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Effects of Maternal Depression and Mother-Child Relationship Quality in Early Childhood on Neural Reactivity to Rejection and Peer Stress in Adolescence: A 9-Year Longitudinal Study

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Abstract

Problems in mother-child relationships are thought to be key to intergenerational transmission of depression. To evaluate neural and behavioral processes involved in these pathways, we tested effects of maternal depression and maternal-child relationship quality in early childhood on neural and interviewer-based indicators of social processes in adolescence. At age 3, children and mothers (*N*=332) completed an observational parenting measure and diagnostic interviews with mothers. At age 12, adolescents completed a task in which event-related potentials (ERPs) were recorded to peer acceptance and rejection feedback and interviews to assess peer stress. Lower mother-child relationship quality at age 3 was associated with enhanced reactivity to rejection, as measured by N1, and greater peer stress at age 12. Indirect effects of maternal depression through mother-child relationship quality were observed for N1 and peer stress. Findings inform understanding of disruptions in social functioning that are likely relevant to the intergenerational transmission of depression.

Offspring of depressed mothers are approximately 3 times more likely than offspring of nondepressed mothers to develop depression (Weissman et al., 2006). Identifying mechanisms of intergenerational transmission of depression is needed to inform prevention. Critically, transmission of depression from mothers to offspring is not fully accounted for by genetics, and parenting and disruptions in the family environment are key mechanisms of the effects of maternal depression on offspring depression (Garber & Cole, 2010; Hammen & Brennan, 2001; Hammen, Shih, & Brennan, 2004; Harold et al., 2011). Despite variability in parenting, there is consistent evidence that compared to non-depressed mothers, depressed mothers exhibit fewer positive parenting behaviors like support and warmth, and more

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Authorship

A.K. and D.N.K. developed the study concept and design. K.B.A. contributed to the computerized social interaction task design and programming. M.C.F. contributed to the design for assessing chronic peer stress. E.M.K. and E.M. contributed to the electroencephalogram assessment design. A.K. performed the data analysis and interpretation and drafted the manuscript along with D.N.K. All authors provided critical revisions and approved the final manuscript.

negative behaviors like criticism and intrusiveness (Cummings & Davies, 1994; Goodman & Gotlib, 1999). Although problematic parenting behaviors are particularly apparent among currently depressed mothers, there is also evidence that mothers with a past history of depression exhibit lower positive parenting (Ewell Foster, Garber, & Durlak, 2008; Weinberg & Tronick, 1998).

It is well-established that the quality of relationships with caregivers in early childhood predicts later relationships with peers (Groh et al., 2014; Schneider, Atkinson, & Tardif, 2001). That is, robust evidence indicates that secure attachments in early childhood and greater mother-child relationship quality are related to better peer functioning, including child popularity, social competence, and romantic relationship quality (Bohlin, Hagekull, & Rydell, 2000; Groh et al., 2014; Katz, Hammen, & Brennan, 2013; Schneider et al., 2001). Similarly, substantial evidence indicates that maternal depression is associated with interpersonal stress and impairment in social functioning in offspring (Feurer, Hammen, & Gibb, 2016; Hammen & Brennan, 2001; Katz et al., 2013). Critically, the interpersonal effects of maternal depression on offspring are not limited to parent-child relationships, but instead, problems in the early family environment disrupt social development, leading to difficulties in later peer and romantic relationships (Feurer et al., 2016; Hammen et al., 2004; Katz et al., 2013). Further, less secure attachment with parents and disruptions in the quality of mother-child relationships are associated with increased risk of psychiatric symptoms, particularly depression (Allen et al., 2007; Eberhart, Shih, Hammen, & Brennan, 2006; Hammen et al., 2004).

The effects of early relationships with caregivers on later relationships with peers is thought to be mediated by the development of social and emotional brain networks (Nelson, Jarcho, & Guyer, 2016; Schriber & Guyer, 2016). Consistent with this, parenting style predicts reward-related brain function in offspring, particularly among offspring of depressed parents (Kujawa, Proudfit, Laptook, & Klein, 2015; Morgan, Shaw, & Forbes, 2014), but only a few small studies have examined the effects of parenting on brain function in the context of peer interactions. In functional magnetic resonance imaging (fMRI) studies, authoritative parenting in middle childhood was associated with activation of the striatum to peer rejection in adolescence (Guyer et al., 2015), and cross-sectional associations were observed between maternal negative affect and adolescents' responses to peer acceptance in the amygdala and anterior cingulate cortex (ACC; Tan et al., 2014). In a recent study of adolescent girls, higher youth-reported parent-child relationship quality was associated with decreased responses in dorsal ACC to social exclusion (Rudolph et al., 2018). Taken together, this literature suggests that parenting quality might shape neural responses to feedback from peers in adolescence, with potential implications for understanding the intergenerational transmission of depression.

The extant literature points to a developmental pathway in which early parent-child relationships serve as a mechanism of the negative effects of maternal depression on the quality of later peer relationships in offspring. In turn, dysfunction in relationships with peers and elevated social stress increase risk for later depression in offspring (Hammen, 2009; Prinstein, Cheah, Borelli, Simon, & Aikins, 2005), particularly among those high in rejection sensitivity (Chango, McElhaney, Allen, Schad, & Marston, 2012). Yet, the neural

processes underlying the effects of maternal depression and early parenting on peer functioning have been largely unexamined.

We developed a computerized peer interaction task for measuring neural responses to peer acceptance and rejection feedback using event-related potentials (ERPs) derived from the electroencephalogram (EEG; Kujawa et al. 2014a, 2017). During the task, participants vote to reject and accept co-players, and receive a combination of rejection and acceptance feedback. The task elicits a series of ERP components that are differentially modulated by peer acceptance and rejection feedback (Kujawa et al., 2017). Although neural responses to social feedback appear to be more complex than those observed in response to monetary feedback (Kujawa et al., 2017, 2018), two components consistently emerge in response to peer rejection and acceptance feedback in this task and appear particularly relevant to depression risk: Reward positivity (RewP) and N1 (Babinski, Kujawa, Kessel, Arfer, & Klein, in press; Ethridge et al., 2017; Kujawa et al., 2017).

