Deficits in doors P300 amplitude during adolescence associated with preschool-onset depression

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Abstract
The psychophysiological underpinnings of preschool-onset depression (POMDD) remain underexplored. Moreover, there is currently a limited understanding of the potential impact that POMDD might have on neurobiological functions later in development such as general cognitive domains and reward processing. Thus, the current study sought to examine potential neurophysiological differences, measured via electroencephalography (EEG), in adolescents with and without a history of POMDD. Participants and their caregivers (N=138) from a large longitudinal study completed semi-structured clinical interviews at a baseline visit (ages 3–7) to determine POMDD status. At a follow-up visit approximately 11 years later, adolescents (ages 13–19) completed the doors gambling task while EEG was recorded to measure event-related potentials (ERPs) elicited by both the doors and feedback stimuli, to index cognitive and reward processing functions (i.e., doors-P300, gain/loss feedback-P300, and RewP). Adolescents with a history of POMDD exhibited significantly smaller doors-P300 compared with adolescents with no history of POMDD, whereas there were no group differences in gain/loss feedback-P300 or RewP. Additionally, reduced doors-P300 was independently associated with lower baseline income-to-needs ratio, older age, and female gender. The current study suggests that reduced doors-P300 amplitude during adolescence might reflect impaired neurophysiological development related to POMDD. Thus, the P300 derived from the doors stimuli might be a valuable neural measure to further our understanding of potential neurophysiological differences associated with early-onset childhood depression.

KEYWORDS
adolescence, EEG, ERP, P300, POMDD

1 | INTRODUCTION

The recognition of preschool-onset depression (i.e., POMDD) is a relatively new but emerging diagnostic classification in the fields of clinical psychology and psychiatry (Luby, 2010; Luby et al., 2003). POMDD is now a well-validated mental health disorder (Donohue et al., 2019) that is associated with significant burden, including impaired psychosocial functioning (Luby et al., 2009) and worsening depression outcomes as children age into later childhood and early adolescence (Luby et al., 2014). Currently, there
is limited insight into the potential impact that PO-MDD might have on neurobiological development, and to what extent this altered developmental trajectory may influence the chronic and relapsing course of depression.

Event-related potentials (ERPs) are measures of neural function, recorded by electroencephalography (EEG), that have been employed to better understand mechanisms implicated in psychopathology (Hajcak et al., 2019). In depressive disorders, it is common to find broad impairments to cognitive domains such as attention, processing speed, executive functions, and memory (Rock et al., 2014). One ERP which has been utilized extensively to examine the association between depression and deficits in cognitive functioning is the P300 component. The P300 is a positive-going waveform that peaks approximately 300 ms after stimulus presentation in experimental tasks and is typically maximal at parietal recording sites of the scalp (Hajcak & Foti, 2020). The P300 is believed to index cognitive processes such as attentional allocation, context updating, and inhibitory control (Hajcak & Foti, 2020) making it well-suited to investigate cognitive functioning commonly impacted by depressive disorders (Roiser et al., 2009).

Past studies consistently find P300 deficits among currently depressed adults across various experimental paradigms in which stimuli require the participant to respond, such as the oddball task, the flanker task, and the go-no-go task (Bruder et al., 2012; Klawohn, Santopetro, et al., 2020; Ruchsov et al., 2008; Santopetro, Brush, Bruchnak, et al., 2021); however, it is important to note that past studies predominately utilized visual or auditory oddball tasks (Bruder et al., 2012).

A recent study focused on extending this work to the P300 elicited in the doors gambling task in adults. In the doors, task participants are presented with two identical doors (the doors stimuli) and are told to select either door, which is followed by feedback indicating monetary gain or loss (Proudfit, 2015). Given that the presentation of the doors is an imperative stimulus on each trial that requires a response, it is possible that the doors-locked P300 could be examined in relation to depression. Indeed, a recent article found that currently depressed adults were characterized by reduced doors-P300 compared with adults with no history of depression; however, gain or loss feedback-P300 did not differ between groups which is in line with other studies reporting inconsistent deficits in feedback-P300 in relation to depression (Chang et al., 2020; Foti & Hajcak, 2009; Thoma et al., 2015)—consistent with the possibility that depression-related deficits may only be observed in contexts in which the P300 is elicited by stimuli that require a response. Moreover, higher anhedonia symptoms within the depressed group were associated with a smaller doors-P300, suggesting that motivational impairments may be especially relevant to deficits in doors-P300 in depression (Santopetro, Brush, Burani, et al., 2021).

Despite extensive work in adult samples, few studies have examined the relationship between P300 and depression in younger populations. Considering risk for depression is higher as youths traverse adolescence (Angold & Rutter, 1992; Costello et al., 2011; Ford et al., 2003; Lawrence et al., 2015) and that early-onset depression is associated with worse course of the disorder (Gollan et al., 2005; Klein et al., 1988), examination of the neurological underpinnings of depression during this critical developmental period can help further elucidate our overall understanding of the etiology of depressive disorders. More recent studies have found that reductions in P300, derived from stimulus presentation in the flanker task, were associated with heightened depressive symptoms (Santopetro, Kallen, Threadgill, et al., 2021) as well as predicted prospective increases in depressive symptoms over a two-year period among female adolescents (Santopetro et al., 2020). Additionally, researchers have reported deficits in P300 in response to stimuli among female adolescents with a lifetime history of depression in the context of a complex visual oddball task (Houston et al., 2003). In sum, research in adult and adolescent samples suggests that depression is characterized by deficits in P300 in response to imperative target stimuli (i.e., oddball stimuli, flanker stimuli, and doors stimuli)—potentially reflecting a neural correlate of the general motivational impairments that are common symptoms of depressive disorders (American Psychiatric Association, 2013; Bruder et al., 2012).

