# Childhood Adversity Is Associated with Left Basal Ganglia Dysfunction During Reward Anticipation in Adulthood

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**Background:** Childhood adversity increases the risk of psychopathology, but the neurobiological mechanisms underlying this vulnerability are not well-understood. In animal models, early adversity is associated with dysfunction in basal ganglia regions involved in reward processing, but this relationship has not been established in humans.

**Methods:** Functional magnetic resonance imaging was used to examine basal ganglia responses to: 1) cues signaling possible monetary rewards and losses; and 2) delivery of monetary gains and penalties, in 13 young adults who experienced maltreatment before age 14 years and 31 nonmaltreated control subjects.

**Results:** Relative to control subjects, individuals exposed to childhood adversity reported elevated symptoms of anhedonia and depression, rated reward cues less positively, and displayed a weaker response to reward cues in the left globus pallidus. There were no group differences in right hemisphere basal ganglia response to reward cues or in basal ganglia response to loss cues, no-incentive cues, gains, or penalties.

**Conclusions:** Results indicate that childhood adversity in humans is associated with blunted subjective responses to reward-predicting cues as well as dysfunction in left basal ganglia regions implicated in reward-related learning and motivation. This dysfunction might serve as a diathesis that contributes to the multiple negative outcomes and psychopathologies associated with childhood adversity. The findings suggest that interventions that target motivation and goal-directed action might be useful for reducing the negative consequences of childhood adversity.

**Key Words:** Anhedonia, basal ganglia, fMRI, maltreatment, reward, stress

Childhood adversity, including abuse, neglect, and exposure to dysfunctional household environments (e.g., witnessing parental violence, living with substance-abusing individuals), increases the risk for psychopathology and substance abuse (1–6) and can lead to dysregulated hypothalamic-pituitary-adrenal stress responses (7), neuropsychological impairments (8), and dysfunction in brain regions implicated in learning and memory (9). However, potential effects on brain reward circuitry in adulthood have gone unexplored, although there is evidence of altered reward processing in maltreated children (10). This is important because reward system dysfunction might underlie anhedonia (11), a core component of stress-related psychopathology (12). Although maltreatment is associated with anhedonia (13) and melancholia (14), neural mechanisms underlying these relationships remain unknown.

In experimental animals, chronic stressors can weaken preferences for sucrose solutions and conditioning for rewarded locations, delay approach to palatable foods, and increase thresholds for brain stimulation reward (15–19). These effects are hypothesized to reflect dysfunction in dopaminergic (DA) circuits that project to the basal ganglia (19), which are sensitive to early adversity (20). Importantly, in experiments using cue-outcome designs these DA circuits are more strongly associated with incentive motivational processes elicited by reward-predicting cues than with hedonic processes triggered by rewarding outcomes (21–23), suggesting that early adversity might preferentially affect responses to reward-predicting cues. Consistent with this assumption, early adversity in marmosets decreased motivation to obtain rewards without affecting consummatory behavior (17). Thus, we hypothesized that childhood adversity in humans could weaken basal ganglia responses to reward-predicting cues while leaving responses to actual rewards intact.

To test this hypothesis, we used functional magnetic resonance imaging (fMRI) and a monetary incentive delay (MID) task (22,23) to investigate reward-processing in young adults exposed to maltreatment (24). This task was selected because it recruits basal ganglia activity across a variety of samples, including adolescents (25), young adults (22,23), and older adults (26). Trials began with cues signaling potential rewards, losses, or no-incentive. Next, participants pressed a button in response to a briefly presented target; they were instructed that rapid reaction times (RTs) increased their chances of receiving gains and avoiding penalties. Finally, feedback indicated whether money was gained or lost. Analyses focused on basal ganglia regions of interest (ROIs). Participants also rated cues and outcomes for arousal and valence.

We predicted that, relative to control subjects, maltreated participants would show slower RT on reward trials, rate reward cues as less positive, and show weaker basal ganglia responses to reward cues. Group differences in response to gains were not predicted, on the basis of recent animal findings (17) and evidence that early adversity affects DA transmission (19) that is most strongly associated with reward anticipation (22,23,27).

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Received November 26, 2008; revised February 20, 2009; accepted February 23, 2009.

0006-3223/09/$36.00
doi:10.1016/j.biopsych.2009.02.019

## Methods and Materials

### Participants

**Maltreated Group.** Maltreated participants were recruited from a study exploring relations between social risk factors and psychopathology in young adulthood (24). Recruitment was directed at 63 individuals: 18 could not be relocated, 21 were excluded (Supplement 1), 3 could not be scheduled, and 2 declined. The remaining 19 underwent fMRI scanning; data from 6 individuals were excluded due to excessive head movement. The final sample consisted of 13 young adults (4 men) (Table 1). Eight have been studied since infancy (mean ± SD age at enrollment = 8.88 months ± 5.36 months), and five have been studied since young adulthood (20.60 years ± 1.34 years).

