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Supplementary Information for

Childhood maltreatment is associated with changes in mitochondrial bioenergetics in maternal, but not in neonatal immune cells

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Supplementary Information Text

SI Materials and Methods

Study participants and design
Study participants were recruited in the Department of Obstetrics and Gynecology at Ulm University Hospital within the scope of the project "My Childhood – Your Childhood". The aim of this longitudinal study was to investigate psychobiological risk and resilience factors in the intergenerational transmission of CM in a community sample (for more details see 1, 2). Mothers were recruited within one week after parturition (*M*=2.32 [SD=1.50] days for the cohort of this paper) for study participation (for exclusion criteria and recruitment process see Figure S2). To avoid potential biases of the energetic system due to extreme parturition-related stress, severe complications during parturition as well as severe health problems among mothers and children were considered as exclusion criteria. Consequently, our cohort consisted of healthy mother-newborn dyads after parturition. Prior to the psychodiagnostic interview, written informed consent was obtained from 548 women. Umbilical cord blood (up to 35 ml) was directly transported to the laboratory of the Department of Clinical & Biological Psychology to isolate umbilical blood mononuclear cells (UBMCs). If mothers met any of the exclusion criteria or declined participation (Figure S2), UBMC samples of their newborns were discarded. Until mothers' written informed consent was obtained, the umbilical cord blood was prepared only for later storage, and no biological analyses were conducted. Except of the isolation of the blood cells and storage of the cells, no further measurements were conducted, and, thus, no participant-related data were collected. Peripheral blood (up to 35 ml) was collected from non-fasting mothers by venipuncture within one week after parturition to isolate peripheral blood mononuclear cells (PBMCs). Participants received a remuneration of 15 € for study participation. All study procedures were in accordance with the Declaration of Helsinki (3) and approved by the Ethics Committee of Ulm University.

Sociodemographic and psychological measures
During the psychodiagnostic interview, mothers were asked about their sociodemographic and clinical data and to provide retrospective information about their childhood. The German short version of the *Childhood Trauma Questionnaire* (CTQ; 4, 5) was used to assess maternal CM exposure. With respect to the emotionally sensitive puerperium situation of the participating mothers, the CTQ was conducted as an interview by trained psychologists. The CTQ sum score was used as a cumulative measure of CM experiences, defined as CM load (6). Using established CTQ cut-off criteria (7), mothers' CM experiences were classified into the categories "none", "mild", "moderate", and "severe". Following the low cut-off, women without CM experiences were classified as CM-, whereas women with at least mild CM experiences in one or more CTQ subscales were categorized as CM+. CM+ mothers and their newborns did not differ from CM- mothers and their newborns with regard to descriptive characteristics, except for the CTQ sum score and the sum scores of the CTQ subscales (Table S1). We did not assess maternal body mass index (BMI) after parturition in our study cohort, as the BMI is not a robust reference measure for mothers shortly after giving birth, since the woman's body undergoes dynamic physiological changes during pregnancy (8, 9).

Blood sampling and isolation of peripheral blood mononuclear cells.
Samples of peripheral blood from mothers (*n*=318) and umbilical cord blood from newborns (*n*=238) were drawn into monovettes (Sarstedt, Nürmbrecht, Germany) buffered with Citrate-phosphate-dextrose-adenine (CPDA) to minimize nutritional stress for blood cells and to compensate for possible differences in storage time between blood collection and processing. PBMCs and UBMCs were isolated by Ficoll-Hypaque density-gradient centrifugation (GE Healthcare, Chalfont St Giles, UK) according to the manufacturer's protocol and stored frozen at –80° C in cryoprotective freezing medium (dimethyl sulphoxide: Sigma-Aldrich, St. Louis, USA; fetal calf serum (FCS): Sigma-Aldrich; dilution 1:10) until biological analyses.

To control for possible differences in blood cell composition, a small volume of whole blood was collected (2.5 ml) into EDTA-buffered blood collection tubes (Sarstedt) to generate a standard hemogram in the Department of Clinical Chemistry at Ulm University Hospital. The hemogram of both, maternal and umbilical cord blood, was analyzed only in the samples of mothers who provided written informed consent. CM+ mothers and their newborns did not differ from CM- mothers and their newborns with regard to blood cell composition (Table 1).

Mitochondrial respiration in intact cells

In short, frozen cells were thawed in pre-warmed Phosphate-buffered saline (PBS; Life Technologies, Carlsbad, USA) supplemented with 2% FCS, washed two times by centrifugation at 270 g for 10 min at room temperature. In a small sample, cell were stained with trypan blue to quantify the amount of living cells. Cell samples were resuspended in 4.3 ml freshly thawed mitochondrial respiration medium (Mir05) (10), 2.1 ml of the cell suspension was transferred into each of the two chambers of an air-calibrated O2k Oxygraph (Oroboros Instruments, Innsbruck, Austria) and supplemented with 10 µl Sodium pyruvate (2 M stock; Sigma-Aldrich). Real-time oxygen concentration (µM) in the chamber, as well as oxygen flux (pmol O_2/sec) per million living cells, were recorded over time using the DatLab software 6.1 (Oroboros Instruments). A standardized Substrate-Uncoupler-Inhibitor-Titration (SUIT) protocol (11, 12) was used according to the manufacturer to measure mitochondrial respiration at 37°C. Samples were measured in duplicates and analyses were performed blinded with respect to clinical variables or group assignment. Following the respirometric analysis, 500,000 cells were shock-frozen in liquid nitrogen for measuring the intracellular mitochondrial density.

SUIT Protocol for the measurement of mitochondrial respiration in intact immune cells.

First, physiological respiration (Routine respiration) was assessed as mitochondrial oxygen consumption of intact peripheral blood mononuclear cells (PBMCs) / umbilical cord blood mononuclear cells (UBMCs). After adding 0.5 µl of the *ATP-synthase* inhibitor Oligomycin (5 mM stock; Sigma-Aldrich), Leak respiration, which compensates for proton leak, slippage, and cation cycling over the inner mitochondrial membrane, was measured (11). The difference between Routine respiration and Leak respiration represents the oxygen consumption related to ATP production reflected by the *ATP-synthase* (*Complex V*) activity (ATP-turnover-related respiration). Stepwise titration (first 1 µl, followed by 0.5 µl steps) of the uncoupler Carbonyl cyanide 4-trifluoro-methoxyphenyl hydrazone (FCCP, 1mM stock; Sigma-Aldrich) induced the maximal capacity of the respiratory chain, which indicates the non-physiological maximal Uncoupled respiration that is not limited by the enzyme activity of the *ATP-synthase* (12). Spare respiratory capacity was calculated as the difference between the maximal respiratory capacity and Routine respiration. Thereafter, the addition of 1µl *Complex I*-inhibitor Rotenone (1 mM stock; Sigma-Aldrich) and of 1 µl *Complex III*-inhibitor Antimycin A (5 mM stock; Sigma-Aldrich) enables to measure the residual oxygen consumption (ROX). ROX estimates the cellular oxygen consumption linked to oxidative side reactions remaining after the complete blocking of the respiratory chain (11) as well as to technical background noise of the measurements. For evaluation of cellular oxygen consumption related to mitochondrial activity, ROX was subtracted from all other values according to the manufacturer's recommendations (11, 12). Representative example measurements of the samples of one mother and her child are presented in Figure S3.

Averaged values of both oxygraph chambers normalized for the number of living cells in the sample were used for statistical analyses. For further qualitative analysis, flux control ratios were calculated based on the measured respiratory values as internal normalization to control for cell size, cell morphology, and mitochondrial content (11): *Routine control ratio* (Routine respiration / Maximal respiratory capacity); *Leak control ratio* (Leak respiration / Maximal respiratory capacity); *Net routine ratio* (ATP-turnover-related respiration / Maximal respiratory capacity); *Coupling efficiency* (ATP-turnover-related respiration / Routine respiration).

Spectrophotometric assessment of the intracellular mitochondrial density

For quantifying the density of the mitochondrial network, *citrate synthase* activity (CSA) was determined spectrophotometrically in freshly thawed samples at 30°C using a standardized and established protocol as previously described (13, 14). Samples were measured in duplicates and

mean values were used for statistical analyses. CSA as a marker for mitochondrial density in human PBMCs has been validated via another marker for mitochondrial density, i.e., mtDNA copy number (mtDNAcn). CSA per cell and mtDNAcn showed a high correlation in human PBMCs (15, 16). Parameters from high-resolution respirometry were normalized for CSA and thus for the intracellular mitochondrial density.

