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Relationship between Borderline Personality Disorder, Emotional Availability, and Cortisol Output in Mother-Child Dyads

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Keywords
Cortisol · Borderline personality disorder · Mother-child interaction · Emotional availability · Synchrony

Abstract
Background: Mothers with borderline personality disorder (BPD) often show altered emotional availability toward their own child and heightened stress vulnerability. The aims of the present study were (1) to examine total cortisol output in saliva during mother-child interaction in mothers with BPD and their children and (2) to test whether maternal nonhostility as a subscale of emotional availability mediates the relationship between maternal BPD and child total cortisol output. ***Methods:*** We investigated 16 mothers with BPD and 30 healthy control mothers (HC) and 29 children of mothers with BPD and 33 children of HC mothers. Children were between 5 and 12 years old. Salivary cortisol was collected prior to and twice after an episode of a 21-min standardized play situation between mother and child. Nonhostility was rated using the emotional availability scales. Analyses of covariance were computed to test for group differences in total cortisol output (measured with area under the curve with respect to ground). Pearson's correlation was calculated to test the association between maternal and child total cortisol output. To test the second question, a mediation analysis according to Preacher and Hayes was conducted. ***Results:*** Mothers with BPD and their children had lower total cortisol output. Maternal and child total cortisol output was significantly correlated. Contrary to our hypothesis, maternal nonhostility did not mediate the relationship between BPD and child total cortisol output. ***Conclusion:*** Results imply that the hormonal stress activity of mothers with BPD and their children is altered, which may reflect modified stress regulation and stress vulnerability in mother and child and may impact

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on mother-child interaction. The finding of a positive association between mother's and child total cortisol output could indicate an intergenerational transmission of these alterations.

Introduction

Cortisol Output in Mothers with BPD and Their Children

Borderline personality disorder (BPD) is associated with altered emotion regulation and heightened vulnerability toward stress [1–3]. For mothers with BPD, it can be especially challenging to deal with stressful mother-child interactions. Previous studies showed that mothers with BPD show a more hostile parenting style toward their own children, which can be characterized by accumulated signs of anger, boredom, and impatience [4]. In addition, a dysregulated hormonal stress response system was found in individuals with BPD, which is indicated by an altered hypothalamic-pituitary-adrenal (HPA) axis [5, 6]. Altered maternal cortisol output may be particularly relevant during mother-child interaction. Interacting with the own child entails recurring stressful situations, inducing HPA axis activity. A dysregulated HPA axis could impact on dealing with these situations.

A majority of individuals with BPD have experienced severe stressful life events, which can lead to continued HPA dysregulation [7]. Such HPA dysregulation is found in experimental studies including psychosocial challenges in individuals with BPD. Specifically, investigating saliva cortisol output in women with BPD during the Trier Social Stress Test (TSST [8]), a paradigm to induce stress under laboratory conditions, previous studies found reduced baseline cortisol levels [9–11], reduced reactive cortisol levels, and reduced cortisol reactivity (change from baseline to reactive cortisol levels) in females with BPD in comparison with healthy females [9–12]. In contrast, some studies also found increased cortisol levels in response to a psychosocial stressor [13, 14] and increased continuous cortisol levels in saliva and urine during the day in individuals with BPD [15]. Discrepancies between studies may be related to factors like group size and different measurement of cortisol (saliva, urine, and blood). Factors like gender [10] and comorbid conditions (e.g., PTSD symptoms, depression, and dissociation [6, 13, 16]) may also impact on cortisol output.

However, in our analysis, mothers with depression or PTSD were excluded. No study so far addressed cortisol output in mothers with BPD during mother-child interaction. The question arises whether a reduced cortisol output may be present during mother-child interaction.

Previous research in healthy and depressed mothers and their children showed that maternal and child cortisol levels may be correlated [17–22], indicating an intergenerational transmission of stress regulation. Hormonal synchrony might be due to the interplay of genetic dispositions, prenatal programming, and postnatal care [23]. Notably, children of mothers with mental disorders like major depressive disorder or anxiety disorder were altered with heightened cortisol levels in reaction to a stressor [18]. To the best of our knowledge, no study so far has investigated cortisol levels of mothers with BPD and their children during mother-child interaction. The question arises if children of mothers with BPD also show modified cortisol levels and if alterations in cortisol levels are correlated between mothers and children.

The first aim of the present study was to investigate cortisol output in mothers with BPD and their children. Cortisol was measured during a standardized mother-child interaction followed by a puzzle task, which was meant to induce stress in both mother and the child. We hypothesized that cortisol output during mother-child interaction is reduced in both mothers with BPD and their children compared to healthy mothers and their children. Specifically, we expected reduced total cortisol output (AUCg) in mothers with BPD (hypothesis 1.1) and their children (1.2). We also expected (1.3) a correlation between maternal and child total cortisol output (AUCg). In explorative analyses, we examined whether maternal and child cortisol levels changed during mother-child interaction and stress task across measure points. To control for factors additionally impacting on HPA axis function, we used variables as covariates, which have potential influence on cortisol output and differed significantly between the groups (number of years of education, axis I disorder (yes/no), age, HAMD score, and partnership status). Although groups did not differ with regard to childhood maltreatment, we performed supplemental regression analyses exploring possible effects of maternal childhood maltreatment on maternal and child total cortisol output, as it is known to have an impact on the HPA axis [24].