Participants were recruited on the basis of evidence of emotional, physical, and/or sexual abuse during childhood that met state guidelines for maltreatment. Evidence of abuse was rated in the original study from multimodal assessments including the Adult Attachment Interview (28,29), the revised Conflict Tactics Scale (30), the Traumatic Stress Schedule (31), whether a report of concern for safety was substantiated by protective services before age 7 years, and whether major disruption of placement with the primary caretaker had occurred. Reliability of abuse ratings was high (intraclass correlation coefficient = .99, $n = 37$). Among the 13 participants, 12 reported abuse before age 12 years (emotional abuse $n = 1$; physical or sexual abuse $n = 6$; multiple types of abuse $n = 5$), with 1 participant reporting abuse beginning at age 13 years (sexual abuse) (see Supplement 1 for details).

Maltreated participants were right-handed (32), reported no history of medical or neurological conditions, and met fMRI safety criteria. Two maltreated participants reported using psychotropic medications in the weeks before scanning (citalopram, $n = 1$; hydrocodone, $n = 1$).

**Control Subjects.** Maltreated participants were compared with community control subjects ($n = 31$) who performed the same task for another study (33). Data from two control subjects were discarded due to excessive head movement. The final sample included 16 men (Table 1). Control subjects were right-handed (32); reported no history of neurological or medical conditions, no current or past psychopathology, no psychotropic medication use; and met fMRI safety criteria. Control subjects were older and more educated than maltreated participants, but gender and racial composition were similar (Table 1). Community control subjects were used because the study from which maltreated individuals were recruited did not yield an adequate number of nonmaltreated individuals for comparison.

**Table 1.** Sociodemographic and Self-Reported Mood Data

| | Maltreated Group | | Control Group | | | |
|---|---|---|---|---|---|---|
| | Mean | SD | Mean | SD | Statistic | *p* |
| % Female | 69% | NA | 45% | NA | $\chi^2(1) = 2.14$ | $> .13$ |
| Age | 24.58 | .88 | 37.08 | 13.77 | $t(40) = 4.87$ | $< .001$ |
| Education | 12.92 | 2.22 | 15.28 | 1.65 | $t(40) = 3.84$ | $< .001$ |
| % Caucasian | 77% | NA | 76% | NA | $\chi^2(1) = .006$ | $> .94$ |
| MASQ-GDD[a] | 22.77 | 12.90 | 14.89 | 2.97 | $t(39) = 3.10$ | $< .005$ |
| MASQ-GDA[a] | 17.15 | 7.10 | 14.00 | 2.46 | $t(39) = 1.56$ | $> .13$ |
| MASQ-AD[a] | 55.69 | 20.84 | 42.57 | 7.81 | $t(39) = 2.20$ | $< .047$ |
| MASQ-AA[a] | 20.62 | 3.93 | 18.54 | 1.95 | $t(39) = 1.81$ | $> .09$ |
| CES-D | 12.15 | 12.93 | NA | NA | NA | NA |
| BDI-II[a] | NA | NA | 2.25 | 2.46 | NA | NA |

MASQ, Mood and Anxiety Symptom Questionnaire (35); GDD, General Distress Depressive symptoms; GDA, General Distress Anxious symptoms; AD, anhedonic depressive symptoms; AA, anxious arousal symptoms; CES-D, Center for Epidemiological Studies Depression Scale (36); BDI-II, Beck Depression Inventory (37).

[a]One control participant had missing values for the MASQ and BDI.

### Procedure

**Informed Consent.** Participants consented to an institutional review board-approved protocol and were debriefed after the study. Maltreated and control participants were compensated $100 and $80, respectively, for the fMRI session and were given $20–$22 as "earnings" from the task.

**Psychopathology Assessments.** Structured clinical interviews for DSM disorders (SCID-I [34]) were administered once to control subjects to rule out psychopathology. Two SCIDs were administered to maltreated participants. The first covered lifetime through young adulthood (age at first SCID: 20.10 ± 1.43 years). The second was administered shortly before the experimental session (1.17 ± 1.58 months before) and focused on the interval between young adulthood and the experimental session (interval between SCIDs: 4.48 ± 1.47 years). Both groups completed the Mood and Anxiety Symptoms Questionnaire (MASQ: 35), which assesses anxious arousal (AA), anhedonic depression (AD), and general distress due to anxiety (GDA) or depression (GDD). Maltreated participants completed the Center for Epidemiological Studies Depression Scale (CES-D: 36); control subjects completed the Beck Depression Inventory (BDI-II: 37).

