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Research paper

Maternal postpartum depressive symptoms: The predictive role of objective and subjective birth experience and hair glucocorticoids

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ABSTRACT

Background: Having a negative childbirth experience is a known risk-factor for developing postpartum depression (PPD). Alterations of the hypothalamus-pituitary-adrenal (HPA)-axis have been discussed as a potential underlying mechanism. However, research on the association between negative birth experiences and long-term integrated glucocorticoids (GCs) is lacking. This study aimed to examine whether objective and subjective birth experience predicted long-term GCs and PPD symptoms.

Methods: Measures of objective and subjective birth experience, PPD symptoms, and hair strands for the assessment of hair cortisol concentrations (HairF), hair cortisone concentrations (HairE), and HairF/HairE ratio, were provided eight weeks after childbirth by 235 mothers participating in the study $DREAM_{HAIR}$.

Results: A negative objective birth experience predicted a higher HairF/HairE ratio but was not associated with HairF or HairE. The subjective birth experience did not explain additional variance in hair GCs but was a significant predictor for PPD symptoms. A higher HairF/HairE ratio predicted PPD symptoms when controlling for prepartum depressive symptoms and number of lifetime traumatic events.

Limitations: Analyses were based on a relatively homogeneous sample and women reported in general positive birth experiences and low levels of depressive symptoms. Therefore, results should be applied to the broader population with caution.

Conclusions: Our results suggest that negative objective birth experience is associated with an altered HairF/HairE ratio, which in turn, seems to be a promising biomarker to identify women at risk for developing PPD. A negative subjective birth experience may be less critical for alterations of the HPA-axis but remains an essential risk factor for PPD.

1. Introduction

The childbirth experience is a multidimensional construct that includes objective and subjective aspects (Reisz et al., 2015). Objective birth experiences can be assessed through cumulative medical complications concerning the mother and the infant, including an unplanned instrumental delivery, extensive labor duration, or a low Apgar score (Garthus-Niegel et al., 2013). A woman's subjective birth experience, on the other hand, comprises physical discomfort, fulfillment, and emotional distress (Stadlmayr et al., 2001).

It is well established that stressful life events can affect the hypothalamus-pituitary-adrenal (HPA)-axis, the body's central stress

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response system (Faravelli et al., 2012; Karin et al., 2020). Childbirth represents a physical and psychological stressor (Horsch and Ayers, 2016), which can impact cortisol levels. For example, Miller et al. (2019) found that the duration of the second stage of delivery was linked to higher salivary cortisol levels assessed 2 min and 2 hr after childbirth. Similarly, total plasma cortisol levels at 1 min postdelivery were higher in women who underwent an instrumental delivery compared to those who had a spontaneous, uncomplicated delivery (Benfield et al., 2014). Furthermore, the subjective appraisal of a stressful event has been suggested to influence HPA-axis activity (Staufenbiel et al., 2015). However, research on the association between negative maternal birth experience, both objective and subjective, and long-term alterations of the HPA-axis is lacking.

On a psychological level, negative overall birth experiences can render women vulnerable to experience postpartum depression (PPD; O'hara and Swain, 1996). The DSM-5 classifies peripartum depression as a major depressive episode, with its onset occurring during pregnancy or within four weeks after childbirth (American Psychiatric Association, 2013). Besides prepartum depression being one of the most substantial risk factors for PPD (Hutchens and Kearney, 2020), women are more likely to develop depressive symptoms following a negative objective birth experience, such as cesarean section, vacuum or forceps delivery (Astbury et al., 2010), and obstetric perineal lacerations (Asif et al., 2020). Further, a growing body of evidence suggests that the subjective birth experience might supersede objective criteria in predicting an increased risk of PPD (McKelvin et al., 2021; Weisman et al., 2010). Maternal PPD can impair social functioning and the relationship with the partner (Garthus-Niegel et al., 2018). It can also affect the child's early social-emotional development (Junge et al., 2017), sleeping and eating patterns, and behavioral disorders beyond childhood (Hutchens and Kearney, 2020). Given the detrimental effects that PPD can have on women's and infants' health, it is of utmost importance to gain a more systematic understanding of the etiology of PPD by shedding light on the underlying biological factors contributing to the development of PPD.

Over the last few years, the role of altered levels of the glucocorticoid (GC) hormone cortisol as biological predictor of PPD has been discussed. Research employing traditional methods that investigate cortisol concentrations in blood, urine, or saliva (Brummelte and Galea, 2010; Yim et al., 2015) has been inconclusive, with some studies showing a link between altered cortisol concentrations and maternal PPD (Hillerer et al., 2012; Seth et al., 2016) and others failing to find significant results (Evans et al., 2008; Fan et al., 2009; Peer et al., 2013). Conventional methods provide cortisol samples at a single time point and are influenced by rapid-changing factors such as circadian rhythm, acute stress, and changes in stress-induced HPA-axis reactivity (Stalder et al., 2017). Hence, these methods are not suitable for evaluating overall *long-term* systemic cortisol exposure.

A promising biomarker in this context includes the assessment of long-term integrated GC secretion in hair samples. Scalp-near hair cortisol concentrations (HairF) which provide a retrospective measure of cumulative cortisol secretion (Wennig, 2000) seem to be a promising biomarker of long-term GC secretion over an extended period. As cortisol can be converted into its inactive cortisone, assessing hair cortisone concentrations (HairE) parallel to HairF may offer a better understanding of the cumulative amount of active and inactive corticosteroids in the body (Perogamvros et al., 2010). Furthermore, the HairF/HairE ratio can be quantified as an indirect marker of the enzymatic activity of 11b-hydroxysteroid-dehydrogenase type 2 (11β-HSD2; Zhang et al., 2013). 11β-HSD2 converts cortisol into cortisone and reflects peripheral tissues' potential to metabolize corticosteroids. Therefore, it is advisable to assess HairF, HairE, and their ratio to quantify a more robust GC index.