Association of Emotional Availability and Child Cortisol Output

Previous research on parental behavior reported less emotional availability (EA) in mothers with BPD, especially nonhostility [4, 25]. Maternal EA is the capacity of a dyad to share an emotionally healthy relationship. A

higher level of EA is a factor that contributes to the mother's ability to respond properly to the emotional needs of the children, which helps the child to regulate its emotions [26]. Maternal EA is considered a "social buffer" against the development of emotional stress in infants in the sense that high EA in mothers may reduce the stress reaction of the child [27]. In accordance with this, previous studies in healthy and depressed mothers and their children showed reduced basal and reactive cortisol levels in children of sensitive mothers [18, 27–29]. Other studies found higher flexibility of cortisol output (for example, higher increase and decrease of cortisol, depending on the stressor) in children, when the mother is more sensitive [19, 30], while some studies found no association between maternal sensitivity and child cortisol secretion [31–33].

While these studies examined the association of EA and child cortisol levels in healthy or depressed mothers, analogous investigations are missing in mothers with BPD. Therefore, the second aim of the present study was to investigate the relationship between maternal EA and child cortisol output. Because mothers with BPD show alterations in nonhostility rather than sensitivity [25], the present study focused on this aspect of EA. We hypothesized that maternal nonhostility mediates the association between maternal BPD and child total cortisol output (AUCg, hypothesis 2). Considering a higher flexibility of the HPA axis in children of more sensitive mothers, we hypothesized that lower nonhostility mediates the effect of maternal BPD on reduced total cortisol output in children.

Methods

Participants

The present study was performed within the UBICA project ("Understanding and Breaking the Intergenerational Cycle of Abuse," "http://www.ubica.de"). The UBICA project investigates the mechanism of intergenerational transmission of maternal psychopathology and history of early-life maltreatment on mother-child interaction and child development [34, 35]. Parts of the present article have previously been published in German in the dissertation "Zusammenhang zwischen mütterlicher Borderline-Persönlichkeitsstörung, emotionaler Verfügbarkeit gegenüber dem eigenen Kind und Cortisolausschüttung bei Mutter und Kind" submitted by M. Roth to the Faculty of Medicine, Charité – Universitätsmedizin Berlin, in 2019 [36].

The current study initially involved 91 mother-child dyads (n = 37 BPD and n = 54 control). Participants were recruited in Berlin between December 2012 and December 2016. Mother-child dyads were recruited by advertisement (flyer and poster) in psychiatric hospitals and in gynecological and family practices. Inclusion criteria were as follows: children were the biological child of the mother and dyads lived together. Children were between 5 and 12 years old and attended primary school. Exclusion criteria for children were previous diagnosis of autistic disorder (according to DSM-IV criteria) and intelligence quotient score below 70 as assessed by the Culture Fair Intelligence Test 1 revised for children between 5 and 8 years of age (CFT 1-R [37]), or the CFT 20-R [38] for children between the age of 9 and 12. Exclusion criteria for all mothers were neurological diseases, lifetime history of schizophrenia or manic episodes, acute depressive episode, current posttraumatic stress disorder as assessed by the Mini-International Neuropsychiatric Interview [39] and anxious-avoidant or antisocial personality disorder assessed by the International Personality Disorder Examination interview (IPDE [40]), and intake of benzodiazepines within the last 6 months. Exclusion criteria for healthy mothers were current or lifetime DSM-IV axis I disorder assessed by Mini-International Neuropsychiatric Interview (M.I.N.I. [39]) or diagnosis of BPD, which was diagnosed using the International Personality Disorder Examination (IPDE [40]). All mothers were required to have a HAMD (Hamilton Depression Scale [41, 42]) score of below 8 to assure full remission in case they had a depressive episode in the past [43]. Exclusion criteria for analyses of the salivary cortisol were current pregnancy or breastfeeding, thyroid disease, use of cannabis or other drugs within the last 2 weeks, eating/drinking/smoking 1 h prior to testing, and cortisol data 3 standard deviations above or below the mean value. Forty-five mothers and 29 children were excluded (mothers: n = 17 eating/drinking/smoking 1 h before testing, n = 14 thyroid diseases, n = 12 pregnancy and breastfeeding, n = 5 use of cannabis, n = 12 cortisol data 3 standard deviations above or below the mean value; children: n = 17 eating/drinking 1 h before testing, n = 1 thyroid disease, and n = 12 cortisol data 3 standard deviations above or below the mean value; multiple reasons of exclusion possible). At group level, the final sample involved 46 mothers (n = 16 BPD and n = 30 control) and 62 children (n = 29 BPD and n = 33 control). At dyadic level, a total number of 35 mother-child dyads (n = 12 BPD and n = 22 HC) were included for the correlational analysis between maternal and child total cortisol output. Mothers were reimbursed for their participation (100 EUR).

Procedure and Measures

The study took place at 2 dates between 9:00 a.m. and 4:00 p.m. The time required per appointment was between 3 and 4 h.