Data analysis

All statistical analyses were performed in R 3.3.3 (R Core Team, 2016). Normal distribution of model residuals was examined with the histogram of standardized residuals, and homogeneity and homoscedasticity were checked by plotting fitted values against standardized residuals. Non-parametric analyses were used where appropriate. Continuous variables of CM+ and CM- group were compared using *t*-tests and Mann–Whitney *U*-tests, or analyses of covariance (ANCOVAs) if additional covariates were included. Categorical data were compared using χ^2 tests or Fisher's exact tests. Kendall's tau correlation coefficients (τ) were calculated for correlation analyses. Parameters of mitochondrial bioenergetics that differed significantly in group comparisons (CM- vs. CM+) were additionally tested for prediction by CM load using linear regression analyses. The unstandardized (*B*) and standardized (β) regression coefficients, standard errors (*SE*), as well as related *t*-statistics and *p*-values are reported. Storage time of cryopreserved cells served as a covariate as it may affect mitochondrial functioning (17–19). As immune cell subsets within the PBMC/UBMC fraction (i.e., lymphocytes, monocytes, and dendritic cells) differ in their bioenergetic profiles (20, 21), we considered the percentage of lymphocytes and monocytes in whole blood as additional covariates in the linear regression analyses. All analyses were repeated for the neonatal bioenergetics. In addition, children's biological sex was controlled as a covariate in the linear regression analyses. As recommended (22), in case of non-normal distributed model residuals and/or heteroscedasticity of residuals, we applied MM-estimator-based robust linear regression models using the R-package "robustbase" (23). All reported analyses used a two-tailed significance level set at $p \leq 0.05$. For the mitochondrial parameters, *p*-values were adjusted for multiple comparisons according to the Benjamini-Hochberg procedure (i.e., false discovery rate, FDR) (24). Effects of $0.01 \leq \eta^2_p \leq 0.04$ were considered small, $0.05 \leq \eta^2_p \leq 0.13$ medium, and $\eta^2_p > 0.14$ large. For τ and β, effects of 0.10-0.22 were considered small, of 0.23-0.35 medium, and of > 0.36 large.

Power analysis for future studies

In our study, we observed significant CM group effects on maternal routine respiration, ATP-turnover-related respiration, and CSA with effect sizes of $\eta^2_p = 0.057$, 0.051, and 0.061, respectively. Using an ANCOVA (two groups, one covariate, $\alpha = 0.05$), the observed power to detect such effects ranged from $1\text{-}\beta = 0.54$ to 0.63 at the given sample size (n=105). Accordingly, future studies which aim at replicating effects ranging between $\eta^2_p = 0.050$ and 0.065 (i.e., $f = 0.23$–0.25) with an ANCOVA and a power of $1\text{-}\beta = 0.80$ would require samples of n=142 to 187 participants. With respect to the CSA in newborns, we observed a nonsignificant CM group difference of $\eta^2_p = 0.039$. The observed power was relatively low with $1\text{-}\beta = 0.36$ (ANCOVA with two groups, two covariates, $\alpha = 0.05$). To enhance the statistical power on $1\text{-}\beta = 0.80$, replication studies would require a sample of 273 newborns. Note that sample sizes need to be further enhanced to enable the adjustment of *p*-values for the testing of multiple outcomes.

Supplementary Figures

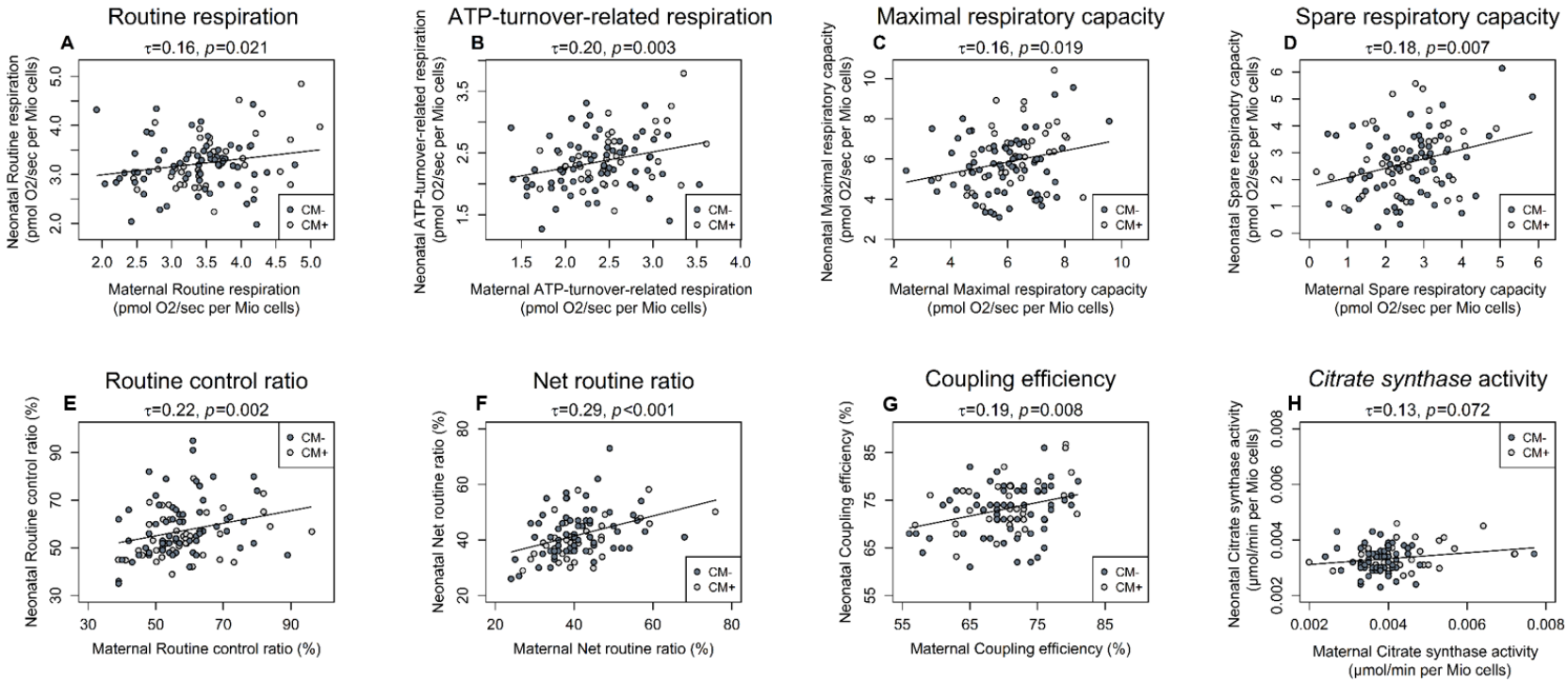


Fig. S1. Scatterplots for the graphical illustration of the significant correlations between maternal and neonatal mitochondrial bioenergetics (*n*=102). Maternal and neonatal mitochondrial respiration parameters showed small to medium-sized positive correlations which were significant for Routine respiration (A), ATP-turnover-related respiration (B), Maximal respiratory capacity (C), and Spare respiratory capacity (D), as well as for the flux control ratios Routine control ratio (E), Net routine ratio (F), and Coupling efficiency (G) for the given sample size. Maternal and neonatal *citrate synthase* activity showed a small-sized positive correlation (H). Kendall's tau correlation coefficients (τ) and the corresponding *p*-value are depicted.