Few studies investigating the association between hair GCs and PPD have shown mixed evidence. Jahangard et al. (2019) found that lower prepartum and postpartum 3-month integrated HairF and HairE predicted PPD 12 weeks postpartum, while Scharlau et al. (2018) determined that depression during pregnancy correlated with HairE and the HairF/HairE ratio but not with HairF alone, underlining the importance of simultaneous assessment of HairF and HairE. However, earlier research has not systematically controlled whether the actual onset of depression occurred prenatally and if other hair-related factors such as hair washing frequency influenced GC levels, which might explain the inconclusive evidence (Bryson et al., 2021; Schnakenberg et al., 2021). Furthermore, lifetime trauma exposure has been shown to be associated with both dysregulated hair GCs (e.g., Steudte-Schmiedgen et al., 2016, 2023) and PPD (e.g., Martini et al., 2022). Therefore, studies that control for both potential hair GC confounders, number of lifetime traumatic events, and prepartum depressive symptoms in community samples are necessary to clarify the relationship between hair GCs and PPD (Jahangard et al., 2019; Psarraki et al., 2021).

In the current study, 1) we hypothesized that objective birth experience would be associated with maternal HairF, HairE, and the HairF/HairE ratio measured eight weeks after childbirth (Braig et al., 2015). Considering that birth is a multifaceted construct (Reisz et al., 2015), we assumed an increase in explained variance in hair GCs by including subjective birth experience as additional predictor. As we are amongst the first to investigate these relationships, we do not postulate a direction in which steroid secretion is modified. 2) We sought to replicate previous findings on the association between birth experience and PPD symptoms. We assumed that a negative objective birth experience would predict higher PPD symptoms eight weeks after birth and expected an increase in explained variance by considering subjective birth experience as an additional predictor (Weisman et al., 2010). 3) We hypothesized that 2-month integrated hair GCs would predict PPD symptoms eight weeks after birth. Given heterogeneous prior results (Psarraki et al., 2021), we did not postulate the direction in which GC secretion is modified. 4) To integrate biological mechanisms into the psychosocial etiology of PPD symptoms associated with the birth experience, we examined in an exploratory way whether GC levels explain the intermediate pathway between objective and subjective birth experience and PPD symptoms, respectively. A more comprehensive biopsychological model of PPD will provide an improved identification of individuals at risk and support the development of interventions on a physiological and psychosocial level (Bergunde et al., 2022).

2. Methods

2.1. Study design and participants

The present study is part of the ongoing prospective cohort Dresden Study on Parenting, Work, and Mental Health (DREAM) investigating the effects of parental work, role distribution, and stress factors on long-term mental and somatic health with currently six measurement points from pregnancy (T1 DREAM) to childhood (T6 DREAM). The study uses a multi-method approach including the sub-study $DREAM_{HAIR}$, which aims to understand the associations between long-term stress-associated biomarkers in hair and mental health-related outcomes in mothers, partners, and their offspring from pregnancy to 4.5 years postpartum (for further details regarding DREAM, see Kress et al., 2019). Participants were included in the DREAM study if they were residents in Dresden (Germany) or surrounding areas and had sufficient German language skills to complete the questionnaires. Inclusion criteria for the $DREAM_{HAIR}$ study comprised a minimal hair length of 2 cm, no hair loss or baldness, no severe somatic disease in the last five years (e.g., cancer, diabetes mellitus), and no use of GC-containing medication over the previous four months. The Ethics Committee of the Faculty of Medicine of the Technical University of Dresden approved DREAM and the associated biological substudies (No: EK 278062015). All participants gave their informed consent according to the Declaration of Helsinki for DREAM and $DREAM_{HAIR}$ before conducting the first assessment.

The current study focused on mothers who completed T1 DREAM, T1

$DREAM_{HAIR}$, T2 DREAM, and T2 $DREAM_{HAIR}$, with both T2 assessments approximately eight weeks after childbirth. Exclusion criteria for this particular investigation comprised: 1) multiple births, due to higher risk for intrapartum complications, which could influence the birth experience, 2) preterm births (childbirth before 37 weeks of pregnancy), 3) stillbirths or infant death after birth, 4) factors affecting hair GC levels (GC intake, consumption of psychotropic drugs, or smoking), and 5) laboratory analyses were not possible (including hair length < 2 cm, hair mass < 5 mg). 6) Not completing the questionnaire at T1 DREAM or T1 $DREAM_{HAIR}$ resulted in exclusion from the present investigation, considering prepartum depressive symptoms and number of lifetime traumatic events were measured during pregnancy and included as a control variable in the present study. 7) Failing to complete the T2 DREAM or T2 $DREAM_{HAIR}$ assessments within 7—14 weeks after childbirth resulted in exclusion. The final sample consisted of $N = 235$ women (for details of final exclusion criteria in this sample, see Fig. 1), although the *n* varied slightly between analyses due to missing data.

