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Impact of perinatal asphyxia on parental mental health and bonding with the infant

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What is already known on this topic

- Perinatal asphyxia is a life threatening event, potentially psychologically traumatic for parents.
- Parental mental health problems may impact on bonding with and development of the child.
- Research examining posttraumatic stress disorder, psychological distress, and bonding with their infant in parents of infants born with perinatal asphyxia is lacking.

What this study adds

- More frequent PTSD symptoms in both parents and poorer bonding with the infant in mothers after perinatal asphyxia were found compared to control parents.
- Parents of infants hospitalized for perinatal asphyxia are more at risk of developing PTSD than control parents.

Abstract

Objective: (1) To compare current symptoms of posttraumatic stress disorder (PTSD), psychological distress, and bonding with the infant in parents who had an infant with perinatal asphyxia in the last two years with parents who had a healthy baby; (2) To investigate which sociodemographic, obstetric, and neonatal variables correlated with mental health symptoms and infant bonding.

Design: Cross-sectional Swiss national cohort study

Setting: Data from Swiss national Asphyxia and Cooling register

Participants: Parents of infants surviving perinatal asphyxia born in 2012 and 2013 and parents of healthy infants born during the same time period

Main outcome measures: Posttraumatic Diagnostic Scale, Hospital Anxiety and Depression Scale, Mother-to-Infant Bonding Scale

Results: Compared with the control group, mothers (U=2291.0, z=-3.14) and fathers (U=892.0, z=-1.77) in the asphyxia group had a higher frequency of PTSD symptoms. Mothers in the asphyxia group reported poorer bonding with the infant (U=2508.5, z=-1.72). In mothers of the asphyxia group, having a trauma in the past was linked to more psychological distress (r=0.31 [95%-CI: 0.04-0.54]) and having a previous pregnancy was linked to poorer bonding (r=0.41 [95%-CI: 0.13-0.63]). In fathers of the asphyxia group, therapeutic hypothermia of the infant was related to less frequent PTSD symptoms (r=-0.37 [95%-CI:-0.61- -0.06]). Past psychological difficulties (r=0.37 [95%-CI: 0.07-0.60]) and past trauma (r=0.35 [95%-CI: 0.05-0.59]) were positively correlated with general psychological distress, and a lower Apgar score was linked to poorer bonding (r=-0.38 [95%-CI:-0.64--0.05]).

Conclusions: Parents of infants hospitalized for perinatal asphyxia are more at risk of developing PTSD than control parents.

Keywords: asphyxia, posttraumatic stress disorder, mother, mental health, bonding

Perinatal asphyxia is a life threatening event affecting 2/1000 infants, which qualifies as a psychologically traumatic stressor for parents[1]. When associated with hypoxic ischemic encephalopathy (HIE), it may lead to disabling brain injuries or death[2-4]. Current treatment of HIE requires immediate transfer to a specialized neonatal unit and therapeutic hypothermia in order to reduce the risk of brain lesions and neurodevelopmental disabilities[5].

Parents of critically ill or premature infants admitted to a neonatal intensive care unit report more stress[6], more adjustment difficulties, and need for support during the first year after delivery[7, 8] compared to parents of healthy infants. They may experience posttraumatic stress disorder (PTSD) [9-11], anxiety, and depression following the birth[12].

Although two qualitative studies described the experiences of becoming a parent after perinatal asphyxia[13, 14] and another showed that fathers may be traumatized[15], PTSD symptoms or psychological distress have not been measured in parents of these children. PTSD consists of four symptom clusters (re-experiencing, avoidance, hyperarousal, and negative cognitions and mood) and is diagnosable 1 month post-trauma[1]. Assessing postnatal PTSD and psychological distress is not only important for the well-being of parents, but PTSD may also significantly interfere with infant bonding, leading to severe and long-term consequences for the development of the baby[16-18].

The current study aimed to compare current symptoms of PTSD, psychological distress, and infant bonding in parents who had an infant with perinatal asphyxia in the last two years with control parents. It was predicted that parents of the asphyxia group would report more PTSD and psychological distress symptoms and less infant bonding than controls. Another objective was to investigate which sociodemographic, psychological, obstetric, and neonatal variables were correlated with mental health symptoms and infant bonding in both groups.

Methods

Study design and sample

This cross-sectional Swiss national cohort study included infants surviving perinatal asphyxia (asphyxia group, AG) born in 2012 and 2013, registered in the national Asphyxia and Cooling register of the Swiss Neonatal Network & Follow-up Group. Parents were sent an invitation letter, a participant information sheet, and the questionnaires in French, German or English, with a pre-stamped envelope.

Parents of the control group (CG) were recruited via flyers in public places, on Swiss internet forums for parents, and on a website of the University of Lausanne. They were eligible if they had given birth to a healthy infant in 2012 or 2013. When accessing the online questionnaire, participants first read the information sheet; informed consent was implied when they completed the anonymous questionnaire in French, German or English.

This study was approved by the cantonal ethical review board (Vaud) and by the Swiss Federal Commission for Privacy Protection in Medical Research.

Measures

Parental PTSD was measured using the 17-item Posttraumatic Diagnostic Scale (PDS)[19-21]. It provides both a diagnosis according to DSM-IV criteria and a measure of PTSD symptom severity[22, 23], and has been widely used in postnatal populations (e.g.[24]). Participants rated how often they experienced each of the symptoms in the past month, using a 4-point frequency scale

ranging from 0 (*not at all or only one time*) to 3 (*5 times per week or almost always*). A *partial* PTSD symptoms diagnosis was defined as meeting the criteria for two of the three PTSD symptom clusters[24]. The PDS has good psychometric properties[19, 20]. Cronbach's alpha of the total PDS frequency score (α=.90), and of the three sub-scales (re-experiencing: α=.85; avoidance: α=.75; hyperarousal: α=.80) was good to excellent.

General psychological distress of parents in the past week was assessed with the Hospital Anxiety and Depression Scale (HADS)[25-27], a 14-item questionnaire. Each item is scored from 0 to 3, with higher scores indicating greater psychological distress[28]. The HADS has good psychometric properties[26], with a Cronbach's alpha of α=.81 in the current study.

The Mother-to-Infant Bonding Scale (MIBS)[29] consists of eight adjectives that describe feelings towards their baby (loving, resentful, neutral or felt nothing, joyful, dislike, protective, disappointed and aggressive) and measures infant bonding. Each adjective is followed by a 4-point scale ranging from 0 (*very much*) to 3 (*not at all*). When the adjective reflects a negative emotional response, the scoring is reversed. Possible scores range between 0 and 24, with high scores indicating problematic bonding[30, 31]. Cronbach's alpha was fair, α=.77.

Parents also completed a demographic questionnaire (age, marital status, migrant status, educational background for mothers, occupation for fathers, previous pregnancy for mothers) with two items assessing whether they had experienced past or current psychological difficulties, and whether they had experienced a past traumatic event. Parental socioeconomic status was determined using the Largo score, a 6-point scale, with recorded mother's education (*1=university and 6=special or no schooling*) and father's occupation (*1=leading position and 6=unskilled labor*)[32]. Parents also reported demographic details related to their infant (gender,

gestational age, birth weight, current age of infant). Neonatal variables were obtained from the national asphyxia register: Apgar score (at 1, 5, and 10 minutes), umbilical cord pH, number of days when full sucking was achieved, whether infant was resuscitated >10 minutes, Sarnat stage [33], whether therapeutic hypothermia had occurred, whether the neurological examination at discharge had been normal, and whether any seizure had occurred.

Statistical analyses

Data were analyzed using IBM SPSS version 22. Descriptive statistics were calculated for each scale. Responders and non-responders within the AG were compared regarding obstetric and neonatal variables using chi-squared tests and independent samples *t*-tests. To compare AG and CG regarding the central tendencies of the non-normal distributed mental health and bonding outcomes (PDS, HADS, MIBS), rank based Mann-Whitney U-tests were performed. Bivariate correlation analyses (Pearson and point-biserial correlations) between sociodemographic, obstetric, and neonatal variables and mental health or infant bonding were carried out. Prior to assessing the correlation, the non-normally distributed scores (PDS, HADS, MIBS, Largo, gestational age, and Apgar index 1 minute) were rank-based inverse normal (RIN) transformed within each gender using Blom's formula[34]. Given that the non-independence of mothers' and fathers' scores may lead to biased estimates[35], mothers and fathers were analysed separately. Within each gender, correlations were calculated separately for AG and CG.

The 95% confidence interval (95%-CI) for correlations and Cohen's *d* were calculated using the Exploratory Software for Confidence Intervals (ESCI)[36]. The effect sizes of frequencies analysed with a chi-squared test were expressed as the differences of the two

independent proportions and the corresponding 95%-CI was calculated using ESCI. The effect size for the Mann-Whitney statistic was estimated by $\hat{\theta}=U/mn$ (i.e., dividing U_1 for the asphyxia group by the product of both group sizes m and n)[37]. The limits of the asymptotic 95%-CI or 90%-CI of $\hat{\theta}=U/mn$ were calculated with the EXCEL macro GENERALISEDMW[38].

Results

Sample characteristics

For the AG, parents of 114 registered infants were contacted and 95 parents (52 mothers and 43 fathers) of 53 infants (47%) responded. The CG was composed of 134 mothers and 58 fathers. Missing data per variable ranged from 0 to 7 (mothers) and 0 to 13 (fathers). Missing data were not replaced. The comparison of responders and non-responders of the asphyxia population according to infant sociodemographic and neonatal variables listed in Tables 1 and 2 resulted in no significant differences (data not shown).

Regarding demographic variables, three significant group differences were found for mothers (see Table 1): AG mothers had a higher Largo score, $U(N=185)=2668.0$, $z=-2.56$, $p=.011$ ($\hat{\theta}=0.39$, 95%-CI: 0.31 to 0.48) and reported a lower frequency of previous pregnancies, $\chi^2(df=1)=18.55$, $p<.001$ (difference between proportions: -33.8%, 95%-CI: -48.0% to -17.8%) compared to controls. Furthermore, the current age of the infant was higher for AG mothers (18 vs. 14 months), $t(df=183)=3.44$, $p<.001$ ($d=0.56$, 95%-CI: 0.24 to 0.89). For fathers, corresponding significant differences were found for Largo score, $U(N=93)=657.5$, $z=-3.06$,

p=.002 ($\hat{\theta}$=0.32, 95%-CI: 0.22 to 0.44), and current age of the infant (18 vs. 14 months), $t(df=89)$ =3.66, p<.001 (d=0.77, 95%-CI: 0.34 to 1.20).

Mental health symptoms and infant bonding: group comparisons

As predicted, AG mothers reported a higher frequency of total PTSD symptoms than controls, U=2291.0, z=-3.14, $p_{1\text{-tailed}}$ <.001 (see Table 3 for descriptive values). This difference was due to a higher frequency of re-experiencing symptoms in AG mothers compared to controls, U=1600.0, z=-5.58, $p_{1\text{-tailed}}$<.001. Consistent with the latter finding, AG mothers were also more likely to have at least one re-experiencing symptom than controls, $\chi^2(1) = 25.21$; p <.001;V=.37 (difference in proportions: 41.7%, 90%-CI: 29.3% to 51.0%). In the AG, n=14 (28.0%) and n=14 (28.0%) mothers met criteria of either a partial or a full PTSD symptom diagnosis. In the CG, these were n=30 (22.4%) and n=22 (16.4%) respectively. The group difference was marginal, $\chi^2(2)$=4.88, p=.087. However, when group membership (high vs. low asphyxia-related stress) and PTSD symptom diagnosis (none, partial, full) were both treated as ordinal, both variables were significantly related, Kendalls' τ = -.16, p=.032, suggesting that AG mothers were more likely to receive a partial or full PTSD symptom diagnosis. As expected, AG mothers reported poorer bonding with the infant compared to controls, U=2508.5, z=-1.72, $p_{1\text{-tailed}}$ =.043 (see Table 3).

The predicted difference for total PTSD symptoms between AG and CG was also found in fathers, U=892.0, z=-1.77, $p_{1\text{-tailed}}$ =.038 (see Table 3). Fathers in the AG reported a higher frequency of re-experiencing symptoms compared to controls, U=612.0, z=-4.29, $p_{1\text{-tailed}}$ <.001 and were significantly more likely to report at least one re-experiencing symptom compared to

controls, $\chi^2(1)=13.16$, $p<.001$; $V=.37$ (difference in proportions: 37.2%, 90%-CI: 20.5% to 51.1%). In the AG , $n=10$ (24.39%) and $n=11$ (26.83%) fathers met criteria of a partial or a full PTSD symptom diagnosis compared to $n=13$ (22.41%) and $n=6$ (10.34%) controls. Again, the group difference was marginal, $\chi^2(2)=5.22$, $p=.074$, but when group membership and PTSD diagnosis were treated as ordinal, both variables were negatively related, Kendall's $\tau = -.20$, $p=.034$, suggesting that AG fathers were more likely to receive a PTSD symptom diagnosis. No other statistically significant group differences were found (all p=ns).

Associations between sociodemographic, psychological, obstetric, and neonatal variables with mental health symptoms and infant bonding

For mothers, two statically significant correlations were found in the AG and six significant correlations were observed in the CG (see Table 4a): in the AG, having a trauma in the past was linked to more psychological distress and having a previous pregnancy was linked to poorer infant bonding. The 95% confidence intervals for these correlations did not intersect suggesting that both correlations differed significantly (AG: $r=.41$, $p=.006$; CG: $r=-.11$, n.s.; $\Delta r=.51$, 95%-CI for Δr: .18 to .79). In the CG, higher Largo scores, past psychological difficulties, and past trauma were linked to more frequent PTSD symptoms. In addition, past psychological difficulties, past trauma, and younger gestational age (although all infants were born at term) were also related to more general psychological distress.

In fathers, four statistically significant correlations were found in the AG and two significant correlations in the CG (see Table 4b). In the AG, therapeutic hypothermia was related to less frequent PTSD symptoms. Past psychological difficulties and past trauma were positively correlated with current general psychological distress, and a lower Apgar score (10 minutes) was

linked to poorer infant bonding. In the CG, general psychological distress was not significantly related to any of the selected variables. In addition, lower current age of the infant and fathers' past trauma were linked to poorer infant bonding.

Discussion

This cross-sectional Swiss national cohort study comparing parents of infants surviving perinatal asphyxia with those of healthy infants found more frequent PTSD (and particularly re-experiencing) symptoms in parents and poorer bonding with the infant in mothers of infants born with asphyxia compared with controls. Results need to be considered with caution, as AG mothers had a lower socioeconomic status, a lower frequency of previous pregnancies, and slightly older infants compared to controls. Compared to control fathers, AG fathers had a lower socioeconomic status and older infants.

These results show for the first time that parents of infants with perinatal asphyxia experience elevated symptoms of PTSD, such as has been reported for other populations of high-risk parents, e.g., those of premature or critically ill infants[9-11]. The lack of differences between the asphyxia and control parents in relation to general psychological distress points to a generally healthy psychological adjustment of parents that might partly be due to a good experience of care regarding their infant and effective staff support.

When investigating potential risk factors for mental health problems in AG mothers, we found that having experienced a past trauma was associated with more general psychological distress. This is in line with research identifying a previous traumatic experience as a risk factor for developing PTSD following childbirth[39] and depression in the general adult population[40]. Our finding that having previously been pregnant was associated with more bonding problems is

novel. It may be that already being a parent makes it harder to invest oneself in a relationship with another child, particularly one that is severely ill. Alternatively, infants who had asphyxia at birth may be less effective in interactions with parents and parents may thus find it harder to bond with them. However, more research is needed to explore this. Given the small number of AG mothers, none of the weak correlations of the other neonatal variables were statistically significant but the small to medium sized effects might be detected with a more powerful design.