Researchers posit that dysfunctions in reward systems, more specifically hyposensitivity to rewards indexed by lower activation of brain areas such as the nucleus accumbens and caudate, are central to the etiology of depressive disorders (Pizzagalli et al., 2009). Therefore, an alternate avenue of ERP research has investigated individual differences in reward processing as indexed by the reward positivity (RewP), which is a positive-going component that typically peaks between 250 and 350 ms at frontal–central electrode sites following presentation of gain compared with loss feedback in experimental paradigms such as the doors task (Proudfit, 2015). Reduced RewP has been reported in adults with depression (Brush et al., 2018; Keren et al., 2018; Klawohn, Burani, et al., 2020) and has been found to prospectively predict onset and course of depression in older children and adolescents (Bress et al., 2013; Nelson et al., 2018). Children with current PO-MDD exhibited reductions in RewP when compared to psychiatrically healthy children (Belden et al., 2013). Additionally, higher reward positivity (RewP) was observed among children with a history of depression (Hajcak et al., 2019). These findings have been consistent across numerous studies demonstrating that reward sensitivity is altered in depression, and thus, RewP may be a useful measure for the evaluation of psychiatric populations.
et al., 2016), and RewP amplitude increased in a sample of children with PO-MDD who improved following a dyadic psychotherapeutic intervention (Barch et al., 2020). This research suggests that reductions in RewP evident in currently depressed adults and children reflect reward processing deficits core to depressive disorders (Whitton et al., 2015).

Recent research has also suggested that childhood poverty is associated with abnormalities in neural development. More specifically, researchers found that decreased income-to-needs ratio during childhood is associated with smaller hippocampus and amygdala volumes during early adolescence, suggesting that economic status may influence neurobiological development (Luby et al., 2013). Poverty during childhood has also been extensively linked to increased risk for psychopathology during childhood and adolescence (Peverill et al., 2021), yet few studies investigate the effects of childhood poverty and early depression simultaneously in relation to neurodevelopment.

The current study sought to examine the associations between PO-MDD assessed in early childhood and reliable neural indices of general cognitive and reward processing functions assessed in mid-to-late adolescence from the same experimental paradigm. More specifically, our primary goal was to examine the association of PO-MDD history status with stimulus-locked (i.e., doors-P300) and feedback-locked (i.e., gain and loss feedback-P300 and RewP) ERPs elicited from the doors gambling task in adolescence as these brain potentials are typically studied in isolation, making it unclear whether deficits in both adolescent cognitive functioning and reward processing might co-occur in relation to PO-MDD. To investigate whether long-term effects of PO-MDD on psychophysiology could be detected, our analyses were focused on assessing differences between adolescents with and without a history of PO-MDD, even when controlling for current differences in depressive symptoms, baseline, and current income-to-needs ratios, and current psychotropic medication use. Specifically, a semi-structured clinical interview was administered to the parents of all child participants at a baseline visit (ages 3–7) to determine the child’s PO-MDD status. At a follow-up visit approximately 11 years later, adolescent participants completed an additional interview to assess current depression status, and were administered the doors gambling task while EEG was recorded to measure ERPs elicited by the presentation of both doors and feedback stimuli. Based on past studies, we predicted that adolescents with a history of PO-MDD would show reductions in doors-P300 and RewP, whereas we predicted that neither gain nor loss feedback-locked P300 would not relate to PO-MDD status.

2 | METHOD

2.1 | Participants

The current study is part of the longitudinal Preschool Depression Study (PDS; Elsayed et al., 2021; Geselowitz et al., 2020; Luby et al., 2013; Luking et al., 2020). A total of 306 children, ages 3 to 6, and their parents/guardians, were recruited to participate in the baseline visit from daycares, preschools, and primary care clinics in the St. Louis area. All families were invited to participate in up to six additional yearly assessments which consisted of clinical interviews, observational assessments, and self-report questionnaires. Furthermore, a subset of these families were invited to participate in an additional three assessments which included similar clinical interviews, five neuroimaging scans, and two waves of EEG/ERP. Exclusion criteria included autism spectrum disorder, chronic illnesses, neurological disorders, and significant speech, language, or cognitive delays. Caregivers provided informed consent and the child provided verbal/written assent prior to participating in the study visits. All study procedures were approved in advance by the Institutional Review Board at Washington University School of Medicine.