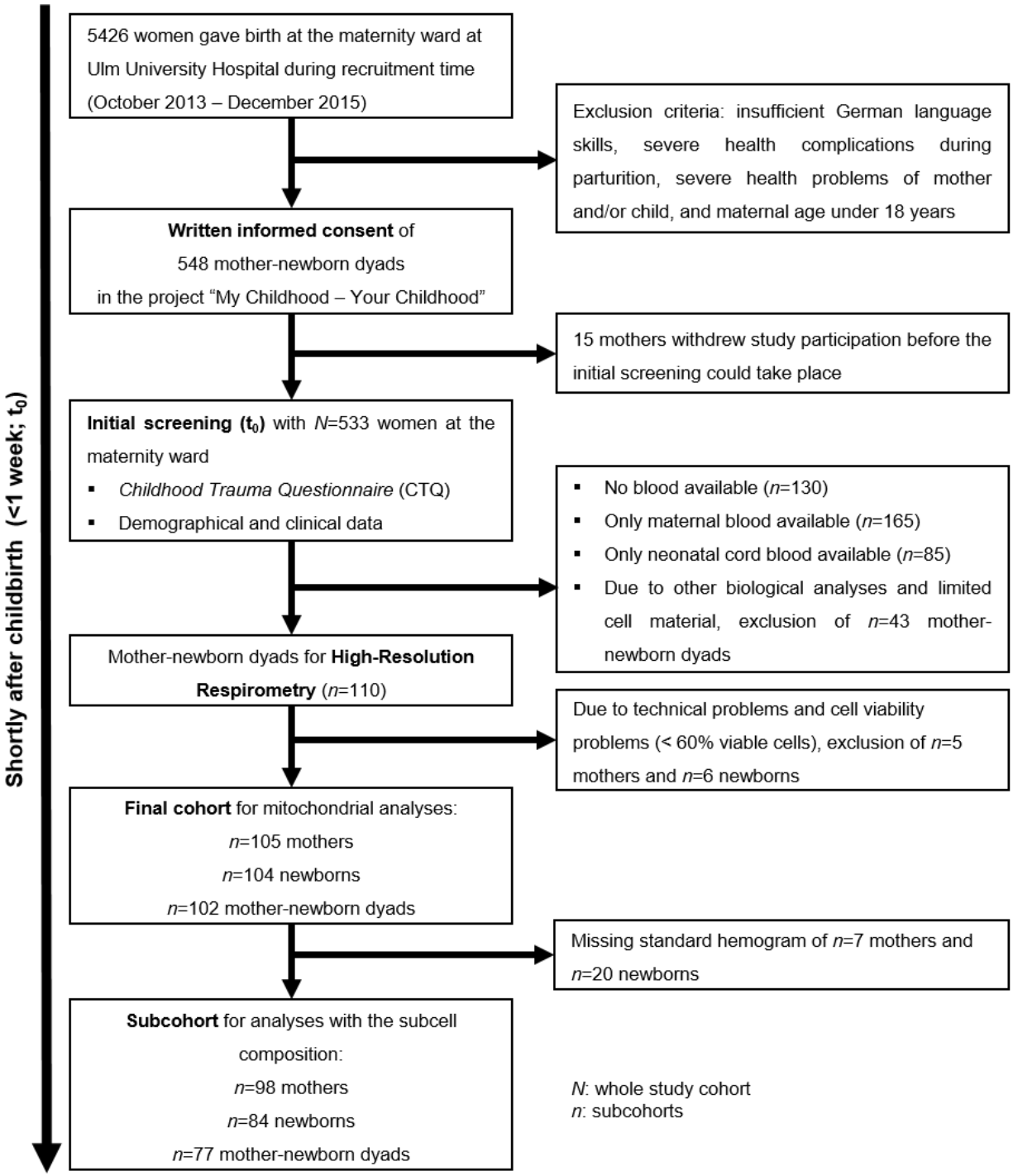
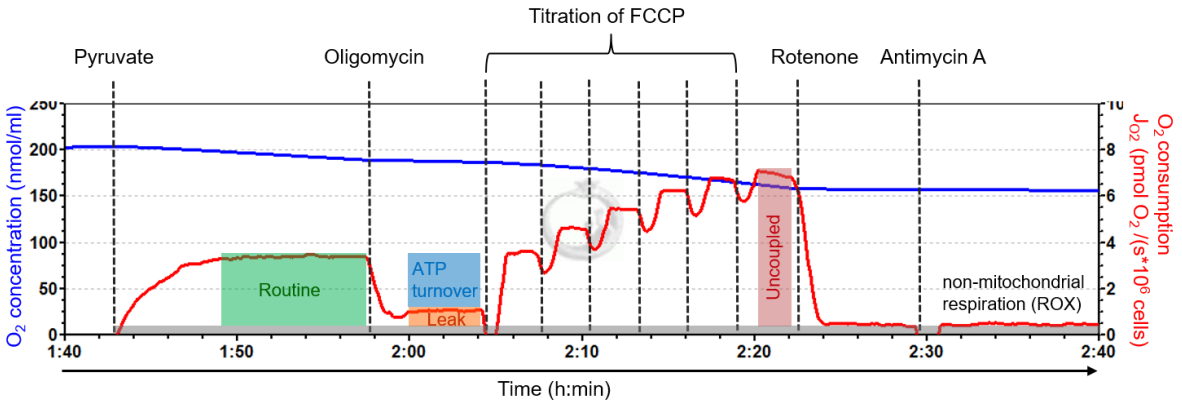


Fig. S2. Overview of final sample sizes after applying exclusion criteria in the study "My Childhood – Your Childhood".

A) Mother



B) Newborn

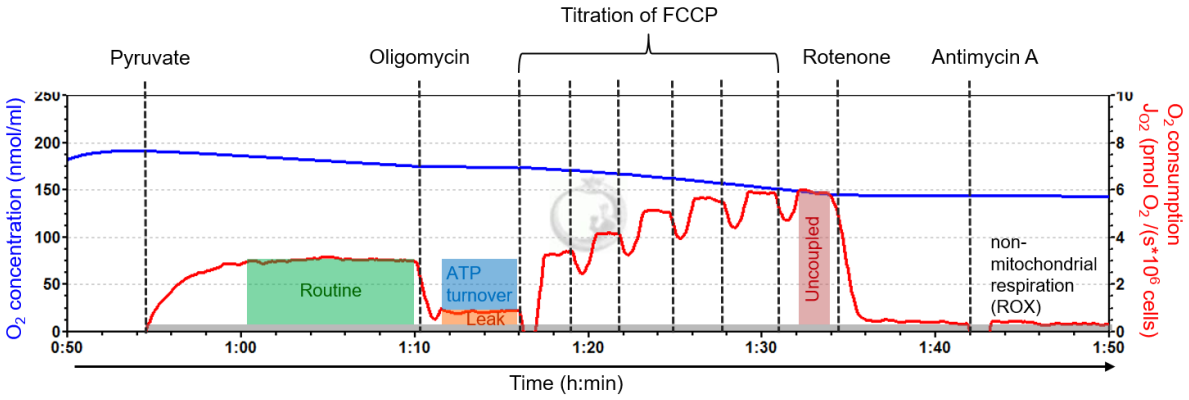


Fig. S3. Representative example for the assessment of immunocellular oxygen consumption in intact peripheral blood mononuclear cells (PBMCs) of the mother (A) and in umbilical cord blood mononuclear cells (UBMCs) of the newborn (B) using high-resolution respirometry. The cellular oxygen consumption (red line) of intact PBMCs/UBMCs was assessed by recording the reduction in oxygen concentration (blue line) over time within the air-sealed chambers of an O2k-Oxygraph. Following the measurement of basal mitochondrial oxygen consumption (Routine respiration, marked in green), Leak respiration (marked in orange), ATP-turnover-related respiration (marked in blue), Uncoupled respiration (maximal capacity of the mitochondrial respiratory chain, marked in red) and the residual oxygen consumption (ROX; marked in grey) were assessed using a standardized Substrate-Uncoupler-Inhibitor-Titration (SUIT) protocol (11, 12) for both, PBMCs and UBMCs.