For AG fathers, therapeutic hypothermia of the infant was related to less frequent PTSD symptoms. This is a novel finding and might be linked to a certain level of reassurance that fathers feel when witnessing a highly technological treatment, thus reducing their perceived threat to their infant's life. Similar to mothers, past psychological difficulties and past trauma were positively correlated with current general psychological distress, which is in line with previous research in the general adult population[40]. Finally, a lower Apgar score (10 min) was associated with more bonding problems. This novel result may be explained by the fact that a lower Apgar score would have indicated a more severe life threat for the infant and fathers might have unintentionally found it harder to develop a bond with their infant for fear of losing it. However, this remains to be explored in future studies.

Strengths of the study are the inclusion of a national cohort, the comparison with a control group, and the use of standardised questionnaires. The response rate is comparable with other studies of high-risk populations[8] and regarded as fair, particularly given the tendency of traumatised parents to avoid reminders of the childbirth or hospital stay. Limitations of the study include the cross-sectional, retrospective design of the study, thus not allowing for causal conclusions and the risk of a reporting bias. The small sample size related to the low prevalence of perinatal asphyxia limited the statistical power, despite it being a national cohort study.

Caution needs to be taken in interpreting the results, given that both groups differed on sociodemographic characteristics. Future studies with a larger cohort, a prospective design, and a control group matched on important sociodemographic variables are needed.

Conclusion

This study found more frequent PTSD (and particularly re-experiencing) symptoms in AG parents and poorer infant bonding in AG mothers compared with the CG. Results show for the first time that AG parents are at risk for developing PTSD.

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Contributors

AH had primary responsibility for the study design, data acquisition, analysis, and writing of the manuscript, and approved the final manuscript as submitted. MBG was involved in the study design, data acquisition, and writing of the manuscript, and approved the final manuscript as

submitted. IJ was responsible for the statistical expertise, performed all final statistical analyses, contributed to the writing of the manuscript, and approved the final manuscript as submitted. CF and LG contributed to the data analysis, critically reviewed and revised the manuscript, and approved the final manuscript as submitted. JS and MMH contributed to the interpretation of data, critically reviewed and revised the manuscript and approved the final manuscript as submitted.

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Competing interests

None declared.

Patient consent

Obtained.

Ethics approval

This study was approved by the cantonal ethical review board (Vaud) and by the Swiss Federal Commission for Privacy Protection in Medical Research.

Provenance and peer review

Not commissioned: externally peer reviewed.

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Table 1: Sample characteristics, test coefficients, and effect size estimates for mothers and fathers

Characteristics	Mothers				Fathers			
	Asphyxia (*n*=52)	Control (*n*=134)	*t, U or* χ^2	*d,* $\hat{\theta}$ or *V*	Asphyxia (*n*=43)	Control (*n*=58)	*t, U or* χ^2	*d,* $\hat{\theta}$ or *V*
Parents								
Age (years)	32.02 ± 4.74	32.44 ± 4.27	-0.57	-0.09	35.12 ± 6.29	34.64 ± 4.53	0.42	0.09
Largo score	2 (1-5)	1 (1-5)	2668.0*	0.39	3 (1-6)	2 (1-4)	657.5**	0.32
Marital status (with partner)	48 (92%)	126 (94%)	0.18	0.03	42 (98%)	56 (97%)	0.11	0.03
Migrant status (yes)	16 (31%)	33 (25%)	0.73	0.06	14 (33%)	19 (33%)	0.00	0.00
Previous pregnancy (yes)	21 (42%)	100 (76%)	18.55***	0.32	-	-	-	-
History of psychological difficulties (yes)	19 (37%)	46 (34%)	0.08	0.02	9 (21%)	7 (12%)	1.59	0.13
Past trauma (yes)	27 (52%)	50 (37%)	3.30	0.13	15 (36%)	21 (36%)	0.00	0.01
Infants								
Gestational age (weeks)	40 (35-42)	40 (35-42)	3378.0	0.50	40 (35-42)	40 (37-46)	964.5	0.50
Birth weight (grams)	3381.25 ± 408.11	3396.53 ± 506.19	-0.19	-0.03	3426.05 ± 421.38	3307.55 ± 504.76	1.20	0.25
Age at survey (months)	18.16 ± 7.46	14.13 ± 7.04	3.44***	0.56	18.76 ± 7.15	13.60 ± 6.28	3.66***	0.77
Gender (female)	21 (40%)	75 (56%)	3.64	0.14	18 (42%)	20 (41%)	0.01	0.01

Notes: Values are expressed as *M* ± *SD*, *Md* (*range*), or *n* (%). *d* = Cohen's *d*, $\hat{\theta} = U_1/mn$ [37], *V* = Cramer's *V*. Due to missing data, effective sample sizes ranged *n* = 182 to 186 (mothers) and *n* = 88 to 101 (fathers). * $p<.05$, ** $p<.01$.

Table 2: Clinical characteristics of the asphyxia children

Characteristics	M ± SD or n (%)
Agpar 1 min	2.12 ± 2.07
Agpar 5 min	3.75 ± 2.30
Agpar 10 min	5.10 ± 2.39
When was full sucking achieved (in days)	7.02 ± 5.13
Resuscitated > 10 min (yes)	27 (52%)
Therapeutic hypothermia (yes)	41 (79%)
Neurological examination normal (yes)	30 (58%)
Seizures (yes)	4 (8%)
Sarnat stage > 1	37 (71%)

Notes: Due to missing data, effective sample size ranges $n = 47$ to 52.

Table 3: Range and median questionnaire scores, Mann-Whitney-U-test coefficients, and effect size estimates ($\hat{\theta}$) for mothers and fathers in the asphyxia group and control group

	Asphyxia				Control						
	M	SD	Md	Range	M	SD	Md	Range	*U*	*z*	$\hat{\theta}$ (90%-*CI*)
Mothers											
PDS total score	8.80	7.19	6.00	0-37	5.95	6.55	4.00	0-30	2291.0	-3.14***	.35 (.28-.43)
PDS re-experiencing	3.29	2.81	3.00	0-12	1.29	2.09	0.00	0-12	1600.0	-5.58***	.24 (.18-.32)
PDS avoidance/numbing	2.52	2.86	1.50	0-12	2.07	2.78	1.00	0-16	2954.0	-1.27	.44 (.37-.52)
PDS hyperarousal	2.88	2.95	2.00	0-13	2.59	2.84	2.00	0-14	3101.5	-0.79	.46 (.39-.54)
HADS total score	9.38	5.88	9.00	0-25	10.83	5.55	10.00	0-33	2871.5	-1.86	.59 (.51-.66)
MIBS total score	3.38	3.65	2.00	0-13	2.38	3.38	1.00	0-20	2508.5	-1.72*	.42 (.34-.498)
Fathers											
PDS total score	8.82	10.61	7.00	0-45	4.62	5.10	3.00	0-20	892.0	-1.77*	.39 (.30-.49)
PDS re-experiencing	2.93	3.56	2.00	0-15	0.66	1.19	0.00	0-5	612.0	-4.29***	.26 (.19-.36)
PDS avoidance/numbing	2.71	3.76	1.00	0-18	1.81	2.59	1.00	0-12	1002.0	-1.39	.42 (.33-.52)
PDS hyperarousal	3.27	3.91	2.00	0-14	2.16	2.18	2.00	0-8	1085.0	-0.76	.46 (.36-.55)
HADS total score	8.57	5.74	7.00	0-27	9.10	5.38	9.00	2-32	1158.0	-0.61	.54 (.44-.63)
MIBS total score	2.09	2.79	1.00	0-11	2.55	3.05	1.00	0-14	843.0	-0.80	.55 (.45-.65)

Notes: *M* = mean; *SD* = standard deviation; *Md* = median; *U* = Mann-Whitney test statistic; *z* = z-test; $\hat{\theta} = U_1/mn$ [37]; *90%-CI* = lower and upper level of the 90% confidence interval for $\hat{\theta}$ (Newcombe, 2006, method 5). *PDS* = Posttraumatic Diagnostic Scale, *HADS* = Hospital Anxiety and Depression Scale, *MIBS* = Mother-Infant Bonding Scale. The effective sample sizes ranged $n = 179$ to 186 (mothers) and $n = 89$ to 101 (fathers). *$p < .05$, ***$p < .001$ (1-tailed).

Table 4a: Pearson correlations and point-biserial correlations between mental health variables and bonding quality with selected study variables for mothers in the asphyxia group and in the control group

	PDS total[a]		HADS total[a]		MIBS[a]	
	r_{Apshyx} (95%-CI)	$r_{Control}$ (95%-CI)	r_{Apshyx} (95%-CI)	$r_{Control}$ (95%-CI)	r_{Apshyx} (95%-CI)	$r_{Control}$ (95%-CI)
Parent's age	.06 (-.23, .34)	-.09 (-.26, .08)	.22 (-.06, .47)	-.06 (-.23, .11)	.11 (-.19, .39)	.04 (-.13, .21)
Migrant status	.03 (-.26, .31)	.04 (-.13, .21)	-.18 (-.43, .10)	.01 (-.16, .18)	-.03 (-.32, .27)	-.02 (-.19, .15)
Largo score[a]	-.10 (-.37, .19)	.21* (.04, .37)	-.04 (-.31, .24)	.16 (-.01, .32)	-.07 (-.35, .23)	.00 (-.17, .17)
Past psychological difficulties	.12 (-.16, .39)	.27** (.10, .42)	.24 (-.03, .48)	.26** (.10, .42)	-.02 (-.31, .28)	.09 (-.08, .25)
Past trauma	.03 (-.26, .31)	.28** (.11, .43)	.31* (.04, .54)	.21* (.04, .37)	.05 (-.25, .34)	.06 (-.11, .22)
Previous pregnancy	.16 (-.13, .42)	-.13 (-.30, .04)	.22 (-.07, .47)	.05 (-.13, .22)	.41** (.13, .63)	-.11 (-.27, .07)
Birth weight	-.01 (-.29, .27)	-.04 (-.21, .13)	-.14 (-.40, .14)	-.07 (-.24, .10)	.09 (-.20, .38)	.13 (-.05, .29)
Age of infant	-.26 (-.50, .02)	.07 (-.10, .24)	.03 (-.24, .31)	.09 (-.08, .25)	.10 (-.20, .38)	.07 (-.11, .23)
Gestational age[a]	-.02 (-.30, .26)	-.15 (-.31, .03)	-.03 (-.30, .25)	-.26** (-.41, -.09)	-.06 (-.35, .24)	.16 (-.02, .32)
Apgar 1 min[a]	.05 (-.24, .33)		.05 (-.23, .32)		.18 (-.12, .45)	
Apgar 5 min	.12 (-.17, .39)		.09 (-.18, .36)		.08 (-.22, .36)	
Apgar 10 min	.16 (-.13, .42)		.19 (-.09, .44)		-.10 (-.39, .20)	
Resuscitation	-.24 (-.49, .04)		-.21 (-.46, .07)		.01 (-.28, .30)	
Therapeutic hypothermia	-.23 (-.48, .05)		-.00 (-.28, .27)		-.01 (-.30, .29)	
Sarnat stage > 1	-.23 (-.49, .06)		-.06 (-.33, .23)		.06 (-.24, .36)	

Notes: [a] scores were rank-based inverse normal transformed using Blom's formula; effective sample size ranges from $n = 43$ to 52 (asphyxia group), and from $n = 131$ to 134 (control group). $^{*}p < .05$, $^{**}p < .01$ (2-tailed).

Table 4b: Pearson correlations and point-biserial correlations between mental health variables and bonding quality with selected study variables for fathers in the asphyxia group and in the control group

	PDS total[a]		HADS total[a]		MIBS[a]	
	r_{Apshyx} (95%-CI)	$r_{Control}$ (95%-CI)	r_{Apshyx} (95%-CI)	$r_{Control}$ (95%-CI)	r_{Apshyx} (95%-CI)	$r_{Control}$ (95%-CI)
Parent's age	-.14 (-.45, .19)	.01 (-.25, .28)	.06 (-.25, .36)	-.11 (-.36, .16)	.26 (-.09, .55)	-.08 (-.34, .19)
Migrant status	.04 (-.28, .36)	.11 (-.16, .36)	.01 (-.29, .31)	-.07 (-.32, .20)	-.08 (-.41, .26)	-.20 (-.44, .07)
Largo score[a]	.07 (-.29, .41)	.11 (-.15, .36)	.20 (-.14, .49)	.19 (-.07, .43)	-.16 (-.51, .22)	.06 (-.21, .32)
Past psychological difficulties	.05 (-.28, .36)	.23 (-.03, .46)	.37* (.07, .60)	.19 (-.07, .43)	-.12 (-.44, .23)	.16 (-.11, .41)
Past trauma	.13 (-.19, .44)	-.02 (-.28, .24)	.35* (.05, .59)	-.03 (-.29, .23)	.02 (-.32, .36)	-.34* (-.56, -.09)
Birth weight	.06 (-.26, .37)	-.17 (-.44, .12)	-.06 (-.35, .24)	-.27 (-.52, .02)	.17 (-.18, .48)	-.24 (-.50, .06)
Age of infant	-.20 (-.48, .13)	.03 (-.26, .31)	.09 (-.21, .38)	.07 (-.22, .35)	.00 (-.34, .34)	-.37* (-.60, -.09)
Gestational age[a]	-.01 (-.33, .31)	.21 (-.09, .47)	-.03 (-.33, .27)	-.11 (-.39, .19)	-.12 (-.44, .22)	.09 (-.21, .38)
Apgar 1 min[a]	-.09 (-.40, .23)		-.14 (-.43, .16)		-.02 (-.35, .32)	
Apgar 5 min	.04 (-.28, .36)		-.02 (-.32, .29)		-.10 (-.43, .24)	
Apgar 10 min	.02 (-.30, .33)		.01 (-.29, .31)		-.38* (-.64, -.05)	
Resuscitation	-.18 (-.47, .15)		-.01 (-.31, .29)		.08 (-.26, .41)	
Therapeutic hypothermia	-.37* (-.61, -.06)		-.17 (-.45, .14)		.09 (-.26, .42)	
Sarnat stage > 1	-.25 (-.53, .08)		-.14 (-.43, .17)		-.05 (-.38, .30)	

Notes: [a] scores were rank-based inverse normal transformed using Blom's formula; effective sample size ranges from $n = 28$ to 43 (asphyxia group), and from $n = 43$ to 58 (control group). *$p < .05$ (2-tailed).

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Impact of perinatal asphyxia on parental mental health and bonding with the infant

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What is already known on this topic

- Perinatal asphyxia is a life threatening event, potentially psychologically traumatic for parents.
- Parental mental health problems may impact on bonding with and development of the child.
- Research examining posttraumatic stress disorder, psychological distress, and bonding with their infant in parents of infants born with perinatal asphyxia is lacking.

What this study adds

- More frequent posttraumatic stress symptoms in both parents and poorer bonding with the infant in mothers after perinatal asphyxia were found compared to control parents.
- Parents of infants hospitalized for perinatal asphyxia are more at risk of developing posttraumatic stress disorder than control parents.
- Parents who experienced a previous traumatic event are particularly vulnerable to experiencing higher psychological distress.

Abstract

Objective: (1) To compare current symptoms of posttraumatic stress disorder (PTSD), psychological distress, and bonding with the infant in parents who had an infant surviving perinatal asphyxia in the last two years with control parents who judged their baby as healthy; (2) To investigate which sociodemographic, obstetric, and neonatal variables correlated with mental health symptoms and infant bonding.