The current study utilized parent-reported clinical interview data collected across three preschool assessments (ages 3 to 7) and stimulus-locked EEG data collected during the doors task and clinical interview data (combination of parent and child report) collected at the ninth follow-up assessment (ages 13 to 19). Of the 306 children and caregivers that attended the baseline visit, 172 returned for the ninth follow-up visit. Of the 172 returning participants, 150 completed the doors tasks while EEG was recorded. Of those, 12 participants were excluded for unusable EEG data. Thus, the final sample for the current analyses included 138 adolescent participants. From this final sample, 43 adolescents met criteria for PO-MDD. Conversely, the remaining 95 adolescents did not meet PO-MDD criteria during the first three preschool assessments. The average age of the sample at the follow-up visit was 16.26 years (SD = 1.20), and 49% were female (n = 67). At the follow-up visit, 51% of participants identified as White (n = 70), 36% identified as Black or African American (n = 50), and 13% identified as belonging to more than one race (n = 18). Table 1 has additional information regarding these variables in relation to PO-MDD status.

1One participant’s P300 data were winsorized as they were more than three standard deviations from the mean; that participants P300 amplitude was reduced to be exactly the three standard deviation value.
2.2 Measures

2.2.1 Preschool age psychiatric assessment

The preschool age psychiatric assessment (PAPA) is a well-validated parent-reported semi-structured diagnostic interview that was administered during the first three assessments (ages 3 to 7; Egger & Angold, 2004; Egger et al., 2006). Interviews were audio recorded and approximately 20% of the audio tapes were reviewed by a master coder. When discrepancies arose, these cases were discussed and recoded under the supervision of a senior child psychiatrist. To maintain calibration and avoid rater drift, weekly coding meetings with a master rater were conducted.

2.2.2 Kiddie schedule for affective disorders and schizophrenia

The kiddie schedule for affective disorders and schizophrenia (K-SADS) is a semi-structured diagnostic interview that assesses various current and lifetime psychological symptoms such as mood, psychosis, and behavioral issues (Kaufman et al., 1997). The K-SADS was administered to both adolescents and their caregivers at the ninth follow-up visit (ages 13 to 19) to assess current symptoms of psychopathology as well as symptoms since their previous assessment. This diagnostic interview is utilized for children between 6 and 18 years, incorporates both child and parent report, and demonstrates good psychometric properties (Birmaher...
et al., 2009). The most severe report of psychopathology, whether it be parent or child report, was utilized for scoring of K-SADS symptoms. The inter-rater reliability for depression diagnoses (i.e., MDD) from K-SADS at the ninth follow-up visit was $\kappa = 0.81$.

2.2.3 Income-to-needs ratio

The income-to-needs ratio was determined by dividing total family income by the federal poverty level based on family size at the time of (1) the baseline visit, and (2) the ninth follow-up visit.

2.3 Procedures

2.3.1 Doors task

The doors task (Proudfit, 2015) was administered using Presentation software and consisted of 60 total trials divided into three blocks. Each trial began with the presentation of two identical doors. Participants were instructed to select either the left or right door to gain ($0.50) or lose money ($0.25). The images of the doors were presented until participants selected a door, followed by a fixation cross displayed for 1000 ms, and then feedback stimulus presentation for 2000 ms. The feedback stimulus was indicated by a green arrow pointing upward to indicate gains or a red arrow pointing downward to indicate losses. Following feedback, another fixation cross was then presented for 1500 ms, followed by the prompt “Click for next round...” until participants responded with a button click to initiate the next trial. Gain and loss trials were equiprobable and presented pseudo-randomly.

2.3.2 EEG recording and processing

Continuous EEG was recorded during the doors task using a 32-channel electrode (Ag/AgCl) actiCHamp system (Brain Products GmbH, Gilching, Germany). The electrodes were placed on the cap in accordance with the international 10/20 system electrode system, and electrode site Cz served as the online recording reference. Electrococulogram (EOG) was collected from four electrodes: one placed above and below the right eye, one to the sides of each eye, and one additional reference electrode was placed above the left eye. Data were sampled at 500 Hz.

Offline EEG analyses were performed in Brain Vision Analyzer (version 2.2; Brain Products, Gilching, Germany). The EEG data were re-referenced to averaged TP9 and TP10, and then filtered with low and high filter cutoffs set at 0.1 and 30 Hz, respectively. Ocular artifacts were corrected following the Gratton et al. (1983) procedure. Automatic artifact rejection was implemented, rejecting any data with a voltage step (gradient) greater than 50 $\mu$V, a voltage difference of 175 $\mu$V within a 400 ms interval, or a maximum voltage difference of less than 0.50 $\mu$V within 100 ms intervals.

2.3.3 ERP quantification

Data were segmented starting 200 ms before the presentation of the doors/feedback stimuli to 800 ms after stimulus presentation and were baseline-corrected using the 200 ms pre-stimulus interval. All ERP measurement windows and electrode sites used were determined using a collapsed localizer approach (Luck & Gaspelin, 2017) such that data were inspected after collapsing groups; parameters were chosen in the time range and electrode sites showing maximal activity for each ERP (see Figures 1–4). First, the doors-P300 was quantified as the mean amplitude at an occipital pool consisting of electrode sites O1, O2, and Pz from 250 to 450 ms following the presentation of the doors stimulus. Next, gains and losses were averaged separately and both gain and loss feedback-P300 were scored from 300 to 450 ms post-feedback at electrode site Pz. Last, gains and losses were scored separately from 250 to 350 ms post-feedback as a fronto-central pool consisting of electrode sites Fz, Cz, FC1, and FC2. A residualized RewP difference score (referred to as RewP) was then calculated by saving the unstandardized residuals in a linear regression that predicted gains from losses (Santopetro, Brush, Burani, et al., 2021). It is important to note that the quantification of the outcome-related ERP components (i.e., feedback-P300s and RewP) in the present study are consistent with past research which displays different timing and scalp topographies for these neural components (i.e., maximal at parietal regions compared with frontal regions) reflecting unique psychological processes (Glazer et al., 2018). The correlation between odd and even trials for each ERP was examined to measure internal consistency (Levinson et al., 2017), which was corrected using the Spearman–Brown prophecy formula (Nunnally et al., 1967; Table 1).