Peer acceptance feedback reliably elicits a RewP component (Ethridge & Weinberg, 2018; Kujawa, Arfer, et al., 2014; Kujawa et al., 2017), which presents as a relative positivity in the ERP wave beginning around 250 ms that is enhanced for positive feedback. RewP is also referred to as the feedback negativity (FN) and was originally thought to present as a negativity in the ERP wave in response to negative performance feedback and losses. More recent evidence from temporospatial principal component analyses (PCA) and other methods indicate that this component is better characterized by a positivity that is enhanced in response to positive performance and reward feedback and reduced to negative feedback (for a review, see Proudfit, 2015). Consistent with this, using PCAs on ERP data obtained from both social and monetary reward tasks in children and adolescents, we found that a positive component consistent with the RewP consistently emerges in response to both social and monetary reward feedback (Kujawa et al., 2018, 2017). Most research on RewP uses performance or monetary reward tasks. In these tasks, RewP correlates with positive emotionality (Kujawa, Proudfit, Kessel, et al., 2015) and activation of the ventral striatum (Becker, Nitsch, Miltner, & Straube, 2014), and prospectively predicts depressive symptoms (Bress, Meyer, & Proudfit, 2015; Kujawa, Hajcak, & Klein, 2019; Nelson, Perlman, Klein, Kotov, & Hajcak, 2016).

Prior to RewP in the ERP wave, we identified an N1 component enhanced for rejection relative to acceptance feedback (Kujawa et al., 2017). N1, an early visual attention component, presents as a negative deflection in the ERP around 100 to 150 ms that is enhanced in response to attended stimuli (Coch & Gullick, 2012; Luck, Woodman, & Vogel, 2000). In Island Getaway, N1 is consistently enhanced in response to rejection vs. acceptance cues (Kujawa et al., 2017), suggesting that rejection feedback may more immediately capture attention. We previously observed a cross-sectional association between an enhanced (i.e., more negative) N1 to rejection and self-reported rejection sensitivity, supporting this component's utility as a measure of individual differences in reactivity to social feedback that may be relevant for depression risk (Babinski et al., in press).

In addition to RewP and N1, our prior work indicates that later ERP components, including P3 and late positive potential (LPP), also appear to be sensitive to social feedback valence and likely reflect sustained attentional allocation towards social feedback cues (Kujawa et al., 2017). In the current study, we focus our analyses on N1 and RewP, given prior evidence that these neural measures reflect individual differences in self-reported rejection sensitivity and positive emotionality, respectively (Babinski et al., in press; Kujawa, Proudfit, Kessel, et al., 2015), and an extensive literature linking RewP to depression risk (Keren et al., 2018; Kujawa & Burkhouse, 2017; Nelson et al., 2016).

The goal of this longitudinal study was to examine pathways from maternal depression and early parenting to later neural processing of social feedback and chronic peer stress using a multi-method approach. We evaluated observed mother-child relationship quality at age 3 as a predictor of multiple indicators of social processes 9 years later (i.e., N1 to peer rejection; RewP to peer acceptance; chronic peer stress), and tested indirect effects of maternal depression on social processes through mother-child relationship quality. Consistent with our prior work on parenting and emotional development (Kujawa, Dougherty, et al., 2014; Kujawa, Proudfit, Laptook, et al., 2015), we examined relationship quality in early childhood because of evidence that the family environment in the first few years of life has lasting impacts on child social and emotional development (Cavanagh & Huston, 2008; Woodward, Fergusson, & Belsky, 2000) and in order to test parenting variables as prospective predictors of neural reactivity to social feedback and peer stress. Given evidence that broad disruption in parent-child attachment and relationship quality are associated with impairments in peer function and depressive symptoms in offspring (Hammen et al., 2004; Schneider et al., 2001), our primary focus was on overall observed quality of mother-child relationships. Social processes measures were obtained in early adolescence, a time when the importance of peer relationships increases but prevalence of clinical depression remains relatively low (Brown, 2004; Hankin et al., 1998), allowing us to examine social problems that might emerge prior to depressive disorders. We focused on maternal, rather than paternal, depression and relationships, given weaker effects of paternal depression on internalizing symptoms in offspring (Connell & Goodman, 2002; Tully, Iacono, & McGue, 2008) and because mothers spend greater time caregiving than fathers on average (Phares, Fields, & Kamboukos, 2009).

Primary analyses examined the overall quality of the reciprocal relationship between mothers and children in early childhood and tested the effects of maternal depression and mother-child relationship quality on 3 indicators of social processes at age 12: N1 to rejection, RewP to acceptance, and interviewer-rated chronic peer stress. We hypothesized that lower mother-child relationship quality at age 3 would be associated with an enhanced N1 to rejection, reduced RewP to acceptance, and greater peer stress at age 12, and mediate the effects of maternal depression on neural reactivity to peer feedback and peer stress. Following significant effects of relationship quality, secondary exploratory analyses evaluated the extent to which these pathways were driven by more specific parenting behaviors by mothers that could be targeted for prevention. Specifically, we examined dimensions of positive (i.e., confidence, support, and instruction) and negative parenting behavior (i.e., hostility and intrusiveness), consistent with our prior work identify distinct associations between these two dimensions of parenting and neural processing of monetary

reward in offspring (Kujawa, Proudfit, Laptook, et al., 2015) and some evidence linking more specific features of maternal positivity and sensitivity to depressive symptoms and social functioning in offspring (Garber & Cole, 2010; Roisman, Booth-LaForce, Cauffman, & Spieker, 2009). To test specificity of these pathways for maternal depression as opposed to maternal psychopathology more broadly defined, we also tested mediation models including maternal history of anxiety and substance use disorders as covariates. Finally, given sex differences in rates of depression and experiences of interpersonal stress (Hankin, Wetter, & Cheely, 2008; Rudolph, 2002), as well as evidence of differential patterns of parental emotion socialization for boys compared to girls (Chaplin, Cole, & Zahn-Waxler, 2005; Fivush, Brotman, Buckner, & Goodman, 2000), additional exploratory analyses examined generalizability of these pathways for both girls and boys by testing sex as a moderator of the direct and indirect effects of maternal depression on neural reactivity to social feedback and peer stress.