Design: Cross-sectional Swiss national cohort study

Setting: Data from Swiss national Asphyxia and Cooling register

Participants: Parents (*n*=52 mothers and *n*=43 fathers) of infants surviving perinatal asphyxia born in 2012 and 2013 and parents (*n*=134 mothers and *n*=58 fathers) of healthy infants born during the same time period

Main outcome measures: Posttraumatic Diagnostic Scale, Hospital Anxiety and Depression Scale, Mother-to-Infant Bonding Scale

Results: Compared with the control group, mothers (*U*=2291.0, *z*=-3.14) and fathers (*U*=892.0, *z*=-1.77) in the asphyxia group had a higher frequency of PTSD symptoms. Mothers in the asphyxia group reported poorer bonding with the infant (*U*=2508.5, *z*=-1.72). In mothers of the asphyxia group, having a trauma in the past was linked to more psychological distress (*r*=0.31 [95%-CI: 0.04-0.54]) and having a previous pregnancy was linked to poorer bonding (*r*=0.41 [95%-CI: 0.13-0.63]). In fathers of the asphyxia group, therapeutic hypothermia of the infant was related to less frequent PTSD symptoms (*r*=-0.37 [95%-CI:-0.61- -0.06]). Past psychological difficulties (*r*=0.37 [95%-CI: 0.07-0.60]) and past trauma (*r*=0.35 [95%-CI: 0.05-0.59]) were positively correlated with general psychological distress, and a lower Apgar score was linked to poorer bonding (*r*=-0.38 [95%-CI:-0.64--0.05]).

Conclusions: Parents of infants hospitalized for perinatal asphyxia are more at risk of developing PTSD than control parents.

Keywords: asphyxia, posttraumatic stress disorder, mother, mental health, bonding

Perinatal asphyxia is a life threatening event affecting 2/1000 infants, which qualifies as a psychologically traumatic stressor for parents[1]. When associated with hypoxic ischemic encephalopathy (HIE), it may lead to disabling brain injuries or death[2-4]. Current treatment of HIE requires immediate transfer to a specialized neonatal unit and therapeutic hypothermia in order to reduce the risk of brain lesions and neurodevelopmental disabilities[5].

Parents of infants admitted to a neonatal intensive care unit report more stress[6], more adjustment difficulties, and need for support during the first year after delivery[7 8] compared to parents of healthy infants. They may experience posttraumatic stress disorder (PTSD) [9-11], anxiety, and depression following the birth[12].

Although two qualitative studies described the experiences of becoming a parent after perinatal asphyxia[13 14] and another showed that fathers may be traumatized[15], PTSD symptoms or psychological distress have not been measured in parents of these children. PTSD consists of four symptom clusters (re-experiencing, avoidance, hyperarousal, and negative cognitions and mood) and is diagnosable from 1 month post-trauma[1]. Assessing postnatal PTSD and psychological distress is not only important for the well-being of parents, but PTSD may also significantly interfere with infant bonding, leading to severe and long-term consequences for the development of the baby[16-18].

The current study aimed to compare current symptoms of PTSD, psychological distress, and infant bonding in parents who had an infant with perinatal asphyxia in the last two years with control parents. It was predicted that parents of the asphyxia group would report more PTSD and psychological distress symptoms and poorerinfant bonding than controls. Another objective was to investigate which sociodemographic, psychological, obstetric, and neonatal variables were correlated with mental health symptoms and infant bonding in both groups.

Methods

Study design and sample

This cross-sectional Swiss national cohort study included infants surviving perinatal asphyxia (asphyxia group) born in 2012 and 2013 (i.e., up to two years after birth), registered in the national Asphyxia and Cooling register of the Swiss Neonatal Network & Follow-up Group. Infants are anonymously entered in the register if they have a gestational age of more than 35 weeks and fulfill criteria for therapeutic hypothermia (low Apgar score, need for ventilatory support or abnormal blood gases during the first hour of life, clinical signs of encephalopathy during the first 6 hours of life)[19]. The questionnaires were sent out to the participating hospitals in May 2014, who then sent them on to the asphyxia group parents. Parents were sent an invitation letter, a participant information sheet, and the questionnaires in French, German or English, with a pre-stamped envelope, by their local referring hospitals.

The control group was recruited during the same time period. Parents of the control group were recruited via flyers in public places, on Swiss internet forums for parents, and on a website of the University of Lausanne. They were eligible if they had given birth in 2012 or 2013 to a full-term infant that they judged to be healthy (i.e., up to two years after birth). When accessing the online questionnaire, participants first read the information sheet; informed consent was implied when they completed the anonymous questionnaire in French, German or English.

This study was approved by the cantonal ethical review board (Vaud) and by the Swiss Federal Commission for Privacy Protection in Medical Research.

Measures

Parental PTSD was measured using the 17-item Posttraumatic Diagnostic Scale (PDS)[20-22]. It provides both a diagnosis according to DSM-IV criteria and a measure of PTSD symptom severity, as well as symptom cluster severity (re-experiencing, avoidance, and hyperarousal) [23 24], and has been widely used in postnatal populations (e.g.[25]). Participants rated how often they experienced each of the symptoms in the past month, using a 4-point frequency scale ranging from 0 (*not at all or only one time*) to 3 (*5 times per week or almost always*). A *partial* PTSD symptoms diagnosis was defined as meeting the criteria for two of the three PTSD symptom clusters[25]. The PDS has good psychometric properties[20 21]. Cronbach's alpha of the total PDS frequency score (α=.90), and of the three sub-scales (re-experiencing: α=.85; avoidance: α=.75; hyperarousal: α=.80) was good to excellent.

General psychological distress of parents in the past week was assessed with the Hospital Anxiety and Depression Scale (HADS)[26-28], a 14-item questionnaire. Each item is scored from 0 to 3, with higher scores indicating greater psychological distress[29]. The HADS has good psychometric properties[27], with a Cronbach's alpha of α=.81 in the current study.

The Mother-to-Infant Bonding Scale (MIBS)[30] consists of eight adjectives that describe feelings towards their baby (loving, resentful, neutral or felt nothing, joyful, dislike, protective, disappointed and aggressive) and measures infant bonding. Each adjective is followed by a 4-point scale ranging from 0 (*very much*) to 3 (*not at all*). When the adjective reflects a negative emotional response, the scoring is reversed. Possible scores range between 0 and 24, with high scores indicating problematic bonding[31 32]. Cronbach's alpha was fair, α=.77.

Parents also completed a demographic questionnaire (age, marital status, migrant status, educational background for mothers, occupation for fathers, previous pregnancy for mothers) with two items assessing whether they had experienced past or current psychological difficulties (In the past, have you already experienced emotional or psychological difficulties? (yes/no) If yes, can you please briefly describe this? Do you currently experience emotional or psychological difficulties? (yes/no) If yes, can you please briefly describe this?), and whether they had experienced a past traumatic event (Have you already experienced a traumatic or particularly stressful situation? (yes/no) If yes, can you please briefly describe this?). Parental socioeconomic status was determined using the Largo score, a 6-point scale, with recorded mother's education (*1=university and 6=special or no schooling*) and father's occupation (*1=leading position and 6=unskilled labor*)[33]. Parents also reported demographic details related to their infant (gender, gestational age, birth weight, current age of infant). Neonatal variables were obtained from the national asphyxia register: Apgar score (at 1, 5, and 10 minutes), umbilical cord pH, number of days when full sucking was achieved, whether infant was resuscitated >10 minutes, Sarnat stage [34], whether therapeutic hypothermia had occurred, whether the neurological examination at discharge had been normal, and whether any seizure had occurred.

Statistical analyses

Data were analyzed using IBM SPSS version 22. Descriptive statistics were calculated for each scale. Responders and non-responders within the asphyxia group were compared regarding obstetric and neonatal variables using chi-squared tests and independent samples *t*-tests. To compare asphyxia group and control group regarding the central tendencies of the non-

normal distributed mental health and bonding outcomes (PDS total score and symptom clusters, HADS, MIBS), rank based Mann-Whitney U-tests were performed. The χ^2 analyses were performed to compare PTSD cluster symptoms and PTSD diagnosis (partial, full) between groups. Bivariate correlation analyses (Pearson and point-biserial correlations) between sociodemographic, obstetric, and neonatal variables and mental health or infant bonding were carried out. Prior to assessing the correlation, the non-normally distributed scores (PDS, HADS, MIBS, Largo, gestational age, and Apgar index 1 minute) were rank-based inverse normal (RIN) transformed within each gender using Blom's formula[35]. Given that the non-independence of mothers' and fathers' scores may lead to biased estimates[36], mothers and fathers were analysed separately. Within each gender, correlations were calculated separately for the asphyxia and control groups.

The 95% confidence interval (95%-CI) for correlations and Cohen's *d* were calculated using the Exploratory Software for Confidence Intervals (ESCI)[37]. Established guidelines for the interpretation of *r* suggest that a large effect is .50, a medium-sized effect is .30, and a small effect is .10[38].The effect sizes of frequencies analysed with a chi-squared test were expressed as the differences of the two independent proportions and the corresponding 95%-CI was calculated using ESCI. The effect size for the Mann-Whitney statistic was estimated as $r = z/\sqrt{N}$ [38]. The limits of the 90%-CI of the effect size estimate *r* obtained for the Mann-Whitney statistic were calculated with ESCI [38].

Results

Sample characteristics

For the asphyxia group, parents of 114 registered infants were contacted and 95 parents (52 mothers and 43 fathers) of 53 infants (46.5%) responded. The control group was composed of 134 mothers and 58 fathers. Missing data per variable ranged from 0 to 7 (mothers) and 0 to 13 (fathers). Missing data were not replaced. The comparison of responders and non-responders according to infant neonatal variables listed in Tables 1 and 2 resulted in no significant differences (see Table S1 in the supplemental material).

Regarding demographic variables, three significant differences between asphyxia and control mothers were found (see Table 1): asphyxia group mothers had a higher Largo score, p=.011 and reported a lower frequency of previous pregnancies, (p<.001) compared to controls. Furthermore, the current age of the infant was higher for the asphyxia group (18 vs. 14 months), (p<.001). For fathers, corresponding significant differences were found for Largo score, (p=.002), and current age of the infant (18 vs. 14 months, p<.001).

Mental health symptoms and infant bonding: group comparisons

As predicted, mothers in the asphyxia group reported a higher frequency of total PTSD symptoms than controls, $p_{1\text{-tailed}}$<.001 (see Table 3 for descriptive values, effect size estimate r, and the respective 90% confidence interval). This difference was due to a higher frequency of re-experiencing symptoms in asphyxia group mothers compared to controls, $p_{1\text{-tailed}}$<.001. Consistent with the latter finding, mothers in the asphyxia group were also more likely to have at least one re-experiencing symptom than controls, $\chi^2(1) = 25.21$; p <.001; (difference in proportions: 41.7%, 90%-CI: 29.3% to 51.0%). In the asphyxia group, n=14 (28.0%) and n=14 (28.0%) mothers met criteria of either a partial or a full PTSD symptom diagnosis. In the control

group, these were *n*=30 (22.4%) and *n*=22 (16.4%) respectively. The group difference was marginal, $\chi^2(2)=4.88$, *p*=.087. However, when group membership and PTSD symptom diagnosis (none, partial, full) were both treated as ordinal, both variables were significantly related, Kendalls' τ =.16, *p*=.032, suggesting that asphyxia mothers were more likely to receive a partial or full PTSD symptom diagnosis. As expected, asphyxia group mothers reported poorer bonding with the infant compared to controls, *U*=2508.5, *z*=1.72, $p_{1\text{-tailed}}$ =.043 (see Table 3).

The difference for total PTSD symptoms between asphyxia and control group was also found in fathers, $p_{1\text{-tailed}}$ =.038 (see Table 3 for descriptive values, effect size estimate *r*, and the respective 90% confidence interval). Fathers in the asphyxia group reported a higher frequency of re-experiencing symptoms compared to controls, $p_{1\text{-tailed}}$ <.001 and were significantly more likely to report at least one re-experiencing symptom compared to controls, $\chi^2(1)=13.16$, *p* <.001; (difference in proportions: 37.2%, 90%-CI: 20.5% to 51.1%). In the asphyxia group , *n*=10 (24.39%) and *n*=11 (26.83%) fathers met criteria of a partial or a full PTSD symptom diagnosis compared to *n*=13 (22.41%) and *n*=6 (10.34%) controls. Again, the group difference was marginal, $\chi^2(2)=5.22$, *p*=.074, but when group membership and PTSD diagnosis were treated as ordinal, both variables were positively related, Kendall's τ =.20, *p*=.034, suggesting that fathers in the asphyxia group were more likely to receive a PTSD symptom diagnosis. No other statistically significant group differences were found (all *p*=ns).

Associations between sociodemographic, psychological, obstetric, and neonatal variables with mental health symptoms and infant bonding

For mothers, different significant correlations were found in the asphyxia and in the control group (see Table 4a): having a trauma in the past was linked to more psychological distress in both groups. In the asphyxia group only, having a previous pregnancy was linked to poorer infant bonding. In the control group, past psychological difficulties were linked to more frequent PTSD symptoms and more general psychological distress. Finally, still in the control group, younger gestational age (although all infants were born at term) was also related to more general psychological distress and higher Largo scores to more frequent PTSD symptoms.

In fathers of the asphyxia group, (see Table 4b) therapeutic hypothermia was related to less frequent PTSD symptoms. Past psychological difficulties and past trauma were linked with current general psychological distress, and a lower Apgar score (10 minutes) was linked to poorer infant bonding. In the control group fathers, general psychological distress and PTSD were not significantly related to any of the selected variables, but lower current age of the infant and past trauma were linked to poorer infant bonding.

Discussion

This cross-sectional Swiss national cohort study comparing parents of infants surviving perinatal asphyxia with those of healthy infants found more frequent PTSD (and particularly re-experiencing) symptoms in parents and poorer bonding with the infant in mothers of infants born with asphyxia compared with controls. Results need to be considered with caution, as mothers in the asphyxia group had a lower socioeconomic status, a lower frequency of previous pregnancies, and slightly older infants compared to controls. Compared to control fathers, fathers in the asphyxia group had a lower socioeconomic status and older infants.

These results show for the first time that parents of infants with perinatal asphyxia experience elevated symptoms of PTSD, such as has been reported for other populations of high-risk parents, e.g., those of premature or critically ill infants[9-11]. The lack of differences between the asphyxia and control parents in relation to general psychological distress points to a generally healthy psychological adjustment of parents that might partly be due to a good experience of care regarding their infant and effective staff support.

When investigating potential risk factors for mental health problems in asphyxia group parents, we found that having experienced a past trauma was associated with more general psychological distress in both mothers and fathers. This is in line with research identifying a previous traumatic experience as a risk factor for developing PTSD following childbirth[39] and depression in the general adult population[40]. Our finding that having previously been pregnant was associated with more bonding problems is novel. It may be that already being a parent makes it harder to invest oneself in a relationship with another child, particularly one that is severely ill. Alternatively, infants who had asphyxia at birth may be less effective in interactions with parents and parents may thus find it harder to bond with them. However, more research is needed to explore this. Given the small number of mothers in the asphyxia group, none of the weak correlations of the other neonatal variables were statistically significant but the small to medium sized effects might be detected with a more powerful design.

For fathers in the asphyxia group, therapeutic hypothermia of the infant was related to less frequent PTSD symptoms. This is a novel finding and might be linked to a certain level of reassurance that fathers feel when witnessing a highly technological treatment, thus reducing their perceived threat to their infant's life. Similar to mothers, past psychological difficulties and past trauma were positively correlated with current general psychological distress, which is in

line with previous research in the general adult population[40]. Finally, a lower Apgar score (10 min) was associated with more bonding problems. This novel result may be explained by the fact that a lower Apgar score would have indicated a more severe life threat for the infant and fathers might have unintentionally found it harder to develop a bond with their infant for fear of losing it. However, this remains to be explored in future studies.