**MID Task.** The MID task was based on previous studies (22) and identical to a prior version (23). There were five blocks of 24 trials. Trials began with one of three visual cues (1.5 sec) signaling potential outcomes (reward: +$; loss: −$; no-incentive: $0) (8 trials/cue/block). After a jittered interstimulus interval (ISI: 3–7.5 sec), a red square was presented for a variable duration. Participants responded to the square with a button press. After a second ISI (4.4–8.9 sec), visual feedback (1.5 sec) indicated delivery of a gain (range: $1.96 to $2.34; mean: $2.15), penalty (range: $1.81 to −$2.19; mean: −$2.00), or "no change". Reward trials ended with gains or no change, loss trials ended with penalties or no change, and no-incentive trials ended in no change. An intertrial-interval separated the trials (3–12 sec).

To achieve a balanced design, one-half the reward and loss trials ended in gains and penalties, respectively. However, participants were told that rapid RTs increased their chances of receiving gains and avoiding penalties, so that RT could be used to probe incentive motivation. After blocks two and four, participants rated cues and outcomes for arousal (1 = low, 5 = high) and valence (1 = negative, 5 = positive). Ratings data were not collected for two maltreated participants due to time constraints, and reward cue valence ratings were not collected from one control subject due to error.

### MRI Acquisition

The MRI data were acquired on a 1.5-T Symphony/Sonata scanner (Siemens Medical Systems; Iselin, New Jersey), with tilted slice acquisition and z-shimming to minimize susceptibility artifacts (38). During structural imaging, a T1-weighted magnetization prepared rapid gradient echo volume was acquired (repetition time [TR]/echo time [TE]: 2730/3.39 msec; field-of-view [FOV]: 256 mm, 1 × 1 × 1.33 mm voxels; 128 slices). During functional imaging, gradient echo T2*-weighted echo planar images were acquired (TR/TE: 2500/35 msec; FOV: 200 mm, 3.125 × 3.125 × 3 mm voxels; 35 slices; 222 volumes).

**Table 2.** Current and Lifetime Axis I Diagnoses for Maltreated Participants

| Subject | Period | Diagnoses |
|---|---|---|
| 1 | Current | Generalized anxiety disorder |
| | Lifetime | Major depressive disorder; alcohol abuse; cannabis abuse |
| 2 | Current | None |
| | Lifetime | Major depressive disorder; specific phobia |
| 3 | Current | None |
| | Lifetime | Alcohol abuse |
| 4 | Current | None |
| | Lifetime | Anxiety disorder, not otherwise specified |
| 5 | Current | Major depressive disorder; agoraphobia without panic disorder; generalized anxiety disorder; post-traumatic stress disorder |
| | Lifetime | Major depressive disorder; alcohol dependence; hallucinogen dependence; eating disorders |
| 6 | Current | None |
| | Lifetime | None |
| 7 | Current | None |
| | Lifetime | Major depressive disorder |
| 8 | Current | None |
| | Lifetime | None |
| 9 | Current | None |
| | Lifetime | Alcohol dependence; bipolar I disorder |
| 10 | Current | None |
| | Lifetime | Alcohol dependence; cannabis dependence; opioid dependence |
| 11 | Current | None |
| | Lifetime | Panic disorder without agoraphobia; cannabis abuse |
| 12 | Current | None |
| | Lifetime | Generalized anxiety disorder; social phobia; alcohol abuse; cannabis abuse |
| 13 | Current | None |
| | Lifetime | None |

### Data Analysis

**Mood.** Between-groups *t* tests tested for differences on the MASQ.

**RT and Affective Ratings.** After removing outliers (RTs exceeding mean ± 3 SD), RTs were entered into a Group × Cue × Block analysis of variance (ANOVA). Ratings were entered into Group × Cue or Group × Outcome ANOVAs. Significant differences were followed-up with *t* tests. The Greenhouse-Geisser correction was used when sphericity was violated.

**fMRI.** Neuroimaging data were analyzed with FS-FAST (http://surfer.nmr.mgh.harvard.edu) and FreeSurfer (39). Preprocessing included motion and slice-time correction, removal of slow trends with a second order polynomial, intensity normalization, and spatial smoothing (6 mm full-width-at-half-maximal Gaussian filter). Hemodynamic responses were modeled as a γ function convolved with stimulus onsets. A temporal whitening filter estimated and corrected for autocorrelation in the noise. Participants with head movement >3.75 mm or degrees were excluded (approximately the size of 1 functional voxel; control: $n = 2$; maltreated: $n = 6$). For remaining participants, motion parameters were included as nuisance regressors.

Four basal ganglia ROIs were defined by FreeSurfer's subcortical segmentation algorithm: nucleus accumbens (NAcc), caudate, putamen, and globus pallidus (39,40) (Supplement 1). Average β weights measuring the fit of the data to the model were extracted from each ROI for the cues and three outcomes (gains, penalties, no change feedback on no-incentive trials) and entered into Group × Cue (or Outcome) × Hemisphere × Structure (NAcc, caudate, putamen, pallidus) ANOVAs. Significant effects were followed-up with ANOVAs and *t* tests. Analysis of covariance (ANCOVA) was not used, because groups differed on the potential covariates, age, and education, violating a key assumption of ANCOVA (41) (Supplement 1).