Supplementary tables

Table S1. Sociodemographic and clinical characteristics of mothers and their newborns

Mothers (*n*=105)						
	Whole cohort (*n*=105) *M [SD]* or *n* (%)	**Range** (Min-Max)	**CM-** (*n*=67) *M [SD]* or *n* (%)	**CM+** (*n*=38) *M [SD]* or *n* (%)	**Test statistics** [a]	***p***
Sociodemographics						
Age (years)	33.0 [4.0]	24-43	33.2 [3.9]	32.8 [4.3]	$t(103)=-0.44$, $d=-0.09$	0.662
Maternal ethnicity [Caucasian] [b]	104 (99%)	-	67 (100%)	37 (97%)	-	0.362
Living in a partnership	105 (100%)	-	67 (100%)	38 (100%)	-	-
Academic education	71 (68%)	-	50 (75%)	21 (55%)	$\chi^2(1)=3.32$, $V=0.18$	0.069
Pregnancy duration (days)	278 [9]	251-294	278 [10]	277 [8]	$U=3682.00$, $r=-0.09$	0.378
Vaginal delivery [c]	80 (77%)	-	50 (76%)	30 (79%)	$\chi^2(1)=0.02$, $V=0.01$	0.897
Psychological & clinical characteristics						
Lifetime psychiatric disorder	24 (23%)	-	12 (18%)	12 (32%)	$\chi^2(1)=1.85$, $V=0.13$	0.174
Lifetime intake of psychotropic medication	26 (25%)	-	15 (22%)	11 (29%)	$\chi^2(1)=0.26$, $V=0.05$	0.608
CTQ sum score	32.3 [10.4]	25-85	27.0 [2.0]	41.7 [12.6]	$U=2325.50$, $r=0.80$	<0.001
Emotional abuse sum score	6.7 [2.8]	5-18	5.6 [0.8]	8.7 [3.9]	$U=2843.00$, $r=0.49$	<0.001
Physical abuse sum score	5.7 [2.3]	5-25	5.1 [0.2]	6.8 [3.7]	$U=3069.00$, $r=0.46$	<0.001
Sexual abuse sum score	6.0 [3.4]	5-23	5.0 [0]	7.8 [5.2]	$U=3149.00$, $r=0.47$	<0.001
Emotional neglect sum score	8.4 [4.0]	5-21	6.3 [1.5]	12.0 [4.5]	$U=2593.50$, $r=0.64$	<0.001
Physical neglect sum score	5.5 [1.5]	5-12	5.0 [0.2]	6.4 [2.2]	$U=3052.50$, $r=0.48$	<0.001
Newborns (*n*=104)						
	Whole cohort (*n*=104) *M [SD]* or *n* (%)	**Range** (Min-Max)	**CM-** (*n*=65) *M [SD]* or *n* (%)	**CM+** (*n*=39) *M [SD]* or *n* (%)	**Test statistics** [a]	***p***
Sex (male)	63 (61%)	-	40 (62%)	23 (59%)	$\chi^2(1)=0.003$, $V=0.01$	0.959
Birth weight (kg)	3.36 [0.47]	2.42-4.63	3.36 [0.48]	3.36 [0.46]	$t(102)=0.02$, $d=0.004$	0.985
Gestational age (days)	278 [9]	251-294	279 [9]	278 [8]	$U=3519.00$, $r=-0.07$	0.471

CM: Childhood maltreatment; CM-: Women without CM experiences; CM+: Women with mild to severe CM experiences; CTQ: *Childhood Trauma Questionnaire*.

[a] Two-tailed Student *t*-tests/ Mann–Whitney *U*-tests/ χ^2-tests/ Fisher's exact tests were calculated where appropriate. CM- group as reference group. As effect size measure Cohen's *d*, *r*, or Cramer's *V* is reported.

[b] One study participant of North American origin

[c] *n* = 104, one missing in CM-group.

Table S2. Biological raw data for mitochondrial respiration of mothers and their newborns without ROX correction

Mothers (*n*=105)						
	Whole cohort (*n*=105) *M [SD]*	**Range** (Min-Max)	**CM-** (*n*=67) *M [SD]*	**Range CM-** (Min-Max)	**CM+** (*n*=38) *M [SD]*	**Range CM+** (Min-Max)
Mitochondrial respiration (pmol O_2/sec per Mio cells)						
Routine respiration	3.66 [0.70]	2.25 – 5.25	3.56 [0.69]	2.25 – 5.24	3.84 [0.69]	2.51 – 5.25
Leak respiration	1.25 [0.33]	0.60 – 2.45	1.22 [0.34]	0.60 – 2.45	1.29 [0.31]	0.80 – 2.22
ATP-turnover-related respiration	2.41 [0.48]	1.38 – 3.61	2.34 [0.47]	1.38 – 3.53	2.55 [0.46]	1.71 – 3.61
Maximal respiratory capacity	6.28 [1.27]	2.86 – 9.64	6.17 [1.32]	2.86 – 9.64	6.46 [1.18]	3.86 – 8.86
Spare respiratory capacity	2.62 [1.06]	0.18 – 5.85	2.62 [1.07]	0.48 – 5.85	2.62 [1.07]	0.18 – 4.90
Residual oxygen consumption (ROX)	0.24 [0.18]	0.00 – 0.70	0.25 [0.19]	0.00 – 0.70	0.22 [0.17]	0.00 – 0.62
Newborns (*n*=104)						
	Whole cohort (*n*=104) *M [SD]*	**Range** (Min-Max)	**CM-** (*n*=65) *M [SD]*	**Range CM-** (Min-Max)	**CM+** (*n*=39) *M [SD]*	**Range CM+** (Min-Max)
Mitochondrial respiration (pmol O_2/sec per Mio cells)						
Routine respiration	3.48 [0.55]	2.22 – 5.01	3.43 [0.53]	2.22 – 5.01	3.57 [0.57]	2.37 – 4.98
Leak respiration	1.12 [0.24]	0.73 – 2.10	1.11 [0.25]	0.73 – 2.10	1.13 [0.24]	0.79 – 1.74
ATP-turnover-related respiration	2.36 [0.44]	1.27 – 3.79	2.32 [0.43]	1.27 – 3.31	2.43 [0.46]	1.56 – 3.79
Maximal respiratory capacity	6.08 [1.44]	3.28 – 10.55	5.91 [1.38]	3.28 – 9.69	6.37 [1.51]	3.71 – 10.55
Spare respiratory capacity	2.60 [1.22]	0.23 – 6.14	2.48 [1.21]	0.23 – 6.14	2.80 [1.24]	0.93 – 5.57
Residual oxygen consumption (ROX)	0.26 [0.18]	0.02 – 0.69	0.25 [0.16]	0.02 – 0.69	0.27 [0.20]	0.05 – 0.63

Table S3. Mitochondrial bioenergetics in newborns: Mitochondrial raw data of male and female newborns

	Male newborns (*n*=63) *M [SD]*	**Female newborns** (*n*=41) *M [SD]*
Mitochondrial respiration (pmol O_2/sec per Mio cells)		
Routine respiration	3.12 [0.54]	3.37 [0.51]
Leak respiration	0.87 [0.21]	0.85 [0.21]
ATP-turnover-related respiration	2.25 [0.42]	2.53 [0.44]
Maximal respiratory capacity	5.61 [1.47]	6.14 [1.50]
Spare respiratory capacity	2.49 [1.20]	2.77 [1.25]
Residual oxygen consumption (ROX)	0.28 [0.19]	0.23 [0.16]
Mitochondrial density (µmol/min per Mio cells)		
Citrate synthase activity	0.0034 [0.0005]	0.0033 [0.0004]

Parameters for mitochondrial respiration are presented corrected for residual oxygen consumption (ROX). For statistics see table S4.

Table S4. Mitochondrial bioenergetics in newborns: Results of ANCOVAs concerning the group comparisons of mitochondrial respiration and density in female (*n*=41) and male (*n*=63) newborns accounting for the storage time of cryopreserved cells as a covariate