Methods

Participants

Participants were from the Stony Brook Temperament Study, a predominantly middle class, community sample of children recruited when they were 3 years old (Klein & Finsaas, 2017; Kujawa, Proudfit, & Klein, 2014; Olino, Klein, Dyson, Rose, & Durbin, 2010). At age 3, a total of 559 children and their parents were enrolled in the larger study. The size of the sample was determined by power analyses for the aims of the parent project. Of these participants, 490 children and biological mothers completed the observational parenting assessment and diagnostic interviews. At age 12, adolescents completed an EEG assessment and both the adolescent and a parent were interviewed concerning stress experienced by the child. A total of 367 youth who completed assessments at age 3 also completed the EEG assessment at age 12. EEG data were excluded for 26 participants due to noisy EEG data or technical errors (Kujawa et al., 2017) and stress data were missing for 9 participants, leaving a final analysis sample of 332. The mean age of the sample was 3.54 years (SD=0.26) at the time of the parenting assessment and 12.66 years (SD=0.43) at the EEG assessment. The analysis sample was 46.7% female, 9.0% Hispanic/Latino, 94.9% Caucasian, 2.1% African American, 2.1% Asian, 0.3% Native American, and 0.6% other race. Participants who completed the measures at age 3 but were missing data at age 12 did not significantly differ from included participants on distributions of maternal depression, child sex, race or ethnicity or on observed mother-child relationship quality (ps > .24).

All task conditions and data exclusions have been reported here, along with all measures for the current research questions. A complete list of parental psychopathology, parenting, functioning, and EEG/ERP measures administered at the age 3 and age 12 assessments is available in the Supplemental Material. This study was not preregistered because data collection and analyses began before preregistrations were common in clinical psychological science. The Stony Brook Temperament Study (SBTS) began in 2004, the EEG peer feedback task was added to the study in 2014, and cross-sectional analyses of the EEG data began in 2015 to characterize the neural response to social acceptance and rejection feedback (Kujawa et al., 2017). Although our primary analyses in the current study were

informed by theories of interpersonal dysfunction in the intergeneration transmission of depression, the analyses for this specific study were not planned at the start of the SBTS and should be considered exploratory.

Procedure

This protocol was approved by Stony Brook University's Institutional Review Board. Informed consent was obtained from parents and assent from participants. At age 3, children and mothers visited the laboratory to complete observational measures of mother-child relationship quality and parenting. Mothers also completed diagnostic interviews to assess depression history. Families returned to the lab around age 12 and the EEG assessment was completed. Following the laboratory assessment, participants completed a home assessment in which one parent and the adolescent were interviewed about stress in the past 12 months.

Measures

Maternal depression.—Biological mothers were interviewed using the Structured Clinical Interview for DSM-IV (First, Spitzer, Gibbon, & Williams, 2002). Interviews were conducted by telephone, which yields comparable results to face-to-face interviews (Rohde, Lewinsohn, & Seeley, 1997; Sobin, Weissman, Goldstein, & Adams, 1993). Two Masters-level raters conducted diagnostic interviews under the supervision of a licensed clinical psychologist. Independent ratings of diagnoses based on audiotapes of 30 interviews indicated that inter-rater reliability (Kappa) was 0.93 for depressive disorders.

Of the 332 children included in the current study, 29.8% (n=99) of mothers had a lifetime history of depression, defined as major depressive disorder (MDD) and/or dysthymia/ persistent depressive disorder (PDD), at the time of the age 3 assessment. Only 12.3% (n=41) were estimated to have experienced depression during the child's first 3 years of life, and 3.3% (n=11) endorsed past month MDD and/or dysthymia/PDD at the time of the age 3 assessment. Although depression and parenting were assessed concurrently, 88.8% of mothers with depression were in remission at the time of the assessment. One mother had a history of bipolar disorder[1]. With regard to other common diagnoses, 31.3% (n=104) of mothers had one or more lifetime DSM-IV anxiety disorders and 25.0% (n=83) had lifetime alcohol or substance abuse or dependence.

Observed mother-child relationship quality.—At age 3, children and mothers completed an observational assessment based on the Teaching Tasks (Egeland et al., 1995), which included six standardized tasks (e.g., book reading, block building). Trained coders rated videotapes of each episode, with ratings then averaged across tasks (Kujawa, Dougherty, et al., 2014; Kujawa, Proudfit, Laptook, et al., 2015). Primary analyses examined global ratings of mother-child relationship quality. High ratings indicate clear evidence that mother and child respond to each other, exhibit reciprocity/harmony, enjoy each other, and are quick to resolve conflicts. Low ratings indicate negative emotions, lack of harmony/ reciprocity, limited enjoyment of each other, and/or failure to resolve conflicts. Coders also

[1]Analyses were computed with the participant with maternal bipolar disorder excluded and no substantive changes in results were observed.

rated each episode for maternal hostility (expression of anger, frustration, or annoyance), intrusiveness (failure to respect the child as an individual), confidence (degree to which mother seems to believe that she can work successfully with the child), support (expression of positive regard and emotional support), and instruction (ability to structure the situation so that the child understands the task). Hostility and confidence were dichotomized to reduce skewness/kurtosis. A negative parenting composite score included standardized scores on hostility and intrusiveness, and a positive parenting composite score included standardized scores on confidence, support, and instruction, similar to our prior work (Kujawa, Proudfit, Laptook, et al., 2015). Inter-rater reliability was acceptable to good for all variables, with the lowest reliability observed for maternal ratings of confidence, included in the positive parenting composite (ICC=.79 for mother-child relationship quality; ICCs=.70 to .83 for negative parenting variables; ICCs=.59 to .85 for positive parenting variables, n=55).

