0)	Cingulate	5016	(4, -25, 40)	
	Cerebellum	4680	(22, -38, -26)	
	Right Precentral Gyrus	3240	(32, -28, 62)	
	Right Thalamus	2720	(8, -19, 19)	
Response: Miss(-) vs. Miss(0)	Left Inferior Frontal Gyrus	4080	(-46, 9, 22)	

Table S1: Brain regions (clusters of voxels) whose activation during the Monetary Incentive Delay task is significantly correlated with childhood stress (YLSI scores) (p<0.05).

Task Condition	Brain Region	Cambridge Gambling Task	cc (ELS – Brain)	cc (Brain – CGT)	cc (ELS – CGT)	p-val (Mediation)
Anticipation of loss	Putamen / Insula	Deliberation Time (6-4)	-0.52	-0.33*	0.63***	0.92
		Deliberation Time (7-3)	-0.52	-0.33*	0.60***	0.67
		Deliberation Time (9-1)	-0.52	-0.34*	0.60***	0.70
		Quality of Decision Making (6-4)	-0.52	0.34*	-0.38*	0.06 +
		Quality of Decision Making (7-3)	-0.52	0.38*	-0.63***	0.42
		Risk adjustment	-0.52	0.42*	-0.39*	0.06 +
Anticipation of win	Lingual Gyrus / Cerebellum	Delay Aversion (9-1)	-0.54	-0.31*	0.49**	0.51
		Deliberation Time (8-2)	-0.54	-0.14	0.64***	0.00*
		Deliberation Time (9-1)	-0.54	-0.21	0.60***	0.08 +
		Quality of Decision Making (7-3)	-0.54	0.46*	-0.63***	0.51
		Quality of Decision Making (8-2)	-0.54	0.31*	-0.40*	0.59
	Precuneus	Delay Aversion (6-4)	-0.63	-0.07	-0.14	0.08 +
		Delay Aversion (9-1)	-0.62	-0.35*	0.49**	0.56
		Deliberation Time (6-4)	-0.62	-0.32*	0.63***	0.46
		Deliberation Time (8-2)	-0.62	-0.23	0.64***	0.04*
		Quality of Decision Making (6-4)	-0.62	0.33*	-0.38*	0.38
		Quality of Decision Making (7-3)	-0.62	0.49**	-0.63***	0.50
		Quality of Decision Making (8-2)	-0.62	0.34*	-0.40*	0.53
	R. Middle Temporal Gyrus	Delay Aversion (9-1)	-0.59	-0.38*	0.49**	0.34
		Deliberation Time (8-2)	-0.59	-0.15	0.64***	0.07 +
		Quality of Decision Making (6-4)	-0.59	0.37*	-0.38*	0.13
		Quality of Decision Making (7-3)	-0.59	0.39*	-0.63***	0.92
Response to avoiding loss	R. Precentral Gyrus	Deliberation Time (8-2)	-0.52	-0.31*	0.64***	0.77
		Deliberation Time (9-1)	-0.52	-0.31*	0.60***	0.92
		Quality of Decision Making (7-3)	-0.52	0.34*	-0.63***	0.97
		Quality of Decision Making (9-1)	-0.52	0.32*	-0.46*	0.50
Response to loss	L. Inferior Frontal Gyrus	Delay Aversion (9-1)	0.60	0.42*	0.49**	0.33
		Deliberation Time (6-4)	0.60	0.22	0.63***	0.02*
		Deliberation Time (7-3)	0.60	0.20	0.60***	0.05*
		Deliberation Time (8-2)	0.60	0.20	0.64***	0.02*
		Quality of Decision Making (7-3)	0.60	-0.43*	-0.63***	0.81
		Quality of Decision Making (8-2)	0.60	-0.31*	-0.40*	0.76

Table S2: Brain areas where the activation during the monetary incentive delay (MID) task was significantly correlated with both childhood stress and reward-related behavior during the Cambridge Gambling Task. The correlation coefficients (cc) of these measures across participants is shown in columns 4-6. The last column indicates the significance of a mediation analysis: early life stress (ELS) \rightarrow brain activation (Brain) \rightarrow Behavior on the Cambridge Gambling Task (CGT). The + sign indicates trend level significance, p<0.1. * p<0.05, ** p<0.001, *** p<0.0001.

	Give a score of 0 if	Give a score of 1 if	
Total Tobacco Use	< 3.9	>= 4	
Alcohol Use per month	<=3	>=4	
History of Arrests	0	>=1	
BMI	<=24.9	>=25	
Total Court Records	0	>=1	
Number of Children	0	>=1	
Drive Without Seatbelt	<=1	>1	
Carry Weapon	0	>1	
Serious Physical Fight	<=1	>1	
Threatened by Gun/Knife	0	>= 1	

Table S3: Criteria used to determine the real-life risky behavior scores. Information about total tobacco use, alcohol use, driving without a seatbelt, carrying a weapon, being in a serious physical fight, and being threatened by a gun or knife are taken from the Youth Risk Behavior Survey (YRBS).