2.2. Measures

The objective birth experience was constructed based on possible childbirth complications registered in maternal and child's medical records. An index was computed by summing the number of possible complications, including: 1) unplanned instrumental vaginal delivery or emergency CS, 2) active phase of labor lasted longer than 12 h, 3) no progress in the second stage of labor, 4) premature or 5) difficult abruption of the placenta, 6) heavy bleeding, 7) perineal tear (3rd or 4th degree), 8) vaginal tear, 9) labial tear, 10) breech birth, 11) transversal lie, 12) pathological heart sound during birth, 13) umbilical cord prolapse, 14) umbilical cord compressing the child's neck, 15) green amniotic liquor, and (16) low neonate Apgar score (< 7) at 5 min (Garthus-Niegel et al., 2013). Scores could range from 0 to 16.

The subjective birth experience was measured with the German version of Salmon's Item List (SIL; Stadlmayr et al., 2001). SIL contains 20 items rated on a numerical scale 1–7, with positive (e. g., happy) and negative (e. g., not happy) adjectives used as anchor statements. A total score range between 0 and 120 was generated, with higher scores indicating a

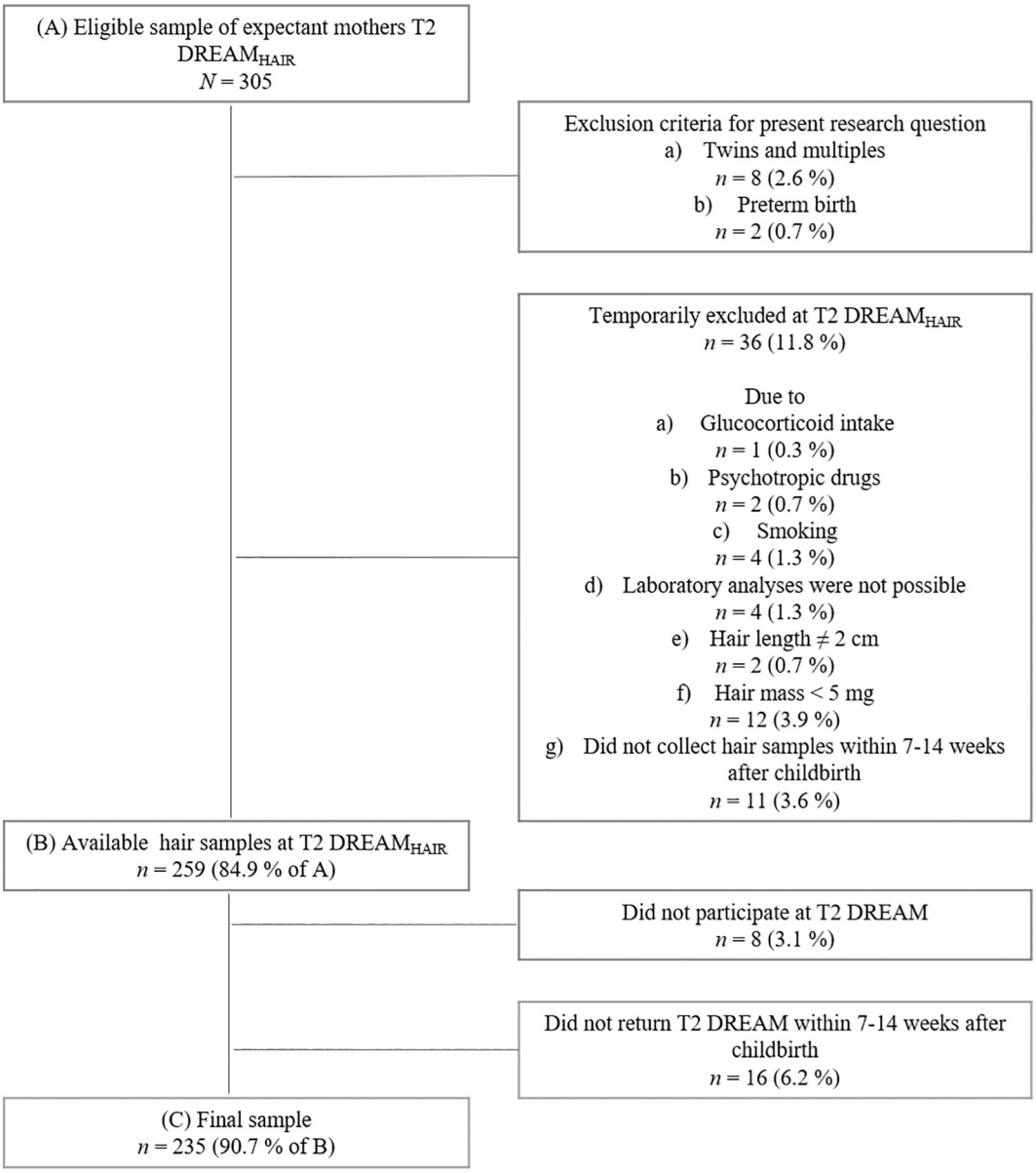

Fig. 1. Flowchart of retention rate and exclusion criteria. The present sample includes data collected until January 31st of 2022 (version 9 of the quality-assured data files, prospective data collection ongoing collection). T2 DREAM and T2 $DREAM_{HAIR}$ = 8 weeks after anticipated birth date.

more positive subjective birth experience. Internal consistency was excellent (α = .92).

Depressive symptoms during the past week were assessed using the Edinburgh Postnatal Depression Scale (EPDS; Bergant et al., 2008; Cox et al., 1987; Weigl and Garthus-Niegel, 2021). The EPDS is a reliable self-report questionnaire containing ten items with response categories that range from 0 to 3 (total score: 0–30). Higher total scores indicate higher symptom severity (Cox et al., 1987). Based on consistent previous findings showing the substantial predictive value of depression during pregnancy for PPD (Hutchens and Kearney, 2020), prepartum depressive symptoms assessed at T1 DREAM during pregnancy were controlled for as a confounding variable for analyses with PPD symptoms as the outcome variable. EPDS scores demonstrated good internal consistency at T1 DREAM (α = .84) and an acceptable internal consistency at T2 DREAM (α = .76).