Neural reactivity to peer feedback.—Participants completed the Island Getaway task (Kujawa, Arfer, et al., 2014) while EEG data were recorded (http://arfer.net/projects/survivor branch klein). Prior evidence indicates that this task elicits reliable ERPs sensitive to social feedback from late childhood to adulthood (Ethridge et al., 2017; Ethridge & Weinberg, 2018). Participants were told that they would play a game with 11 peers of similar ages to participants in which they will travel the Hawaiian Islands, vote whether they want each peer to continue on with them to the next island, and then receive feedback on how peers voted for them. All co-player profiles and responses were fabricated. In the first round, participants created a profile including their photograph and reviewed co-player profiles. Stock photographs and a child face stimulus set (Egger et al., 2011) were used for co-player photographs. Co-player photographs were selected such that co-players appeared to be diverse with regard to race/ethnicity. In subsequent rounds, participants responded to a poll question (e.g., “Who do you most admire?”) and reviewed co-player responses to facilitate an exchange of personal information for the remaining voting/feedback phases.

Following review of profiles/poll responses, participants were prompted to vote to accept (“Keep”) or reject (“Kick out”) each co-player. After each vote, participants saw feedback indicating whether that co-player voted to accept or reject them. Acceptance feedback was indicated by a green “thumbs up” and rejection feedback was indicated by a red “thumbs down.” Each voting trial began with a co-player profile presented until participants voted. To simulate variability in co-player response speed, a co-player voting speed was selected for each trial based on actual variability in participants’ voting patterns from previously collected data. If participants voted faster than the simulated voting time for that co-player, the message “Waiting for [co-player] to vote…” was displayed. Lastly, a fixation “+” was presented for 1000 ms, followed by feedback for 2000 ms. A blank screen was presented for 1500 ms before the start of the next trial. After each round, participants were told that one of the co-players had been sent home, and after completing the sixth round, participants were informed that they made it to the “Big Island.” The task included a total of 51 feedback trials over 6 rounds split evenly between acceptance and rejection, with the last trial type determined randomly.

Continuous EEG was recorded using a 34-electrode cap (32 channels, FCz, and Iz) and a BioSemi system (Amsterdam, Netherlands). Eye movements and blinks were recorded using

facial electrodes placed approximately 1 cm above and below one eye and 1 cm from the outer corners of the eyes. Electrodes were also placed on the left and right mastoids. Recordings were digitized with a sampling rate of 1024 Hz.

Offline processing was conducted using BrainVision Analyzer software (Munich, Germany). Data were referenced to the average mastoids, filtered with cutoffs of 0.1 and 30 Hz, and segmented 200 ms before until 1000 ms after feedback onset. Eye movement correction (Gratton, Coles, & Donchin, 1983) and artifact rejection procedures were conducted. Criteria of a voltage step of 50 μV between sample points, maximum difference of 300 μV within a 200 ms interval, and minimum activity of 0.5 μV were used to automatically detect artifacts, with additional artifacts removed manually. All included participants had a minimum of 22 trials per condition remaining after artifact rejection (*M*s = 25.42 for acceptance, 25.48 for rejection). ERPs were averaged for acceptance and rejection, and baseline corrected to the 200 ms prior to feedback onset. ERPs were scored in accordance with a prior PCA using these data (Babinski et al., in press; Kujawa et al., 2017): N1 was scored 140–180 ms at Cz and RewP was scored 300–375 ms at Cz (Figure1). Consistent with recommendations (Meyer, Lerner, de los Reyes, Laird, & Hajcak, 2017) and our prior work examining ERPs from the Island Getaway task (Babinski et al., 2017; Kujawa et al., 2017), residual scores were computed for each component to isolate the relative variance in the ERP attributed to processing of rejection or acceptance feedback. Specifically, we evaluated residual scores for N1 to rejection adjusting for responses to acceptance, with more negative values indicating enhanced early attention towards rejection cues, and residual scores for RewP to acceptance adjusting for responses to rejection, with more positive values indicating enhanced reactivity to acceptance feedback.

Peer stress in early adolescence.—At age 12, adolescents and one parent (92.2% biological mother, 7.8% biological father) were separately interviewed using the youth version of the UCLA Chronic Life Stress Interview (LSI) (Rudolph & Hammen, 1999). The LSI has been extensively validated in adolescent and adult samples, with consistent evidence of associations between chronic stress, particularly interpersonal stress, and depressive risk and symptoms (Adrian & Hammen, 1993; Hammen et al., 2004; Rudolph et al., 2000). The LSI uses a semi-structured interview format to assess chronic stress in the 12 months prior to the interview. Stress in each domain was rated by interviewers on a scale from 1 to 5, with higher scores indicating greater stress. Ratings based on parent and adolescent reports were highly correlated (*r*s > .64). Interviewers incorporated information obtained from participants and parents to derive combined ratings that reflect the best estimate of adolescents' chronic stress based on all available information. Given our interest in social functioning beyond the parent-child relationship, we averaged ratings of chronic stress in close friendships (which integrated information obtained from parent and adolescent reports of number of close friends and degree of satisfaction with friendships, conflict, confiding, and stability) and broader social life (which included parent and adolescent reports of degrees of popularity, bullying, and engagement in social activities with a wider peer group). Independent ratings of 35 videotaped interviews indicated that inter-rater reliability (ICCs) for chronic stress in friendships and social life was .82 and .86, respectively.