Outcome variable	Predictor	*B (SE)*	95%CI (*B*)	*F* (1,101)	$\eta^2_{partial}$	*p*	p_{FDR}
Routine respiration (pmol O_2/sec per Mio cells)	Intercept	3.01 (0.28)	[2.46, 3.56]	118.30		<0.001	<0.001
	Female sex	0.26 (0.11)	[0.05, 0.47]	5.77	0.053	**0.018**	**0.036**
	Storage time of cryopreserved cells	$9.86*10^{-5}$ ($2.35*10^{-4}$)	[$-3.67*10^{-4}$, $5.64*10^{-4}$]	0.18	0.002	0.675	0.759
	Overall model statistics: $F(2,101)=2.89$, $p=0.060$, $R^2=0.054$, $R^2_{adj}=0.035$						
Leak respiration (pmol O_2/sec per Mio cells)	Intercept	0.56 (0.09)	[0.38, 0.73]	40.11		<0.001	<0.001
	Female sex	$-2.43*10^{-3}$ (0.04)	[-0.08, 0.08]	0.004	<0.001	0.951	0.951
	Storage time of cryopreserved cells	$2.60*10^{-4}$ ($7.20*10^{-5}$)	[$1.17*10^{-4}$, $4.03*10^{-4}$]	13.00	0.114	<0.001	0.001
	Overall model statistics†: $F(2,101)=6.64$, $p=0.002$, $R^2=0.089$, $R^2_{adj}=0.071$						
ATP-turnover related respiration (pmol O_2/sec per Mio cells)	Intercept	2.42 (0.22)	[1.98, 2.86]	118.69		<0.001	<0.001
	Female sex	0.26 (0.09)	[0.09, 0.44]	9.40	0.094	**0.003**	**0.008**
	Storage time of cryopreserved cells	$-1.47*10^{-4}$ ($1.89*10^{-4}$)	[$-5.21*10^{-4}$, $2.27*10^{-4}$]	0.61	0.006	0.436	0.523
	Overall model statistics: $F(2,101)=5.54$, $p=0.005$, $R^2=0.099$, $R^2_{adj}=0.081$						
Maximal respiratory capacity (pmol O_2/sec per Mio cells)	Intercept	4.02 (0.76)	[2.51, 5.53]	27.85		<0.001	<0.001
	Female sex	0.64 (0.30)	[0.05, 1.22]	4.61	0.032	**0.034**	0.051
	Storage time of cryopreserved cells	$1.39*10^{-3}$ ($6.46*10^{-4}$)	[$1.08*10^{-4}$, $2.67*10^{-3}$]	4.62	0.044	0.034	0.051
	Overall model statistics: $F(2,101)=3.97$, $p=0.022$, $R^2=0.073$, $R^2_{adj}=0.055$						
Spare respiratory capacity (pmol O_2/sec per Mio cells)	Intercept	1.02 (0.62)	[-0.22, 2.25]	2.65		0.107	0.148
	Female sex	0.38 (0.24)	[-0.10, 0.86]	2.43	0.014	0.122	0.157
	Storage time of cryopreserved cells	$1.29*10^{-3}$ ($5.29*10^{-4}$)	[$2.39*10^{-4}$, $2.34*10^{-3}$]	5.93	0.055	0.017	0.036
	Overall model statistics: $F(2,101)=3.66$, $p=0.029$, $R^2=0.068$, $R^2_{adj}=0.049$						
***Citrate synthase* activity** (µmol/min per Mio cells)	Intercept	$2.82*10^{-3}$ ($2.37*10^{-4}$)	[$2.35*10^{-3}$, $3.28*10^{-3}$]	141.67		<0.001	<0.001
	Female sex	$-2.58*10^{-5}$ ($9.20*10^{-5}$)	[$-2.08*10^{-4}$, $1.57*10^{-4}$]	0.08	0.004	0.779	0.825
	Storage time of cryopreserved cells	$4.68*10^{-7}$ ($2.01*10^{-7}$)	[$6.97*10^{-8}$, $8.65*10^{-7}$]	5.43	0.051	0.022	0.040
	Overall model statistics: $F(2,101)=2.94$, $p=0.057$, $R^2=0.055$, $R^2_{adj}=0.036$						

Significant sex effects are given in bold. Robust models (†) where appropriate. Male newborns as reference group. *P*-values were adjusted for multiple comparisons according to the Benjamini-Hochberg procedure (i.e., false discovery rate, FDR) (24).

Table S5. Results of ANCOVAs concerning the group comparisons of mitochondrial respiration and density in CM- and CM+ women accounting for the storage time of cryopreserved cells as a covariate (*n*=105)

Outcome variable	Predictor	*B (SE)*	95%CI (B)	*F* (1,102)	$\eta^2_{partial}$	*p*	p_{FDR}
Routine respiration (pmol O_2/sec per Mio cells)	Intercept	3.98 (0.31)	[3.37, 4.59]	166.36		<0.001	<0.001
	CM group	0.34 (0.13)	[0.09, 0.59]	7.11	0.057	**0.009**	**0.019**
	Storage time of cryopreserved cells	$-6.08*10^{-4}$ ($2.72*10^{-4}$)	[-0.001, $-6.83*10^{-5}$]	4.99	0.047	0.028	0.047
	Overall model statistics: $F(2,102)=5.56$, $p=0.005$, $R^2=0.098$, $R^2_{adj}=0.081$						
Leak respiration (pmol O_2/sec per Mio cells)	Intercept	0.94 (0.13)	[0.69, 1.19]	56.16		<0.001	<0.001
	CM group	0.06 (0.06)	[-0.06, 0.17]	1.03	0.010	0.314	0.428
	Storage time of cryopreserved cells	$2.19*10^{-5}$ ($1.13*10^{-4}$)	[$-2.02*10^{-4}$, $2.46*10^{-4}$]	0.04	<0.001	0.847	0.932
	Overall model statistics†: $F(2,102)=0.62$, $p=0.542$, $R^2=0.013$, $R^2_{adj}=-0.007$						
ATP-turnover-related respiration (pmol O_2/sec per Mio cells)	Intercept	3.04 (0.22)	[2.59, 3.48]	185.61		<0.001	<0.001
	CM group	0.24 (0.09)	[0.06, 0.42]	6.87	0.051	**0.010**	**0.020**
	Storage time of cryopreserved cells	$-6.36*10^{-4}$ ($1.96*10^{-4}$)	[$-1.02*10^{-3}$, $-2.47*10^{-4}$]	10.49	0.093	0.002	0.005
	Overall model statistics: $F(2,102)=7.98$, $p<0.001$, $R^2=0.135$, $R^2_{adj}=0.118$						
Maximal respiratory capacity (pmol O_2/sec per Mio cells)	Intercept	5.58 (0.64)	[4.31, 6.85]	76.04		<0.001	<0.001
	CM group	0.30 (0.26)	[-0.22, 0.82]	1.33	0.014	0.252	0.360
	Storage time of cryopreserved cells	$3.14*10^{-4}$ ($5.64*10^{-4}$)	[$-8.04*10^{-4}$, $1.43*10^{-3}$]	0.31	0.003	0.579	0.695
	Overall model statistics: $F(2,102)=0.88$, $p=0.417$, $R^2=0.017$, $R^2_{adj}=-0.002$						
Spare respiratory capacity (pmol O_2/sec per Mio cells)	Intercept	1.60 (0.53)	[0.56, 2.65]	9.24		0.003	0.007
	CM group	-0.04 (0.21)	[-0.46, 0.39]	0.03	<0.001	0.870	0.932
	Storage time of cryopreserved cells	$9.22*10^{-4}$ ($4.64*10^{-4}$)	[$1.17*10^{-6}$, $1.84*10^{-3}$]	3.94	0.037	0.050	0.079
	Overall model statistics: $F(2,102)=1.97$, $p=0.144$, $R^2=0.037$, $R^2_{adj}=0.018$						
Routine control ratio (%)	Intercept	0.69 (0.05)	[0.58, 0.79]	166.05		<0.001	<0.001
	CM group	0.02 (0.02)	[-0.03, 0.06]	0.57	0.006	0.450	0.587
	Storage time of cryopreserved cells	$-1.12*10^{-4}$ ($4.69*10^{-5}$)	[$-2.05*10^{-4}$, $-1.89*10^{-5}$]	5.70	0.053	0.019	0.034
	Overall model statistics†: $F(2,102)=2.85$, $p=0.063$, $R^2=0.061$, $R^2_{adj}=0.042$						
Leak control ratio (%)	Intercept	0.16 (0.02)	[0.12, 0.20]	63.47		<0.001	<0.001
	CM group	$4.19*10^{-3}$ ($1.02*10^{-2}$)	[-0.02, 0.02]	0.17	0.002	0.682	0.787