Appendix

Young Adult Behavior Survey

This survey is about health behavior. The answers you give will be kept confidential. It is important that you answer questions based on what you really do and how you really behave in your everyday life. If there are questions that you feel uncomfortable with, it will help us if you simply leave the question unanswered rather than providing a response that is not accurate or truthful.

For each question, circle the letter for the answer that best describes your behavior over the past year or two.

- 1. When you ride a bicycle, how often do you wear a helmet?
 - a. I have not ridden a bicycle recently.
 - b. Never wear a helmet
 - c. Rarely wear a helmet
 - d. Sometimes wear a helmet
 - e. Most of the time wear a helmet
 - f. Always wear a helmet
- 2. How often do you wear a seat belt when riding in a car driven by someone else?
 - a. Never
 - b. Rarely
 - c. Sometimes
 - d. Most of the time
 - e. Always
- 3. How many times have you ridden in a car/vehicle driven by someone who had been drinking alcohol?
 - a. 0 times
 - b. 1 time
 - c. 2 or 3 times
 - d. 4 or 5 times
 - e. 6 or more times
- 4. How many times did you drive a car or other vehicle when you had been drinking alcohol?
 - a. I do not drive
 - b. 0 times
 - c. 1 time
 - d. 2 or 3 times
 - e. 4 or 5 times

- f. 6 or more times
- 5. About how many times have you texted or emailed while driving a car or other vehicle?
 - a. I do not drive
 - b. Never
 - c. Rarely (1-2 times)
 - d. Sometimes (3-6 times)
 - e. Often (more than 6 times)
 - f. Always
- 6. How many days did you carry a weapon such as a gun, knife, or club?
 - a. Never (0 days)
 - b. Rarely (1 or 2 days a month)
 - c. Sometimes (3 days a month)
 - d. Often (more than 5 a month)
 - e. Always (nearly every day)
- 7. During the past 30 days, on how many days did you carry a weapon such as a gun, knife, or club to class or work?
 - a. 0 days
 - b. 1 day
 - c. 2 or 3 days
 - d. 4 or 5 days
 - e. 6 or more days
- 8. How many times has someone threatened or injured you with a weapon such as a gun, knife, or club?
 - a. 0 times
 - b. 1 time
 - c. 2 or 3 times
 - d. 4 or 5 times
 - e. 6 or 7 times
 - f. 8 or 9 times
 - g. 10 or 11 times
 - h. 12 or more times
- 9. How many times were you in a physical fight?
 - a. 0 times
 - b. 1 time
 - c. 2 or 3 times
 - d. 4 or 5 times
 - e. 6 or 7 times
 - f. 8 or 9 times
 - g. 10 or 11 times
 - h. 12 or more times

- 10. How many times were you in a physical fight in which you were injured and had to be treated by a doctor or nurse?
 - a. 0 times
 - b. 1 time
 - c. 2 or 3 times
 - d. 4 or 5 times
 - e. 6 or more times
- 11. Have you ever been physically forced to have sex when you did not want to?
 - a. Yes
 - b. No
- 12. How many times did someone you were dating or going out with physically hurt you on purpose? (Count such things as being hit, slapped, slammed into something, or injured with an object or weapon.)
 - a. 0 times
 - b. 1 time
 - c. 2 or 3 times
 - d. 4 or 5 times
 - e. 6 or more times
- 13. How many times did someone you were dating or going out with force you to do sexual things that you did not want to do or felt uncomfortable with?
 - a. 0 times
 - b. 1 time
 - c. 2 or 3 times
 - d. 4 or 5 times
 - e. 6 or more times
- 14. How many times have you intentionally tried to hurt yourself? (Consider such actions as attempted suicide, poisoning, overdose, and cutting.)
 - a. 0 times
 - b. 1 time
 - c. 2 or 3 times
 - d. 4 or 5 times
 - e. 6 or more times
- 15. How old were you when you smoked a whole cigarette for the first time?
 - a. I have never smoked a whole cigarette.
 - b. 8 years old or younger
 - c. 9 or 10 years old
 - d. 11 or 12 years old
 - e. 13 or 14 years old
 - f. 15 or 16 years old
 - g. 17 years old or older