Data Analysis

First, bivariate correlations were computed to examine descriptive associations between maternal depression (presence or absence of lifetime depressive disorder), age 3 parenting variables, and age 12 social processes measures. Next, 3 simple mediation analyses were conducted using ordinary least squares path analyses in PROCESS (Hayes, 2013) to test mother-child relationship quality at age 3 as a mediator of the association between maternal depression and indicators of social processes and relationships at age 12 (N1 to rejection residual, RewP to acceptance residual, chronic peer stress). Models with significant effects of mother-child relationship were followed up with exploratory parallel mediation analyses to examine positive and negative parenting behaviors as mediators of the association between maternal depression and indicators of social processes. Finally, exploratory analyses tested sex as a moderator of the direct and indirect effects of maternal depression on social processes at age 12.[2]

Results

Bivariate Correlations

Descriptive statistics and bivariate associations between study variables are presented in Table 1. Maternal depression at age 3 correlated with lower mother-child relationship quality and positive parenting, but the association between maternal depression and negative parenting was not significant. The association between maternal depression at age 3 and low peer stress in early adolescence did not reach significance. Both low relationship quality and positive parenting in early childhood were modestly correlated with greater peer stress in adolescence. Maternal depression was not significantly correlated with ERP measures, but lower mother-child relationship quality and positive parenting were modestly correlated with an enhanced N1 to rejection. No significant correlations were observed between parenting measures and RewP or between peer stress and ERP measures (ps>.41), suggesting that neural and interviewer-based measures reflect distinct aspects of social processes.

Mediation Models

Three simple mediation models were computed to test direct and indirect effects of maternal depression on outcome variables (N1 to rejection residuals, RewP to acceptance residual, LSI chronic peer stress), with age 3 relationship quality as the mediator. Model coefficients for primary analyses are presented in Table 2 and model coefficients for exploratory follow-up analyses of positive and negative parenting behaviors are presented in Table 3.

Maternal depression in early childhood had an indirect effect on an enhanced (i.e., more negative) N1 to rejection cues through its effect on mother-child relationship quality. Maternal depression was associated with lower mother-child relationship quality (unstandardized coefficient [b]=−.18), which related to an enhanced N1 to rejection feedback (i.e., enhanced early attention towards rejection cues; b=.84). A bias-corrected bootstrap 95% confidence interval for the indirect effect of maternal depression on N1 to rejection (b=−.15, SE=.10) based on 5000 bootstrap samples was below 0 (−.38 to −.002)[3].

[2]The deidentified dataset is available by contacting the first author.

The partially standardized effect size was −.04 (*SE*=.02), which indicates that the maternal depression groups differ on average .04 standard deviations in N1 to rejection as a result of the indirect pathway through mother-child relationship quality (Hayes, 2013). The direct effect of maternal depression on N1 to rejection was not significant (*b*=.23, *SE*=.51, *p*=.66).

Next, an exploratory parallel mediation model was computed to test the indirect effect of maternal depression through positive and negative parenting (Table 3). Bootstrap 95% confidence intervals for the indirect effects of maternal depression on N1 to rejection through positive parenting were entirely below 0 (−.47 to −.004), supporting an indirect effect of maternal depression on N1 to rejection through positive parenting. The partially standardized effect size indicated a comparable effect size as was observed for relationship quality (*b*=−.04, *SE*=.03). The indirect effect through negative parenting included 0 (−.07 to .20).

A comparable pathway for RewP to acceptance feedback was not supported. Mother-child relationship quality was not significantly associated with RewP to acceptance (*p*=.93), the direct effect of maternal depression on RewP to acceptance feedback was not significant (*p*=.49), and the bootstrap 95% confidence interval for the indirect effect included 0 (−.28 to .30)[4].

Similar to the N1 results, maternal depression had an indirect effect on peer stress through mother-child relationship quality. Lower mother-child relationship quality was observed among mothers with a history of depression (*b*=−.18), and lower mother-child relationship quality was related to greater peer stress in early adolescence (*b*=−.11). A bias-corrected bootstrap 95% confidence interval for the indirect effect of maternal depression on peer stress (*b*=.02, *SE*=.01) based on 5000 bootstrap samples was above 0 (.001 to .05)[5]. The partially standardized effect size was comparable to that observed for the indirect effect on N1 (*b*=.04, *SE*=.03). The direct effect of maternal depression on age 12 peer stress did not reach significance (*b*=.09, *SE*=.06, *p*=.14). Next, parallel mediation models were computed to test the indirect effect of maternal depression through positive and negative parenting. Bootstrap 95% confidence intervals for indirect effects of maternal depression on peer stress through positive and negative parenting reached or included 0 (0 to .04 and −.01 to .02, respectively). Thus, the pathway appeared to be best explained by global ratings of relationship quality, which included both parent and child behaviors in relating to one another.

Although the primary focus of the current study was on developmental pathways involved in the intergenerational transmission of depression, to examine specificity of effects of

[3]We also tested mediation models with a Holm-Bonferroni correction (Holm, 1979) applied to tests of the 3 primary indirect effects of interest (i.e., maternal depression effects on N1 to rejection, RewP to acceptance, and chronic peer stress through mother-child relationship quality). With 3 tests, this correction requires $p < .017$ for the model with the lowest p value and $p < .025$ for the model with the second lowest p value. The Holm-Bonferroni-corrected test of the indirect effect of maternal depression on N1 to rejection through mother-child relationship quality using a 97.5% confidence interval reached 0 (−.43 to .01).

[4]Given evidence of interactive effects of depression and parenting behavior on RewP to monetary reward (Kujawa, Proudfit, Laptook, et al., 2015), exploratory analyses tested the maternal depression X mother-child relationship quality interactions for RewP to acceptance. The interaction effect did not reach significance (*p*=.10).

[5]The Holm-Bonferroni-corrected test of the indirect effect of maternal depression on peer stress through mother-child relationship quality using a 98.3% confidence interval reached 0 (−.002 to .06).

maternal depression rather than maternal psychopathology more broadly, mediation models were computed with the addition of maternal anxiety and substance use disorders as covariates. Neither maternal anxiety or substance use disorders were significantly associated with mother-child relationship quality (ps > .84), the association between maternal depression and relationship quality remained significant when controlling for anxiety and substance use disorders (p = .01), and the bootstrap 95% confidence intervals of the indirect effects of maternal depression on both N1 to rejection and chronic peer stress through mother-child relationship quality remained entirely below and above 0 (−.38 to −.002 and .001 to .05, respectively).