**Basal Ganglia Volumetry.** Basal ganglia volumes were extracted from FreeSurfer, divided by intracerebral volume, multiplied by 100 to yield percent intracerebral volume scores, and entered into a Group × Hemisphere × Structure ANOVA.

**Regression Analyses Including Age and Education.** Group differences were followed-up with hierarchical regressions to determine whether they remained after removing variance associated with age and education. Possible effects of age on findings were also investigated by comparing maltreated participants to a subsample of 13 age-matched control subjects (Supplement 1); it was not possible to select a subsample of education-matched control subjects.

## Results

### Clinical Data

Seventy-seven percent of maltreated participants met DSM-IV criteria for an Axis I disorder at some time (Table 2). On the SCID proximal to scanning, one participant met criteria for MDD, agoraphobia, Generalized Anxiety Disorder (GAD), and post-traumatic stress disorder; another met criteria for GAD (see Supplement 1 for results excluding these participants). No other participants displayed current axis I disorder.

The mean CES-D score for the maltreated group was low (Table 1). The CES-D scores of 16–26 indicate mild depression, whereas scores above 26 indicate increasingly severe depression (42); by these criteria, the maltreated group was not depressed. Ten maltreated participants indicated no depression (CES-D < 16), two indicated mild depression (CES-D = 17, 23), and one indicated more severe depression (CES-D = 49) (see Supplement 1 for results excluding these participants). However, despite absence of clinical depression, maltreated and control groups differed on MASQ GDD and AD scores (Table 1).

### RT

There was a significant Cue effect [$F(2,80) = 23.40$, $p < .001$]. The RT was fastest on reward trials (335.16 ± 68.15 msec), intermediate on loss trials (354.54 ± 69.50 msec), and slowest on no-incentive trials (397.90 ± 88.82 msec) (all *p* values < .001) (Figure 1), indicating that participants were motivated to obtain gains and avoid penalties. There was a trend for Group [$F(1,40) = 2.89$, $p = .097$], because maltreated participants responded more slowly (389.07 ± 68.69 msec) than control subjects (350.63 ± 67.42

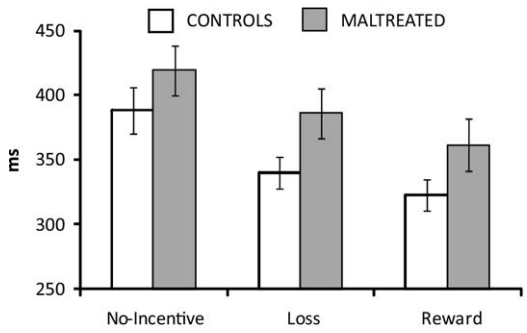


**Figure 1.** Reaction time to the target by Group and Cue. Error bars reflect the SEM.

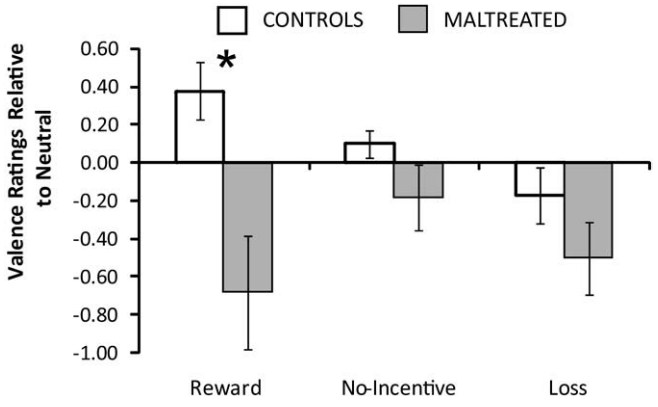


**Figure 2.** Valence ratings in response to cues. Data are plotted as change scores relative to neutral valence, which was 3 on the 5-point scale (1 = most negative, 3 = neutral, 5 = most positive). Maltreated participants rated reward cues significantly less positively than control subjects. Bars indicate the SEM. *$p < .05$.

msec). However, contrary to predictions, group differences were not specific to reward trials, Group × Cue [$F(2,80) < 1$].

### Affective Ratings

As predicted, analysis of cue-elicited valence revealed a Group effect [$F(1,37) = 10.33$, $p = .003$], and a Group × Cue interaction [$F(2,74) = 4.14$, $p = .02$]. Reward cues were rated less positively by maltreated participants (2.32 ± .98) relative to control subjects (3.38 ± .78) [$t(37) = 3.55$, $p = .001$, Hedges' $G = 1.24$ (SE = .38; 95% CI: .49−1.99)] (Figure 2). Group differences for no-incentive and loss cues were nonsignificant ($p$ values > .13).