- 16. How often do you smoke cigarettes?
 - a. Never
 - b. Rarely (1 or 2 times a month)
 - c. Sometimes (3 to 5 times a month)
 - d. Often (6 to 10 times a month)
 - e. Frequently (10 to 19 times a month)
 - f. Always (nearly every day)
- 17. During the past year, did you ever try to quit smoking cigarettes?
 - a. I did not smoke during the past 12 months
 - b. Yes- I tried and was successful
 - c. Yes- I tried but was unsuccessful
 - d. No- But I would like to try
 - e. No- I have no interest in quitting at this time
- 18. How often do you use chewing tobacco, snuff, or dip such as Redman, Levi Garrett, Beechnut, Skoal Bandits, or Copenhagen?
 - a. Never
 - b. Rarely (1 or 2 times a month)
 - c. Sometimes (3 to 5 times a month)
 - d. Often (6 to 10 times a month)
 - e. Frequently (10 to 19 times a month)
 - f. Always (nearly every day)
- 19. How often do you smoke cigars, cigarillos, or little cigars?
 - a. Never
 - b. Rarely (1 or 2 times a month)
 - c. Sometimes (3 to 5 times a month)
 - d. Often (6 to 10 times a month)
 - e. Frequently (10 to 19 times a month)
 - f. Always (nearly every day)
- 20. How often do you have at least one drink of alcohol?
 - a. Never
 - b. Rarely (1 drink a week or less)
 - c. Sometimes (2-3 drinks a week)
 - d. Often (4 drinks a week)
 - e. Frequently (more than 5 drinks a week)
 - f. Always (nearly every day)
- 21. How old were you when you had your first drink of alcohol other than a few sips?
 - a. I have never had a drink of alcohol other than a few sips
 - b. 8 years old or younger
 - c. 9 or 10 years old

- d. 11 or 12 years old
- e. 13 or 14 years old
- f. 15 or 16 years old
- g. 17 years old or older
- 22. During the past 30 days, on how many days did you have at least one drink of alcohol?
 - a. 0 days
 - b. 1 or 2 days
 - c. 3 to 5 days
 - d. 6 to 9 days
 - e. 10 to 19 days
 - f. 20 to 29 days
 - g. All 30 days
- 23. As an adult, what is the largest number of alcoholic drinks you have had in a row, that is, within a couple of hours?
 - a. I do not drink alcohol
 - b. 1 or 2 drinks
 - c. 3 drinks
 - d. 4 drinks
 - e. 5 drinks
 - f. 6 or 7 drinks
 - g. 8 or 9 drinks
 - h. 10 or more drinks
- 24. How often do you use marijuana?
 - a. Never
 - b. Rarely (1 or 2 times a year)
 - c. Sometimes (3 to 6 times a year)
 - d. Often (about once or twice a month)
 - e. Frequently (several days a month)
 - f. Always (nearly every day)
- 25. How old were you when you tried marijuana for the first time?
 - a. I have never tried marijuana
 - b. 8 years old or younger
 - c. 9 or 10 years old
 - d. 11 or 12 years old
 - e. 13 or 14 years old
 - f. 15 or 16 years old
 - g. 17 years old or older

- 26. During the past 30 days, how many times did you use marijuana?
 - a. 0 times
 - b. 1 or 2 times
 - c. 3 to 9 times
 - d. 10 to 19 times
 - e. 20 to 39 times
 - f. 40 or more times
- 27. During your life, how many times have you used any form of cocaine, including powder, crack, or freebase?
 - a. Never
 - b. Rarely (1 or 2 times a year)
 - c. Sometimes (3 to 6 times a year)
 - d. Often (about once or twice a month)
 - e. Frequently (several days a month)
 - f. Always (nearly every day)
- 28. During your life, how many times have you sniffed glue, breathed the contents of aerosol spray cans, inhaled gasoline fumes, or inhaled any paints or sprays to get high?
 - a. 0 times
 - b. 1 or 2 times
 - c. 3 to 9 times
 - d. 10 to 19 times
 - e. 20 to 39 times
 - f. 40 or more times
- 29. During your life, how many times have you used heroin (also called smack, junk, or China White)?
 - a. 0 times
 - b. 1 or 2 times
 - c. 3 to 9 times
 - d. 10 to 19 times
 - e. 20 to 39 times
 - f. 40 or more times
- 30. During your life, how many times have you used methamphetamines (also called speed, crystal, crank, or ice)?
 - a. 0 times
 - b. 1 or 2 times
 - c. 3 to 9 times
 - d. 10 to 19 times

- e. 20 to 39 times
- f. 40 or more times
- 31. During your life, how many times have you used Ecstasy (also called MDMA)?
 - a. 0 times
 - b. 1 or 2 times
 - c. 3 to 9 times
 - d. 10 to 19 times
 - e. 20 to 39 times
 - f. 40 or more times
- 32. During your life, how many times have you taken steroid pills or shots without a doctor's prescription?
 - a. 0 times
 - b. 1 or 2 times
 - c. 3 to 9 times
 - d. 10 to 19 times
 - e. 20 to 39 times
 - f. 40 or more times
- 33. During your life, how many times have you taken a prescription drug (such as OxyContin, Percocet, Vicodin, Codeine, Adderall, Ritalin, or Xanax) without a doctor's prescription?
 - a. 0 times
 - b. 1 or 2 times
 - c. 3 to 9 times
 - d. 10 to 19 times
 - e. 20 to 39 times
 - f. 40 or more times
- 34. During your life, how many times have you used a needle to inject any illegal drug into your body?
 - a. 0 times
 - b. 1 time
 - c. 2 or more times
- 35. During the past 12 months, has anyone offered, sold, or given you an illegal drug at school or work?
 - a. Yes
 - b. No