Finally, exploratory moderated mediation analyses were conducted to evaluate whether child sex moderates indirect or direct effects of maternal depression on N1 to rejection or chronic peer stress. Male and female participants did not significantly differ on parenting variables, N1 to rejection, RewP to acceptance, or chronic peer stress (ps > .42). Further, the maternal depression x child sex interaction was not a significant predictor of N1 or chronic peer stress (ps > .67). In addition, the 95% confidence interval for the index of moderated mediation examining the difference between conditional indirect effects for males vs. females included 0 for both N1 to rejection (−.36 to .18) and chronic peer stress (−.02 to .04).

Discussion

We examined longitudinal associations between maternal depression and observed mother-child relationship quality in early childhood and neural and interviewer-based indicators of social processes 9 years later. Lower observed mother-child relationship quality in early childhood was modestly related to enhanced neural reactivity to peer rejection cues during a computerized peer interaction task (i.e., more negative N1 ERP to rejection) and greater chronic stress in peer relationships in early adolescence. Moreover, indirect effects of maternal depression on social measures though mother-child relationship quality were observed. That is, maternal depression was associated with lower mother-child relationship quality at age 3 which was associated with an enhanced N1 to peer rejection cues and greater chronic peer stress at age 12, highlighting a mechanism by which maternal depression shapes social development. The pathway from maternal depression to enhanced neural reactivity to peer rejection cues appeared to be driven by lower levels of positive parenting behaviors, including support, instruction, and confidence, while the pathway to chronic peer stress was best accounted for by observations of the overall quality of the relationship between mothers and children. Although lower relationship quality with mothers in early childhood was associated with multiple measures of social processing and functioning in early adolescence, neural reactivity to social feedback cues and chronic peer stress were not significantly associated with each other.

An enhanced N1 to peer rejection in the peer interaction task likely reflects greater early attention towards rejection relative to acceptance cues (Coch & Gullick, 2012; Kujawa et al., 2017; Luck et al., 2000). We previously observed an association between N1 to rejection and self-reported rejection sensitivity, such that adolescents who demonstrated an enhanced N1 to rejection feedback reported higher levels of rejection sensitivity in hypothetical scenarios (Babinski et al., in press). Self-reported rejection sensitivity has also been linked to the later

emergence of depression (Chango et al., 2012). Thus, one potential pathway by which maternal depression shapes risk for depression is through problems in the quality of relationships with mothers, which then leads to maladaptive processing of peer rejection cues and potentially heightened sensitivity to possible rejection in peer interactions. Although in need of replication, exploratory analyses indicated that positive parenting behaviors at age 3 were also associated with N1 to rejection cues, suggesting that lower parent support, instruction, and confidence in their parenting might lead to heightened sensitivity to peer rejection in offspring. These findings provide support for prevention efforts targeting positive parenting behaviors in early childhood and highlight a specific outcome to examine (i.e., neural reactivity to peer rejection cues). At the same time, we did not directly measure other aspects of parenting that might be relevant to social competence, such as positive and negative emotion socialization (e.g., Garner, Jones, & Miner, 1994), and future research is needed to further examine possible components of parenting that might be important to target.

Indirect effects of maternal depression through mother-child relationship quality were also observed for chronic peer stress in adolescence. In contrast with the N1 model, neither positive nor negative parenting behaviors accounted for these associations, but instead, the overall quality of the reciprocal relationship between mothers and children appears to set the framework for adolescents' later relationships with peers. Critically, our measure of peer stress did not include stress in family relationships, providing evidence that the effects of maternal depression and early relationship quality on social functioning in offspring extend beyond the family, generalizing to peer functioning. Strain in peer relationships is a well-established risk factor for depression (Hammen, 2009; La Greca & Harrison, 2005; Prinstein et al., 2005), and this pathway may also be a key to understanding the intergenerational transmission of depression.

Neural and interviewer-based measures index distinct aspects of social processes, with N1 reflecting attentional allocation towards peer rejection cues and LSI reflecting broader stress and impairment in relationships. Given the lack of a correlation between these measures, neural reactivity to peer feedback as assessed by this task does not appear to be a mechanism of the effects of early relationships on peer relationships in adolescence. Instead, the current findings highlight two distinct pathways by which maternal depression disrupts mother-child relationship quality leading to both increased neural reactivity to rejection and chronic peer stress. That is, some adolescents might demonstrate enhanced attention towards rejection cues but still establish meaningful, supportive relationships, while others might have impairments in relationships that are not accounted for by reactivity to rejection cues. Both heightened reactivity to rejection cues and peer stress are likely to predict the emergence of depression later in adolescence. Further assessment of this sample will provide insight into the extent to which these two processes might reflect independent or interactive vulnerabilities for depressive symptoms across adolescence.

Despite consistent indirect effects across methods, direct and bivariate associations between maternal depression and age 12 social processes were not significant. Direct effects would indicate that the effects of maternal depression were significant independent of the influence of mother-child relationship quality. As such, the current results suggest that early

relationships between mothers and children are key to understanding social processing and functioning in offspring at risk for depression. The lack of a significant total effect might be due to the fact that intergenerational transmission of depression is characterized by multiple additive and interactive pathways and mechanisms, which might have opposing effects (Hayes, 2013; Shrout & Bolger, 2002). Further research is needed to identify additional mediators of the association between maternal depression and social processes in adolescence. It should also be noted that the lack of significant associations between maternal depression and social outcomes is likely to be partly explained by the length of time between the maternal depression and age 12 assessments.

No significant associations were observed between relationship quality and RewP to social acceptance. While N1 reflects early attentional allocation to social cues, RewP is thought to index reward prediction signals (Holroyd, Krigolson, & Lee, 2011; Proudfit, 2015). As reward systems undergo substantial developmental change from childhood to adolescence (Casey, Jones, & Hare, 2008; Galvan, 2010), effects of early parenting on reward-related brain function may be weaker in adolescence or only observable when examining developmental change in RewP. In addition, much of the literature on RewP comes from monetary reward or performance tasks. Although there is growing research directly comparing RewP in both monetary and social reward tasks (Distefano et al., 2018; Ethridge et al., 2017; Ethridge & Weinberg, 2018), further research is needed to better understand the specific processes reflected by RewP in social interaction tasks.