2.3.4 Statistical analyses

All analyses were performed using SPSS software (Version 25.0; IBM Corp., Armonk, N.Y., USA). Current demographic, clinical interview, and ERP data were analyzed between the history of PO-MDD and no history...
PO-MDD groups utilizing independent samples t tests or chi-squared tests. Additionally, bivariate Pearson correlations or independent samples t tests were conducted across the sample to examine associations between adolescent ERPs and other variables of interest (e.g., age, gender, and baseline/current income-to-needs ratio). Lastly, four separate multiple linear regressions were conducted predicting (1) doors-P300, (2) gain

**FIGURE 1** Doors stimulus-locked waveform at an occipital pool in the entire sample (n = 138).

**FIGURE 2** Doors stimulus-locked waveforms and head maps of adolescents with a history of preschool-onset depression (PO-MDD; n = 43) and adolescents with no history of preschool-onset depression (No PO-MDD; n = 95).
feedback-P300, (3) loss feedback-P300, and (4) RewP. All regression models included PO-MDD status, current depression status, gender, baseline income-to-needs ratio, current income-to-needs ratio, and age at follow-up as independent variables. The criterion of statistical significance for all analyses was .05.
3 | RESULTS

3.1 | Demographic and clinical

There were no significant differences regarding age, gender, or racial composition between adolescents with and without a history of PO-MDD. However, adolescents with a history of PO-MDD had a lower income-to-needs ratio at baseline, \( t(122) = 2.53, p = .013, d = 0.47 \), as well as lower income-to-needs ratio at the time of the follow-up visit, \( t(131) = 2.03, p = .045, d = 0.38 \). Adolescents with a history of PO-MDD were also significantly more likely to be taking psychotropic medications at follow-up, \( X^2(1, 138) = 6.63, p = .010 \). Refer to Table 1 for information regarding these variables.

3.2 | ERPs

Doors-P300 amplitude was reduced among adolescents with a history of PO-MDD, \( t(136) = 3.18, p = .002, d = 0.60 \) (Figure 2 and Table 1). However, there was no significant difference in gain feedback-P300, loss feedback-P300, or RewP between adolescents with a history of PO-MDD compared with those with no history of PO-MDD.\(^3\) Gain feedback-P300 (\( M = 14.26 \mu V, SD = 6.13 \)) was significantly larger than loss feedback-P300 (\( M = 13.33 \mu V, SD = 6.54 \)), \( t(136) = 2.91, p = .004 \) (Figure 3). Similarly, gain activity (\( M = 10.08 \mu V, SD = 6.45 \)) scored at fronto-central sites, was significantly larger than loss activity (\( M = 6.24 \mu V, SD = 5.77 \)), \( t(136) = 10.67, p < .001 \) (Figure 4). Doors-P300 amplitude was positively correlated with both gain feedback-P300 amplitude, \( r(136) = .31, p < .001 \), and loss feedback-P300 amplitude, \( r(136) = .29, p = .001 \). Doors-P300 did not significantly differ in adolescents with a current depression diagnosis compared with adolescents with no current depressive disorders.

Adolescents with higher income-to-needs ratios at the baseline assessment exhibited larger doors-P300, \( r(122) = .22, p = .012 \), as well as larger gain and loss feedback-P300, \( r(122) = .20, p = .028 \), and \( r(122) = .20, p = .023 \), respectively. However, adolescents with higher current income-to-needs ratio were characterized only by larger gain and loss feedback-P300, \( r(131) = .20, p = .025 \), and \( r(131) = .22, p = .011 \), respectively, while doors-P300 was not significantly associated with current income-to-needs ratio. There was no significant association between baseline or current income-to-needs ratios and RewP at follow-up. Older adolescents were characterized by smaller doors-P300, \( r(136) = -.31, p < .001 \), and larger RewP, \( r(136) = .18, p = .034 \), relative to younger adolescents. There were no significant associations between adolescent age and gain or loss feedback-P300. Female adolescents were characterized by reductions in doors-P300 (\( M = 4.28 \mu V, SD = 3.79 \)) compared with males (\( M = 5.56 \mu V, SD = 3.63 \)), \( t(136) = 2.01, p = .047, d = 0.34 \). There were no significant gender differences in terms of gain feedback-P300, loss feedback-P300, or RewP.