Number of lifetime traumatic events was assessed at T1 $DREAM_{HAIR}$ using the Trauma Checklist of the Posttraumatic Diagnostic Scale (PDS; Foa et al., 1997) and investigated as a control variable that can influence hair GCs and PPD symptoms. Participants were asked to indicate whether they had experienced any of 12 listed traumatic events (e.g., accident, violent or sexual attack), including an "other" open category for additional events. Number of lifetime traumatic events was calculated by adding up the number of previous traumatic events, with possible scores ranging from 0 to 12.

Hair GCs were assessed in participants' scalp-near 2-cm hair strands taken from a posterior vertex position. With a hair growth rate of approximately 1 cm/month and steroids cumulating into growing hair (Stalder et al., 2017; Wennig, 2000), hair GCs at T2 $DREAM_{HAIR}$ in this proximal segment are assumed to represent integrated hormone levels from delivery up to two months postpartum. The samples were stored in aluminum foil in a dry and dark place at room temperature until they were sent to the Institute of Biological Psychology at the Technische Universität Dresden, in four batches. Laboratory analyses were performed via liquid chromatography-tandem mass spectrometry (LCMS/MS) to quantify HairF and HairE following a validated protocol (Gao et al., 2013).

Potential confounders for the association between birth experience and hair GCs pertained to hair-related characteristics (hair washing frequency, hair treatment, time point of hair sampling after childbirth) and health and lifestyle-related questions (sunlight exposure, and use of oral contraceptives). Relevant variables were considered based on meta-analytic research (Stalder et al., 2017) and obtained from an in-house hair protocol at T2 $DREAM_{HAIR}$ (Stalder et al., 2014). Maternal age and BMI were measured at T2 DREAM. We also included storage time and batch effects as possible confounders.

2.3. Statistical analyses

All analyses were conducted with IBM SPSS Statistics 28 (IBM Corp, 2021). Mean values replaced missing items if participants filled in at least 80 % of the items from psychometric scales. If complete scales were missing, SPSS used pairwise deletion by default. As HairF and HairE lacked normality, GC data were log-transformed to reduce biased results (Miller and Plessow, 2013). Log-transformation of HairF and HairE reduced skewness and kurtosis, however data did not satisfy normality. The HairF/HairE ratio was calculated by dividing the logarithmized HairE by the logarithmized HairF. Univariate outliers in hair GCs (3 SD ± mean) were excluded from further analyses, resulting in the following final samples: Hair*F*: $n = 232$; Hair*E*: $n = 230$; HairF/HairE ratio: $n = 224$.

We conducted descriptive analyses for sociodemographic characteristics and primary study variables. None of the primary variables (i.e., objective and subjective birth experience, GC concentrations, number of lifetime traumatic events, prepartum and PPD symptoms) were normally distributed. Therefore, Spearman rank correlations were performed firstly to analyze associations between primary study variables and subsequently to identify significant confounders on HairF, HairE, and their ratio. Analyses to identify confounders of hair GC levels showed that the following variables correlated significantly: hair treatment with all hair GCs, storage time and time point of hair sampling with HairF and HairE, and hair washing frequency with HairE (p's $< .05$, r's $< |-.17|$). All statistically significantly associated confounders were included in the hierarchical regressions with the respective GC as the outcome variable.

As data collection took place before and during the COVID-19 pandemic, we accounted for possible pandemic-related effects on hair GCs (Jia et al., 2023) and mental health (Gloster et al., 2020; Wall and Dempsey, 2023). Participants were grouped in two categories relating to the date of completion of T2 (cut-off date March 9th, 2020), i.e., the date when participants reported the outcome variable. We conducted hierarchical regression analyses with batch effects coded as dummy variables in Model 1 and COVID-19 pandemic exposure in Model 2 to predict hair GC concentrations. A potential association between COVID-19 pandemic exposure and PPD symptoms was tested via Spearman rank correlation analysis. Results revealed that batch effects were significantly associated with all hair GCs and were included in the primary analyses described below. COVID-19 pandemic exposure affected neither GC concentrations nor PPD symptoms and was therefore not included in regression analyses (see Supplements 1 for full analyses).

Thereupon, hierarchical regression analyses were conducted: 1) After controlling for relevant hair confounding variables and number of lifetime traumatic events, the effect of objective birth experience and then subjective birth experience on HairF, HairE, and the HairF/HairE ratio, respectively was investigated. 2) We also investigated the effect of objective and subjective birth experience on PPD symptoms controlling for prepartum depressive symptoms and number of lifetime traumatic events. 3) Each hair GC was investigated as predictor for PPD symptoms while controlling for prepartum depressive symptoms and number of lifetime traumatic events. 4) Finally, SPSS modelling tool PROCESS was used to test in an exploratory way whether GCs mediate the relationship between birth experience and PPD symptoms (Hayes, 2018). After identifying multivariate outliers for hierarchical regressions and mediation analyses using Mahalanobis distance (Yan et al., 2018), sensitivity analyses for the influence of possible multivariate outliers were performed. We detected two multivariate outliers for all regression analyses in which objective and subjective experience were included as predictors. The first participant reported a negative objective birth experience above average (six childbirth complications), the second the highest possible score for subjective birth experience (SIL = 120). Analyses are reported excluding these outliers.