Strengths of the study are the inclusion of a national cohort, the comparison with a control group, and the use of standardised questionnaires. The relatively low response rate (47%) is comparable with other studies of high-risk populations[8] and regarded as fair, particularly given the tendency of traumatised parents to avoid reminders of the childbirth or hospital stay. Limitations of the study include the cross-sectional, retrospective design of the study, thus not allowing for causal conclusions and the risk of a reporting bias. The small sample size related to the low prevalence of perinatal asphyxia limited the statistical power, despite it being a national cohort study. The MIBS has so far not been validated for the use with fathers, for whom a bonding questionnaire remains to be developed. Caution needs to be taken in interpreting the results, given that both groups differed on sociodemographic characteristics. Further limitations are the recruitment of the anonymous control group via flyers in public places, not allowing us to check for health problems of their infants and relying on the self-report of the parents. Finally, the temporal nature of the associations, and the potential impact of events between birth and the parental responses, which we did not ask for in either group, may have potentially influenced the study outcomes. We also did not ask parents in either group about infant health issues or events since birth, which may have potentially influenced the study outcomes. Future studies with a larger cohort, a prospective design, and a control group matched on important sociodemographic

variables are needed. Furthermore, investigating the effects of PTSD and bonding on infant outcomes would be of interest.

Conclusion

This study found more frequent PTSD (and particularly re-experiencing) symptoms in asphyxia group parents and poorer infant bonding in asphyxia group mothers compared with the control group. Results show for the first time that parents in the asphyxia group are at risk for developing PTSD. Furthermore, we found that a history of past trauma puts parents at increased risk of general psychological distress after perinatal asphyxia.

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Contributors

AH had primary responsibility for the study design, data acquisition, analysis, and writing of the manuscript, and approved the final manuscript as submitted. MBG was involved in the study

design, data acquisition, and writing of the manuscript, and approved the final manuscript as submitted. IJ was responsible for the statistical expertise, performed all final statistical analyses, contributed to the writing of the manuscript, and approved the final manuscript as submitted. CF and LG contributed to the data analysis, critically reviewed and revised the manuscript, and approved the final manuscript as submitted. JS and MMH contributed to the interpretation of data, critically reviewed and revised the manuscript and approved the final manuscript as submitted.

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Competing interests

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Patient consent

Obtained.

Ethics approval

This study was approved by the cantonal ethical review board (Vaud) and by the Swiss Federal Commission for Privacy Protection in Medical Research.

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Table 1: Sample characteristics, test coefficients, and probability values for mothers and fathers

Characteristics	Mothers				Fathers			
	Asphyxia (*n*=52)	Control (*n*=134)	*t, U or* χ^2	*p*-value	Asphyxia (*n*=43)	Control (*n*=58)	*t, U or* χ^2	*p*-value
Parents								
Age (years)	32.02 ± 4.74	32.44 ± 4.27	-0.57	.567	35.12 ± 6.29	34.64 ± 4.53	0.42	.679
Largo score	2 (1-5)	1 (1-5)	2668.0	.011	3 (1-6)	2 (1-4)	657.5	.002
Marital status (with partner)	48 (92%)	126 (94%)	0.18	.668	42 (98%)	56 (97%)	0.11	.742
Migrant status (yes)	16 (31%)	33 (25%)	0.73	.393	14 (33%)	19 (33%)	0.00	.983
Previous pregnancy (yes)	21 (42%)	100 (76%)	18.55	<.001	-	-	-	
History of psychological difficulties (yes)	19 (37%)	46 (34%)	0.08	.777	9 (21%)	7 (12%)	1.59	.208
Past trauma (yes)	27 (52%)	50 (37%)	3.30	.069	15 (36%)	21 (36%)	0.00	.960
Infants								
Gestational age (weeks)	40 (35-42)	40 (35-42)	3378.0	.929	40 (35-42)	40 (37-46)	964.5	.979
Birth weight (grams)	3381.25 ± 408.11	3396.53 ± 506.19	-0.19	.846	3426.05 ± 421.38	3307.55 ± 504.76	1.20	.232
Age at survey (months)	18.16 ± 7.46	14.13 ± 7.04	3.44	<.001	18.76 ± 7.15	13.60 ± 6.28	3.66	<.001
Gender (female)	21 (40%)	75 (56%)	3.64	.056	18 (42%)	20 (41%)	0.01	.919

Notes: Values are expressed as *M* ± *SD*, *Md* (*range*), or *n* (%). Due to missing data, effective sample sizes ranged from *n* = 182 to 186 (mothers) and from *n* = 88 to 101 (fathers).

Table 2: Clinical characteristics of the asphyxia children

Characteristics	M ± SD or n (%)
Agpar 1 min	2.11 ± 2.05
Agpar 5 min	3.74 ± 2.27
Agpar 10 min	5.06 ± 2.37
When was full sucking achieved (in days)	6.88 ± 5.11
Resuscitated > 10 min (yes)	27 (50.9%)
Therapeutic hypothermia (yes)	41 (77.4%)
Neurological examination normal (yes)	31 (58.5%)
Seizures (yes)	4 (7.5%)
Sarnat stage 1	14 (32.6%)
Sarnat stage 2	25 (58.1%)
Sarnat stage 3	4(9.3%)

Notes: Due to missing data, effective sample size ranges $n = 43$ to 53.

Table 3: Range and median questionnaire scores, Mann-Whitney-U-test coefficients, and effect size estimates *r* for mothers and fathers in the asphyxia group and control group

	Asphyxia				Control						
	M	SD	Md	Range	M	SD	Md	Range	*U*	*z*	*r* (90%-*CI*)
Mothers											
PDS total score	8.80	7.19	6.00	0-37	5.95	6.55	4.00	0-30	2291.0	3.14***	.23 (.11, .34)
PDS re-experiencing	3.29	2.81	3.00	0-12	1.29	2.09	0.00	0-12	1600.0	5.58***	.40 (.29, .50)
PDS avoidance/numbing	2.52	2.86	1.50	0-12	2.07	2.78	1.00	0-16	2954.0	1.27	.09 (-.03, .21)
PDS hyperarousal	2.88	2.95	2.00	0-13	2.59	2.84	2.00	0-14	3101.5	0.79	.06 (-.06, .18)
HADS total score	9.38	5.88	9.00	0-25	10.83	5.55	10.00	0-33	2871.5	-1.86	-.14 (-.25, -.02)
MIBS total score	3.38	3.65	2.00	0-13	2.38	3.38	1.00	0-20	2508.5	1.72*	.13 (.01, .25)
Fathers											
PDS total score	8.82	10.61	7.00	0-45	4.62	5.10	3.00	0-20	892.0	1.77*	.18 (.01, .34)
PDS re-experiencing	2.93	3.56	2.00	0-15	0.66	1.19	0.00	0-5	612.0	4.29***	.41 (.26, .54)
PDS avoidance/numbing	2.71	3.76	1.00	0-18	1.81	2.59	1.00	0-12	1002.0	1.39	.14 (-.02, .30)
PDS hyperarousal	3.27	3.91	2.00	0-14	2.16	2.18	2.00	0-8	1085.0	0.76	.06 (-.11, .22)
HADS total score	8.57	5.74	7.00	0-27	9.10	5.38	9.00	2-32	1158.0	-0.61	-.06 (-.22, .11)
MIBS total score	2.09	2.79	1.00	0-11	2.55	3.05	1.00	0-14	843.0	-0.80	-.08 (-.26, .09)

Notes: *M* = mean; *SD* = standard deviation; *Md* = median; *U* = Mann-Whitney test statistic; *z* = z-test (a positive z-score denotes higher scale scores in the asphyxia group); $r = z/\sqrt{N}$ [41]; *90%-CI* = lower and upper level of the 90% confidence interval . *PDS* = Posttraumatic Diagnostic Scale, *HADS* = Hospital Anxiety and Depression Scale, *MIBS* = Mother-Infant Bonding Scale. The total sample sizes ranged from $n = 179$ to 186 (mothers) and from $n = 89$ to 101 (fathers). $^{*}p < .05$, $^{***}p < .001$ (1-tailed).

Table 4a: Pearson correlations and point-biserial correlations between mental health variables and bonding quality with selected study variables for mothers in the asphyxia group and in the control group

	PDS total[a]		HADS total[a]		MIBS[a]	
	r_{Apshyx} (95%-CI)	$r_{Control}$ (95%-CI)	r_{Apshyx} (95%-CI)	$r_{Control}$ (95%-CI)	r_{Apshyx} (95%-CI)	$r_{Control}$ (95%-CI)
Parent's age	.06 (-.23, .34)	-.09 (-.26, .08)	.22 (-.06, .47)	-.06 (-.23, .11)	.11 (-.19, .39)	.04 (-.13, .21)
Migrant status	.03 (-.26, .31)	.04 (-.13, .21)	-.18 (-.43, .10)	.01 (-.16, .18)	-.03 (-.32, .27)	-.02 (-.19, .15)
Largo score[a]	-.10 (-.37, .19)	.21* (.04, .37)	-.04 (-.31, .24)	.16 (-.01, .32)	-.07 (-.35, .23)	.00 (-.17, .17)
Past psychological difficulties	.12 (-.16, .39)	.27** (.10, .42)	.24 (-.03, .48)	.26** (.10, .42)	-.02 (-.31, .28)	.09 (-.08, .25)
Past trauma	.03 (-.26, .31)	.28** (.11, .43)	.31* (.04, .54)	.21* (.04, .37)	.05 (-.25, .34)	.06 (-.11, .22)
Previous pregnancy	.16 (-.13, .42)	-.13 (-.30, .04)	.22 (-.07, .47)	.05 (-.13, .22)	.41** (.13, .63)	-.11 (-.27, .07)
Birth weight	-.01 (-.29, .27)	-.04 (-.21, .13)	-.14 (-.40, .14)	-.07 (-.24, .10)	.09 (-.20, .38)	.13 (-.05, .29)
Age of infant	-.26 (-.50, .02)	.07 (-.10, .24)	.03 (-.24, .31)	.09 (-.08, .25)	.10 (-.20, .38)	.07 (-.11, .23)
Gestational age[a]	-.02 (-.30, .26)	-.15 (-.31, .03)	-.03 (-.30, .25)	-.26** (-.41, -.09)	-.06 (-.35, .24)	.16 (-.02, .32)
Apgar 1 min[a]	.05 (-.24, .33)		.05 (-.23, .32)		.18 (-.12, .45)	
Apgar 5 min	.12 (-.17, .39)		.09 (-.18, .36)		.08 (-.22, .36)	
Apgar 10 min	.16 (-.13, .42)		.19 (-.09, .44)		-.10 (-.39, .20)	
Resuscitation	-.24 (-.49, .04)		-.21 (-.46, .07)		.01 (-.28, .30)	
Therapeutic hypothermia	-.23 (-.48, .05)		-.00 (-.28, .27)		-.01 (-.30, .29)	
Sarnat stage > 1	-.23 (-.49, .06)		-.06 (-.33, .23)		.06 (-.24, .36)	

Notes: [a] scores were rank-based inverse normal transformed using Blom's formula; effective sample size ranges from $n = 43$ to 52 (asphyxia group), and from $n = 131$ to 134 (control group). $^{*}p < .05$, $^{**}p < .01$ (2-tailed).

Table 4b: Pearson correlations and point-biserial correlations between mental health variables and bonding quality with selected study variables for fathers in the asphyxia group and in the control group

	PDS total[a]		HADS total[a]		MIBS[a]	
	r_{Apshyx} (95%-CI)	$r_{Control}$ (95%-CI)	r_{Apshyx} (95%-CI)	$r_{Control}$ (95%-CI)	r_{Apshyx} (95%-CI)	$r_{Control}$ (95%-CI)
Parent's age	-.14 (-.45, .19)	.01 (-.25, .28)	.06 (-.25, .36)	-.11 (-.36, .16)	.26 (-.09, .55)	-.08 (-.34, .19)
Migrant status	.04 (-.28, .36)	.11 (-.16, .36)	.01 (-.29, .31)	-.07 (-.32, .20)	-.08 (-.41, .26)	-.20 (-.44, .07)
Largo score[a]	.07 (-.29, .41)	.11 (-.15, .36)	.20 (-.14, .49)	.19 (-.07, .43)	-.16 (-.51, .22)	.06 (-.21, .32)
Past psychological difficulties	.05 (-.28, .36)	.23 (-.03, .46)	.37* (.07, .60)	.19 (-.07, .43)	-.12 (-.44, .23)	.16 (-.11, .41)
Past trauma	.13 (-.19, .44)	-.02 (-.28, .24)	.35* (.05, .59)	-.03 (-.29, .23)	.02 (-.32, .36)	-.34* (-.56, -.09)
Birth weight	.06 (-.26, .37)	-.17 (-.44, .12)	-.06 (-.35, .24)	-.27 (-.52, .02)	.17 (-.18, .48)	-.24 (-.50, .06)
Age of infant	-.20 (-.48, .13)	.03 (-.26, .31)	.09 (-.21, .38)	.07 (-.22, .35)	.00 (-.34, .34)	-.37* (-.60, -.09)
Gestational age[a]	-.01 (-.33, .31)	.21 (-.09, .47)	-.03 (-.33, .27)	-.11 (-.39, .19)	-.12 (-.44, .22)	.09 (-.21, .38)
Apgar 1 min[a]	-.09 (-.40, .23)		-.14 (-.43, .16)		-.02 (-.35, .32)	
Apgar 5 min	.04 (-.28, .36)		-.02 (-.32, .29)		-.10 (-.43, .24)	
Apgar 10 min	.02 (-.30, .33)		.01 (-.29, .31)		-.38* (-.64, -.05)	
Resuscitation	-.18 (-.47, .15)		-.01 (-.31, .29)		.08 (-.26, .41)	
Therapeutic hypothermia	-.37* (-.61, -.06)		-.17 (-.45, .14)		.09 (-.26, .42)	
Sarnat stage > 1	-.25 (-.53, .08)		-.14 (-.43, .17)		-.05 (-.38, .30)	

Notes: [a] scores were rank-based inverse normal transformed using Blom's formula; effective sample size ranges from $n = 28$ to 43 (asphyxia group), and from $n = 43$ to 58 (control group). *$p < .05$ (2-tailed).

Table S1 (supplemental material): Characteristics of asphyxia infants in the responder and non-responder groups

Characteristics	Non-responders (*n*=61)	Responders (*n*=53)	*t or* χ^2	*p*-value
Agpar 1 min	2.57 ± 2.36	2.11 ± 2.05	1.11	.272
Agpar 5 min	4.61 ± 2.42	3.74 ± 2.27	1.97	.051
Agpar 10 min	5.56 ± 2.41	5.06 ± 2.37	1.11	.268
When was full sucking achieved (in days)	6.42 ± 5.06	6.88 ± 5.11	-0.46	.650
Resuscitated > 10 min (yes)	26 (43.3%)	27 (50.9%)	0.65 [a]	.419
Therapeutic hypothermia (yes)	45 (73.8%)	41 (77.4%)	0.20	.657
Neurological examination normal (yes)	33 (55.0%)	31 (58.5%)	0.14 [a]	.709
Seizures (yes)	6 (9.8%)	4 (7.5%)	0.19	.667
Sarnat stage 1	14 (28.0%)	14 (32.6%)	0.34 [b]	.855
Sarnat stage 2	32 (64.0%)	25 (58.1%)		
Sarnat stage 3	4 (8.0%)	4 (9.3%)		
Gestational age (weeks)	39 (34-42)	40 (35-42)	1309.00	.072
Birth weight (grams)	3248.26 ± 612.46	3415.57 ± 442.32	-1.69	.095
Gender (female)	25 (41.0%)	21 (39.6%)	0.02	.883

Notes: Values are expressed as *M* ± *SD*, *Md* (*range*), or *n* (%); *p*-values are 2-tailed; [a] $N = 113$; [b] $N = 93$.

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Impact of perinatal asphyxia on parental mental health and bonding with the infant: a questionnaire survey of Swiss parents

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Impact of perinatal asphyxia on parental mental health and bonding with the infant: a questionnaire survey of Swiss parents.