To further assess unique predictors of doors-P300 at follow-up, PO-MDD status, baseline income-to-needs ratio, current income-to-needs ratio, current depression status, gender, and age were entered simultaneously as predictors in a multiple linear regression with doors-P300 as the dependent variable (Table 2). The overall regression was significant. Participants without a history of PO-MDD exhibited larger doors-P300, as did adolescents in households with higher income-to-needs ratio at baseline. These variables uniquely predicted 2.9% and 5.9% of variation in adolescent doors-P300, respectively. Additionally, both male and younger adolescents showed larger doors-P300. Current depression status and current income-to-needs ratio were not significant predictors of doors-P300 in this multivariate model.\(^4\)

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\(^2\)Baseline income-to-needs ratio was collected in 40 history of PO-MDD and 84 participants with no history of PO-MDD, and current income-to-needs ratio was collected in 42 history of PO-MDD and 91 participants with no history of PO-MDD.

\(^3\)Three additional depressive symptom severity scores, derived from additional clinical interviews administered between the second and ninth visits, were examined; average depressive symptoms from ages 3 to 5 (preschool), average depressive symptoms from ages 6 to 9 (school age), and average depressive symptoms from 11 to 14 (early adolescence). Doors-P300 amplitude was negatively associated with average preschool depressive symptoms, \( r(109) = -.26, p = .005 \), and depressive symptoms during the earlier adolescence period, \( r(133) = -.21, p = .016 \), but was not significantly associated with depressive symptoms during school age, \( r(125) = -.09, p = .304 \). A significant multiple regression model predicting doors-P300, \( F(2,107) = 4.90, p = .009 \), revealed that only preschool symptoms emerged as a unique predictor (\( p = .015 \)) and average depressive symptoms recorded between ages 11 to 14 was a nonsignificant predictor (\( p = .683 \)). Lastly, there were no significant zero-order associations between RewP, gain feedback-P300, or loss feedback-P300 with any of the average depressive scores collected during the preschool, school age, or early adolescence time frames (\( r^2 \) ranging –.109 to .110, \( p \)'s > .252).

\(^4\)Including current psychotropic medication status, gain feedback-P300, and loss feedback-P300 into the model as additional predictors does not change the current results. The overall model was still significant, \( F(9, 109) = 6.28, p < .001 \). PO-MDD remained a significant predictor of adolescent doors-P300 amplitude, \( b = -1.85, t(118) = -2.78, p = .006, sr = -.22, 95\% CI [−3.17, −0.53], \) as were age and gender. Baseline income-to-needs ratio was trending as significant predictor of doors-P300 amplitude in this specific model, \( b = 0.70, t(118) = 1.78, p = .078, sr = .14, 95\% CI [−0.08, 1.48] \). Gain feedback-P300 was also a significant predictor in the model, \( b = 0.20, t(118) = 2.29, p = .024, sr = .18, 95\% CI [0.03, 0.37] \). Current medication status and loss feedback-P300 were not significant predictors of adolescent doors-P300.
In the second regression model, gain feedback-P300 was predicted utilizing PO-MDD history, baseline income-to-needs ratio, current income-to-needs ratio, current depression status, gender, and age as predictors. The overall model was not significant and none of the independent variables emerged as unique predictors of gain feedback-P300 (Table 3).

In the third regression model, loss feedback-P300 was predicted utilizing PO-MDD history, baseline income-to-needs ratio, current income-to-needs ratio, current depression status, gender, and age as predictors. The overall model was not significant and none of the independent variables emerged as unique predictors of loss feedback-P300 (Table 4).

In the final regression model, RewP was the dependent variable, and PO-MDD history, baseline income-to-needs ratio, current income-to-needs ratio, current depression status, gender, and age were utilized as predictors. The overall model was not significant and only age emerged as a unique significant predictor of RewP (Table 5).

**DISCUSSION**

Children with PO-MDD were characterized by reduced doors-P300 amplitude in adolescence compared with adolescents with no history of PO-MDD. This effect was independent of current depression diagnosis, current income-to-needs ratio, and current psychotropic

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**TABLE 2** Multiple regression results using doors-P300 amplitude as the criterion.

<table>
<thead>
<tr>
<th>Predictors</th>
<th>b</th>
<th>95% CI [LL, UL]</th>
<th>Beta</th>
<th>95% CI [LL, UL]</th>
<th>sr²</th>
<th>95% CI [LL, UL]</th>
<th>r</th>
<th>Fit</th>
</tr>
</thead>
<tbody>
<tr>
<td>PO-MDD</td>
<td>−1.45*</td>
<td>[−2.79, −0.11]</td>
<td>−0.18</td>
<td>[−0.35, −0.01]</td>
<td>.03</td>
<td>[−.02, .08]</td>
<td>−.26**</td>
<td>0.081</td>
</tr>
<tr>
<td>Baseline income-to-needs</td>
<td>0.99*</td>
<td>[0.19, 1.80]</td>
<td>0.30</td>
<td>[0.06, 0.54]</td>
<td>.04</td>
<td>[−.02, 10]</td>
<td>.24**</td>
<td>0.249**</td>
</tr>
<tr>
<td>Current income-to-needs</td>
<td>−0.20</td>
<td>[−0.59, 0.19]</td>
<td>−0.12</td>
<td>[−0.36, 0.11]</td>
<td>.01</td>
<td>[−.02, .03]</td>
<td>.09</td>
<td></td>
</tr>
<tr>
<td>Current MDD</td>
<td>1.21</td>
<td>[−0.52, 2.94]</td>
<td>0.12</td>
<td>[−0.05, 0.28]</td>
<td>.01</td>
<td>[−.02, .05]</td>
<td>.00</td>
<td></td>
</tr>
<tr>
<td>Gender</td>
<td>−1.56*</td>
<td>[−2.78, −0.35]</td>
<td>−0.21</td>
<td>[−0.38, −0.05]</td>
<td>.04</td>
<td>[−.02, .11]</td>
<td>−1.9*</td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>−1.02**</td>
<td>[−1.54, −0.49]</td>
<td>−0.32</td>
<td>[−0.49, −0.15]</td>
<td>.10</td>
<td>[−.00, .19]</td>
<td>−.32**</td>
<td></td>
</tr>
</tbody>
</table>