Salivary Cortisol

We measured maternal and child salivary cortisol levels prior to, immediately after, and 20 min after mother-child interaction using noninvasive Salivette devices (Sarstedt, Rommelsdorf, Germany). All samples were stored immediately at −20°C until assaying. Salivary free cortisol was analyzed in the Department of Medical Psychology, Charité (Berlin, Germany) using immunoassay (Salimetrics, Cortisol ELISA Kit [Saliva]). Intra- and interassay coefficients of variation were 11.63% und 8.34 %. For total cortisol output, we calculated the area under the curve from ground (AUCg [44]). This is a frequently used method which provides an index of total hormone output over repeated measurements. Cortisol data with 3 standard deviations above or below the mean were excluded (mothers: n = 12 and children: n = 12). Log transformation was used to reduce skewness of data.

Maternal Nonhostility

It was measured using the Emotional Availability Scales (EAS, 4th Edition [45]). Mother-child dyads were videotaped during a

standardized play situation for 21 min. For the first 15 min, mother and child were asked to play as they normally do. For the following 6 min, the dyads performed a puzzle task ("Shape by Shape"), which was designed to be too difficult for the child. This task was meant to induce stress in both mother and the child. In our previous work, we showed that the puzzle task is a mild stressor. Therefore, we expected an increase of cortisol levels from T1 (baseline) to T3 (response) [46].

The EA scales (adult scales: nonhostility, sensitivity, structuring, and intrusiveness; child scales: involvement and responsiveness) are rated on a 7-point scale across the 2 situations. Coders of the EA scales were 3 researchers (1 senior clinical psychologist and 2 psychologists who hold a master's degree of clinical psychology), who have been approved as reliable to code by Zeynep Biringen after an extensive training period. They were blinded to maternal diagnoses, and videos were randomly assigned to them. Every video was rated independently by at least 2 coders; coding discrepancies were resolved through discussion. Due to the dimensional approach of the EAS [47], intraclass correlations for ordinal/interval variables were computed. For the maternal subscales, interrater reliability (average-measure intraclass correlations) for pairs of raters in the present study ranged between $r = 0.80$ and $r = 0.87$ for "sensitivity," between $r = 0.81$ and $r = 0.87$ for "structuring," between $r = 0.82$ and $r = 0.87$ for "nonintrusiveness," and between $r = 0.83$ and $r = 0.92$ for "hostility." For the child subscales, interrater reliability ranged between $r = 0.77$ and $r = 0.83$ for "responsiveness" and between $r = 0.79$ and $r = 0.87$ for "involvement" [25], indicating excellent agreement [48].

Maternal Psychopathology

Maternal BPD and other DSM-IV axis II disorders were assessed by the International Personality Disorder Examination (IPDE [40]), which is a structured diagnostic interview (administered by clinicians) that has well-established reliability and validity [40, 49]. Comorbid diagnoses of acute and lifetime DSM-IV axis I disorders were assessed by the Mini-International Neuropsychiatric Interview (M.I.N.I. [39]). The M.I.N.I. is a structured diagnostic interview, administered by clinicians or researchers for diagnostic purposes. The interview was reported to achieve good interrater reliability [39]. To assess depressive symptomatology, we applied the HAMD interview [41, 42].

Maternal History of Child Maltreatment

It was assessed using the CECA interview (Childhood Experience of Care and Abuse [50]) which is regarded as the golden standard in retrospective assessment of childhood maltreatment [51]. We used a sum score of the 5 main scales (physical abuse, sexual abuse, emotional abuse, antipathy, and neglect) to compare it between groups and account for the possible impact of childhood abuse on maternal or child total cortisol output.

Statistical Analyses

To account for possibly confounding effects, we examined group differences with univariate analyses of variance for continues variables and χ^2 analyses for categorical variables. To compare maternal nonhostility between groups, a multivariate analysis of covariance was performed with group as the fixed factor and EA subscales as dependent variables (see covariates below). For exploratory purposes, we also report group comparisons for those EA scales that are not focused in the present investigation (online suppl. material; for all online suppl. material, see www.karger.com/doi/10.1159/000521519).

For the first hypothesis, 2 separate univariate analyses of covariance were performed with maternal and children's total cortisol output as outcome variables. We used variables as covariates, which have potential influence on cortisol output and differed significantly between the groups. In mothers, we used number of years of education, axis I disorder (yes/no), age, HAMD score, and partnership status as covariates. In an extra analysis, we still checked whether time of the first saliva sample as an additional covariate would impact the study results, even if it did not differ between groups. In children, we used time of taking the first saliva sample as a covariate. We also used the maternal number of years of education as a covariate because it differed significantly between groups, and it was shown that the socioeconomic status impacts on the child total cortisol output [52].

In a second step, the correlation between maternal and child total cortisol output using two-tailed Pearson's correlation was computed. Because not all mother-child dyads were visiting the laboratory at the same time, we used in a second analysis two-tailed partial correlation with time of first cortisol measurement as the control variable.

In additional explorative analyses, we conducted a repeated-measures analysis of covariance (ANCOVA) with cortisol as the within-subject factor and diagnostic group as the between-subject factor (same covariates as above) to examine whether maternal and child cortisol levels changed during mother-child interaction across measure points. We performed 2 supplemental regression analyses to explore how much variance in maternal and child total cortisol output is explained by current axis I disorder/BPD diagnosis (disorder-specific effects) above the variance explained by the CECA sum scores (trans-diagnostic effects). If the correlation was significant, the variable was used as a covariate. Maternal total cortisol output (AUCg) served as the dependent variable. Time of testing and childhood maltreatment (sum score of the 5 main scales of CECA interview) were entered as covariates in the first step; current axis I disorders (except acute depression which was defined as exclusion criterion) and maternal BPD (yes/no) were entered in the second step. In a second analysis, we used child total cortisol output as a dependent variable, with childhood maltreatment in the first step and current axis I disorders and maternal BPD (yes/no) in the second step.