	Storage time of cryopreserved cells	$1.91*10^{-6}$ ($1.84*10^{-5}$)	[$3.45*10^{-5}$, $3.84*10^{-5}$]	0.01	<0.001	0.918	0.938
		Overall model statistics†: $F(2,102)=0.11$, $p=0.895$, $R^2=0.003$, $R^2_{adj}=-0.017$					
Net routine ratio (%)	Intercept	0.52 (0.04)	[0.44, 0.59]	183.69		<0.001	<0.001
	CM group	0.01 (0.02)	[-0.02, 0.04]	0.33	0.003	0.568	0.695
	Storage time of cryopreserved cells	$-1.09*10^{-4}$ ($3.32*10^{-5}$)	[$-1.75*10^{-4}$, $-4.33*10^{-5}$]	10.81	0.096	0.001	0.003
		Overall model statistics†: $F(2,102)=5.46$, $p=0.006$, $R^2=0.107$, $R^2_{adj}=0.089$					
Coupling efficiency (%)	Intercept	0.79 (0.02)	[0.74, 0.83]	1209.55		<0.001	<0.001
	CM group	$8.89*10^{-4}$ (0.01)	[-0.02, 0.02]	0.006	<0.001	0.938	0.938
	Storage time of cryopreserved cells	$-6.98*10^{-5}$ ($2.01*10^{-5}$)	[$-1.10*10^{-4}$, $-3.00*10^{-5}$]	12.10	0.106	<0.001	0.002
		Overall model statistics†: $F(2,102)=6.06$, $p=0.003$, $R^2=0.084$, $R^2_{adj}=0.066$					
***Citrate synthase* activity** (µmol/min per Mio cells)	Intercept	$3.26*10^{-3}$ ($2.97*10^{-4}$)	[$2.67*10^{-3}$, $3.85*10^{-3}$]	120.07		<0.001	<0.001
	CM group	$3.71*10^{-4}$ ($1.44*10^{-4}$)	[$8.50*10^{-5}$, $6.57*10^{-4}$]	6.62	0.061	**0.012**	**0.023**
	Storage time of cryopreserved cells	$4.44*10^{-7}$ ($2.59*10^{-7}$)	[$-7.01*10^{-8}$, $9.58*10^{-7}$]	2.93	0.028	0.090	0.135
		Overall model statistics†: $F(2,102)=4.32$, $p=0.016$, $R^2=0.129$, $R^2_{adj}=0.112$					

Significant CM group effects are given in bold. Robust models (†) where appropriate. *P*-values were adjusted for multiple comparisons according to the Benjamini-Hochberg procedure (i.e., false discovery rate, FDR) (24). CM: Childhood maltreatment; CM group: CM- and CM+ according the low cut-off criteria for the CTQ (7). CM- group as reference group.

Table S6. Results of multiple linear regression analyses concerning associations between CM load and mitochondrial oxygen consumption in mothers accounting for PBMC subcell composition (n=98[1])

Outcome variable	Predictor	*B (SE)*	β	95% CI (β)	*t*	$\eta^2_{partial}$	*p*
Routine respiration (pmol O_2/sec per Mio cells)	Intercept	3.19 (0.46)			6.99		<0.001***
	CTQ sum score	0.02 (0.01)	0.25	[0.07, 0.42]	2.80	0.078	0.006**
	Storage time of cryopreserved cells	$-5.97*10^{-4}$ ($2.50*10^{-4}$)	-0.21	[-0.39, -0.04]	-2.39	0.045	0.019*
	Lymphocytes (% in whole blood)	-0.03 (0.01)	-0.27	[-0.45, -0.09]	-2.98	0.052	0.004**
	Monocytes (% in whole blood)	0.16 (0.04)	0.39	[0.21, 0.57]	4.34	0.168	<0.001***
	Overall model statistics: $F(4,93)=9.04$, $p<0.001^{***}$, $R^2=0.280$, $R^2_{adj.}=0.249$						
ATP-turnover-related respiration (pmol O_2/sec per Mio cells)	Intercept	2.77 (0.35)			7.95		<0.001***
	CTQ sum score	0.01 ($4.66*10^{-3}$)	0.17	[-0.01, 0.35]	1.90	0.038	0.061#
	Storage time of cryopreserved cells	$-6.36*10^{-4}$ ($1.90*10^{-3}$)	-0.30	[-0.49, -0.12]	-3.34	0.093	0.001**
	Lymphocytes (% in whole blood)	-0.02 (0.01)	-0.26	[-0.44, -0.08]	-2.80	0.054	0.006**
	Monocytes (% in whole blood)	0.08 (0.03)	0.28	[0.09, 0.46]	3.00	0.088	0.003**
	Overall model statistics: $F(4,93)=6.91$, $p<0.001^{***}$, $R^2=0.229$, $R^2_{adj.}=0.196$						
***Citrate synthase* activity** (µmol/min per Mio cells)	Intercept	$2.71*10^{-3}$ ($6.50*10^{-4}$)			4.17		<0.001***
	CTQ sum score	$1.83*10^{-5}$ ($1.12*10^{-5}$)	0.19	[-0.04, 0.42]	1.63	0.028	0.106
	Storage time of cryopreserved cells	$4.77*10^{-7}$ ($2.87*10^{-7}$)	0.12	[-0.02, 0.26]	1.88	0.029	0.100
	Lymphocytes (% in whole blood)	$-2.37*10^{-5}$ ($1.20*10^{-5}$)	-0.14	[-0.27, 0.001]	-1.98	0.040	0.051#
	Monocytes (% in whole blood)	$8.43*10^{-5}$ ($4.34*10^{-5}$)	0.15	[-0.003, 0.30]	1.94	0.039	0.055#
	Overall model statistics†: $F(4,93)=1.71$, $p=0.154$, $R^2=0.164$, $R^2_{adj.}=0.128$						

< 0.10, * <0.05, **<0.01, *** <0.001
Multiple linear regression or robust multiple regression (†) where appropriate
CTQ: *Childhood Trauma Questionnaire*
B: unstandardized regression coefficient, β: standardized regression coefficient, *SE*: standard error
[1] Blood counts available from n=98 mothers (CM+ group: n=34, CM- group: n=64)

Table S7. Results of multiple linear regression analyses concerning associations between CM load and mitochondrial respiration parameters normalized for *citrate synthase* activity in mothers (*n*=105)

Outcome variable	Predictor	*B (SE)*	β	95%CI (β)	*t*	$\eta^2_{partial}$	*p*
Routine respiration normalized for *citrate synthase* activity	Intercept	0.08 ($5.23*10^{-3}$)			14.99		<0.001***
	CTQ sum score	$-7.12*10^{-5}$ ($5.89*10^{-5}$)	-0.07	[-0.19, 0.05]	-1.21	0.014	0.230
	Storage time of cryopreserved cells	$-2.13*10^{-5}$ ($4.16*10^{-6}$)	-0.47	[-0.65, -0.29]	-5.13	0.205	<0.001***
	Overall model statistics†: $F(2,102)=13.27$, $p<0.001^{***}$, $R^2=0.245$, $R^2_{adj.}=0.231$						
ATP-turnover-related respiration normalized for *citrate synthase* activity	Intercept	0.06 ($3.72*10^{-3}$)			16.44		<0.001***
	CTQ sum score	$-7.46*10^{-5}$ ($4.29*10^{-5}$)	-0.10	[-0.21, 0.01]	-1.74	0.029	0.085#
	Storage time of cryopreserved cells	$-1.96*10^{-5}$ ($2.94*10^{-6}$)	-0.54	[-0.71, -0.38]	-6.68	0.304	<0.001***
	Overall model statistics†: $F(2,102)=22.85$, $p<0.001^{***}$, $R^2=0.323$, $R^2_{adj.}=0.310$						

< 0.10, * <0.05, **<0.01, *** <0.001
Multiple linear regression or robust multiple regression (†) where appropriate
CTQ: *Childhood Trauma Questionnaire*
B: unstandardized regression coefficient, β: standardized regression coefficient, *SE*: standard error

Table S8. Results of ANCOVAs concerning the group comparisons of mitochondrial function and density in newborns of CM- and CM+ women accounting for the storage time of cryopreserved cells and sex of the child as covariates (*n*=104)