R² = .249**

95% CI [0.09, 0.34]

**TABLE 3** Multiple regression results using gain feedback-P300 amplitude as the criterion.

<table>
<thead>
<tr>
<th>Predictors</th>
<th>b</th>
<th>95% CI [LL, UL]</th>
<th>Beta</th>
<th>95% CI [LL, UL]</th>
<th>sr²</th>
<th>95% CI [LL, UL]</th>
<th>r</th>
<th>Fit</th>
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<tbody>
<tr>
<td>PO-MDD</td>
<td>−1.85*</td>
<td>[−2.79, −0.91]</td>
<td>−0.25</td>
<td>[−0.35, −0.15]</td>
<td>.03</td>
<td>[−.02, .08]</td>
<td>−.26**</td>
<td></td>
</tr>
<tr>
<td>Baseline income-to-needs</td>
<td>0.77</td>
<td>[0.19, 1.35]</td>
<td>0.30</td>
<td>[0.06, 0.54]</td>
<td>.04</td>
<td>[−.02, 10]</td>
<td>.24**</td>
<td></td>
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<tr>
<td>Current income-to-needs</td>
<td>0.10</td>
<td>[−0.59, 0.79]</td>
<td>0.04</td>
<td>[−0.22, 0.30]</td>
<td>.00</td>
<td>[−.01, .01]</td>
<td>.19*</td>
<td></td>
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<tr>
<td>Current MDD</td>
<td>1.08</td>
<td>[−1.97, 4.14]</td>
<td>0.07</td>
<td>[−0.12, 0.25]</td>
<td>.00</td>
<td>[−.02, .03]</td>
<td>.04</td>
<td></td>
</tr>
<tr>
<td>Gender</td>
<td>−0.40</td>
<td>[−2.19, 2.11]</td>
<td>−0.00</td>
<td>[−0.18, 0.18]</td>
<td>.00</td>
<td>[−.00, .00]</td>
<td>−.02</td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>0.59</td>
<td>[−0.34, 1.52]</td>
<td>0.12</td>
<td>[−0.07, 0.30]</td>
<td>.01</td>
<td>[−.03, .05]</td>
<td>.14</td>
<td></td>
</tr>
</tbody>
</table>

R² = .081

95% CI [0.00, 0.14]

Note: PO-MDD is coded 0 = no PO-MDD, 1 = PO-MDD. Current MDD is coded 0 = no MDD, 1 = MDD. Gender is coded 0 = male, 1 = female. LL and UL indicate the lower and upper limits of a confidence interval, respectively.

* p < .05; ** p < .01.
medication status (see footnote 4). Having no history of PO-MDD, a higher baseline family income, being younger, and being male were all independently associated with larger doors-P300. In contrast, gain and loss feedback-P300 were unrelated to history of PO-MDD, age, or gender, but both were associated with higher baseline and current family income in zero-order correlations; however, neither of these income measures uniquely predicted either gain or loss feedback-P300 while utilized in the same models. Lastly, in contrast to expectations, no associations between RewP measured during adolescence and PO-MDD status, baseline/current income-to-needs ratios, or gender, were observed.

The current results linking reduced doors-P300 to history of PO-MDD echo findings from a recent study that found that doors-P300, but not gain or loss feedback-P300, was significantly reduced among adults with depression (Santopetro, Brush, Burani, et al., 2021). Additionally, these results are consistent with extant literature reporting cross-sectional and prospective reductions in P300 derived from the oddball and flanker task in depressed adults (Bruder et al., 2012; Klawohn, Santopetro, et al., 2020; Santopetro, Brush, Bruchnak, et al., 2021). Moreover, these results support findings from studies conducted in adolescent samples that suggest that lifetime history of depression, current depressive symptoms, and risk for future depressive symptoms were all associated with reductions in current P300 elicited from visual oddball and flanker tasks (Houston et al., 2003; Santopetro et al., 2020; Santopetro, Kallen, Threadgill, et al., 2021). Additional analyses seen in footnote 3 further underscore the unique association of heightened preschool depressive symptoms with lower current P300.