Although we identified effects of mother-child relationship quality across methods, the association between early childhood relationship quality and indicators of social processing and functioning, including both N1 and chronic peer stress, were modest in magnitude. Further, we tested mediation models for 3 distinct indicators of social processes in adolescence, and given the number of models tested, significant results must be interpreted cautiously pending replication. We examined longitudinal associations between observed parenting and both neural and interviewer-based measures of social functioning, and the lack of shared method variance and length of time between assessment may partly account for modest effects. In addition, peer functioning in early adolescence is complex and shaped by a range of factors, and one aspect of the environment may not be expected to account for large amounts of variance. Despite the small effects, the current study is unique in its multi-method longitudinal approach to examining social processes and highlights a specific neural process (N1 to rejection) that warrants further study in research on peer functioning.

A few additional limitations of the current study should be noted. We did not administer an observational assessment of mother-child relationship quality at age 12 and were unable to test the distinct and combined effects of relationship quality in early childhood and adolescence on neural or behavioral indicators of social processing at age 12. Likewise, we did not collect neural and interview measures of social functioning in early childhood and cannot test bidirectional associations between neural reactivity to rejection cues, peer stress, and mother-child relationship quality. Although most cases of maternal depression were not current at the age 3 assessment, supporting the theory that maternal depression shapes later relationship quality with offspring, maternal depression and parenting variables were assessed concurrently, and as such, we did not examine bidirectional associations between

these variables across time. Finally, it should be noted that neural response to social acceptance and rejection feedback might differ as function of participant votes to accept or reject peers. The current task design is not well-suited to examine this possibility because of variability in the proportion of participant votes to reject and accept peers (Kujawa et al., 2017), but further research is needed to evaluate this possibility.

The current findings are consistent with attachment theory and interpersonal perspectives on the intergenerational transmission of depression (Groh et al., 2014; Hammen & Brennan, 2001; Schneider et al., 2001), but this study is among the first to identify a specific neural process that appears to be shaped by the effects of maternal depression on early relationships with mothers—neural reactivity to peer rejection cues. We tested developmental pathways across levels of analysis from observed behavior to neurophysiology and gold-standard measures of peer chronic stress spanning 9 years of development. Results provide insight into the lasting effects of maternal depression and early mother-child relationships on brain function and social behavior and identify specific mechanisms of the effects of maternal depression on peer relationships and processing of social cues in adolescence. These findings have important implications for prevention, suggesting that among mothers with depression history, enhancing positive parenting behaviors and mother-child relationship quality in the preschool years might alter the course of social development in offspring and promote later resilience. Further, results highlight a potential neural process (i.e., N1 to peer rejection cues) to examine in depression risk and prevention research.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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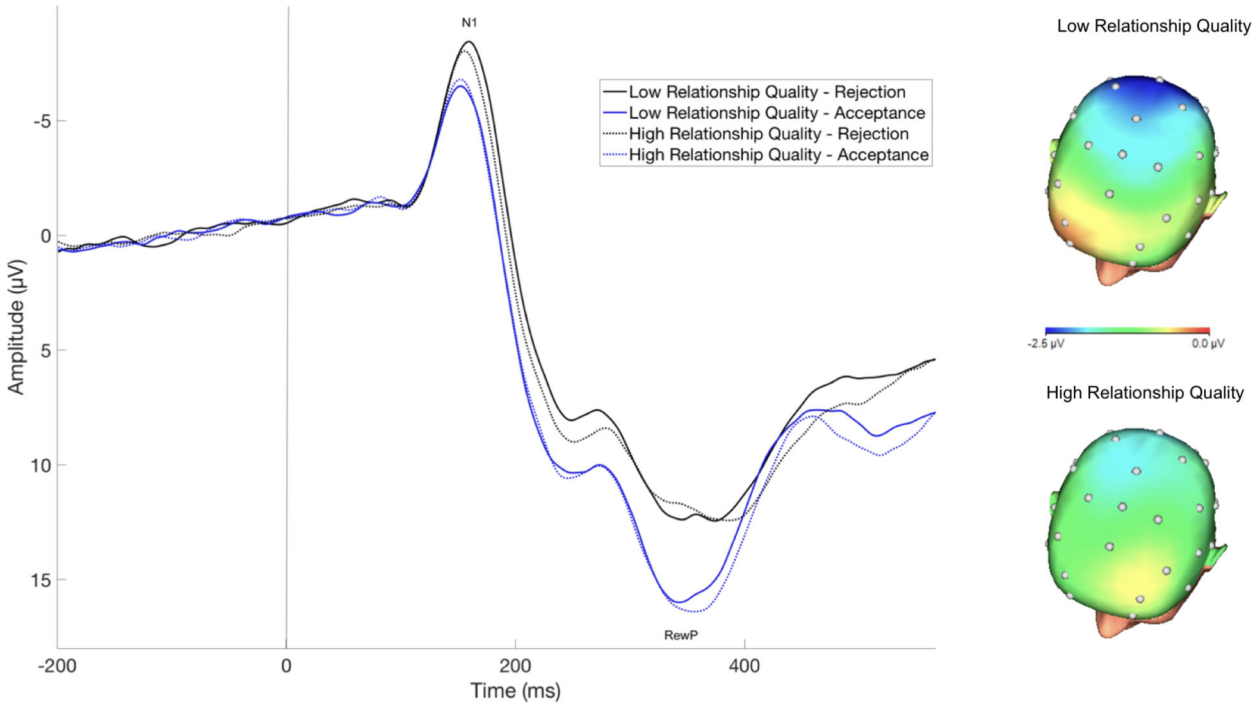

Figure 1.