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What is already known on this topic

- Perinatal asphyxia is a life threatening event, potentially psychologically traumatic for parents.
- Parental mental health problems may impact on bonding with and development of the child.
- Research examining posttraumatic stress disorder, psychological distress, and bonding with their infant in parents of infants born with perinatal asphyxia is lacking.

What this study adds

- More frequent posttraumatic stress symptoms in both parents and poorer bonding with the infant in mothers after perinatal asphyxia were found compared to control parents.
- Parents of infants hospitalized for perinatal asphyxia are more at risk of developing posttraumatic stress disorder than control parents.

Abstract

Objective: To compare current mental health symptoms and infant bonding in parents whose infants survived perinatal asphyxia in the last two years with control parents and to investigate which sociodemographic, obstetric, and neonatal variables correlated with parental mental health and infant bonding in the asphyxia group.

Design: Cross-sectional questionnaire survey of parents whose children were registered in Swiss national Asphyxia and Cooling register and control parents (Posttraumatic Diagnostic Scale, Hospital Anxiety and Depression Scale, Mother-to-Infant Bonding Scale).

Results: The response rate for the asphyxia group was 46.5%. Compared with controls, mothers and fathers in the asphyxia group had a higher frequency of PTSD symptoms (p <0.001). More mothers received a partial or full PTSD symptom diagnosis (n=28, 56%) than controls (n=54, 39%), (p=0.032). Similarly, more fathers (n=31, 51%) compared to controls (n=19, 33%) received a partial or full PTSD symptom diagnosis (p=0.034). Mothers reported poorer bonding with the infant (p =0.043) than controls. Having a trauma in the past was linked to more psychological distress in mothers (r=0.31 [95%-CI: 0.04-0.54]) and fathers(r=0.35 [95%-CI: 0.05-0.59]). For mothers, previous pregnancy was linked to poorer bonding (r=0.41 [95%-CI: 0.13-0.63]). In fathers, therapeutic hypothermia of the infant was related to less frequent PTSD symptoms (r=-0.37 [95%-CI:-0.61- -0.06]) and past psychological difficulties (r=0.37 [95%-CI: 0.07-0.60]) to more psychological distress. A lower Apgar score was linked to poorer bonding (r=-0.38 [95%-CI:-0.64--0.05]).

Conclusions: Parents of infants hospitalized for perinatal asphyxia report more PTSD symptoms and more partial or full PTSD symptom diagnosis.

Conclusions: Parents of infants hospitalized for perinatal asphyxia are more at risk of developing PTSD than control parents.

Keywords: asphyxia, posttraumatic stress disorder, mother, mental health, bonding

Perinatal asphyxia is a life threatening event affecting 2/1000 infants, which qualifies as a psychologically traumatic stressor for parents[1]. When associated with hypoxic ischemic encephalopathy (HIE), it may lead to disabling brain injuries or death[2-4]. Current treatment of HIE requires immediate transfer to a specialized neonatal unit and therapeutic hypothermia in order to reduce the risk of brain lesions and neurodevelopmental disabilities[5].

Parents of infants admitted to a neonatal intensive care unit report more stress[6], more adjustment difficulties, and need for support during the first year after delivery[7 8] compared to parents of healthy infants. They may experience posttraumatic stress disorder (PTSD) [9-11], anxiety, and depression following the birth[12].

Although two qualitative studies described the experiences of becoming a parent after perinatal asphyxia[13 14] and another showed that fathers may be traumatized[15], PTSD symptoms or psychological distress have not been measured in parents of these children. PTSD consists of four symptom clusters (re-experiencing, avoidance, hyperarousal, and negative cognitions and mood) and is diagnosable from 1 month post-trauma[1]. Assessing postnatal PTSD and psychological distress is not only important for the well-being of parents, but PTSD may also significantly interfere with infant bonding, leading to severe and long-term consequences for the development of the baby[16-18].

The current study aimed to compare current symptoms of PTSD, psychological distress, and infant bonding in parents who had an infant with perinatal asphyxia in the last two years with control parents. It was predicted that parents of the asphyxia group would report more PTSD and psychological distress symptoms and poorer infant bonding than controls. Another objective was to investigate which sociodemographic, psychological, obstetric, and neonatal variables were correlated with mental health symptoms and infant bonding in both groups.

Methods

Study design and sample

This cross-sectional Swiss national cohort study (questionnaire survey of Swiss parents) included infants surviving perinatal asphyxia (asphyxia group) born in 2012 and 2013 (i.e., up to two years after birth), registered in the national Asphyxia and Cooling register of the Swiss Neonatal Network & Follow-up Group. Infants are anonymously entered in the register if they have a gestational age of more than 35 weeks and fulfill criteria for therapeutic hypothermia (low Apgar score, need for ventilatory support or abnormal blood gases during the first hour of life, clinical signs of encephalopathy during the first 6 hours of life)[19]. The questionnaires were sent out to the participating hospitals in May 2014, who then sent them on to the asphyxia group parents. Parents were sent an invitation letter, a participant information sheet, and the questionnaires in French, German or English, with a pre-stamped envelope, by their local referring hospitals.

The control group was recruited during the same time period. Parents of the control group were recruited via flyers in public places, on Swiss internet forums for parents, and on a website of the University of Lausanne. They were eligible if they had given birth in 2012 or 2013 to a full-term infant that they judged to be healthy (i.e., up to two years after birth). When accessing the online questionnaire, participants first read the information sheet; informed consent was implied when they completed the anonymous questionnaire in French, German or English.

This study was approved by the cantonal ethical review board (Vaud) and by the Swiss Federal Commission for Privacy Protection in Medical Research.

Measures

Parental PTSD was measured using the 17-item Posttraumatic Diagnostic Scale (PDS)[20-22]. It provides both a diagnosis according to DSM-IV criteria and a measure of PTSD symptom severity, as well as symptom cluster severity (re-experiencing, avoidance, and hyperarousal) [23 24], and has been widely used in postnatal populations (e.g.[25]). Participants rated how often they experienced each of the symptoms in the past month, using a 4-point frequency scale ranging from 0 (*not at all or only one time*) to 3 (*5 times per week or almost always*). A *partial* PTSD symptoms diagnosis was defined as meeting the criteria for two of the three PTSD symptom clusters[25]. The PDS has good psychometric properties[20 21]. Cronbach's alpha of the total PDS frequency score (α=.90), and of the three sub-scales (re-experiencing: α=.85; avoidance: α=.75; hyperarousal: α=.80) was good to excellent.

General psychological distress of parents in the past week was assessed with the Hospital Anxiety and Depression Scale (HADS)[26-28], a 14-item questionnaire. Each item is scored from 0 to 3, with higher scores indicating greater psychological distress[29]. The HADS has good psychometric properties[27], with a Cronbach's alpha of α=.81 in the current study.

The Mother-to-Infant Bonding Scale (MIBS)[30] consists of eight adjectives that describe feelings towards their baby (loving, resentful, neutral or felt nothing, joyful, dislike, protective, disappointed and aggressive) and measures infant bonding. Each adjective is followed by a 4-point scale ranging from 0 (*very much*) to 3 (*not at all*). When the adjective reflects a negative emotional response, the scoring is reversed. Possible scores range between 0 and 24, with high scores indicating problematic bonding[31 32]. Cronbach's alpha was fair, α=.77.

Parents also completed a demographic questionnaire (age, marital status, migrant status, educational background for mothers, occupation for fathers, previous pregnancy for mothers) with two items assessing whether they had experienced past or current psychological difficulties (In the past, have you already experienced emotional or psychological difficulties? (yes/no) If yes, can you please briefly describe this? Do you currently experience emotional or psychological difficulties? (yes/no) If yes, can you please briefly describe this?), and whether they had experienced a past traumatic event (Have you already experienced a traumatic or particularly stressful situation? (yes/no) If yes, can you please briefly describe this?). Parental socioeconomic status was determined using the Largo score, a 6-point scale, with recorded mother's education (*1=university and 6=special or no schooling*) and father's occupation (*1=leading position and 6=unskilled labor*)[33]. Parents also reported demographic details related to their infant (gender, gestational age, birth weight, current age of infant). Neonatal variables were obtained from the national asphyxia register: Apgar score (at 1, 5, and 10 minutes), umbilical cord pH, number of days when full sucking was achieved, whether infant was resuscitated >10 minutes, Sarnat stage [34], whether therapeutic hypothermia had occurred, whether the neurological examination at discharge had been normal, and whether any seizure had occurred.

Statistical analyses

Data were analyzed using IBM SPSS version 22. Descriptive statistics were calculated for each scale. Mothers and fathers of the asphyxia and control group were compared separately regarding sociodemographic characteristics using chi-squared tests, independent samples *t*-tests, and Mann-Whitney U-tests. Responders and non-responders within the asphyxia group were

compared regarding obstetric and neonatal variables using chi-squared tests and independent samples *t*-tests. To compare the asphyxia and control groups regarding the central tendencies of the non-normal distributed mental health and bonding outcomes (PDS total score and symptom clusters, HADS, MIBS), rank based Mann-Whitney U-tests were performed. The effect size for the Mann-Whitney statistic was estimated as $r = z/\sqrt{N}$ [35]. The limits of the 95%-CI of the effect size estimate *r* obtained for the Mann-Whitney statistic were calculated with ESCI [35]. Established guidelines for the interpretation of *r* suggest that a large effect is 0.50, a medium-sized effect is 0.30, and a small effect is 0.10[35].

The χ^2 tests were performed to compare PTSD cluster symptoms between groups. The effect sizes of frequencies analysed with a chi-squared test were expressed as the differences of the two independent proportions and the corresponding 95%-CI was calculated using ESCI[35]. To compare groups regarding PTSD diagnosis (none, partial, full), a Kendall rank correlation analysis was carried out. Bivariate correlation analyses (Pearson and point-biserial correlations) between sociodemographic, obstetric, and neonatal variables and mental health or infant bonding were carried out. Prior to assessing the correlation, the non-normally distributed scores (PDS, HADS, MIBS, Largo, gestational age, and Apgar index 1 minute) were rank-based inverse normal (RIN) transformed within each gender using Blom's formula[36]. Given that the non-independence of mothers' and fathers' scores may lead to biased estimates[37], mothers and fathers were analysed separately. Within each gender, correlations with 95 % CI were calculated. . The 95% confidence interval (95%-CI) for correlations and effect size estimates *r* were calculated using the Exploratory Software for Confidence Intervals (ESCI)[38].

Results

Sample characteristics

For the asphyxia group, parents of 114 registered infants were contacted and 95 parents (52 mothers and 43 fathers) of 53 infants (46.5%) responded. The control group was composed of 134 mothers and 58 fathers. Missing data per variable ranged from 0 to 7 (mothers) and 0 to 13 (fathers). Missing data were not replaced. The comparison of responders and non-responders according to infant neonatal variables listed in Tables 1 and 2 resulted in no significant differences (see Table S1 in the supplemental material).

Regarding demographic variables, three significant differences between asphyxia and control mothers were found (see Table 1): asphyxia group mothers had a higher Largo score, p=0.011 and reported a lower frequency of previous pregnancies, (p<0.001) compared to controls. Furthermore, the current age of the infant was higher for the asphyxia group (18 vs. 14 months), (p<0.001). For fathers, corresponding significant differences were found for Largo score, (p=0.002), and current age of the infant (18 vs. 14 months, p<0.001).

Mental health symptoms and infant bonding: group comparisons

Mothers in the asphyxia group reported a higher frequency of total PTSD symptoms than controls, $p_{1\text{-tailed}}$ <0.001 (see Table 3). This difference was due to a higher frequency of re-experiencing symptoms in asphyxia group mothers compared to controls, $p_{1\text{-tailed}}$<0.001. Consistent with the latter finding, mothers in the asphyxia group were also more likely to have at least one re-experiencing symptom than controls, $\chi^2(1) = 25.21$; p <0.001; (difference in

proportions: 41.7%, 90%-CI: 29.3% to 51.0%). Criteria for partial PTSD were met by *n*=14 (28.0%) in the asphyxia group and *n*=30 (22.4%) in the control group. Criteria for a full PTSD symptom diagnosis were met by *n*=14 (28.0%) by mothers of the asphyxia group and *n*=22 (16.4%) of the control group. . When comparing both groups, asphyxia mothers were more likely to receive a partial or full PTSD symptom diagnosis (Kendalls' τ =.16, *p*=0.032). Asphyxia group mothers also reported poorer bonding with the infant compared to controls, *U*=2508.5, *z*=1.72, $p_{1\text{-tailed}}$=0.043 (see Table 3). No significant group difference for the HADS total score was found.

The difference for total PTSD symptoms between asphyxia and control group was also found in fathers, $p_{1\text{-tailed}}$=0.038 (see Table 3). Fathers in the asphyxia group reported a higher frequency of re-experiencing symptoms compared to controls, $p_{1\text{-tailed}}$<.001 and were significantly more likely to report at least one re-experiencing symptom compared to controls, $\chi^2(1)=13.16$, $p<0.001$; (difference in proportions: 37.2%, 90%-CI: 20.5% to 51.1%). Criteria for partial PTSD were met by *n*=10 (24.39%) in the asphyxia group and *n*=13 (22.41%) in the control group. Criteria for a full PTSD symptom diagnosis were met by *n*=11 (26.83%) fathers of the asphyxia group and *n*=6 (10.34%) of the control group. When comparing both groups, asphyxia fathers were more likely to receive a partial or full PTSD symptom diagnosis (Kendall's τ =.20, *p*=0.034). No significant group differences for the HADS total score or for the MIBS total score were found. In mothers of the asphyxia group, having a trauma in the past was linked to more psychological distress (*r*=0.31 [95%-CI: 0.04-0.54]) and having a previous pregnancy was linked to poorer bonding (*r*=0.41 [95%-CI: 0.13-0.63]) (see supplementary table S2). In fathers of the asphyxia group, therapeutic hypothermia of the infant was related to less frequent PTSD symptoms (*r*=-0.37 [95%-CI:-0.61- -0.06]). Past psychological difficulties

(*r*=0.37 [95%-CI: 0.07-0.60]) and past trauma (*r*=0.35 [95%-CI: 0.05-0.59]) were positively correlated with general psychological distress, and a lower Apgar score was linked to poorer bonding (*r*=-0.38 [95%-CI:-0.64--0.05]) (see supplementary table S3).

Discussion

This cross-sectional questionnaire-based Swiss national cohort study comparing parents of infants surviving perinatal asphyxia with those of healthy infants found more frequent PTSD (and particularly re-experiencing) symptoms and more frequent partial or full PTSD symptom diagnosis in asphyxia parents compared with control parents. Furthermore, poorer bonding with the infant in mothers of infants born with asphyxia compared with controls was found. Results need to be considered with caution, as mothers in the asphyxia group had a lower socioeconomic status, a lower frequency of previous pregnancies, and slightly older infants compared to controls. Compared to control fathers, fathers in the asphyxia group had a lower socioeconomic status and older infants.

These results show for the first time that parents of infants with perinatal asphyxia experience elevated symptoms of PTSD, such as has been reported for other populations of high-risk parents, e.g., those of premature or critically ill infants[9-11]. Our finding that mothers of the asphyxia group reported poorer bonding with their infant is in line with other studies of traumatized mothers.[18] The lack of differences between the asphyxia and control parents in relation to general psychological distress (HADS total score) points to a generally healthy

psychological adjustment of parents that might partly be due to a good experience of care regarding their infant and effective staff support.

When investigating potential risk factors for mental health problems in asphyxia group parents, we found that having experienced a past trauma was moderately associated with more general psychological distress in both mothers and fathers. This is in line with research identifying a previous traumatic experience as a risk factor for developing PTSD following childbirth[39] and depression in the general adult population[40]. Our finding that having previously been pregnant was moderately associated with more bonding problems in mothers is novel. It may be that already being a mother makes it harder to invest oneself in a relationship with another child, particularly one that is severely ill. Alternatively, infants who had asphyxia at birth may be less effective in interactions with mothers and mothers may thus find it harder to bond with them. However, more research is needed to explore this. Given the small number of mothers in the asphyxia group, none of the weak correlations of the other neonatal variables were statistically significant but the small to medium sized effects might be detected with a more powerful design.