### TABLE 4 Multiple regression results using loss feedback-P300 amplitude as the criterion.

<table>
<thead>
<tr>
<th>Predictors</th>
<th>b</th>
<th>95% CI [LL, UL]</th>
<th>Beta</th>
<th>95% CI [LL, UL]</th>
<th>r</th>
<th>Fit</th>
</tr>
</thead>
<tbody>
<tr>
<td>PO-MDD</td>
<td>0.52</td>
<td>[−2.06, 3.10]</td>
<td>0.04</td>
<td>[−0.15, 0.23]</td>
<td>.00</td>
<td>−02</td>
</tr>
<tr>
<td>Baseline income-to-needs</td>
<td>1.24</td>
<td>[−0.31, 2.79]</td>
<td>0.22</td>
<td>[−0.05, 0.49]</td>
<td>.02</td>
<td>.24**</td>
</tr>
<tr>
<td>Current income-to-needs</td>
<td>0.16</td>
<td>[−0.59, 0.91]</td>
<td>0.06</td>
<td>[−0.21, 0.32]</td>
<td>.00</td>
<td>.20*</td>
</tr>
<tr>
<td>Current MDD</td>
<td>0.96</td>
<td>[−2.37, 4.28]</td>
<td>0.05</td>
<td>[−0.13, 0.24]</td>
<td>.00</td>
<td>.01</td>
</tr>
<tr>
<td>Gender</td>
<td>−0.32</td>
<td>[−2.66, 2.01]</td>
<td>−0.03</td>
<td>[−0.21, 0.16]</td>
<td>.00</td>
<td>.03</td>
</tr>
<tr>
<td>Age</td>
<td>0.01</td>
<td>[−1.00, 1.03]</td>
<td>0.00</td>
<td>[−0.18, 0.19]</td>
<td>.00</td>
<td>.02</td>
</tr>
</tbody>
</table>

R² = .064  
95% CI [0.00, 0.12]  
*Note: PO-MDD is coded 0 = no PO-MDD, 1 = PO-MDD. Current MDD is coded 0 = no MDD, 1 = MDD. Gender is coded 0 = male, 1 = female. LL and UL indicate the lower and upper limits of a confidence interval, respectively.  **p < .01.

### TABLE 5 Multiple regression results using RewP amplitude as the criterion.

<table>
<thead>
<tr>
<th>Predictors</th>
<th>b</th>
<th>95% CI [LL, UL]</th>
<th>Beta</th>
<th>95% CI [LL, UL]</th>
<th>r</th>
<th>Fit</th>
</tr>
</thead>
<tbody>
<tr>
<td>PO-MDD</td>
<td>−0.24</td>
<td>[−1.87, 1.39]</td>
<td>−0.03</td>
<td>[−0.22, 0.16]</td>
<td>.00</td>
<td>.01</td>
</tr>
<tr>
<td>Baseline income-to-needs</td>
<td>0.05</td>
<td>[−0.93, 1.02]</td>
<td>0.01</td>
<td>[−0.26, 0.28]</td>
<td>.00</td>
<td>.04</td>
</tr>
<tr>
<td>Current income-to-needs</td>
<td>0.00</td>
<td>[−0.47, 0.48]</td>
<td>0.00</td>
<td>[−0.26, 0.26]</td>
<td>.00</td>
<td>.03</td>
</tr>
<tr>
<td>Current MDD</td>
<td>−0.79</td>
<td>[−2.89, 1.30]</td>
<td>−0.07</td>
<td>[−0.26, 0.12]</td>
<td>.00</td>
<td>.05</td>
</tr>
<tr>
<td>Gender</td>
<td>−0.56</td>
<td>[−2.03, 0.92]</td>
<td>−0.07</td>
<td>[−0.25, 0.11]</td>
<td>.00</td>
<td>.09</td>
</tr>
<tr>
<td>Age</td>
<td>0.91**</td>
<td>[0.27, 1.55]</td>
<td>0.26</td>
<td>[0.08, 0.45]</td>
<td>.07</td>
<td>.25**</td>
</tr>
</tbody>
</table>

R² = .076  
95% CI [0.00, 0.14]  
*Note: PO-MDD is coded 0 = no PO-MDD, 1 = PO-MDD. Current MDD is coded 0 = no MDD, 1 = MDD. Gender is coded 0 = male, 1 = female. LL and UL indicate the lower and upper limits of a confidence interval, respectively. **p < .01; *p < .05; **p < .01.
with reductions in adolescent doors-P300 amplitude. These present findings further suggest that PO-MDD is associated with long-lasting deficits to cognitive and motivational functions, such as attentiveness and salience allocation to stimuli that requires a response, as indexed by future reductions in doors-P300, but not gain or loss feedback-P300, during adolescence.

Considering that target detection and motor preparation processes involve the dopaminergic system and that striatal dopamine D_{1}/D_{3} receptor status has been linked to P300 elicited from an oddball task (Pogarell et al., 2011), one possibility is that P300 elicited from stimuli with a response requirement, such as the doors stimuli, are likely indexing dopaminergic activity of the striatum during target detection and response selection. Altogether, there is initial evidence that deficits in P300 can predate (Santopetro et al., 2020; Santopetro, Brush, Bruchnak, et al., 2021), as well as precede depressive symptom onset as seen in the current study, suggesting a potential bidirectional relationship between this neural component and depression.