For the second hypothesis, we examined maternal nonhostility as a mediator between maternal BPD and child total cortisol output according to the method suggested by Preacher and Hayes [53]. Mediation can be assumed if the confidence interval of the indirect effect of the predictor on the outcome through the proposed mediator does not include zero [53]. All calculations were conducted using SPSS for Windows (version 23). For all analyses, the statistical significance threshold was set at $p = 0.05$.

Results

Subject Characteristics

Sample demographics are summarized in Table 1. Mothers did not differ in BMI, time of testing (pre-interaction cortisol), menstrual cycle, intake of oral contracep-

Table 1. Sample characteristics

Mothers	BPD (n = 16) M ± SE	Control (n = 30) M ± SE
Age	35.25±1.36	40.2±0.94*
BMI	26.62±1.81[a]	23.08±0.69
Years of education	15.44±0.79	17.67±0.48*
HAMD	3.5±0.62	0.93±0.26*
Time of testing, hh:mm	02:02 p.m.±0:22[a]	01:57 p.m.±0:23[b]
Cohabiting with child father, %	31.25	73.33*
Hormonal contraception, %	25	6.67
First half of menstruation cycle, %	46.15[c]	52.17[d]
DSM-IV axis I disorder, %	25	0*
IPDE score	13.87±0.51	0.76±0.25*
Childhood maltreatment	20.44±5.05	22.9±1.45
Children	**BPD (n = 29) M ± SE**	**Control (n = 33) M ± SE**
Sex (girls), %	41.38	57.58
Age	8.69±0.4	7.82±0.29
IQ	103.59±2.87	107.59±1.85[a]
Years of education (mother)	15.6±0.7	18.67±0.49*
Time of testing	14:09±0:19[a]	12:54±0:26[d,*]
Siblings	1.31±0.12	1.17±0.14
Childhood maltreatment (of mother)	20.59±3	22.85±1.3

Characteristics for individuals included into the analyses on group level are reported. A subgroup of n = 35 mother-child dyads were included into correlational analyses. Childhood maltreatment = lower scores indicate higher severity of maltreatment. M, mean; SE, standard error; BPD, borderline personality disorder; HAMD, Hamilton Depression Scale; BMI, body mass index (kg/m^2); DSM-IV, Diagnostic and Statistical Manual of Mental Disorders; IPDE, International Personality Disorder Examination; IQ, intelligence quotient. * $p < 0.05$. [a] One missing data. [b] Two missing data. [c] Seven missing data. [d] Three missing data.

tion, and maternal childhood trauma. Mothers with BPD were younger, were less likely to cohabit with the child father, reported less number of years of education, and had higher scores of HAMD, IPDE, and more of those comorbid current axis I disorders, which were not exclusion criteria (n = 3 dysthymia, n = 2 alcohol abuse, n = 1 obsessive-compulsive disorder, and n = 1 social phobia; some mothers had more than one axis I disorder).

At trend level, children of mothers with BPD were older (p = 0.078). Children did not differ with regard to IQ, sex, siblings, or maternal childhood trauma between groups.

Nonhostility

In a multivariate analyses of covariance with group as the fixed factor, EA subscales as dependent variables and number of years of education, axis I disorder (yes/no), age, HAMD score, and partnership status as covariates, there was a significant effect of group on the EA subscales (V = 0.36, $F_{(6, 32)} = 2.994$, $p < 0.05$, $\eta^2 = 0.36$) using Pillai's trace. Subsequent separate univariate ANCOVAs on the outcome variables revealed a significant group effect on nonhostility, $F_{(1, 44)} = 7.475$, $p < 0.05$, $\eta^2 = 0.168$. Mothers with BPD had lower scores of nonhostility (M = 4.66, SE = 0.17) compared to healthy mothers (M = 5.89, SE = 0.31). There was at trend level, a group difference for sensitivity ($F_{(1, 37)} = 3.956$, $p = 0.054$, $\eta^2 = 0.097$). At trend level, mothers with BPD had lower scores of sensitivity (M = 3.70, SE = 0.16) compared to healthy mothers (M = 4.56, SE = 0.16). Comparisons of the other subscales (sensitivity, structuring, nonintrusiveness, responsiveness, and involvement) are reported in online supplementary material.

Cortisol

Mother

Total Cortisol Output (AUCg Mothers). The main effect of group was significant ($F_{(1, 38)} = 5.531$, $p = 0.024$, $\eta^2 = 0.127$). Mothers with BPD showed significantly less total cortisol output (M = −2.08, SE = 0.14) compared to

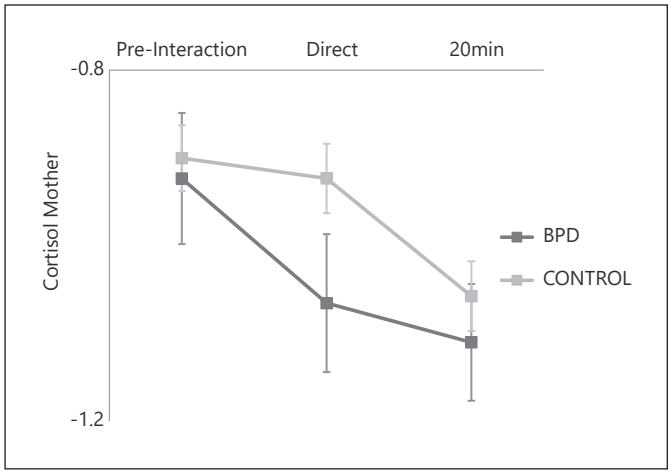

Fig. 1. Salivary cortisol levels over the course of mother-child interaction in mothers with BPD and controls. Data represent the mean ± SE. Negative values are due to log transformation.