No further evidence for group differences emerged, although there was a trend ($p < .09$) for maltreated participants to rate all outcomes as less positive than control subjects. Additional analyses revealed that cues and outcomes elicited intended affective responses (Supplement 1).

### Basal Ganglia Responses

**Cues.** There were two effects involving Group: a Group × Structure interaction [$F(3,120) = 3.26$, $p < .05$] and a Group × Cue × Hemisphere interaction [$F(2,80) = 3.77$, $p = .03$]. To evaluate the triple interaction, Group × Cue ANOVAs were performed in each hemisphere. The interaction was significant in the left hemisphere [$F(2,80) = 3.84$, $p < .04$] [right hemisphere, $F(2,80) < 1$]. Two steps were taken to decompose this interaction. First, within-group tests examined whether cues elicited differential activity in each group. In control subjects, a one-way ANOVA on data averaged across left hemisphere ROIs confirmed the predicted Cue effect [$F(2,56) = 7.54$, $p = .005$]: responses to reward cues (.048 ± .06) were stronger ($p$ values < .006) than responses to no-incentive (.006 ± .05) or loss cues (.021 ± .05), which did not differ ($p = .17$). By contrast, a similar ANOVA in maltreated participants was nonsignificant [$F(2,24) = 1.18$, $p = .32$]: follow-up $t$ tests revealed no differences among responses to no-incentive (.021 ± .04), loss (.039 ± .04), or reward cues (.019 ± .05) ($p$ values > .10). Second, a between-groups $t$ test investigated the predicted difference in reward cue responses averaged across left hemisphere ROIs; the test was nonsignificant [$t(40) = 1.42$, $p = .16$].

In light of the Group × Structure interaction, additional Group × Cue ANOVAs were conducted for each left hemisphere structure to investigate whether group differences were stronger in particular ROIs. The Group × Cue interaction was not significant in the left NAcc or caudate [all $F(2,80) < 2.74$, $p$ values > .08] but was significant in the left putamen [$F(2,80) = 3.60$, $p < .05$] and left pallidus [$F(2,80) = 3.73$, $p = .03$]. Accordingly, between-groups $t$ tests were conducted in these regions (Figure 3).

For the left putamen, control subjects generated a marginally stronger response to reward cues (.052 ± .07) than maltreated participants (.018 ± .04) [$t(40) = 1.73$, $p = .09$, Hedges' $G = .57$ (SE = .34; 95% CI: −.10–1.23), but responses to no-incentive and loss cues were similar ($p$ values > .36). For the left pallidus, control subjects generated a stronger response to reward cues (.052 ± .05) than maltreated participants (.001 ± .05) [$t(40) = 2.55$, $p = .02$, Hedges' $G = .83$ (SE = .35; 95% CI: .16–1.51], but responses to no-incentive and loss cues were again similar, $p$ values > .53. Finally, within-group one-way ANOVAs confirmed that the Cue effect was significant in both regions for control subjects [all $F > 12.18$, $p$ values < .001] but in neither