For fathers in the asphyxia group, therapeutic hypothermia of the infant was moderately related to less frequent PTSD symptoms. This is a novel finding and might be linked to a certain level of reassurance that fathers feel when witnessing a highly technological treatment, thus reducing their perceived threat to their infant's life. Similar to mothers, past psychological difficulties and past trauma were positively and moderately correlated with current general psychological distress, which is in line with previous research in the general adult population[40]. Finally, a lower Apgar score (10 min) was moderately associated with more bonding problems. This novel result may be explained by the fact that a lower Apgar score would have indicated a

more severe life threat for the infant and fathers might have unintentionally found it harder to develop a bond with their infant for fear of losing it. However, this remains to be explored in future studies.

Strengths of the study are the inclusion of a national cohort, the comparison with a control group, and the use of standardised questionnaires. The effect sizes of the significant correlations were all moderate and are thus of potential clinical relevance. The relatively low response rate (47%) is comparable with other studies of high-risk populations[8] and regarded as fair, particularly given the tendency of traumatised parents to avoid reminders of the childbirth or hospital stay. Limitations of the study include the cross-sectional, retrospective design of the study, thus not allowing for causal conclusions, the risk of a reporting bias, and potential problems with multiple testing. The small sample size related to the low prevalence of perinatal asphyxia limited the statistical power, despite it being a national cohort study. The MIBS has so far not been validated for the use with fathers, for whom a bonding questionnaire remains to be developed. Caution needs to be taken in interpreting the results, given that both groups differed on sociodemographic characteristics. Further limitations are the recruitment of the anonymous control group via flyers in public places, not allowing us to check for health problems of their infants and relying on the self-report of the parents. Finally, the temporal nature of the associations, and the potential impact of events between birth and the parental responses, which we did not ask for in either group, may have potentially influenced the study outcomes. We also did not ask parents in either group about infant health issues or events since birth, which may have potentially influenced the study outcomes. Future studies with a larger cohort, a prospective design, and a control group matched on important sociodemographic variables are needed.

Furthermore, investigating the effects of PTSD and bonding on infant outcomes would be of interest.

Conclusion

This study showed for the first time more frequent PTSD (and particularly re-experiencing) symptoms and more partial or full PTSD diagnosis in asphyxia group parents and poorer infant bonding in asphyxia group mothers compared with the control group. Furthermore, we found that a history of past trauma puts parents at increased risk of general psychological distress after perinatal asphyxia.

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Contributors

AH had primary responsibility for the study design, data acquisition, analysis, and writing of the manuscript, and approved the final manuscript as submitted. MBG was involved in the study design, data acquisition, and writing of the manuscript, and approved the final manuscript as submitted. IJ was responsible for the statistical expertise, performed all final statistical analyses, contributed to the writing of the manuscript, and approved the final manuscript as submitted. CF and LG contributed to the data analysis, critically reviewed and revised the manuscript, and approved the final manuscript as submitted. JS and MMH contributed to the interpretation of data, critically reviewed and revised the manuscript and approved the final manuscript as submitted.

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Competing interests

None declared.

Patient consent

Obtained.

Ethics approval

This study was approved by the cantonal ethical review board (Vaud) and by the Swiss Federal Commission for Privacy Protection in Medical Research.

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Table 1: Sample characteristics for mothers and fathers of the asphyxia and control groups

Characteristics	Mothers				Fathers			
	Asphyxia (*n*=52)	Control (*n*=134)	*t, U or* χ^2	*p*-value	Asphyxia (*n*=43)	Control (*n*=58)	*t, U or* χ^2	*p*-value
Parents								
Age (years)	32.02 ± 4.74	32.44 ± 4.27	-0.57	0.567	35.12 ± 6.29	34.64 ± 4.53	0.42	0.679
Largo score	2 (1-5)	1 (1-5)	2668.0	0.011	3 (1-6)	2 (1-4)	657.5	0.002
Marital status (with partner)	48 (92%)	126 (94%)	0.18	0.668	42 (98%)	56 (97%)	0.11	0.742
Migrant status (yes)	16 (31%)	33 (25%)	0.73	0.393	14 (33%)	19 (33%)	0.00	0.983
Previous pregnancy (yes)	21 (42%)	100 (76%)	18.55	<0.001	-	-	-	
History of psychological difficulties (yes)	19 (37%)	46 (34%)	0.08	0.777	9 (21%)	7 (12%)	1.59	0.208
Past trauma (yes)	27 (52%)	50 (37%)	3.30	0.069	15 (36%)	21 (36%)	0.00	0.960
Infants								
Gestational age (weeks)	40 (35-42)	40 (35-42)	3378.0	0.929	40 (35-42)	40 (37-46)	964.5	0.979
Birth weight (grams)	3381.25 ± 408.11	3396.53 ± 506.19	-0.19	0.846	3426.05 ± 421.38	3307.55 ± 504.76	1.20	.232
Age at survey (months)	18.16 ± 7.46	14.13 ± 7.04	3.44	<0.001	18.76 ± 7.15	13.60 ± 6.28	3.66	<0.001
Gender (female)	21 (40%)	75 (56%)	3.64	0.056	18 (42%)	20 (41%)	0.01	0.919

Notes: Values are expressed as *M* ± *SD*, *Md* (*range*), or *n* (%). Due to missing data, effective sample sizes ranged from *n* = 182 to 186 (mothers) and from *n* = 88 to 101 (fathers).

Table 2: Clinical characteristics of the asphyxia children

Characteristics	M ± SD or n (%)
Apgar 1 min	2.11 ± 2.05
Apgar 5 min	3.74 ± 2.27
Apgar 10 min	5.06 ± 2.37
When was full sucking achieved (in days)	6.88 ± 5.11
Resuscitated > 10 min (yes)	27 (51%)
Therapeutic hypothermia (yes)	41 (77%)
Neurological examination normal (yes)	31 (59%)
Seizures (yes)	4 (8%)
Sarnat stage 1	14 (33%)
Sarnat stage 2	25 (58%)
Sarnat stage 3	4(9%)

Notes: Due to missing data, effective sample size ranges $n = 43$ to 53.

Table 3: Range and median questionnaire scores, Mann-Whitney-U-test coefficients, and effect size estimates *r* for mothers and fathers in the asphyxia group and control group

	Asphyxia				Control						
	M	SD	Md	Range	M	SD	Md	Range	*U*	*z*	*r* (95%-*CI*)
Mothers											
PDS total score	8.80	7.19	6.00	0-37	5.95	6.55	4.00	0-30	2291.0	3.14***	0.23 (0.11, 0.34)
PDS re-experiencing	3.29	2.81	3.00	0-12	1.29	2.09	0.00	0-12	1600.0	5.58***	0.40 (0.29, 0.50)
PDS avoidance/numbing	2.52	2.86	1.50	0-12	2.07	2.78	1.00	0-16	2954.0	1.27	0.09 (-0.03, 0.21)
PDS hyperarousal	2.88	2.95	2.00	0-13	2.59	2.84	2.00	0-14	3101.5	0.79	0.06 (-0.06, 0.18)
HADS total score	9.38	5.88	9.00	0-25	10.83	5.55	10.00	0-33	2871.5	-1.86	-0.14 (-0.25, -0.02)
MIBS total score	3.38	3.65	2.00	0-13	2.38	3.38	1.00	0-20	2508.5	1.72*	0.13 (0.01, 0.25)
Fathers											
PDS total score	8.82	10.61	7.00	0-45	4.62	5.10	3.00	0-20	892.0	1.77*	0.18 (0.01, 0.34)
PDS re-experiencing	2.93	3.56	2.00	0-15	0.66	1.19	0.00	0-5	612.0	4.29***	0.41 (0.26, 0.54)
PDS avoidance/numbing	2.71	3.76	1.00	0-18	1.81	2.59	1.00	0-12	1002.0	1.39	0.14 (-0.02, 0.30)
PDS hyperarousal	3.27	3.91	2.00	0-14	2.16	2.18	2.00	0-8	1085.0	0.76	0.06 (-0.11, 0.22)
HADS total score	8.57	5.74	7.00	0-27	9.10	5.38	9.00	2-32	1158.0	-0.61	-0.06 (-0.22, 0.11)
MIBS total score	2.09	2.79	1.00	0-11	2.55	3.05	1.00	0-14	843.0	-0.80	-0.08 (-0.26, 0.09)

Notes: *M* = mean; *SD* = standard deviation; *Md* = median; *U* = Mann-Whitney test statistic; *z* = z-test (a positive z-score denotes higher scale scores in the asphyxia group); $r = z/\sqrt{N}$; *95%-CI* = lower and upper level of the 95% confidence interval . *PDS* =

Posttraumatic Diagnostic Scale, *HADS* = Hospital Anxiety and Depression Scale, *MIBS* = Mother-Infant Bonding Scale. The total sample sizes ranged from $n = 179$ to 186 (mothers) and from $n = 89$ to 101 (fathers). *$p < 0.05$, ***$p < 0.001$ (1-tailed).

Table S1: Characteristics of asphyxia infants in the responder and non-responder groups

Characteristics	Non-responders (*n*=61)	Responders (*n*=53)	*t or* χ^2	*p*-value
Agpar 1 min	2.57 ± 2.36	2.11 ± 2.05	1.11	.272
Agpar 5 min	4.61 ± 2.42	3.74 ± 2.27	1.97	.051
Agpar 10 min	5.56 ± 2.41	5.06 ± 2.37	1.11	.268
When was full sucking achieved (in days)	6.42 ± 5.06	6.88 ± 5.11	-0.46	.650
Resuscitated > 10 min (yes)	26 (43.3%)	27 (50.9%)	0.65 [a]	.419
Therapeutic hypothermia (yes)	45 (73.8%)	41 (77.4%)	0.20	.657
Neurological examination normal (yes)	33 (55.0%)	31 (58.5%)	0.14 [a]	.709
Seizures (yes)	6 (9.8%)	4 (7.5%)	0.19	.667
Sarnat stage 1	14 (28.0%)	14 (32.6%)	0.34 [b]	.855
Sarnat stage 2	32 (64.0%)	25 (58.1%)		
Sarnat stage 3	4 (8.0%)	4 (9.3%)		
Gestational age (weeks)	39 (34-42)	40 (35-42)	1309.00	.072
Birth weight (grams)	3248.26 ± 612.46	3415.57 ± 442.32	-1.69	.095
Gender (female)	25 (41.0%)	21 (39.6%)	0.02	.883

Notes: Values are expressed as *M* ± *SD*, *Md* (*range*), or *n* (%); *p*-values are 2-tailed; [a] *N* = 113; [b] *N* = 93.

Table S2: Pearson correlations and point-biserial correlations between mental health variables and bonding quality with selected study variables for mothers in the asphyxia group and in the control group

	PDS total[a]	HADS total[a]	MIBS[a]
	r (95%-CI)	r_{Apshyx} (95%-CI)	*r* (95%-CI)
Parent's age	0.06 (-0.23, 0.34)	0.22 (-0.06, 0.47)	0.11 (-0.19, 0.39)
Migrant status	0.03 (-0.26, 0.31)	-0.18 (-0.43, 0.10)	-0.03 (-0.32, 0.27)
Largo score[a]	-0.10 (-0.37, 0.19)	-0.04 (-0.31, 0.24)	-0.07 (-0.35, 0.23)
Past psychological difficulties	0.12 (-0.16, 0.39)	0.24 (-0.03, 0.48)	-0.02 (-0.31, 0.28)
Past trauma	0.03 (-0.26, 0.31)	0.31* (0.04, 0.54)	0.05 (-0.25, 0.34)
Previous pregnancy	0.16 (-0.13, 0.42)	0.22 (-0.07, 0.47)	0.41** (0.13, 0.63)
Birth weight	-0.01 (-0.29, 0.27)	-0.14 (-0.40, 0.14)	0.09 (-0.20, 0.38)
Age of infant	-0.26 (-0.50, 0.02)	0.03 (-0.24, 0.31)	0.10 (-0.20,0 .38)
Gestational age[a]	-0.02 (-0.30, 0.26)	-0.03 (-0.30, 0.25)	-0.06 (-0.35, 0.24)
Apgar 1 min[a]	0.05 (-0.24, 0.33)	0.05 (-0.23, 0.32)	0.18 (-0.12, 0.45)
Apgar 5 min	0.12 (-0.17, 0.39)	0.09 (-0.18, 0.36)	0.08 (-0.22, 0.36)
Apgar 10 min	0.16 (-0.13, 0.42)	0.19 (-0.09, 0.44)	-0.10 (-0.39, 0.20)
Resuscitation	-0.24 (-0.49, 0.04)	-0.21 (-0.46, 0.07)	0.01 (-0.28, 0.30)
Therapeutic hypothermia	-0.23 (-0.48, 0.05)	-0.00 (-0.28, 0.27)	-0.01 (-0.30, 0.29)
Sarnat stage > 1	-0.23 (-0.49,0	-0.06 (-0.33,	0.06 (-0.24,

	.06)	.23)	0.36)

Notes: [a] scores were rank-based inverse normal transformed using Blom's formula; effective sample size ranges from $n = 43$ to 52. *$p < 0.05$, **$p < 0.01$ (2-tailed).

Table S3: Pearson correlations and point-biserial correlations between mental health variables and bonding quality with selected study variables for fathers in the asphyxia group

	PDS total[a]	HADS total[a]	MIBS[a]
	r (95%-CI)	r_{Apshyx} (95%-CI)	r_{Apshyx} (95%-CI)
Parent's age	-0.14 (-0.45, 0.19)	0.06 (-0.25, 0.36)	0.26 (-0.09, 0.55)
Migrant status	0.04 (-0.28, 0.36)	0.01 (-0.29, 0.31)	-0.08 (-0.41, 0.26)
Largo score[a]	0.07 (-0.29, 0.41)	0.20 (-0.14, 0.49)	-0.16 (-0.51, 0.22)
Past psychological difficulties	0.05 (-0.28, 0.36)	0.37* (0.07, 0.60)	-0.12 (-0.44, 0.23)
Past trauma	0.13 (-0.19, 0.44)	0.35* (0.05, 0.59)	0.02 (-0.32, 00.36)
Birth weight	0.06 (-0.26, 0.37)	-0.06 (-0.35, 0.24)	0.17 (-0.18, 0.48)
Age of infant	-0.20 (-0.48, 0.13)	0.09 (-0.21, 0.38)	0.00 (-0.34, 0.34)
Gestational age[a]	-0.01 (-0.33, 0.31)	-0.03 (-0.33, 0.27)	-0.12 (-0.44, 0.22)
Apgar 1 min[a]	-0.09 (-0.40, 0.23)	-0.14 (-0.43, 0.16)	-0.02 (-0.35, 0.32)
Apgar 5 min	0.04 (-0.28, 0.36)	-0.02 (-0.32, 0.29)	-0.10 (-0.43, 0.24)
Apgar 10 min	0.02 (-0.30, 0.33)	0.01 (-0.29, 0.31)	-0.38* (-0.64, -0.05)
Resuscitation	-0.18 (-0.47,0 .15)	-0.01 (-0.31, 0.29)	0.08 (-0.26,0 .41)
Therapeutic hypothermia	-0.37* (-0.61, -0.06)	-0.17 (-0.45, 0.14)	0.09 (-0.26, 0.42)
Sarnat stage > 1	-0.25 (-0.53, 0.08)	-0.14 (-0.43, 0.17)	-0.05 (-0.38, 0.30)

Notes: [a] scores were rank-based inverse normal transformed using Blom's formula; effective sample size ranges from $n = 28$ to 43. $*p < .05$ (2-tailed).