3. Results

3.1. Sample characteristics

The present sample's demographic, psychophysiological, and hair-related characteristics are summarized in Table 1. Most participants of this investigation reported a relatively high educational level compared to the overall German population. Regarding the objective birth experience, 23.8 % of participants reported zero complications during childbirth, around one third (32.8 %) of women experienced one complication, almost one quarter (24.3 %) of participants reported two birth complications, and 19.1 % reported having three or more birth complications. Furthermore, 71.9 % of women recounted a positive subjective birth experience (SIL ≥ 70). Regarding EPDS scores during pregnancy, 9.8 % women reported scores ranging between 10 and 12, i.e., suspected minor depression, and 6.4 % of scores were above the recommended cut-off ≥ 13 for major depression (Bergant et al., 2008; Cox et al., 1987). At eight weeks postpartum, 5.5 % of mothers met the cut-off for minor depression, and 3.4 % for major depression.

As expected for LC-based methods, absolute hair GC values were relatively low compared to immunoassay protocols (Stalder et al.,

Table 1
Sample characteristics (n[a] = 235).

Variables	n (%) or Mean ± *SD* (Range)
Demographic variables	
Age (*M*, *SD*, Range)[b]	30.66 ± 3.91 (22–42)
Mother tongue German (*n*, %)[b]	221 (94.0)
University degree (*n*, %)[b]	153 (65.1)
Marital status, (*n*, %)[b]	
Married	110 (46.8)
Unmarried	118 (50.2)
Divorced	6 (2.6)
Primiparous (*n*, %)[b]	196 (83.4)
Body Mass Index (kg/m^2; *M*, *SD*, Range)[c]	24.81 ± 4.14 (16.9–41.2)
Psychophysiological variables	
Index objective birth experience (*M*, *SD*, Range)[c]	1.44 ± 1.18 (0–6)
Subjective birth experience (SIL; *M*, *SD*, Range)[c]	80.93 ± 21.14 (20–120)
Prepartum depressive symptoms (EPDS; *M*, *SD*, Range)[b]	5.30 ± 4.07 (0–19)
Postpartum depressive symptoms (EPDS; *M*, *SD*, Range)[c]	5.05 ± 3.44 (0–17)
Number of prior potentially traumatic events (PDS; *M*, *SD*, Range)[d]	0.76 ± 1.01 (0–5)
Hair-related variables	
Time point of hair sampling (weeks after birth; *M*, *SD*, Range)[e]	8.36 ± 1.03 (7–14)
Hair washing (per week; *M*, *SD*, Range)[e]	2.74 ± 1.15 (0.25–7)
Hair treatment (*n*, %)[e]	47 (20.3)
Storage time (in weeks; *M*, *SD*, Range)[e]	39.85 ± 14.40 (10–72)
Raw glucocorticoid concentrations in hair[e]	
HairF (pg/mg; *M*, *SD*, *Mdn*, Range)	10.07 ± 10.70, 6.81 (0.73–79.09)
HairE (pg/mg; *M*, *SD*, *Mdn*, Range)	22.31 ± 16.40, 18.33 (2.93–136.96)
HairF/HairE ratio (pg/mg; *M*, *SD*, *Mdn*, Range)	0.43 ± 0.25, 0.37 (0.12–2.07)

Note. SIL = Salmon's Item List; EPDS = Edinburgh Postnatal Depression Scale; PDS = Trauma Checklist of the Posttraumatic Diagnostic Scale; HairF = hair cortisol concentrations; HairE = hair cortisone concentrations.
[a] Total *n* varies slightly due to missing values and exclusion of cases with outliers in hair GCs.
[b] T1 DREAM (*M* = 27.14 pregnancy week).
[c] T2 DREAM (*M* = 8.45 weeks after birth date).
[d] T1 DREAM$_{HAIR}$ (*M* = 36.96 pregnancy week).
[e] T2 DREAM$_{HAIR}$ (*M* = 8.36 weeks after birth date).

2017). The existence of inter-laboratory differences poses a challenge to the establishment of normative GC data. However, HairF and HairE in the present sample are comparable to those reported in earlier studies in white female samples during the postpartum period (e.g., King et al., 2022; Lang et al., 2021).

3.2. Baseline associations and confounding variables

Spearman rank correlations between primary study variables are shown in Table 2. The objective and subjective birth experience were significantly correlated, indicating that a higher number of birth complications was linked to lower SIL scores (i.e., a more negative subjective birth experience). A more negative subjective but not objective birth experience was linked to higher levels of PPD symptoms. HairF and HairE did not correlate with either the objective or subjective birth experience, or PPD symptoms. A higher HairF/HairE ratio was not linked to the objective birth experience but significantly correlated with a more negative subjective birth experience and higher levels of PPD symptoms.

Table 2
Spearman rank correlations between primary study variables[a] (*n* = 235[b]).

Variable	1	2	3	4	5	6	7	8
1. Postpartum depressive symptoms (EPDS)	–	.02 [−.10, 16]	−.23** [−.34, −.11]	.50** [.40, .59]	.16* [.03, .29]	.10 [−.02, .22]	.03 [−.10, .16]	.14* [.01, .25]
2. Index objective birth experience		–	−.43** [−.53, −.32]	−.05 [−.18, .08]	.00 [−.13, .13]	.05 [−.10, .18]	−.06 [−.20, .07]	.12 [−.01, .24]
3. Subjective birth experience (SIL)			–	−.10 [−.22, .03]	−.05 [−.19, .10]	−.08 [−.22, .07]	−.02 [−.16, .13]	.16* [−.29, −.01]
4. Prepartum depressive symptoms (EPDS)				–	.11 [−.03, .23]	. 02 [−11, .15]	.04 [−.09, .18]	−.02 [−.15, .12]
5. Number of lifetime traumatic events (PDS)					–	.06 [−.07, .20]	06 [−.07, .19]	01 [−.13, .14]
6. HairF						–	.75** [.66, .81]	87** [.81, .91]
7. HairE							–	.42** [.29, .55]
8. HairF/HairE ratio								–