Outcome variable	Predictor	*B (SE)*	95%CI (B)	*F* (1,100)	$\eta^2_{partial}$	*p*	p_{FDR}
Routine respiration (pmol O_2/sec per Mio cells)	Intercept	2.99 (0.28)	[2.44, 3.54]	70.51		<0.001	<0.001
	CM group	0.11 (0.11)	[-0.10, 0.32]	1.04	0.012	0.309	0.412
	Storage time of cryopreserved cells	$7.71*10^{-5}$ ($2.36*10^{-4}$)	[$-3.90*10^{-4}$, $5.44*10^{-4}$]	0.11	<0.001	0.744	0.804
	Female sex	0.25 (0.11)	[0.04, 0.47]	5.58	0.053	0.020	0.053
	Overall model statistics: $F(3,100)=2.27$, $p=0.085$, $R^2=0.064$, $R^2_{adj.}=0.036$						
Leak respiration (pmol O_2/sec per Mio cells)	Intercept	0.56 (0.09)	[0.38, 0.73]	39.50		<0.001	<0.001
	CM group	-0.03 (0.04)	[-0.11, 0.06]	0.37	0.004	0.543	0.639
	Storage time of cryopreserved cells	$2.70*10^{-4}$ ($7.88*10^{-5}$)	[$1.13*10^{-4}$, $4.26*10^{-4}$]	11.74	0.105	<0.001	0.003
	Female sex	$-1.70*10^{-3}$ (0.04)	[-0.08, 0.08]	0.002	<0.001	0.966	0.966
	Overall model statistics†: $F(3,100)=4.65$, $p=0.004$, $R^2=0.095$, $R^2_{adj.}=0.068$						
ATP-turnover-related respiration (pmol O_2/sec per Mio cells)	Intercept	2.40 (0.22)	[1.97, 2.84]	117.69		<0.001	<0.001
	CM group	0.12 (0.09)	[-0.05, 0.29]	1.84	0.018	0.178	0.274
	Storage time of cryopreserved cells	$-1.70*10^{-4}$ ($1.88*10^{-4}$)	[$-5.44*10^{-4}$, $2.04*10^{-4}$]	0.81	0.020	0.369	0.476
	Female sex	0.26 (0.09)	[0.09, 0.43]	9.14	0.084	0.003	0.009
	Overall model statistics: $F(3,100)=4.34$, $p=0.006$, $R^2=0.115$, $R^2_{adj.}=0.089$						
Maximal respiratory capacity (pmol O_2/sec per Mio cells)	Intercept	3.97 (0.76)	[2.46, 5.48]	27.20		<0.001	0.001
	CM group	0.37 (0.30)	[-0.22, 0.95]	1.53	0.021	0.219	0.313
	Storage time of cryopreserved cells	$1.32*10^{-3}$ ($6.47*10^{-4}$)	[$3.44*10^{-5}$, $2.60*10^{-3}$]	4.15	0.029	0.044	0.088
	Female sex	0.62 (0.30)	[0.03, 1.21]	4.42	0.042	0.038	0.084
	Overall model statistics: $F(3,100)=3.17$, $p=0.028$, $R^2=0.087$, $R^2_{adj.}=0.060$						
Spare respiratory capacity (pmol O_2/sec per Mio cells)	Intercept	0.61 (0.74)	[-0.26, 2.22]	0.69		0.408	0.510
	CM group	0.26 (0.24)	[-0.23, 0.74]	1.11	0.017	0.294	0.406
	Storage time of cryopreserved cells	$1.24*10^{-3}$ ($5.31*10^{-4}$)	[$1.85*10^{-4}$, $2.29*10^{-3}$]	5.44	0.043	0.022	0.055
	Female sex	0.37 (0.24)	[-0.11, 0.85]	2.30	0.023	0.132	0.211
	Overall model statistics: $F(3,100)=2.81$, $p=0.043$, $R^2=0.078$, $R^2_{adj.}=0.050$						

Routine control ratio (%)	Intercept	0.72 (0.05)	[0.62, 0.82]	215.32		<0.001	<0.001
	CM group	-3.97*10^{-3} (0.02)	[-0.05, 0.04]	0.03	<0.001	0.861	0.906
	Storage time of cryopreserved cells	-1.27*10^{-4} (4.43*10^{-5})	[-2.15*10^{-4}, -3.93*10^{-5}]	8.25	0.076	0.005	0.014
	Female sex	-0.03 (0.02)	[-0.07, 0.01]	2.32	0.023	0.131	0.211
	Overall model statistics†: F(3,100)=3.95, p=0.010, R^2=0.084, $R^2_{adj.}$=0.056						
Leak control ratio (%)	Intercept	0.15 (0.02)	[0.10, 0.20]	43.03		<0.001	<0.001
	CM group	-0.01 (0.01)	[-0.03, 0.01]	1.58	0.016	0.212	0.313
	Storage time of cryopreserved cells	1.13*10^{-5} (2.07*10^{-5})	[-2.98*10^{-5}, 5.24*10^{-5}]	0.30	0.003	0.586	0.670
	Female sex	-0.02 (0.01)	[-0.04, 2.06*10^{-3}]	3.16	0.031	0.078	0.142
	Overall model statistics†: F(3,100)=1.68, p=0.177, R^2=0.054, $R^2_{adj.}$=0.026						
Net routine ratio (%)	Intercept	0.56 (0.03)	[0.50, 0.63]	261.73		<0.001	<0.001
	CM group	1.89e-03 (0.02)	[-0.03, 0.03]	0.01	<0.001	0.903	0.926
	Storage time of cryopreserved cells	-1.31*10^{-4} (3.09*10^{-5})	[-1.93*10^{-4}, -6.99*10^{-5}]	18.01	0.153	<0.001	<0.001
	Female sex	-0.01 (0.02)	[-0.04, 0.02]	0.59	0.006	0.444	0.538
	Overall model statistics†: F(3,100)=6.38, p<0.001, R^2=0.145, $R^2_{adj.}$=0.119						
Coupling efficiency (%)	Intercept	0.80 (0.02)	[0.76, 0.85]	1049.42		<0.001	<0.001
	CM group	0.01 (0.01)	[-4.20*10^{-3}, 0.03]	2.40	0.017	0.125	0.211
	Storage time of cryopreserved cells	-7.71*10^{-5} (2.11*10^{-5})	[-1.19*10^{-4}, -3.52*10^{-5}]	13.32	0.141	<0.001	0.002
	Female sex	0.02 (0.01)	[9.00*10^{-4}, 0.04]	4.32	0.041	0.040	0.084
	Overall model statistics: F(3,100)=7.46, p<0.001, R^2=0.183, $R^2_{adj.}$=0.158						
***Citrate synthase* activity** (µmol/min per Mio cells)	Intercept	2.79*10^{-3} (2.34*10^{-4})	[2.33*10^{-3}, 3.26*10^{-3}]	142.16		<0.001	<0.001
	CM group	1.67*10^{-4} (9.10*10^{-5})	[-1.39*10^{-5}, 3.47*10^{-4}]	3.35	0.039	0.070	0.133
	Storage time of cryopreserved cells	4.35*10^{-7} (1.99*10^{-7})	[4.01*10^{-8}, 8.30*10^{-7}]	4.78	0.049	0.031	0.073
	Female sex	-3.24*10^{-5} (9.10*10^{-5})	[-2.13*10^{-4}, 1.48*10^{-4}]	0.13	0.001	0.722	0.802
	Overall model statistics: F(3,100)=3.12, p=0.029, R^2=0.086, $R^2_{adj.}$=0.058						

Robust models (†) where appropriate. *P*-values were adjusted for multiple comparisons according to the Benjamini-Hochberg procedure (i.e., false discovery rate, FDR) (24).CM: Childhood maltreatment; CM group: CM- and CM+ according the low cut-off criteria for the CTQ (7). CM- group as reference group.

Table S9. Results of multiple linear regression analyses concerning associations between CM load and mitochondrial oxygen consumption in newborns accounting for UBMC subcell composition (n=84[1])