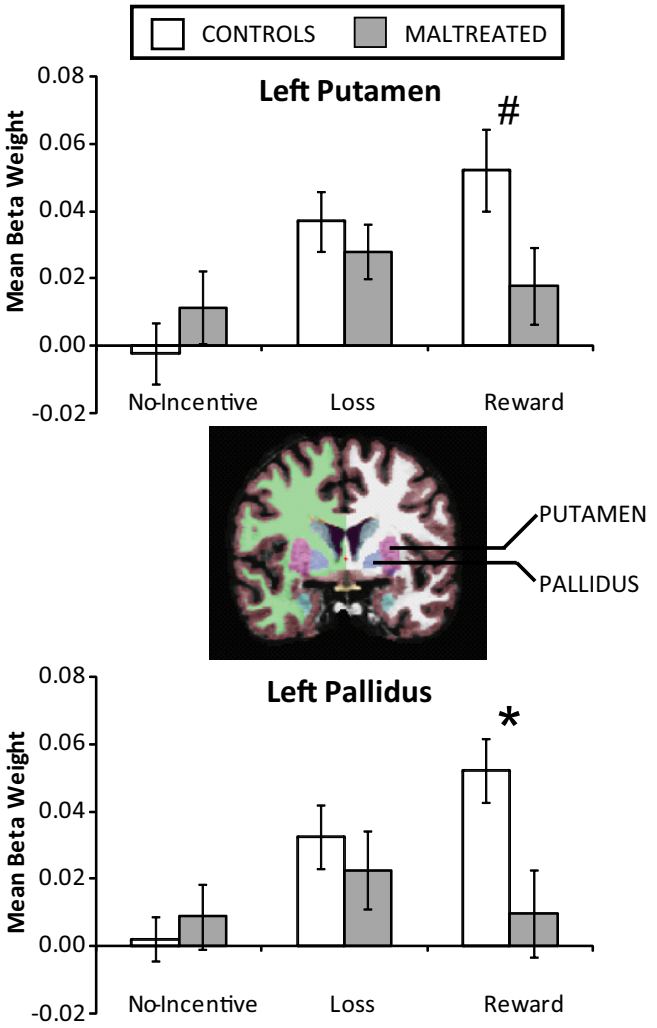


**Figure 3.** Left hemisphere reward anticipation deficit in the maltreated group. Mean β weights in the left putamen (top) and left globus pallidus (bottom) by Group and Cue. The coronal image in the center depicts the FreeSurfer subcortical segmentation for a representative participant, with the putamen in pink and the globus pallidus in blue. The maltreated group showed a blunted response to reward cues in both structures. Furthermore, whereas control subjects showed significant modulation of activity as a function of Cue in both regions, the maltreated group did not. *$p < .05$; #$p < .10$.

region for maltreated participants [all $F < 1.03$, $p > .36$]. Thus, the predicted group difference in reward cue response emerged for the left pallidus, with a similar trend in the left putamen.

**Outcomes.** The ANOVA revealed no evidence for between-group differences in outcome responses (all effects involving Group, $p$ values $> .18$).

### Basal Ganglia Volumes

There was a Group effect [$F(1,40) = 18.60$, $p < .001$] and several interactions involving Group: Group × Hemisphere [$F(1,40) = 4.43$, $p = .04$], Group × Structure [$F(3,120) = 5.86$, $p = .003$], and Group × Hemisphere × Structure [$F(3,120) = 3.24$, $p = .04$]. Group × Hemisphere ANOVAs were conducted at each structure, to decompose the highest-order interaction. The interaction was only significant for the putamen [$F(1,40) = 5.77$, $p = .02$] [all $F(1,40) < 1.24$, $p$ values $> .26$ for other structures]. The $t$ tests revealed larger putamen volumes for maltreated participants in the left hemisphere (maltreated: .406 ± .03; control subjects: .356 ± .04) [$t(40) = -3.80$, $p < .001$, Hedges' $G = -1.24$ (SE = .36; 95% CI: −1.95 to −.54)] and right hemisphere (maltreated: .385 ± .03; control subjects: .348 ± .04), [$t(40) = -2.98$, $p = .005$, Hedges' $G = -.95$ (SE = .35; 95% CI: −1.66 to −.29)].

These results likely reflect the group difference in age. Indeed, among control subjects, age was significantly negatively correlated with putamen volume in the left (control subjects: $r = -.70$, $p < .001$; maltreated: $r = -.47$, $p = .11$) and right (control subjects: $r = -.60$, $p = .001$; maltreated: $r = -.33$, $p = .27$) hemispheres. Accordingly, hierarchical regressions predicting putamen volume by age (entered first) and group (entered second) revealed strong effects for age (left putamen: $\beta = -.61$, $p < .001$; right putamen: $\beta = -.56$, $p < .001$), whereas Group was not a significant predictor of volume (left putamen: $\beta = .24$, $p = .06$; right putamen: $\beta = .17$, $p = .22$).

### Regression Analyses

Additional regressions tested for effects of Group (entered second: 0 = control, 1 = maltreated) on reward cue valence ratings, MASQ AD, and MASQ GDD after accounting for age and education (entered first). For each variable, Group emerged as a significant predictor after accounting for age and education (MASQ AD: $\beta = .39$, $p < .05$; MASQ GDD: $\beta = .37$, $p = .05$; reward cue valence ratings: $\beta = -.47$, $p = .01$). Furthermore, Group improved each model ($\Delta R$s$^2 > .08$, $\Delta F$s $> 4.02$, $p$ values $< .053$).

Next, two sets of regressions evaluated whether group differences in left putamen and left pallidus reward cue responses remained after accounting for other variables. In the first models, variables not hypothesized to relate specifically to reward processing (volumetric data, age, education, MASQ GDA, MASQ AA) were entered first, and Group was entered second. Group predicted left putamen and left pallidus reward cue responses in these models (Table 3), although the putamen results narrowly missed significance (left putamen: Group $\beta = -.39$, $p = .06$; left pallidus: Group $\beta = -.52$, $p = .04$). Furthermore, Group improved the models (left putamen: $\Delta R^2 = .08$, $\Delta F = 3.80$, $p = .06$; left pallidus: $\Delta R^2 = .10$, $\Delta F = 4.66$, $p = .04$).