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Impact of perinatal asphyxia on parental mental health and bonding with the infant: a questionnaire survey of Swiss parents

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Impact of perinatal asphyxia on parental mental health and bonding with the infant: a questionnaire survey of Swiss parents.

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What is already known on this topic

- Perinatal asphyxia is a life threatening event, potentially psychologically traumatic for parents.
- Parental mental health problems may impact on bonding with and development of the child.
- Research examining posttraumatic stress disorder, psychological distress, and bonding with their infant in parents of infants born with perinatal asphyxia is lacking.

What this study adds

- More frequent posttraumatic stress symptoms in both parents and poorer bonding with the infant in mothers after perinatal asphyxia were found compared to control parents.
- Parents of infants hospitalized for perinatal asphyxia are more at risk of developing posttraumatic stress disorder than control parents.

Abstract

Objective: To compare current mental health symptoms and infant bonding in parents whose infants survived perinatal asphyxia in the last two years with control parents and to investigate which sociodemographic, obstetric, and neonatal variables correlated with parental mental health and infant bonding in the asphyxia group.

Design: Cross-sectional questionnaire survey of parents whose children were registered in Swiss national Asphyxia and Cooling register and control parents (Posttraumatic Diagnostic Scale, Hospital Anxiety and Depression Scale, Mother-to-Infant Bonding Scale).

Results: The response rate for the asphyxia group was 46.5%. Compared with controls, mothers and fathers in the asphyxia group had a higher frequency of PTSD symptoms (p <0.001). More mothers (n=28,56%) had symptom diagnostis of either full or partial PTSD than controls (n=54,39%)(p=0.032). Similarly, more fathers (n=31,51%) had symptom diagnostis of either partial or full PTSD than controls (n=19,33%)(p=0.034). Mothers reported poorer bonding with the infant (p =0.043) than controls. Having a trauma in the past was linked to more psychological distress in mothers (r=0.31 [95%-CI: 0.04-0.54]) and fathers(r=0.35 [95%-CI: 0.05-0.59]). For mothers, previous pregnancy was linked to poorer bonding (r=0.41 [95%-CI: 0.13-0.63]). In fathers, therapeutic hypothermia of the infant was related to less frequent PTSD symptoms (r=-0.37 [95%-CI:-0.61- -0.06]) and past psychological difficulties (r=0.37 [95%-CI: 0.07-0.60]) to more psychological distress. A lower Apgar score was linked to poorer bonding (r=-0.38 [95%-CI:-0.64--0.05]).

Conclusions: Parents of infants hospitalized for perinatal asphyxia are more at risk of developing PTSD than control parents.

Keywords: asphyxia, posttraumatic stress disorder, mother, mental health, bonding

Perinatal asphyxia is a life threatening event affecting 2/1000 infants, which qualifies as a psychologically traumatic stressor for parents[1]. When associated with hypoxic ischemic encephalopathy (HIE), it may lead to disabling brain injuries or death[2-4]. Current treatment of HIE requires immediate transfer to a specialized neonatal unit and therapeutic hypothermia in order to reduce the risk of brain lesions and neurodevelopmental disabilities[5].

Parents of infants admitted to a neonatal intensive care unit report more stress[6], more adjustment difficulties, and need for support during the first year after delivery[7 8] compared to parents of healthy infants. They may experience posttraumatic stress disorder (PTSD) [9-11], anxiety, and depression following the birth[12].

Although two qualitative studies described the experiences of becoming a parent after perinatal asphyxia[13 14] and another showed that fathers may be traumatized[15], PTSD symptoms or psychological distress have not been measured in parents of these children. PTSD consists of four symptom clusters (re-experiencing, avoidance, hyperarousal, and negative cognitions and mood) and is diagnosable from 1 month post-trauma[1]. Assessing postnatal PTSD and psychological distress is not only important for the well-being of parents, but PTSD may also significantly interfere with infant bonding, leading to severe and long-term consequences for the development of the baby[16-18].

The current study aimed to compare current symptoms of PTSD, psychological distress, and infant bonding in parents who had an infant with perinatal asphyxia in the last two years with control parents. It was predicted that parents of the asphyxia group would report more PTSD and psychological distress symptoms and poorer infant bonding than controls. Another objective was to investigate which sociodemographic, psychological, obstetric, and neonatal variables were correlated with mental health symptoms and infant bonding in both groups.

Methods

Study design and sample

This cross-sectional Swiss national cohort study (questionnaire survey of Swiss parents) included infants surviving perinatal asphyxia (asphyxia group) born in 2012 and 2013 (i.e., up to two years after birth), registered in the national Asphyxia and Cooling register of the Swiss Neonatal Network & Follow-up Group. Infants are anonymously entered in the register if they have a gestational age of more than 35 weeks and fulfill criteria for therapeutic hypothermia (low Apgar score, need for ventilatory support or abnormal blood gases during the first hour of life, clinical signs of encephalopathy during the first 6 hours of life)[19]. The questionnaires were sent out to the participating hospitals in May 2014, who then sent them on to the asphyxia group parents. Parents were sent an invitation letter, a participant information sheet, and the questionnaires in French, German or English, with a pre-stamped envelope, by their local referring hospitals.

The control group was recruited during the same time period. Parents of the control group were recruited via flyers in public places, on Swiss internet forums for parents, and on a website of the University of Lausanne. They were eligible if they had given birth in 2012 or 2013 to a full-term infant that they judged to be healthy (i.e., up to two years after birth). When accessing the online questionnaire, participants first read the information sheet; informed consent was implied when they completed the anonymous questionnaire in French, German or English.

This study was approved by the cantonal ethical review board (Vaud) and by the Swiss Federal Commission for Privacy Protection in Medical Research.

Measures

Parental PTSD was measured using the 17-item Posttraumatic Diagnostic Scale (PDS)[20-22]. It provides both a diagnosis according to DSM-IV criteria and a measure of PTSD symptom severity, as well as symptom cluster severity (re-experiencing, avoidance, and hyperarousal) [23 24], and has been widely used in postnatal populations (e.g.[25]). Participants rated how often they experienced each of the symptoms in the past month, using a 4-point frequency scale ranging from 0 (*not at all or only one time*) to 3 (*5 times per week or almost always*). A *partial* PTSD symptoms diagnosis was defined as meeting the criteria for two of the three PTSD symptom clusters[25]. The PDS has good psychometric properties[20 21]. Cronbach's alpha of the total PDS frequency score (α=.90), and of the three sub-scales (re-experiencing: α=.85; avoidance: α=.75; hyperarousal: α=.80) was good to excellent.

General psychological distress of parents in the past week was assessed with the Hospital Anxiety and Depression Scale (HADS)[26-28], a 14-item questionnaire. Each item is scored from 0 to 3, with higher scores indicating greater psychological distress[29]. The HADS has good psychometric properties[27], with a Cronbach's alpha of α=.81 in the current study.

The Mother-to-Infant Bonding Scale (MIBS)[30] consists of eight adjectives that describe feelings towards their baby (loving, resentful, neutral or felt nothing, joyful, dislike, protective, disappointed and aggressive) and measures infant bonding. Each adjective is followed by a 4-point scale ranging from 0 (*very much*) to 3 (*not at all*). When the adjective reflects a negative emotional response, the scoring is reversed. Possible scores range between 0 and 24, with high scores indicating problematic bonding[31 32]. Cronbach's alpha was fair, α=.77.

Parents also completed a demographic questionnaire (age, marital status, migrant status, educational background for mothers, occupation for fathers, previous pregnancy for mothers) with two items assessing whether they had experienced past or current psychological difficulties (In the past, have you already experienced emotional or psychological difficulties? (yes/no) If yes, can you please briefly describe this? Do you currently experience emotional or psychological difficulties? (yes/no) If yes, can you please briefly describe this?), and whether they had experienced a past traumatic event (Have you already experienced a traumatic or particularly stressful situation? (yes/no) If yes, can you please briefly describe this?). Parental socioeconomic status was determined using the Largo score, a 6-point scale, with recorded mother's education (*1=university and 6=special or no schooling*) and father's occupation (*1=leading position and 6=unskilled labor*)[33]. Parents also reported demographic details related to their infant (gender, gestational age, birth weight, current age of infant). Neonatal variables were obtained from the national asphyxia register: Apgar score (at 1, 5, and 10 minutes), umbilical cord pH, number of days when full sucking was achieved, whether infant was resuscitated >10 minutes, Sarnat stage [34], whether therapeutic hypothermia had occurred, whether the neurological examination at discharge had been normal, and whether any seizure had occurred.

Statistical analyses

Data were analyzed using IBM SPSS version 22. Descriptive statistics were calculated for each scale. Mothers and fathers of the asphyxia and control group were compared separately regarding sociodemographic characteristics using chi-squared tests, independent samples *t*-tests, and Mann-Whitney U-tests. Responders and non-responders within the asphyxia group were

compared regarding obstetric and neonatal variables using chi-squared tests and independent samples *t*-tests. To compare the asphyxia and control groups regarding the central tendencies of the non-normal distributed mental health and bonding outcomes (PDS total score and symptom clusters, HADS, MIBS), rank based Mann-Whitney U-tests were performed. The effect size for the Mann-Whitney statistic was estimated as $r = z/\sqrt{N}$ [35]. The limits of the 95%-CI of the effect size estimate *r* obtained for the Mann-Whitney statistic were calculated with ESCI [35]. Established guidelines for the interpretation of *r* suggest that a large effect is 0.50, a medium-sized effect is 0.30, and a small effect is 0.10[35].

The χ^2 tests were performed to compare PTSD cluster symptoms between groups. The effect sizes of frequencies analysed with a chi-squared test were expressed as the differences of the two independent proportions and the corresponding 95%-CI was calculated using ESCI[35]. To compare groups regarding PTSD diagnosis (none, partial, full), a Kendall rank correlation analysis was carried out. Bivariate correlation analyses (Pearson and point-biserial correlations) between sociodemographic, obstetric, and neonatal variables and mental health or infant bonding were carried out. Prior to assessing the correlation, the non-normally distributed scores (PDS, HADS, MIBS, Largo, gestational age, and Apgar index 1 minute) were rank-based inverse normal (RIN) transformed within each gender using Blom's formula[36]. Given that the non-independence of mothers' and fathers' scores may lead to biased estimates[37], mothers and fathers were analysed separately. Within each gender, correlations -with 95 % CI were calculated. . The 95% confidence interval (95%-CI) for correlations and effect size estimates *r* were calculated using the Exploratory Software for Confidence Intervals (ESCI)[38].

Results

Sample characteristics

For the asphyxia group, parents of 114 registered infants were contacted and 95 parents (52 mothers and 43 fathers) of 53 infants (46.5%) responded. The control group was composed of 134 mothers and 58 fathers. Missing data per variable ranged from 0 to 7 (mothers) and 0 to 13 (fathers). Missing data were not replaced. The comparison of responders and non-responders according to infant neonatal variables listed in Tables 1 and 2 resulted in no significant differences (see Table S1 in the supplemental material).

Regarding demographic variables, three significant differences between asphyxia and control mothers were found (see Table 1): asphyxia group mothers had a higher Largo score, p=0.011 and reported a lower frequency of previous pregnancies, (p<0.001) compared to controls. Furthermore, the current age of the infant was higher for the asphyxia group (18 vs. 14 months), (p<0.001). For fathers, corresponding significant differences were found for Largo score, (p=0.002), and current age of the infant (18 vs. 14 months, p<0.001).

Mental health symptoms and infant bonding: group comparisons

Mothers in the asphyxia group reported a higher frequency of total PTSD symptoms than controls, $p_{1\text{-tailed}}$ <0.001 (see Table 3). This difference was due to a higher frequency of re-experiencing symptoms in asphyxia group mothers compared to controls, $p_{1\text{-tailed}}$<0.001. Consistent with the latter finding, mothers in the asphyxia group were also more likely to have at least one re-experiencing symptom than controls, $\chi^2(1) = 25.21$; p <0.001; (difference in

proportions: 41.7%, 90%-CI: 29.3% to 51.0%). 14 mothers (28%) in the asphyxia group met the criteria for partial PTSD compared with 30 (22%) in the control group. An additional 14 mothers (28%) met the criteria for full PTSD diagnosis compared with 22 (16%) in the control group. When comparing both groups, asphyxia mothers were more likely to receive a partial or full PTSD symptom diagnosis (Kendalls' τ =.16, p=0.032). Asphyxia group mothers also reported poorer bonding with the infant compared to controls, U=2508.5, z=1.72, $p_{1\text{-tailed}}$=0.043 (see Table 3). No significant group difference for the HADS total score was found.

The difference for total PTSD symptoms between asphyxia and control group was also found in fathers, $p_{1\text{-tailed}}$=0.038 (see Table 3). Fathers in the asphyxia group reported a higher frequency of re-experiencing symptoms compared to controls, $p_{1\text{-tailed}}$<.001 and were significantly more likely to report at least one re-experiencing symptom compared to controls, $\chi^2(1)=13.16$, p<0.001; (difference in proportions: 37.2%, 90%-CI: 20.5% to 51.1%). Criteria for partial PTSD were met by n=10 (24%) in the asphyxia group and n=13 (22%) in the control group. Criteria for a full PTSD symptom diagnosis were met by n=11 (27%) fathers of the asphyxia group and n=6 (10%) of the control group. When comparing both groups, asphyxia fathers were more likely to receive a partial or full PTSD symptom diagnosis (Kendall's τ =.20, p=0.034). No significant group differences for the HADS total score or for the MIBS total score were found. In mothers of the asphyxia group, having a trauma in the past was linked to more psychological distress (r=0.31 [95%-CI: 0.04-0.54]) and having a previous pregnancy was linked to poorer bonding (r=0.41 [95%-CI: 0.13-0.63]) (see supplementary table S2). In fathers of the asphyxia group, therapeutic hypothermia of the infant was related to less frequent PTSD symptoms (r=-0.37 [95%-CI:-0.61- -0.06]). Past psychological difficulties (r=0.37 [95%-CI: 0.07-0.60]) and past trauma (r=0.35 [95%-CI: 0.05-0.59]) were positively correlated with general

psychological distress, and a lower Apgar score was linked to poorer bonding (r=-0.38 [95%-CI:-0.64--0.05]) (see supplementary table S3).

Discussion

This cross-sectional questionnaire-based Swiss national cohort study comparing parents of infants surviving perinatal asphyxia with those of healthy infants found more frequent PTSD (and particularly re-experiencing) symptoms and more frequent partial or full PTSD symptom diagnosis in asphyxia parents compared with control parents. Furthermore, poorer bonding with the infant in mothers of infants born with asphyxia compared with controls was found. Results need to be considered with caution, as mothers in the asphyxia group had a lower socioeconomic status, a lower frequency of previous pregnancies, and slightly older infants compared to controls. Compared to control fathers, fathers in the asphyxia group had a lower socioeconomic status and older infants.

These results show for the first time that parents of infants with perinatal asphyxia experience elevated symptoms of PTSD, such as has been reported for other populations of high-risk parents, e.g., those of premature or critically ill infants[9-11]. Our finding that mothers of the asphyxia group reported poorer bonding with their infant is in line with other studies of traumatized mothers.[18] The lack of differences between the asphyxia and control parents in relation to general psychological distress (HADS total score) points to a generally healthy psychological adjustment of parents that might partly be due to a good experience of care regarding their infant and effective staff support.

When investigating potential risk factors for mental health problems in asphyxia group parents, we found that having experienced a past trauma was moderately associated with more general psychological distress in both mothers and fathers. This is in line with research identifying a previous traumatic experience as a risk factor for developing PTSD following childbirth[39] and depression in the general adult population[40]. Our finding that having previously been pregnant was moderately associated with more bonding problems in mothers is novel. It may be that already being a mother makes it harder to invest oneself in a relationship with another child, particularly one that is severely ill. Alternatively, infants who had asphyxia at birth may be less effective in interactions with mothers and mothers may thus find it harder to bond with them. However, more research is needed to explore this. Given the small number of mothers in the asphyxia group, none of the weak correlations of the other neonatal variables were statistically significant but the small to medium sized effects might be detected with a more powerful design.