There were no significant differences in doors-P300, gain/loss feedback-P300, or RewP between adolescents with or without a current diagnosis of depression in the present study. These findings contrast with prior research demonstrating reductions in P300 (Bruder et al., 2012; Klawohn, Santopetro, et al., 2020; Ruchsow et al., 2008; Santopetro, Brush, Bruchnak, et al., 2021) and RewP (Brush et al., 2018; Keren et al., 2018; Klawohn, Burani, et al., 2020) in individuals with current depressive disorder. However, it is important to note that the sample size of currently depressed individuals was quite small (i.e., 18) relative to previous studies; therefore, this analysis was not properly powered to detect current depression-related differences in neural activity. Additionally, the context of the experimental paradigm (i.e., doors task) in the current study could impact the association between the P300 and current depressive symptoms. For example, past researchers have posited that cognitive demand or difficulty of an experimental paradigm could potentially influence the expected P300 and depression association (Bruder et al., 2012). Indeed, compared with tasks such as the faster-paced flanker and oddball tasks, the doors task is much less cognitively demanding which could result in less consistent associations with current symptoms of depression.

PO-MDD was associated with both lower baseline and current income-to-needs ratios, and thus, we also assessed the relationship between income-to-needs and all ERP components. Children from households with lower income-to-needs ratio exhibited blunted doors-P300 during adolescence, independent of their PO-MDD status and current income-to-needs status. Alternatively, both gain and loss feedback-P300 were associated with both childhood and current income-to-needs in separate analyses; however, neither of these measures uniquely predicted gain or loss feedback-P300 when entered into the same models. These findings regarding doors-P300 are consistent with recent findings from this project indicating that childhood poverty influences brain development. More specifically, low income-to-needs ratio at baseline was associated with smaller hippocampus and amygdaloid volumes during early adolescence (Luby et al., 2013). In sum, the current data suggest that childhood poverty may impact development of brain activity that is unique to the doors-P300 component as compared to the RewP, though more research is needed to determine the exact relationships that may exist between childhood poverty, concurrent poverty, and feedback-P300.

Female adolescents were also characterized by significantly smaller doors-P300, but not gain or loss feedback-P300; these results are in line with a recent study conducted in a large (N = 619) sample of adolescents that reported reductions in flanker P300 in female participants (Santopetro, Kallen, Threadgill, et al., 2021). It is possible that unique pubertal changes experienced by females might directly influence cognitive and motivational functioning, and therefore, P300. However, it remains unclear whether the neurological mechanisms underlying reductions in P300 seen in adolescent females are directly related to those mechanisms influencing P300 deficits linked to depressive disorders.

Adolescent RewP was unrelated to history of PO-MDD. These results were unexpected as past research has found RewP reductions in relation to depression in adults, adolescents, and children (Barch et al., 2020; Belden et al., 2016; Bress et al., 2013; Brush et al., 2018; Keren et al., 2018; Klawohn, Burani, et al., 2020; Nelson et al., 2018). One possible explanation is that deficits in RewP associated with PO-MDD are only evident during depressive episodes. That is, PO-MDD may result in longer-term reductions in doors-P300, but not RewP. It is also possible that differences in internal consistencies between these separate neural measures impacted the present findings; the RewP exhibits lower internal consistency (e.g., .54–.61) compared with the doors-P300 (e.g., .86–.92). It will be important for future studies to characterize the developmental relationships of PO-MDD, remission, doors-P300, and RewP using longitudinal designs.

The current study had limitations. Neither doors-P300, gain/loss feedback-P300, nor RewP were collected at earlier time points in the project. This information would have allowed direct comparisons in changes in neural activity with changes in depression status, which would have allowed more direct inferences about the directionality of the relationships between depression and these.
neural measures. In general, more research examining ERP differences in adolescent depression is needed as this specific area of the literature is extremely understudied despite heightened levels of depression that occur during this critical developmental period (Lawrence et al., 2015).

5 | CONCLUSION

Overall, the present study suggests that PO-MDD and low baseline income-to-needs ratio independently relate to reductions in adolescent doors-P300. These relationships appear to be specific to the doors-P300, as adolescent gain feedback-P300, loss feedback-P300, and RewP were not uniquely associated with history of PO-MDD or baseline income-to-needs ratio. Furthermore, gender differences in doors-P300, but not gain/loss feedback-P300 or RewP, were evident in the current sample. Thus, the doors-P300 might be a valuable neural measure to further our understanding of neurobiological changes that result from both childhood depression and poverty.

AUTHOR CONTRIBUTIONS
Nicholas J. Santopetro: Conceptualization; formal analysis; writing – original draft; writing – review and editing. Deanna M Barch: Conceptualization; data curation; funding acquisition; investigation; methodology; project administration; resources; writing – original draft; writing – review and editing. Joan L Luby: Conceptualization; data curation; funding acquisition; investigation; project administration; resources; writing – original draft; writing – review and editing. Laura Hennefield: Conceptualization; data curation; investigation; project administration; writing – original draft; writing – review and editing. Kirsten Gilbert: Conceptualization; data curation; investigation; project administration; writing – original draft; writing – review and editing. Diana J. Whalen: Conceptualization; data curation; investigation; project administration; writing – original draft; writing – review and editing. Greg Hajcak: Conceptualization; formal analysis; supervision; writing – original draft; writing – review and editing.

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CONFLICT OF INTEREST STATEMENT
The authors have no conflicts of interest to declare that are relevant to the content of this article.

DATA AVAILABILITY STATEMENT
Data or other materials are available through correspondence with the author.

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REFERENCES


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