In the second models, reward cue valence ratings and MASQ AD scores were added in step one. The MASQ AD was used rather than MASQ GDD, because the scales were correlated ($r = .85$, $p < .001$), and anhedonia is directly related to reward responsiveness (43). Not surprisingly, the Group effect was weakened (Table 3). Group no longer predicted reward cue response in left putamen ($\beta = -.18$, $p = .44$) or left pallidus ($\beta = -.34$, $p = .24$) and no longer improved the models (left putamen: $\Delta R^2 = .02$, $\Delta F < 1$, $p = .44$; left pallidus: $\Delta R^2 = .04$, $\Delta F = 1.45$, $p = .24$). These results indicate that group differences in reward cue valence ratings, MASQ AD, and left putamen/left pallidus reward cue responses share common variance. Indeed, left hemisphere basal ganglia reward responses were negatively correlated with MASQ AD across groups (putamen: $r = -.31$, $p = .05$; pallidus: $r = -.26$, $p = .097$) and positively correlated with reward cue valence ratings (putamen: $r = .36$, $p = .02$; pallidus: $r = .29$, $p = .07$).

**Table 3.** Hierarchical Regression Results for Left Putamen and Left Pallidus Reward Cue Response

| Predictor | Step | β | *t* | *p* |
|---|---|---|---|---|
| Left Putamen | | | | |
| First model | | | | |
| Volume | 1 | .01 | .05 | .96 |
| Age | 1 | −.39 | −1.78 | .08 |
| Education | 1 | −.04 | −.20 | .85 |
| MASQ-GDA | 1 | .24 | .99 | .33 |
| MASQ-AA | 1 | −.43 | −1.74 | .09 |
| Group | 2 | −.39 | −1.95 | .06 |
| Second model | | | | |
| Volume | 1 | −.07 | −.28 | .78 |
| Age | 1 | −.38 | −1.65 | .11 |
| Education | 1 | −.10 | −.55 | .59 |
| MASQ-GDA | 1 | .31 | 1.14 | .26 |
| MASQ-AA | 1 | −.27 | −1.05 | .30 |
| MASQ-AD | 1 | −.27 | −1.08 | .29 |
| Reward Cue valence ratings | 1 | .26 | 1.37 | .18 |
| Group | 2 | −.18 | −.79 | .44 |
| Left Pallidus | | | | |
| First model | | | | |
| Volume | 1 | .13 | .52 | .61 |
| Age | 1 | −.21 | −1.01 | .32 |
| Education | 1 | −.06 | −.31 | .76 |
| MASQ-GDA | 1 | .24 | 1.01 | .32 |
| MASQ-AA | 1 | −.42 | −1.75 | .09 |
| Group | 2 | −.52 | −2.16 | .04 |
| Second model | | | | |
| Volume | 1 | .12 | .43 | .67 |
| Age | 1 | −.19 | −.79 | .44 |
| Education | 1 | −.11 | −.55 | .58 |
| MASQ-GDA | 1 | .18 | .62 | .54 |
| MASQ-AA | 1 | −.31 | −1.20 | .24 |
| MASQ-AD | 1 | .00 | .00 | .99 |
| Reward Cue valence ratings | 1 | .28 | 1.43 | .16 |
| Group | 2 | −.34 | −1.21 | .24 |

Group was coded 0 = control subjects, 1 = maltreated. See Table 1 for additional details. Abbreviations as in Table 1.

## Discussion

Consistent with findings in nonhuman animals (15–19), maltreated participants reported elevated depressive and anhedonic symptoms, rated reward-predicting cues less positively, and showed decreased anticipatory reward activity in the left pallidus relative to control subjects. Results indicate that childhood adversity that includes maltreatment is associated with impaired reward processing (13,14). Furthermore, the findings highlight a neural mechanism that could contribute to relationships between childhood adversity and psychopathology: decreased anticipatory reward activity in the left basal ganglia. The pallidus

integrates reward information and conveys it to motor cortex via the thalamus (44). Thus, pallidus dysfunction might weaken the ability of reward-predicting cues to elicit goal-directed actions.

The relationship between childhood adversity and decreased subjective and neural responses to reward-predicting cues rather than rewards themselves was predicted on the basis of findings in nonhuman animals. For example, early maternal deprivation in marmosets impaired motivation to work for liquid reinforcement but did not affect consummatory behavior (17). We expected similar results, because DA neurons that project to the basal ganglia are susceptible to stress-related dysfunction (18,19) and critical for incentive motivation (21,27). However, it should be noted that early adversity can also weaken the hedonic impact of obtained rewards (16,19), possibly via effects on opioid systems (45). Accordingly, group differences in consummatory responses might emerge in larger samples or different paradigms.

The findings are consistent with the hypothesis that childhood adversity might have affected the development of DA systems. However, any strong causal interpretation of the data would be premature. In this small sample, we cannot disentangle effects of maltreatment per se from many potential correlates of maltreatment, such as inherited dysfunction in neural activity, parental depression or substance abuse, or the contribution of previous psychiatric issues (Table 2). Prospective studies using larger samples are needed to distinguish among such correlated factors.