For fathers in the asphyxia group, therapeutic hypothermia of the infant was moderately related to less frequent PTSD symptoms. This is a novel finding and might be linked to a certain level of reassurance that fathers feel when witnessing a highly technological treatment, thus reducing their perceived threat to their infant's life. Similar to mothers, past psychological difficulties and past trauma were positively and moderately correlated with current general psychological distress, which is in line with previous research in the general adult population[40]. Finally, a lower Apgar score (10 min) was moderately associated with more bonding problems. This novel result may be explained by the fact that a lower Apgar score would have indicated a more severe life threat for the infant and fathers might have unintentionally found it harder to

develop a bond with their infant for fear of losing it. However, this remains to be explored in future studies.

Strengths of the study are the inclusion of a national cohort, the comparison with a control group, and the use of standardised questionnaires. The effect sizes of the significant correlations were all moderate and are thus of potential clinical relevance. The relatively low response rate (47%) is comparable with other studies of high-risk populations[8] and regarded as fair, particularly given the tendency of traumatised parents to avoid reminders of the childbirth or hospital stay. Limitations of the study include the cross-sectional, retrospective design of the study, thus not allowing for causal conclusions, the risk of a reporting bias, and potential problems with multiple testing. The small sample size related to the low prevalence of perinatal asphyxia limited the statistical power, despite it being a national cohort study. The MIBS has so far not been validated for the use with fathers, for whom a bonding questionnaire remains to be developed. Caution needs to be taken in interpreting the results, given that both groups differed on sociodemographic characteristics. Further limitations are the recruitment of the anonymous control group via flyers in public places, not allowing us to check for health problems of their infants and relying on the self-report of the parents. Finally, the temporal nature of the associations, and the potential impact of events between birth and the parental responses, which we did not ask for in either group, may have potentially influenced the study outcomes. We also did not ask parents in either group about infant health issues or events since birth, which may have potentially influenced the study outcomes. Future studies with a larger cohort, a prospective design, and a control group matched on important sociodemographic variables are needed. Furthermore, investigating the effects of PTSD and bonding on infant outcomes would be of interest.

Conclusion

This study showed for the first time more frequent PTSD (and particularly re-experiencing) symptoms and more partial or full PTSD diagnosis in asphyxia group parents and poorer infant bonding in asphyxia group mothers compared with the control group. Furthermore, we found that a history of past trauma puts parents at increased risk of general psychological distress after perinatal asphyxia.

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Contributors

AH had primary responsibility for the study design, data acquisition, analysis, and writing of the manuscript, and approved the final manuscript as submitted. MBG was involved in the study design, data acquisition, and writing of the manuscript, and approved the final manuscript as submitted. IJ was responsible for the statistical expertise, performed all final statistical analyses,

contributed to the writing of the manuscript, and approved the final manuscript as submitted. CF and LG contributed to the data analysis, critically reviewed and revised the manuscript, and approved the final manuscript as submitted. JS and MMH contributed to the interpretation of data, critically reviewed and revised the manuscript and approved the final manuscript as submitted.

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Competing interests

None declared.

Patient consent

Obtained.

Ethics approval

This study was approved by the cantonal ethical review board (Vaud) and by the Swiss Federal Commission for Privacy Protection in Medical Research.

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Table 1: Sample characteristics for mothers and fathers of the asphyxia and control groups

Characteristics	Mothers				Fathers			
	Asphyxia (*n*=52)	Control (*n*=134)	*t, U or* χ^2	*p*-value	Asphyxia (*n*=43)	Control (*n*=58)	*t, U or* χ^2	*p*-value
Parents								
Age (years)	32.02 ± 4.74	32.44 ± 4.27	-0.57	0.567	35.12 ± 6.29	34.64 ± 4.53	0.42	0.679
Largo score	2 (1-5)	1 (1-5)	2668.0	0.011	3 (1-6)	2 (1-4)	657.5	0.002
Marital status (with partner)	48 (92%)	126 (94%)	0.18	0.668	42 (98%)	56 (97%)	0.11	0.742
Migrant status (yes)	16 (31%)	33 (25%)	0.73	0.393	14 (33%)	19 (33%)	0.00	0.983
Previous pregnancy (yes)	21 (42%)	100 (76%)	18.55	<0.001	-	-	-	
History of psychological difficulties (yes)	19 (37%)	46 (34%)	0.08	0.777	9 (21%)	7 (12%)	1.59	0.208
Past trauma (yes)	27 (52%)	50 (37%)	3.30	0.069	15 (36%)	21 (36%)	0.00	0.960
Infants								
Gestational age (weeks)	40 (35-42)	40 (35-42)	3378.0	0.929	40 (35-42)	40 (37-46)	964.5	0.979
Birth weight (grams)	3381.25 ± 408.11	3396.53 ± 506.19	-0.19	0.846	3426.05 ± 421.38	3307.55 ± 504.76	1.20	.232
Age at survey (months)	18.16 ± 7.46	14.13 ± 7.04	3.44	<0.001	18.76 ± 7.15	13.60 ± 6.28	3.66	<0.001
Gender (female)	21 (40%)	75 (56%)	3.64	0.056	18 (42%)	20 (41%)	0.01	0.919

Notes: Values are expressed as *M* ± *SD*, *Md* (*range*), or *n* (%). Due to missing data, effective sample sizes ranged from *n* = 182 to 186 (mothers) and from *n* = 88 to 101 (fathers).

Table 2: Clinical characteristics of the asphyxia children

Characteristics	M ± SD or n (%)
Apgar 1 min	2.11 ± 2.05
Apgar 5 min	3.74 ± 2.27
Apgar 10 min	5.06 ± 2.37
When was full sucking achieved (in days)	6.88 ± 5.11
Resuscitated > 10 min (yes)	27 (51%)
Therapeutic hypothermia (yes)	41 (77%)
Neurological examination normal (yes)	31 (59%)
Seizures (yes)	4 (8%)
Sarnat stage 1	14 (33%)
Sarnat stage 2	25 (58%)
Sarnat stage 3	4(9%)

Notes: Due to missing data, effective sample size ranges $n = 43$ to 53.

Table 3: Range and median questionnaire scores, Mann-Whitney-U-test coefficients, and effect size estimates *r* for mothers and fathers in the asphyxia group and control group

	Asphyxia				Control						
	M	SD	Md	Range	M	SD	Md	Range	*U*	*z*	*r* (95%-*CI*)
Mothers											
PDS total score	8.80	7.19	6.00	0-37	5.95	6.55	4.00	0-30	2291.0	3.14***	0.23 (0.11, 0.34)
PDS re-experiencing	3.29	2.81	3.00	0-12	1.29	2.09	0.00	0-12	1600.0	5.58***	0.40 (0.29, 0.50)
PDS avoidance/numbing	2.52	2.86	1.50	0-12	2.07	2.78	1.00	0-16	2954.0	1.27	0.09 (-0.03, 0.21)
PDS hyperarousal	2.88	2.95	2.00	0-13	2.59	2.84	2.00	0-14	3101.5	0.79	0.06 (-0.06, 0.18)
HADS total score	9.38	5.88	9.00	0-25	10.83	5.55	10.00	0-33	2871.5	-1.86	-0.14 (-0.25, -0.02)
MIBS total score	3.38	3.65	2.00	0-13	2.38	3.38	1.00	0-20	2508.5	1.72*	0.13 (0.01, 0.25)
Fathers											
PDS total score	8.82	10.61	7.00	0-45	4.62	5.10	3.00	0-20	892.0	1.77*	0.18 (0.01, 0.34)
PDS re-experiencing	2.93	3.56	2.00	0-15	0.66	1.19	0.00	0-5	612.0	4.29***	0.41 (0.26, 0.54)
PDS avoidance/numbing	2.71	3.76	1.00	0-18	1.81	2.59	1.00	0-12	1002.0	1.39	0.14 (-0.02, 0.30)
PDS hyperarousal	3.27	3.91	2.00	0-14	2.16	2.18	2.00	0-8	1085.0	0.76	0.06 (-0.11, 0.22)
HADS total score	8.57	5.74	7.00	0-27	9.10	5.38	9.00	2-32	1158.0	-0.61	-0.06 (-0.22, 0.11)
MIBS total score	2.09	2.79	1.00	0-11	2.55	3.05	1.00	0-14	843.0	-0.80	-0.08 (-0.26, 0.09)

Notes: *M* = mean; *SD* = standard deviation; *Md* = median; *U* = Mann-Whitney test statistic; *z* = z-test (a positive z-score denotes higher scale scores in the asphyxia group); $r = z/\sqrt{N}$; *95%-CI* = lower and upper level of the 95% confidence interval . *PDS* =

Posttraumatic Diagnostic Scale, *HADS* = Hospital Anxiety and Depression Scale, *MIBS* = Mother-Infant Bonding Scale. The total sample sizes ranged from $n = 179$ to 186 (mothers) and from $n = 89$ to 101 (fathers). *$p < 0.05$, ***$p < 0.001$ (1-tailed).

Table S1: Characteristics of asphyxia infants in the responder and non-responder groups

Characteristics	Non-responders (*n*=61)	Responders (*n*=53)	*t or* χ^2	*p*-value
Agpar 1 min	2.57 ± 2.36	2.11 ± 2.05	1.11	.272
Agpar 5 min	4.61 ± 2.42	3.74 ± 2.27	1.97	.051
Agpar 10 min	5.56 ± 2.41	5.06 ± 2.37	1.11	.268
When was full sucking achieved (in days)	6.42 ± 5.06	6.88 ± 5.11	-0.46	.650
Resuscitated > 10 min (yes)	26 (43.3%)	27 (50.9%)	0.65 [a]	.419
Therapeutic hypothermia (yes)	45 (73.8%)	41 (77.4%)	0.20	.657
Neurological examination normal (yes)	33 (55.0%)	31 (58.5%)	0.14 [a]	.709
Seizures (yes)	6 (9.8%)	4 (7.5%)	0.19	.667
Sarnat stage 1	14 (28.0%)	14 (32.6%)	0.34 [b]	.855
Sarnat stage 2	32 (64.0%)	25 (58.1%)		
Sarnat stage 3	4 (8.0%)	4 (9.3%)		
Gestational age (weeks)	39 (34-42)	40 (35-42)	1309.00	.072
Birth weight (grams)	3248.26 ± 612.46	3415.57 ± 442.32	-1.69	.095
Gender (female)	25 (41.0%)	21 (39.6%)	0.02	.883

Notes: Values are expressed as *M* ± *SD*, *Md* (*range*), or *n* (%); *p*-values are 2-tailed; [a] *N* = 113; [b] *N* = 93.

Table S2: Pearson correlations and point-biserial correlations between mental health variables and bonding quality with selected study variables for mothers in the asphyxia group and in the control group

	PDS total[a]	HADS total[a]	MIBS[a]
	r (95%-CI)	r_{Apshyx} (95%-CI)	*r* (95%-CI)
Parent's age	0.06 (-0.23, 0.34)	0.22 (-0.06, 0.47)	0.11 (-0.19, 0.39)
Migrant status	0.03 (-0.26, 0.31)	-0.18 (-0.43, 0.10)	-0.03 (-0.32, 0.27)
Largo score[a]	-0.10 (-0.37, 0.19)	-0.04 (-0.31, 0.24)	-0.07 (-0.35, 0.23)
Past psychological difficulties	0.12 (-0.16, 0.39)	0.24 (-0.03, 0.48)	-0.02 (-0.31, 0.28)
Past trauma	0.03 (-0.26, 0.31)	0.31* (0.04, 0.54)	0.05 (-0.25, 0.34)
Previous pregnancy	0.16 (-0.13, 0.42)	0.22 (-0.07, 0.47)	0.41** (0.13, 0.63)
Birth weight	-0.01 (-0.29, 0.27)	-0.14 (-0.40, 0.14)	0.09 (-0.20, 0.38)
Age of infant	-0.26 (-0.50, 0.02)	0.03 (-0.24, 0.31)	0.10 (-0.20,0 .38)
Gestational age[a]	-0.02 (-0.30, 0.26)	-0.03 (-0.30, 0.25)	-0.06 (-0.35, 0.24)
Apgar 1 min[a]	0.05 (-0.24, 0.33)	0.05 (-0.23, 0.32)	0.18 (-0.12, 0.45)
Apgar 5 min	0.12 (-0.17, 0.39)	0.09 (-0.18, 0.36)	0.08 (-0.22, 0.36)
Apgar 10 min	0.16 (-0.13, 0.42)	0.19 (-0.09, 0.44)	-0.10 (-0.39, 0.20)
Resuscitation	-0.24 (-0.49, 0.04)	-0.21 (-0.46, 0.07)	0.01 (-0.28, 0.30)
Therapeutic hypothermia	-0.23 (-0.48, 0.05)	-0.00 (-0.28, 0.27)	-0.01 (-0.30, 0.29)
Sarnat stage > 1	-0.23 (-0.49,0	-0.06 (-0.33,	0.06 (-0.24,

	.06)	.23)	0.36)

Notes: [a] scores were rank-based inverse normal transformed using Blom's formula; effective sample size ranges from $n = 43$ to 52. *$p < 0.05$, **$p < 0.01$ (2-tailed).

Table S3: Pearson correlations and point-biserial correlations between mental health variables and bonding quality with selected study variables for fathers in the asphyxia group

	PDS total[a]	HADS total[a]	MIBS[a]
	r (95%-CI)	r_{Apshyx} (95%-CI)	r_{Apshyx} (95%-CI)
Parent's age	-0.14 (-0.45, 0.19)	0.06 (-0.25, 0.36)	0.26 (-0.09, 0.55)
Migrant status	0.04 (-0.28, 0.36)	0.01 (-0.29, 0.31)	-0.08 (-0.41, 0.26)
Largo score[a]	0.07 (-0.29, 0.41)	0.20 (-0.14, 0.49)	-0.16 (-0.51, 0.22)
Past psychological difficulties	0.05 (-0.28, 0.36)	0.37* (0.07, 0.60)	-0.12 (-0.44, 0.23)
Past trauma	0.13 (-0.19, 0.44)	0.35* (0.05, 0.59)	0.02 (-0.32, 00.36)
Birth weight	0.06 (-0.26, 0.37)	-0.06 (-0.35, 0.24)	0.17 (-0.18, 0.48)
Age of infant	-0.20 (-0.48, 0.13)	0.09 (-0.21, 0.38)	0.00 (-0.34, 0.34)
Gestational age[a]	-0.01 (-0.33, 0.31)	-0.03 (-0.33, 0.27)	-0.12 (-0.44, 0.22)
Apgar 1 min[a]	-0.09 (-0.40, 0.23)	-0.14 (-0.43, 0.16)	-0.02 (-0.35, 0.32)
Apgar 5 min	0.04 (-0.28, 0.36)	-0.02 (-0.32, 0.29)	-0.10 (-0.43, 0.24)
Apgar 10 min	0.02 (-0.30, 0.33)	0.01 (-0.29, 0.31)	-0.38* (-0.64, -0.05)
Resuscitation	-0.18 (-0.47,0 .15)	-0.01 (-0.31, 0.29)	0.08 (-0.26,0 .41)
Therapeutic hypothermia	-0.37* (-0.61, -0.06)	-0.17 (-0.45, 0.14)	0.09 (-0.26, 0.42)
Sarnat stage > 1	-0.25 (-0.53, 0.08)	-0.14 (-0.43, 0.17)	-0.05 (-0.38, 0.30)

Notes: [a] scores were rank-based inverse normal transformed using Blom's formula; effective sample size ranges from $n = 28$ to 43. $*p < .05$ (2-tailed).