Note. EPDS = Edinburgh Postnatal Depression Scale; SIL = Salmon's Items List; PDS = Trauma Checklist of the Posttraumatic Diagnostic Scale; HairF = hair cortisol concentrations; HairE = hair cortisone concentrations.
*$p < .05$. ** $p < .001$.
[a] Values in brackets show BCa CI 95 % confidence interval for each correlation. Bootstrap results are based on 2000 bootstrap iterations. Two-tailed testing.
[b] *n* varies slightly due to missing data and excluding outliers in hair GCs. The sample ranges from *n* = 224 to *n* = 235.

Table 3
Hierarchical regression analysis predicting the HairF/HairE ratio ($n = 214$)[a]

Model	Predictor	*SEB*[b]	β	*p*[b]	R^2 *adj.*
1[c]	Hair treatment	.03	−.22	<.001	.11
	Batch 2 vs. Batch 1	.03	−.30	<.001	
	Batch 3 vs. Batch 1	.03	−.19	.01	
	Number of lifetime traumatic events (PDS)	.01	−.07	.32	
2[d]	Hair treatment	.03	−.24	<.001	.15
	Batch 2 vs. Batch 1	.03	−.31	<.001	
	Batch 3 vs. Batch 1	.03	−.22	.00	
	Number of lifetime traumatic events (PDS)	.01	−.07	.31	
	Index objective birth experience	.01	.19	.00	
3[e]	Hair treatment	.03	−.24	<.001	.15
	Batch 2 vs. Batch 1	.03	−.31	<.001	
	Batch 3 vs. Batch 1	.03	−.22	.00	
	Number of lifetime traumatic events (PDS)	.01	−.07	.30	
	Index objective birth experience	.01	.14	.04	
	Subjective birth experience (SIL)	.00	−.11	.13	

Note. HairF/HairE ratio = Ratio hair cortisol concentrations – hair cortisone concentrations; PDS = Trauma Checklist of the Posttraumatic Diagnostic Scale, SIL = Salmon's Item List.

[a] Results are reported excluding one multivariate outlier that reported six childbirth complications.

[b] based on 95 % bias corrected and accelerated bootstrap confidence interval (2000 iterations).

[c] $F(4, 210) = 7.83$, $p < .001$.

[d] $F(5, 209) = 8.35$, $p < .001$.

[e] $F(6, 208) = 7.39$, $p < .001$. When including the multivariate outliers in the hierarchical regression analyses, the effect of objective birth experience on HairF/HairE ratio was no longer significant in Model 3.

3.3. Regression and mediation analyses

3.3.1. Objective and subjective birth experience as predictors of 2-month postpartum hair GCs

Hierarchical multiple regression analyses predicting HairF and HairE revealed that, after controlling for relevant hair confounders (Model 1), the standardized coefficients of objective birth experience (Model 2) and subjective birth experience (Model 3) failed statistical significance (p's > .77).

Analyses with HairF/HairE ratio as the outcome variable are shown in Table 3. After controlling for relevant confounders in Model 1, objective birth experience emerged as a significant predictor (β = .19, $p = .003$; Model 2), indicating that a higher number of birth complications was linked to a higher HairF/HairE ratio. Including subjective birth experience did not account for a significant increase in explained variance ($\Delta R^2 = .00$; Model 3) and the predictor itself failed significance.

3.3.2. Objective and subjective birth experience as predictors of PPD symptoms

Next, we investigated the role of objective and subjective birth experience on PPD symptoms. Objective birth experience was not significantly related to EPDS scores in Model 1, however adding subjective birth experience as a predictor accounted for a significant increase in explained variance ($F(2,223) = 5.25$, $p < .01$; $\Delta R^2 = .05$; Model 2), and the predictor itself was statistically significant (β = -.24, $p = .001$), indicating that a more negative subjective birth experience was associated with higher levels of PPD symptoms. This association remained significant even after controlling for prepartum depressive symptoms and number of lifetime traumatic events ($F(4,221) = 19.35$, $p < .001$; Model 3).

3.3.3. Hair GCs as predictors of PPD symptoms

Further, we investigated the predictive value of GCs integrated in the 2-month period after childbirth on PPD symptoms. Neither HairF nor HairE significantly predicted EPDS scores eight weeks after childbirth. Similarly, Model 1 with the HairF/HairE ratio as a predictor of PPD symptoms revealed no significant results. However, after controlling for prepartum depressive symptoms and number of lifetime traumatic events, the HairF/HairE ratio significantly predicted PPD symptoms (β = .13, $p = .03$) indicating that a higher ratio is associated with higher levels of depressive symptoms eight weeks after childbirth ($F(3,217) = 23.25$, $p < .001$; Model 2).

3.3.4. Exploratory analyses

Mediation analyses with PROCESS Model 4 were conducted to test whether hair GCs levels in the 2-month postpartum period mediate the effect between objective or subjective birth experience and PPD symptoms, controlling for relevant hair confounders and prepartum depressive symptoms. None of the models indicated significant indirect effects (see Supplements 2 for results).