Although the SCID and CES-D revealed little evidence of current clinical depression in maltreated participants, the groups differed on self-reported symptoms of depression and anhedonia. Moreover, when MASQ-AD scores and reward cue valence ratings were controlled, the Group effect on left pallidus reward cue responses became nonsignificant. One possibility is that the anhedonic symptoms and basal ganglia dysfunction are two manifestations of the same dysfunction. Indeed, MASQ-AD scores and reward cue responses in the left pallidus and left putamen were negatively correlated. In addition, the attenuated response to reward-predicting cues in the left pallidus is consistent with evidence of basal ganglia dysfunction in clinical depression. For example, relative to control subjects, depressed individuals showed weaker basal ganglia responses to reward-predicting cues and gains in the MID task (33), reduced ventral striatal responses to positive words (46), decreased caudate glucose metabolism (47) and blood flow (48), and reduced extracellular caudate and putamen DA (49).

The restriction of deficits to the left hemisphere was not predicted but echoes reports that poststroke depression more often follows damage to the left versus right hemisphere (50), with globus pallidus lesions highly predictive of depression (51). Moreover, a study in healthy participants reported a positive correlation between D2-receptor availability in the left putamen and incentive motivation (52), consistent with the fact that left hemisphere group differences were specific to reward anticipation. Findings are also consistent with reported relationships between childhood maltreatment and electrophysiological abnormalities over the left hemisphere (53). The reason for this hemispheric asymmetry is unclear, but asymmetrical projections of DA neurons might play a role (54).

Critically, results do not reflect a global deficit in maltreated participants. There were no significant group differences in affective ratings to any stimulus except reward cues and no differences in basal ganglia response to: 1) loss or no-incentive cues in the left hemisphere, 2) any cue in the right hemisphere, or 3) any outcome. Furthermore, group differences in left pallidus reward cue responses remained after controlling for anxiety and general distress (Table 3).

The study possesses several limitations. First, several maltreated individuals were excluded due to active substance abuse, and the striatum is tonically hypoactive in substance abusers (55). Thus, we might have excluded individuals with severe reward processing dysfunction, yielding a conservative estimate of effects of maltreatment on reward processing. Second, the lack of group differences in response to loss cues and penalties might reflect a weakness of the MID task: because participants knew they would be paid for participation, the loss cues and penalties might not have been sufficiently aversive to elicit group differences. Notably, other studies report relationships between childhood adversity and sensitivity to emotionally negative stimuli (e.g., [56]). Third, the current sample was too small to determine whether a dose–response relationship exists between extent or age of onset of maltreatment and responses to reward cues or to examine whether specific types of maltreatment have different effects on reward processing. Larger studies are needed to address these issues and to investigate whether particular genetic backgrounds or social supports can protect reward systems from adversity-induced dysfunction (57,58).

Fourth, because control subjects and maltreated participants were from different cohorts, variables besides maltreatment might have affected the results. Three considerations mitigate this concern. First, the loss and no-incentive conditions and cue/outcome design served as internal controls that allowed us to pinpoint the predicted differences in reward anticipation; the lack of differences in other conditions argues against a general deficit in maltreated participants. Second, the strong basal ganglia response to reward cues demonstrated by the control subjects is the norm in the MID task and has been demonstrated in samples differing in age, education, and sociodemographic data (22,23,25,26). Thus, the findings reflect a deficit in maltreated participants rather than atypical results in the control subjects. Third, Group predicted left pallidus reward cue responses after adjusting for age, education, anxiety, and basal ganglia volumes. Nonetheless, groups might have differed on other variables not measured, especially because maltreated individuals tend to be exposed to multiple forms of childhood adversity (59). Consequently, results should be interpreted in terms of childhood adversity rather than maltreatment per se.

*This work was supported by grants from the National Institute of Mental Health to Dr. Pizzagalli (R01MH68376, R21MH078979) and Dr. Lyons-Ruth (R01MH062030) as well as Harvard University's Robert Wood Johnson Health and Society Scholars program and Talley Fund award to Dr. Pizzagalli. We are grateful to Kyle Ratner, Elena Goetz, James O'Shea, and Decklin Foster for their skilled assistance, to Drs. Lawrence L. Wald and Christopher Wiggins for their help implementing the optimized fMRI pulse sequence used in the present study, and to Dr. Douglas N. Greve for his expert assistance with the FS-FAST and FreeSurfer packages.*

*Dr. Pizzagalli has received research support from GlaxoSmithKline and Merck & Co. for studies unrelated to this project. The other authors report no biomedical financial interests or potential conflicts of interest.*

*Supplementary material cited in this article is available online.*

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