ERPs (negative up) at Cz following rejection and acceptance feedback and scalp distributions depicting the rejection minus acceptance difference 140–180 ms after feedback onset (i.e., N1) for adolescents low and high in mother-child relationship quality at age 3. A median split of relationship quality was calculated to group participants for illustrative purposes only (all analyses used continuous measures of relationship quality).

Figure 2.

Scatterplots depicting the association between age 3 mother-child relationship quality and age 12 social variables (i.e., N1 to peer rejection cues [top] and chronic peer stress [bottom]).

Table 1.

Descriptive statistics and bivariate correlations (with 95% confidence intervals) between key study variables

	1.	2.	3.	4.	5.	6.	*M*(*SD*)	Range
1. Maternal depression	-						-	-
2. Age 3 relationship quality	−.15(−.26 to −.04)**	-					4.00(.56)	1.83–5.00
3. Age 3 positive parenting	−.12(−.24 to −.003)*	.61(.52 to .69)***	-				0.00(2.50)	−10.80–2.85
4. Age 3 negative parenting	.06(−.05 to .18)	−.45(−.55 to −.33)***	−.58(−.66 to .47)***	-			0.00(1.64)	−1.84–6.92
5. N1 residual	.01(−.11 to .12)	.11(.01 to .21)*	.12(.01 to .23)*	.01(−.13 to .10)	-		0.00(4.22)	−12.66–12.99
6. RewP residual	−.04(−.16 to .08	.01(−.11 to .13)	.05(−.06 to .15)	−.04(−.15 to .07)	−.26(−.35 to −.16)***	-	0.00(6.48)	−16.13–20.66
7. Chronic peer stress	.10(−.02 to .22)†	−.14(−.24 to −.03)*	−.12(−.22 to −.01)*	.06(−.07 to .18)	.04(−.09 to .16)	−.04(−.14 to .06)	2.13(.50)	1.00–4.50

*** $p<.001$;

** $p<.01$;

* $p<.05$;

† $p=.07$; RewP=reward positivity

Table 2.

Model coefficients for simple mediation models testing effects of age 3 maternal depression and relationship quality on age 12 social processes.

	Consequent			
	M (Relationship quality)		Y (N1 residual)	
Antecedent	***b* (95% CI)**	**SE**	***b* (95% CI)**	**SE**
X (Maternal depression)	−.18(−.31 to −.05)**	.07	.23(−.78 to 1.23)	.51
M (Relationship quality)	-	-	.84(.03 to 1.66)*	.42
Constant	4.05(3.98 to 4.12)***	.04	−3.44(−6.80 to −.09)***	1.71
	R^2=.02, F(1, 330)=7.42**		R^2=.01, F(2, 329)=2.07	
	M (Relationship quality)		**Y (RewP residual)**	
Antecedent	***b* (95% CI)**	**SE**	***b* (95% CI)**	**SE**
X (Maternal depression)	−.18(−.31 to −.05)**	.07	−.54(−2.09 to 1.01)	.79
M (Relationship quality)	-	-	.05(−1.21 to 1.32)	.65
Constant	4.05(3.98 to 4.12)***	.04	−.05(−5.24 to 5.14)	2.64
	R^2=.02, F(1, 330)=7.42**		R^2=.00, F(2, 329)=.25	
	M (Relationship quality)		**Y (Peer stress)**	
Antecedent	***b* (95% CI)**	**SE**	***b* (95% CI)**	**SE**
X (Maternal depression)	−.18(−.31 to −.05)*	.07	.09(−0.03 to .21)	.06
M (Relationship quality)	-	-	−.11(−.21 to −.02)*	.05
Constant	4.05(3.98 to 4.12)***	.04	2.55(2.15 to 2.94)***	.20
	R^2=.02, F(1, 330)=7.42**		R^2=.03, F(2, 329)=4.29*	

*** p<.001;

** p<.01;

* p<.05; RewP=reward positivity; *b*=unstandardized regression coefficients; CI=confidence intervals from 5000 bootstrap samples; SE=standard error

Table 3.

Model coefficients for exploratory parallel mediation models testing effects of age 3 maternal depression and parenting behaviors on age 12 N1 to rejection and chronic peer stress.

	Consequent M (Negative parenting)		Consequent M (Positive parenting)		Consequent Y (N1 residual)	
Antecedent	***b* (95% CI)**	**SE**	***b* (95% CI)**	**SE**	***b* (95% CI)**	**SE**
X (Maternal depression)	.23(−.16 to .61)	.20	−.66(−1.25 to −.07)*	.30	.21(−.79 to 1.21)	.51
M (Negative parenting)	-	-	-	-	.22(−.12 to .56)	.17
M (Positive Parenting	-	-	-	-	.28(.06 to .50)*	.11
Constant	−.07(−.28 to .14)	.11	.20(−.12 to .52)	.16	−.06(−.60 to .48)	.28
	R^2=.00, F(1, 330)=1.32		R^2=.01, F(1, 330)=4.85*		R^2=.02, F(3, 328)=2.06†	
	M (Negative parenting)		**M (Positive parenting)**		**Y (Chronic peer stress)**	
Antecedent	***b* (95% CI)**	**SE**	***b* (95% CI)**	**SE**	***b* (95% CI)**	**SE**
X (Maternal depression)	.23(−.16 to .61)	.20	−.66(−1.25 to −.07)*	.30	.09(−.02 to .21)	.03
M (Negative parenting)	-	-	-	-	.00(−.04 to .04)	.02
M (Positive parenting)	-	-	-	-	−.02(−.05 to .00)†	.01
Constant	−.07(−.28 to .14)	.11	.20(−.12 to .52)	.16	2.10(2.03 to 2.16)**	.03
	R^2=.00, F(1, 330)=1.32		R^2=. 01, F(1, 330)=4.85*		R^2=.02, F(3, 328)=2.46†	

** p<.001;

* p<.05;

† p≤.1; RewP=reward positivity; *b*=unstandardized regression coefficients; CI=confidence intervals from 5000 bootstrap samples; SE=standard error