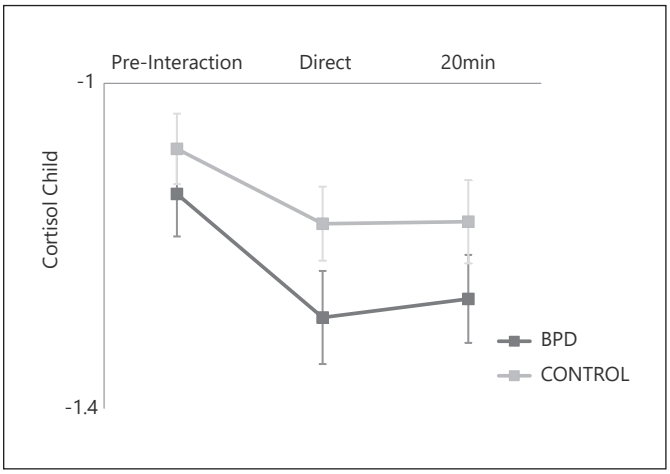

Fig. 2. Salivary cortisol levels over the course of mother-child interaction in children of mothers with BPD and controls. Data represent the mean ± SE. Negative values are due to log transformation.

control mothers (M = −1.89, SE = 0.07) (hypothesis 1.1 confirmed).

Cortisol Levels over the Course of Mother-Child Interaction (Explorative Analysis). The ANCOVA with cortisol as the within-subject factor and diagnostic group as the between-subject factor showed a main effect of group ($F_{(1, 38)} = 4.619$, $p = 0.038$, $\eta^2 = 0.108$), with lower cortisol levels in the BPD group (shown in Fig. 1). There was no main effect of time ($F_{(2, 76)} = 0.917$, $p = 0.404$, $\eta^2 = 0.024$). However, the group × time interaction ($F_{(2, 76)} = 3.121$, $p = 0.050$, $\eta^2 = 0.076$) was significant: compared to healthy controls, mothers with BPD showed significantly lower cortisol levels measured directly after the mother-child interaction (BPD: M = −1.07, SE = 0.08; control: M = −0.92, SE = 0.04; $F_{(1, 38)} = 7.465$, $p = 0.009$, $\eta^2 = 0.164$) and, at trend level, for pre-interaction cortisol (BPD: M = −0.92, SE = 0.07; control: M = −0.9, SE = 0.04; $F_{(1, 39)} = 4.593$, $p = 0.038$, $\eta^2 = 0.105$). Twenty-minutes-after-interaction cortisol did not differ significantly between the groups (BPD: M = −1,11, SE = 0.07; control: M = −1.06, SE = 0.04; $F_{(1, 39)} = 0.824$, $p = 0.37$, $\eta^2 = 0.021$). Post hoc tests were corrected according to Bonferroni ($p = 0.017$).

Using time of the first saliva sample as an additional covariate, effect of group for total cortisol output (AUCg) was still significant ($F_{(1,34)} = 5.188$, $p = 0.008$, $\eta^2 = 0.188$), and group × time interaction was for cortisol levels over the course of mother-child interaction at trend level significant ($F_{(2, 68)} = 2.884$, $p = 0.063$, $\eta^2 = 0.078$). Effect of time was at trend level significant ($F_{(2, 68)} = 0.554$, $p = 0.063$, $\eta^2 = 0.016$).

We performed supplemental regression analyses to analyze how much variance in maternal and child total cortisol output is explained by current axis I disorder/BPD diagnosis (disorder-specific effect) above the variance explained by CECA sum scores (trans-diagnostic effects) (online supplementary material). The analyses revealed that the first step significantly contributed to increased variance explanation ($p = 0.021$) with time of testing ($p = 0.032$) as a significant negative predictor of maternal total cortisol output. Maternal childhood maltreatment was not a significant predictor in the first step ($p > 0.5$). In the second step, neither maternal axis I disorder nor maternal BPD was a predictor. For child total cortisol output, the analyses revealed that the first step significantly contributed to increased variance explanation ($p = 0.04$) with maternal childhood maltreatment ($p = 0.04$) as a significant negative predictor of child total cortisol output. Neither axis I disorder nor maternal BPD was a predictor.

Child

Total Cortisol Output. The main effect of group was significant ($F_{(1, 54)} = 5.633$, $p = 0.021$, $\eta^2 = 0.094$). Children of mothers with BPD showed significantly less total cortisol output (M = −2.50, SE = 0.09) compared to children of control mothers (M = −2.30, SE = 0.08) (hypothesis 1.2 confirmed).