Outcome variable	Predictor	*B (SE)*	β	95%CI (β)	*t*	$\eta^2_{partial}$	*p*
Routine respiration (pmol O_2/sec per Mio cells)	Intercept	2.67 (0.46)			5.79		<0.001***
	CTQ sum score	$-1.86*10^{-3}$ ($5.84*10^{-3}$)	-0.03	[-0.25, 0.18]	-0.32	<0.001	0.751
	Storage time of cryopreserved cells	$1.65*10^{-4}$ ($2.52*10^{-4}$)	0.07	[-0.15, 0.29]	0.65	0.001	0.515
	Female sex	0.35 (0.12)	0.33	[0.11, 0.55]	3.02	0.104	0.003**
	Lymphocytes (% in whole blood)	$2.36*10^{-3}$ ($7.75*10^{-3}$)	0.03	[-0.18, 0.25]	0.31	0.001	0.761
	Monocytes (% in whole blood)	0.02 (0.02)	0.11	[-0.11, 0.33]	1.01	0.012	0.317
	Overall model statistics: $F(5,78)=2.04$, $p=0.082^{\#}$, $R^2=0.116$, $R^2_{adj.}=0.059$						
ATP-turnover-related respiration (pmol O_2/sec per Mio cells)	Intercept	2.19 (0.38)			5.76		<0.001***
	CTQ sum score	$-1.77*10^{-3}$ ($4.80*10^{-3}$)	-0.04	[-0.25, 0.17]	-0.37	<0.001	0.714
	Storage time of cryopreserved cells	$-5.51*10^{-5}$ ($2.07*10^{-4}$)	-0.03	[-0.24, 0.19]	-0.27	0.010	0.791
	Female sex	0.33 (0.09)	0.38	[0.17, 0.60]	3.52	0.135	<0.001***
	Lymphocytes (% in whole blood)	$3.55*10^{-3}$ ($6.38*10^{-3}$)	0.06	[-0.15, 0.27]	0.56	0.004	0.579
	Monocytes (% in whole blood)	$6.85*10^{-3}$ (0.02)	0.04	[-0.17, 0.25]	0.36	0.001	0.722
	Overall model statistics: $F(5,78)=2.67$, $p=0.028^{*}$, $R^2=0.146$, $R^2_{adj.}=0.091$						
***Citrate synthase* activity** (µmol/min per Mio cells)	Intercept	$2.22*10^{-3}$ ($3.96*10^{-4}$)			5.61		<0.001***
	CTQ sum score	$-9.82*10^{-7}$ ($5.01*10^{-6}$)	-0.02	[-0.23, 0.19]	-0.20	<0.001	0.845
	Storage time of cryopreserved cells	$4.30*10^{-7}$ ($2.16*10^{-7}$)	0.22	[-0.00, 0.43]	1.99	0.075	0.050#
	Female sex	$-4.07*10^{-6}$ ($9.90*10^{-5}$)	-0.004	[-0.22, 0.21]	-0.04	<0.001	0.967
	Lymphocytes (% in whole blood)	$6.35*10^{-6}$ ($6.65*10^{-6}$)	0.10	[-0.11, 0.31]	0.96	0.012	0.342
	Monocytes (% in whole blood)	$5.27*10^{-5}$ ($2.01*10^{-5}$)	0.28	[0.07, 0.49]	2.63	0.079	0.010*
	Overall model statistics: $F(5,78)=2.78$, $p=0.023^{*}$, $R^2=0.151$, $R^2_{adj.}=0.097$						

< 0.10, * <0.05, **<0.01, *** <0.001
Multiple linear regression or robust multiple regression (†) where appropriate
CTQ: *Childhood Trauma Questionnaire*
B: unstandardized regression coefficient, β: standardized regression coefficient, *SE*: standard error
[1] Blood counts available from n=84 newborns (CM- group: n=54, CM+ group: n=30)

Table S10. Results of multiple linear regression analyses concerning associations between CM load and mitochondrial oxygen consumption in newborns additionally accounting for newborns gestational age and birth weight (*n*=104)

Outcome variable	Predictor	*B (SE)*	β	95%CI (β)	*t*	$\eta^2_{partial}$	*p*
Routine respiration (pmol O_2/sec per Mio cells)	Intercept	3.28 (1.73)			1.90		0.060#
	CTQ sum score	$3.26*10^{-3}$ ($5.09*10^{-3}$)	0.06	[-0.13, 0.26]	0.64	0.008	0.524
	Storage time of cryopreserved cells	$1.08*10^{-4}$ ($2.38*10^{-4}$)	0.05	[-0.15, 0.24]	0.46	<0.001	0.650
	Female sex	0.24 (0.11)	0.22	[0.02, 0.43]	2.18	0.053	0.032*
	Gestational age	$-4.36*10^{-4}$ ($6.35*10^{-3}$)	-0.01	[-0.21, 0.20]	-0.07	0.001	0.945
	Birth weight	$-7.78*10^{-5}$ ($1.20*10^{-4}$)	-0.07	[-0.28, 0.14]	-0.65	0.004	0.520
	Overall model statistics: $F(5,98)=1.34$, $p=0.255$, $R^2=0.064$, $R^2_{adj.}=0.016$						
ATP-turnover-related respiration (pmol O_2/sec per Mio cells)	Intercept	2.99 (1.39)			2.16		0.033*
	CTQ sum score	$3.61*10^{-3}$ ($4.08*10^{-3}$)	0.09	[-0.11, 0.28]	0.89	0.012	0.378
	Storage time of cryopreserved cells	$-1.43*10^{-4}$ ($1.91*10^{-4}$)	-0.07	[-0.26. 0.12]	-0.75	0.017	0.456
	Female sex	0.26 (0.09)	0.29	[0.09, 0.49]	2.89	0.083	0.005**
	Gestational age	$-2.24*10^{-3}$ ($5.10*10^{-3}$)	-0.04	[-0.24, 0.15]	-0.44	0.003	0.662
	Birth weight	$-1.89*10^{-5}$ ($9.66*10^{-5}$)	-0.02	[-0.22, 0.18]	-0.20	<0.001	0.845
	Overall model statistics: $F(5,98)=2.42$, $p=0.041^*$, $R^2=0.110$, $R^2_{adj.}=0.064$						
***Citrate synthase* activity** (µmol/min per Mio cells)	Intercept	$4.94*10^{-3}$ ($1.46*10^{-3}$)			3.38		0.001***
	CTQ sum score	$8.90*10^{-7}$ ($4.31*10^{-6}$)	0.02	[-0.17, 0.21]	0.21	0.002	0.837
	Storage time of cryopreserved cells	$4.91*10^{-7}$ ($2.02*10^{-7}$)	0.24	[0.04, 0.44]	2.44	0.056	0.017*
	Female sex	$-3.92*10^{-5}$ ($9.36*10^{-5}$)	-0.04	[-0.24, 0.16]	-0.42	0.001	0.677
	Gestational age	$-7.19*10^{-6}$ ($5.39*10^{-6}$)	-0.14	[-0.34, 0.07]	-1.33	0.024	0.185
	Birth weight	$-5.07*10^{-8}$ ($1.02*10^{-7}$)	-0.05	[-0.26, 0.15]	-0.50	0.003	0.620
	Overall model statistics: $F(5,98)=1.72$, $p=0.136$, $R^2=0.081$, $R^2_{adj.}=0.034$						

< 0.10, * <0.05, **<0.01, *** <0.001
Multiple linear regression or robust multiple regression (†) where appropriate
CTQ: *Childhood Trauma Questionnaire*
B: unstandardized regression coefficient, β: standardized regression coefficient, *SE*: standard error

Table S11. Results of multiple linear regression analyses concerning associations between CM load and mitochondrial respiration normalized for c*itrate synthase* activity in newborns (*n*=104)

Outcome variable	Predictor	*B (SE)*	β	95% CI (β)	*t*	$\eta^2_{partial}$	*p*
Routine respiration normalized for *citrate synthase* activity	Intercept	0.06 ($6.23*10^{-3}$)			10.02		<0.001***
	CTQ sum score	$1.55*10^{-5}$ ($6.87*10^{-5}$)	0.02	[-0.13, 0.16]	0.23	0.001	0.822
	Storage time of cryopreserved cells	$-5.88*10^{-6}$ ($4.19*10^{-6}$)	-0.13	[-0.32, 0.06]	-1.40	0.019	0.164
	Female sex	$5.16*10^{-3}$ ($2.00*10^{-3}$)	0.26	[0.06, 0.46]	2.59	0.063	0.011*
	Overall model statistics†: $F(3,100)=4.74$, $p=0.004^{**}$, $R^2=0.099$, $R^2_{adj.}=0.072$						
ATP-turnover-related respiration normalized for *citrate synthase* activity	Intercept	0.05 ($4.74*10^{-3}$)			10.78		<0.001***
	CTQ sum score	$1.54*10^{-5}$ ($7.47*10^{-5}$)	0.02	[-0.16, 0.20]	0.21	0.001	0.837
	Storage time of cryopreserved cells	$-9.36*10^{-6}$ ($3.51*10^{-6}$)	-0.25	[-0.43, -0.06]	-2.67	0.094	0.009**
	Female sex	$5.05*10^{-3}$ ($1.61*10^{-3}$)	0.30	[0.11, 0.48]	3.13	0.089	0.002**
	Overall model statistics: $F(3,100)=6.76$, $p<0.001^{***}$, $R^2=0.169$, $R^2_{adj.}=0.144$						

< 0.10, * <0.05, **<0.01, *** <0.001
Multiple linear regression or robust multiple regression (†) where appropriate
CTQ: *Childhood Trauma Questionnaire*
B: unstandardized regression coefficient, β: standardized regression coefficient, *SE*: standard error

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