4. Discussion

The present study aimed to test the role of both objective and subjective birth experience as potential predictors of maternal 2-month integrated HairF, HairE, the HairF/HairE ratio, and PPD symptoms. A negative objective birth experience significantly predicted a higher HairF/HairE ratio, however not the absolute concentrations in HairF nor HairE. Taking subjective birth experience into account did not contribute to an additional explanation of variance in hair GCs. Furthermore, a negative subjective birth experience and a higher HairF/HairE ratio predicted PPD symptoms eight weeks after childbirth when controlling for prepartum depressive symptoms and number of lifetime traumatic events.

Our findings provide evidence for the predictive role of a negative objective birth experience for a higher HairF/HairE ratio after controlling for relevant confounders. Considering that a higher HairF/HairE ratio is an indirect marker of lower enzymatic activity of 11β-HSD2 (Zhang et al., 2013), our results suggest that stressful intrapartum events might be linked to a lower 11ß-HDS2 activity. Number of lifetime traumatic events was not linked to the 2-month integrated HairF/HairE ratio, however it is conceivable that more recent stress, measured in this study as the number of childbirth complications, leads to epigenetic changes in CpG sites within the promoter region of the 11ß-HSD2 gene, which in turn results in a lower concentration of 11β-HSD2 and therefore an altered GC metabolism (Jensen Peña et al., 2012).

On the other hand, we did not find an association between objective birth experience and HairF or HairE contrasting with studies using traditional cortisol measures showing a link between childbirth complications and altered cortisol levels (Benfield et al., 2014; Miller et al., 2019). Yet research outside the peripartum context reveals increased HairF in samples with ongoing chronic stress but not in conditions with

past stress or recent adversity (such as physical abuse) (Oresta et al., 2021; Stalder et al., 2017). In reconciling these findings, it is conceivable that medical childbirth complications affect acute GC hormone secretion but not long-term systemic cortisol or cortisone levels.

We postulated that subjective birth experience would be associated with hair GCs. Subjective birth experience did not predict HairF or HairE but correlation analyses revealed a link to a higher HairF/HairE ratio. However, this association disappeared after controlling for relevant confounders, showing that subjective birth experience did not explain additional variance beyond objective birth experience. It is possible that the variance of objective and subjective birth experience overlapped, given that both measures were significantly moderately correlated. Recall bias, social desirability, or individual heterogeneity in emotional introspection may explain the lack of covariance between psychological and endocrine assessments (Stalder et al., 2017).

The second aim of the present investigation was to replicate previous findings on the association between birth experience and PPD symptoms. The objective birth experience did not predict PPD symptoms eight weeks after childbirth. Other studies investigating isolated complications have found that PPD is linked to cesarean section (Zhao and Zhang, 2020), moderate to severe lacerations (Dunn et al., 2015), placental insufficiency, hemorrhages, prolapse, and umbilical cord pressing the infant's neck (Mathisen et al., 2013). While previous studies have mainly investigated isolated complications, we measured objective birth experience as an index of cumulative delivery complications concerning the mother and the infant. This index may have been limited in its ability to accurately capture a negative objective birth experience, as the variable's category widths may not represent equal increments (e.g., experiencing labial tear might contribute more to physical stress compared to the infant lying in breech position). Furthermore, some complications are not independent of each other (e.g., placental abruption can lead to the infant not getting sufficient oxygen and, therefore, a lower Apgar score; Su et al., 2021), whereas others might be mutually exclusive (e.g., if a woman undergoes a cesarean section, it is improbable that she will report perineal tear). However, we believe that our index depicts the complexity of a negative objective birth experience by considering several medical complications. Considering that 80.9 % of women in our sample reported having two or fewer birth complications, the limited variance regarding objective birth experience might have reduced the power to detect significant effects, irrespective of the limitations in assessing the objective birth experience.

On the other hand, consistent with our hypothesis, subjective birth experience predicted PPD symptoms. Therefore, we replicated previous research showing that women satisfied with their birth experience have a lower risk of developing PPD (McKelvin et al., 2021). The effects remained significant after controlling for prepartum depressive symptoms and number of lifetime traumatic events. These results highlight the importance of interventions that aim to increase women's satisfaction with their birth experience. Medical staff and others present at birth may have limited control over childbirth complications but can promote a respectful, safe environment by including women in the decision-making process, listening to their needs, and providing clear communication in order to increase birth satisfaction and therefore women's long-term mental health (Bell and Andersson, 2016; Winter et al., 2022).

The third aim of this study was to test whether 2-month integrated hair GC levels predict PPD symptoms eight weeks after childbirth. We found that a higher HairF/HairE ratio, which is assumed to reflect a lower 11ß-HSD2 enzymatic activity (Zhang et al., 2013), significantly predicted higher levels of PPD symptoms after controlling for prepartum depressive symptoms and number of lifetime traumatic events. The downregulation of 11ß-HSD2 may increase cortisol levels in different organs and tissues, leading to several pathologies (Jensen Peña et al., 2012; Zhou et al., 2017) . For example, lower urine 11ß-HSD2 levels have been found in depressed patients and alterations persist even after antidepressant treatment (Römer et al., 2009). Similarly, adverse events during pregnancy may lead to reduced activity of placental 11ß-HSD2 (Jensen Peña et al., 2012), associated with prenatal depressive and anxiety symptoms (Seth et al., 2016). In line with previous research, we found higher HairE compared to HairF (Raul et al., 2004), which might indicate that 11ß-HSD2 locally metabolizes a portion of systemic cortisol into cortisone and in turn, the converted cortisone is incorporated into hair together with systemic cortisone concentrations. However, it remains unclear whether the HairF/HairE ratio reflects systemic 11ß-HSD2 activity in other relevant areas outside the hair follicles. Therefore, further methodological research is required to elucidate the underlying processes behind the HairF/HairE ratio and how these psychobiological systems are implicated in PPD.