Cortisol Levels over the Course of Mother-Child Interaction (Explorative Analysis). In the ANCOVA with cortisol as the within-subject factor and diagnostic group as

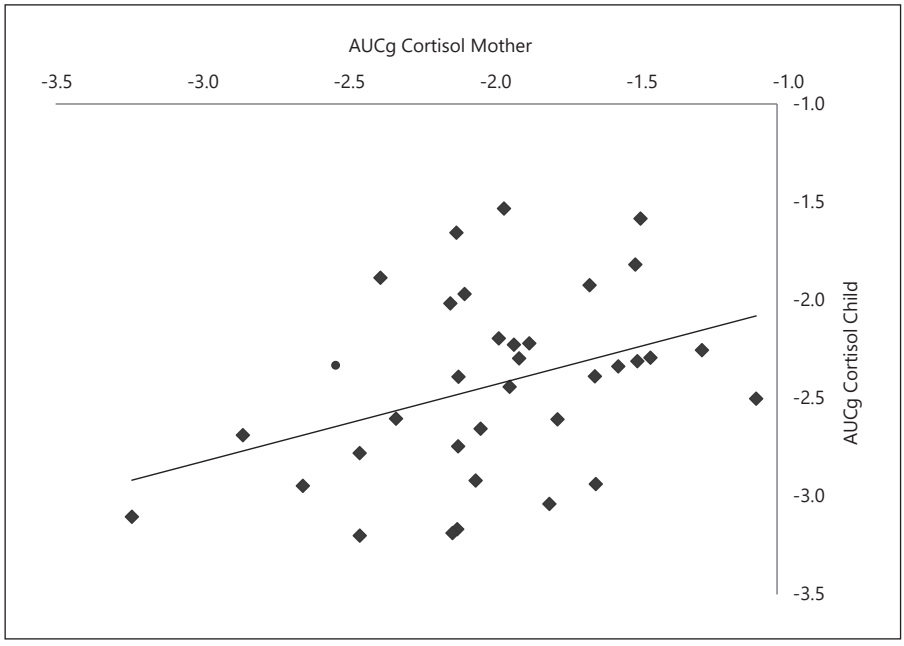

Fig. 3. Correlation between maternal and child salivary total cortisol output (AUCg). Negative values are due to log transformation.

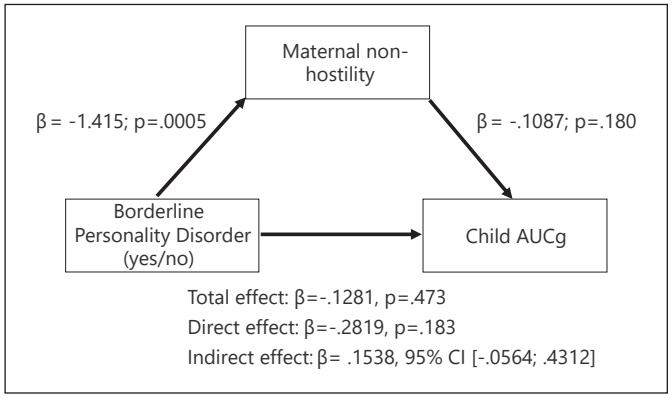

Fig. 4. Mediation analysis with maternal nonhostility as the mediator, maternal BPD as the predictor, and child AUCg as the outcome; the indirect effect is not significant. Hamilton score was used as the covariate.

the between-subject factor, the main effect of group was significant ($F_{(1, 54)}$ = 5.402, p = 0.024, η^2 = 0.091), with lower cortisol levels in children of mothers with BPD (pre-interaction cortisol: BPD: M = −1.14, SE = 0.05; control: M = −1.08, SE = 0.04; immediate-after-interaction cortisol BPD: M = −1.29, SE = 0.06; control: M = −1.17, SE = 0.05; 20-min-after-interaction cortisol: BPD: M =−1.27, SE = 0.05; control: M = −1.17, SE = 0.05). Both the main effect of time ($F_{(1, 108)}$ = 0.699, p = 0.499, η^2 = 0.013) and time × group interaction ($F_{(2, 108)}$ = 0.330, p = 0.719, η^2 = 0.006) were not significant (see Fig. 2).

Correlation between Maternal and Child Total Cortisol Output

In the total sample, total cortisol outputs of mother and child were significantly correlated (r = 0.376, p = 0.026, n = 35), see Figure 3. With time of first cortisol measurement as the control variable, total cortisol outputs of mother and child were significantly correlated (r = 0.375, p = 0.038, n = 29; 6 missing data of time) (hypothesis 1.3 confirmed).

Mediating Effect of Maternal Nonhostility on Child Total Cortisol Output

As displayed in Figure 4, the indirect effect of maternal BPD (predictor) on child total cortisol output (outcome) through maternal nonhostility (proposed mediator) was not significant, indicating that mediation was not present (β = 0.1538, 95% CI [−0.0564; 4,312]) (hypothesis 2 not confirmed). The HAMD score was used as a covariate.

We also calculated our statistical analyses without covariates, as suggested by Simmons, Nelson, and Simonsohn [54]. In these analyses performed in both mothers and children, we found no significant group difference for total cortisol output and no significant time × group interaction for the cortisol levels over the course of the mother-child interaction (see online supplementary material). It is known that the HPA axis can be impacted by different factors. These analyses demonstrate that these covariates play a relevant role in the analysis of the cortisol data.