- 36. During the past 12 months, how often have you used a liquid (such as 5-hour Energy or Red Bull) or a pill (such as NoDoze) to keep yourself awake?
 - a. Never
 - b. Rarely (1 or 2 times a year)
 - c. Sometimes (3 to 6 times a year)
 - d. Often (about once or twice a month)
 - e. Frequently (several days a month)
 - f. Always (nearly every day)
- 37. How old were you when you had sexual intercourse for the first time?
 - a. I have not had sexual intercourse
 - b. 11 years old or younger
 - c. 12 years old
 - d. 13 years old
 - e. 14 years old
 - f. 15 years old
 - g. 16 years old
 - h. 17 years old or older
- 38. During your life, with how many people have you had sexual intercourse?
 - a. I have not had sexual intercourse
 - b. 1 2 people
 - c. 3 4 people
 - d. 5-8 people
 - e. 9 14 people
 - f. 15-20 people
 - g. more than 20 people
- 39. During the past 30 days, with how many people did you have sexual intercourse?
 - a. I have never had sexual intercourse
 - b. I have had sexual intercourse, but not during the past 30 days
 - c. 1 person
 - d. 2 people
 - e. 3 people
 - f. 4 people
 - g. 5 people
 - h. 6 or more people
- 40. The last time you had sexual intercourse, did you drink alcohol or use drugs first?
 - a. I have not had sexual intercourse
 - b. Yes
 - c. No
- 41. The last time you had sexual intercourse, did you or your partner use a condom?
 - a. I have not had sexual intercourse

- b. Yes
- c. No
- 42. The last time you had sexual intercourse, what one method did you or your partner use to prevent pregnancy? (Select only ONE response.)
 - a. I have not had sexual intercourse
 - b. No method was used to prevent pregnancy
 - c. Birth control pills
 - d. Condoms
 - e. An IUD (such as Mirena or ParaGard) or implant (such as Implanon or Nexplanon)
 - f. A shot (such as Depo-Provera), a patch (such as Ortho Evra), or a birth control ring (such as NuvaRing)
 - g. Withdrawal or some other method
 - h. Not sure
- 43. How do you describe your weight?
 - a. Very underweight
 - b. Slightly underweight
 - c. About the right weight
 - d. Slightly overweight
 - e. Very overweight
- 44. Which of the following are you trying to do about your weight?
 - a. Lose weight
 - b. Gain weight
 - c. Stay the same weight
 - d. I am not trying to do anything about my weight
- 45. During the past 30 days, did you take any diet pills, powders, or liquids without a doctor's advice to lose weight or to keep from gaining weight? (Do NOT count meal replacement products such as Slim Fast.)
 - a. Yes
 - b. No
- 46. During the past 30 days, did you vomit or take laxatives to lose weight or to keep from gaining weight?
 - a. Yes
 - b. No
- 47. How many times have you been arrested?
 - a. I have never been arrested
 - b. 1 time

- c. 2 times
- d. 3 times
- e. 4-5 times
- f. 6 or more times
- 48. How many of your close friends have been arrested?
 - a. 0 friends
 - b. 1 friend
 - c. 2 friends
 - d. 3 friends
 - e. 4-5 friends
 - f. 6 or more friends
- 49. How many speeding tickets have you received?
 - a. I have never received a speeding ticket
 - b. 1 ticket
 - c. 2 tickets
 - d. 3 tickets
 - e. 4-5 tickets
 - f. 6 or more tickets
- 50. How many times have you been caught for DUI (driving while under the influence of alcohol or drugs)?
 - a. I have never been caught for DUI
 - b. 1 time
 - c. 2 times
 - d. 3 times
 - e. 4-5 times
 - f. 6 or more times
- 51. How many times have you shoplifted or stolen something that you didn't really need just for fun?
 - a. I have never shoplifted or stolen something just for fun
 - b. 1 time
 - c. 2 times
 - d. 3 times
 - e. 4-5 times
 - f. 6 or more times
- 52. How many times have you shoplifted or stolen something that you really DID need?
 - a. I have never shoplifted or stolen something if even I needed it
 - b. 1 time

- c. 2 times
- d. 3 times
- e. 4-5 times
- f. 6 or more times

This is the end of the survey. Thank you very much for your time.

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