Contrary to our hypothesis, HairF and HairE were not associated with the postpartum EPDS score. This result opposes previous research demonstrating that hair GCs are altered in participants with PPD symptoms (Caparros-Gonzalez et al., 2017; Jahangard et al., 2019). However, some studies using self-report measures usually find that HairF or HairE are weak or non-significant at predicting PPD symptoms (Braig et al., 2017; Lang et al., 2021), whereas the effects seem to be more robust for a diagnosed depressive disorder, implying that altered cortisol levels may be evident in the context of more severe symptomatology (Bryson et al., 2021; O'Connor et al., 2014). Considering that participants in the present sample reported relatively low levels of PPD symptoms, future research may benefit from investigating a more heterogeneous sample regarding mental health including a higher amount of diagnostic relevant depressive symptoms.

Finally, we tested in an exploratory way whether hair GC levels mediate the relationship between birth experience and PPD. Analyses did not indicate a mediating role of long-term GC hair concentrations between birth experience and PPD symptoms. Prospective studies are needed to investigate whether negative birth experiences impact other endocrinological parameters and whether those alterations might be relevant for depressive symptoms. Specifically, the longitudinal multimethod study DREAM offers the opportunity to broaden research and investigate the possible mediating and moderating role of several long-term stress-associated biomarkers (i.e., hair GCs, progesterone, and endocannabinoids) on birth experiences and mental health of mothers, partners, and their children (e.g., Kress et al., 2021; Steudte-Schmiedgen et al., 2023).

Primary strengths of this investigation include our considerably large sample size, the use of objective and subjective measures to characterize the complexity of the birth experience, and the use of non-invasive GC measures analyzed by LC-MS/MS, a current gold standard approach for the quantification of hair steroids (Gao et al., 2013; Keevil, 2016). The assessment of hair GCs circumvents substantial variability and otherwise difficult to interpret results that may arise in traditional GC measures due to acute changes in steroid hormone circulation. Further, the assessment of a robust GC index by simultaneously investigating HairF, HairE, and the HairF/HairE ratio distinguishes our study from others in the field of birth experiences and PPD. Following empirical recommendations, we included hair-related variables, as well as number of lifetime traumatic events and prepartum depressive symptoms as possible confounders that could affect GC concentrations or PPD symptoms (Abell et al., 2016; Martini et al., 2022; Stalder et al., 2017; Steudte-Schmiedgen et al., 2016).

Notwithstanding, the current study presents some limitations. Our analyses were based on a relatively homogeneous community sample, characterized by primarily primiparas with high education and income. Furthermore, the subjective birth experience was assessed retrospectively at eight weeks after childbirth, making this measure prone to recall bias. Although the main variables included in the current study (e.g., childbirth, hair GCs cumulating into growing hair, and perceived PPD symptoms several weeks after childbirth) occur consecutively, all data were collected at one point in time, limiting therefore the determination of temporal associations between birth experience and PPD. Women reported, in general, having positive birth experiences and low levels of depressive symptoms. Thus, the results should be applied to the broader

population with caution. It would be valuable to include populations with more variability regarding birth experiences and PPD symptoms in the future.

5. Conclusion

In the present study, objective birth experience significantly predicted a higher HairF/HairE ratio but was not associated with absolute levels of HairF or HairE. The subjective birth experience did not contribute to an additional explanation of the variance of hair GCs but was linked to PPD symptoms eight weeks after childbirth. Further, a higher HairF/HairE ratio predicted PPD symptoms after controlling for prepartum depressive symptoms and number of lifetime traumatic events. Our results suggest that birth complications may play a less critical role in developing PPD symptoms but are associated with an altered GC metabolism postpartum. Hence, future research should devote attention to the objective birth experience and its possible physiological and psychological impact. We also showed that subjective birth experiences might be less critical for long-term endocrine correlates, but they remain an essential risk factor for PPD. Thus, we emphasize supporting women's right to experience a positive birth, which is pivotal for their long-term mental health (Nakić Radoš et al., 2022; Webb et al., 2021) including bonding (Junge-Hoffmeister et al., 2022; Seefeld et al., 2022). Our study adds knowledge to the discussion about the predictive role of GCs on PPD symptoms as we tested the applicability of these markers to a community sample. We showed that total HairF and HairE might not predict PPD symptoms. However, alterations in their ratio may reflect differential metabolic pathways in women with higher levels of PPD symptoms. Future research should explore the potential of the HairF/HairE ratio as a biomarker to identify women at risk for developing PPD and evaluate its use for prevention purposes.

CRediT authorship contribution statement

SG-N, SSc, and IJ conceived the research question. IJ undertook the statistical analyses and manuscript draft under supervision of SG-N, SSc, LB, and MK. VW, JM, LB, and MK supported the conduction of the study through data collection and preparation for statistical analyses. SG-N acquired the funding, was responsible for the conception and design of DREAM with its sub-studies as well as for the coordination and supervision of the data collection and the ongoing cohort study. KW and WG provided resources for the acquisition of data in the $DREAM_{HAIR}$ study. All authors contributed to manuscript revision, read, and approved the submitted version.

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Declaration of competing interest

None.

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Data were collected and managed using Research Electronic Data Capture (Harris et al., 2009, 2019). REDCap is a secure, web-based application designed to support data capture for research studies, hosted at the “Koordinierungszentrum für Klinische Studien” at the Faculty of Medicine of the Technische Universität Dresden, Germany.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jad.2023.07.034.

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