Discussion

The aim of the present study was (1) to examine total cortisol output in saliva during mother-child interaction in mothers with BPD and their children and (2) to test whether maternal nonhostility as a subscale of EA mediates the relationship between maternal BPD and child total cortisol output. The main findings are (1) total cortisol output in saliva is reduced in mothers with BPD and their children compared to healthy mothers and their children, and total cortisol output of mothers and their children is positively correlated. (2) Maternal nonhostility did not mediate the association between maternal BPD and child total cortisol output.

Total Cortisol Output during Mother-Child Interaction

We found reduced total cortisol output in mothers during the interaction with their own child, confirming hypothesis 1.1. This finding is in line with previous studies with individuals with BPD reporting reduced salivary cortisol before and in reaction to psychosocial stress (induced by the TSST) compared to healthy controls [9–12]. Principally, one explanation for reduced salivary cortisol concentrations to stressful situations in BPD could be that many individuals with BPD report a long history of physical, sexual, or emotional abuse during childhood [55, 56] and persistent severe problems like abuse in adulthood [57, 58]. It has repeatedly been shown that individuals with repeated childhood trauma initially show chronic extensive activation of the HPA axis which can cause hyporesponsiveness and attenuated cortisol release later in life [11, 24, 59–62].

It is possible that our finding is not specific to the diagnosis of BPD but could be a trans-diagnostic marker of several mental disorders and possibly driven by chronic stress and childhood adversity. However, given that groups did not significantly differ with regard to early-life maltreatment in our study and that our supplemental regression analysis did not show a significant effect of early-life maltreatment or mental disorder on maternal cortisol output, the reduced total cortisol output observed in the present study may rather not reflect such attenuated cortisol release resulting from repeated and chronic early-life maltreatment. Another explanation may be that individuals with BPD exhibit a biological disposition for lower HPA activity independent of early childhood maltreatment. Given the relatively high rate of early childhood maltreatment in both groups, a third explanation may be that specific dispositions or moderators exist in individuals who develop BPD after a history of early-life maltreatment. Further studies would be necessary to investigate these moderators.

Another explanation might be that difficulties in emotion regulation characteristic for individuals with BPD could result in repeated and chronic experiences of stress and altered stress vulnerability. Previous studies assumed that acute stress contributes to hypercortisolism, whereas long-term stress may result in downregulation of the HPA axis [63], leading to hypocortisolism. In accordance with this, animal experiments show that primates [64] and rodents [65], who were exposed to chronic stress, showed hyporesponsiveness of the HPA axis in response to acute stressors. Thus, chronic stress was assumed as the main cause for the development of HPA hyporeactivity to acute stress [7, 66]. Although we did not assess systematic measures of chronic stress (e.g., number of daily hassles) in our investigation, we suggest that chronic stress may contribute to the low total cortisol output observed in the present study.

Exploring cortisol levels over the course of mother-child interaction (repeated-measures ANCOVA), we found a significant group and a significant group × time interaction with reduced salivary cortisol levels in mothers with BPD immediately after mother-child interaction, and, at trend level, before interaction. The significant group effect observed in this analysis is in line with our finding of a reduced total cortisol output in mothers with BPD. Across groups, we did not find a significant increase from pre-interaction to immediate-post-interaction cortisol levels, raising the question which measurements represent basal and reactive levels of cortisol, respectively. We had expected the saliva cortisol level to be lower at the first measurement because the mother-child interaction had not yet begun. We had assumed a cortisol increase at the third measurement point because we implemented a stress-task paradigm in our interaction [46]. Contrary to our expectation, cortisol levels decreased from the first to the third measurement in both groups. It is possible that taking part in the present study raised concerns in mothers that were experienced as stressful (e.g., being on time, being aware of being assessed, and new situation) and therefore increased their pre-interaction cortisol levels. These so-called arrival effects have already been described in previous studies [67]. Another explanation could be that the greater part of the 21-min paradigm was actually a free play activity which might not have been stressful.

Extending previous studies on cortisol levels in individuals with BPD [9–12], we also investigated children of mothers with BPD. In our analyses, children of mothers with BPD also showed reduced cortisol total output during mother-child interaction (hypothesis 1.2) which may

reflect reduced HPA axis activity. Exploring cortisol levels over the course of mother-child interaction (repeated-measures ANCOVA), we did not find a significant group × time interaction but a significant group effect showing that child cortisol levels of BPD mothers were lower at all points of measurement. The question arises whether this reduced total cortisol output in children might make them prone to impaired emotion regulation and the development of mental disorder later in life. Previous studies already showed that altered HPA axis function is related to dysregulation in youth [68] and the development of psychopathology like depression, anxiety, substance abuse, or emotional and behavioral problems [69–72].

Additionally, we found a significant correlation between maternal and child total cortisol output across groups (hypothesis 1.3). Previous studies, which examined healthy and depressed mothers, already found a correlation between maternal and child cortisol levels [17–22]. To the best to our knowledge, none of the previous studies examined mothers with BPD and their child.

One might speculate that this similar pattern of reduced cortisol output in BPD mothers and their children points to hormonal synchrony which may represent a mechanism of intergenerational transmission of stress vulnerability and dysregulation. It would be desirable to investigate if interventions, focusing on maternal mentalization and attachment competencies and the quality of mother-child relationship [73], can modify the mother-child HPA axis synchrony, which could in turn maybe lead to better parenting outcome and child mental health.

Mediating Effect of Maternal Nonhostility on Child Total Cortisol Output

Contrary to our hypothesis 2, we did not find a mediating effect of maternal nonhostility on the relationship between maternal BPD and child total cortisol output. In contrast to this finding, some previous studies, which examined healthy or depressed mothers, reported a relationship between maternal EA and child cortisol levels. They found that higher maternal EA was associated with reduced basal and reactive cortisol levels in the child [18, 27–29]. Other studies found higher flexibility of cortisol output (for example, higher increase and decrease of cortisol, depending on the stressor) in children, when the mother was more sensitive [19, 30]. While these previous studies examined infants and toddlers aged 1–2 years, children in our study attended primary school. It is possible that the relationship between child cortisol output and maternal availability depends on child age. Hormonal levels of children of primary school age might not be as strongly associated with the mother's EA. The results could indicate that HPA axis function of the child is more closely associated with maternal availability during early age, whereas with increasing age, child cortisol output becomes more independent of the EA of the mother. It could be possible that lesser amount of shared time with the mother and greater influence of other caregivers or lesser sensitivity of the child HPA axis for the external factor with increasing age could lead to such increasing independence of the child HPA axis. Underlining such influence of child age, longitudinal analyses failed to show correlation between maternal sensitivity and cortisol reactivity in infants aged 8–9 months compared to an initial correlation in infants aged 3–6 months [28, 29]. One could speculate that child HPA regulation is more strongly dependent on maternal EA during early infancy and that interventions are especially important for this age group. Further potential explanations for our nonfinding of a significant mediation include the relatively small sample size and other factors that might have impacted on the mediation, but have not been considered here (e.g., social support of mother and child and involvement of the father).

Strengths and Limitations

To our knowledge, the present study is the first to investigate cortisol output of mothers with BPD and their primary school aged children during mother-child interaction. Structured clinical interviews were used to assess maternal psychopathology and history of child abuse, and mother-child interaction was rated by blind raters using EAS.

The following limitations may be considered. First, we did not assess a number of factors like sleep quality and physical activity that can influence cortisol secretion. Second, menstrual cycle was assessed by maternal reports retrospectively. Third, testing took place at several times which could have influenced cortisol levels. However, time of testing did not differ significantly between groups. Fourth, our final patient sample was relatively small. It is acknowledged that unequal group sizes (n = 16 BPD and n = 30 control) might have impacted the results of the ANCOVA (equal variance assumption, statistical power based on the smaller sample). Additionally, due to our rather small sample size, we decided to keep the analytic model for the cortisol output of maternal and child cortisol over time as simple as possible [74]. We acknowledge that there are other analytic approaches like latent growth curve analysis or cross-lagged model for exploring mother-child-cortisol attunement [75], which was not our focus in this study. Future research with larger samples should consider such analyses.

Despite our small sample size, our study did not include participants with posttraumatic disorder, current depression, or thyroid disease. All 3 conditions have been shown to impact on cortisol levels.

Fifth, our study did not involve individuals with comorbid disorders like depression or PTSD, which are common comorbid disorders in individuals with BPD and which are known to impact on cortisol levels [6]. While excluding these disorders helped to avoid confounding effects, one could also argue that excluding these disorders made the BPD sample a very selective one, which could explain why some of the expected results were not obtained in this study. Including individuals with comorbidities and controlling for these comorbidities in analyses should be considered in future studies.

Sixth, we used variables as covariates, which have potential influence on cortisol output and differed significantly between the groups. In additional analyses without these covariates, we did not find a significant group difference for total cortisol output for both the mother and the child. Further studies with lower group difference in potentially confounding variables will be necessary to address this limitation.

Seventh, we did not ask for "income of parents" during the assessment of the socioeconomic status, although income was shown to be associated with child cortisol levels [52]. However, we obtained years of education of the mother and used this measure as a covariate in the present analyses. Eight, as mentioned before, future studies should include a "resting phase" of 30–40 min prior to testing in order to avoid confounding "arrival effects" on cortisol release [10–12, 59].

Conclusion

In sum, we found reduced total cortisol output in mothers with BPD and their children during mother-child interaction. This reduced output may reflect altered stress regulation and stress vulnerability in both mother and child and may impact on mother-child interaction. Moreover, we found a correlation between maternal and child total cortisol output which might represent a mechanism underlying intergenerational transmission of altered stress regulation. Further research is needed to further elucidate how synchrony between mother and child may alter over the course of infanthood and to determine if interventions can prevent the intergenerational transmission of altered cortisol output. It will be of interest to find out which other factors (e.g., maternal emotional regulation) may mediate the relationship between maternal BPD and child cortisol output.

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Statement of Ethics

The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008. Approval for the study was obtained from the Ethics Committees of the Charité – Universitätsmedizin Berlin (EA2/097/13). Written informed consent was obtained from all participants after the procedure had been explained.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

Roth, Kluczniok, and Bermpohl wrote the first draft of the manuscript. All authors revised the manuscript. Bermpohl, Kluczniok, Herpertz, Röpke, Heim, and Winter designed the study and wrote the protocol. Roth managed the literature searches. Roth, Kluczniok, Bödeker, Hindi Attar, Dittrich, Winter, Ridder, and Poppinga were responsible for data collection. Kluczniok undertook the statistical analysis. Roth, Kluczniok, and Bermpohl were responsible for data interpretation. All authors approved the final version of the article.

Data Availability Statement

All data generated or analyzed during this study are included in this article and its online supplementary material files. Further enquiries can be directed to the corresponding author.

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