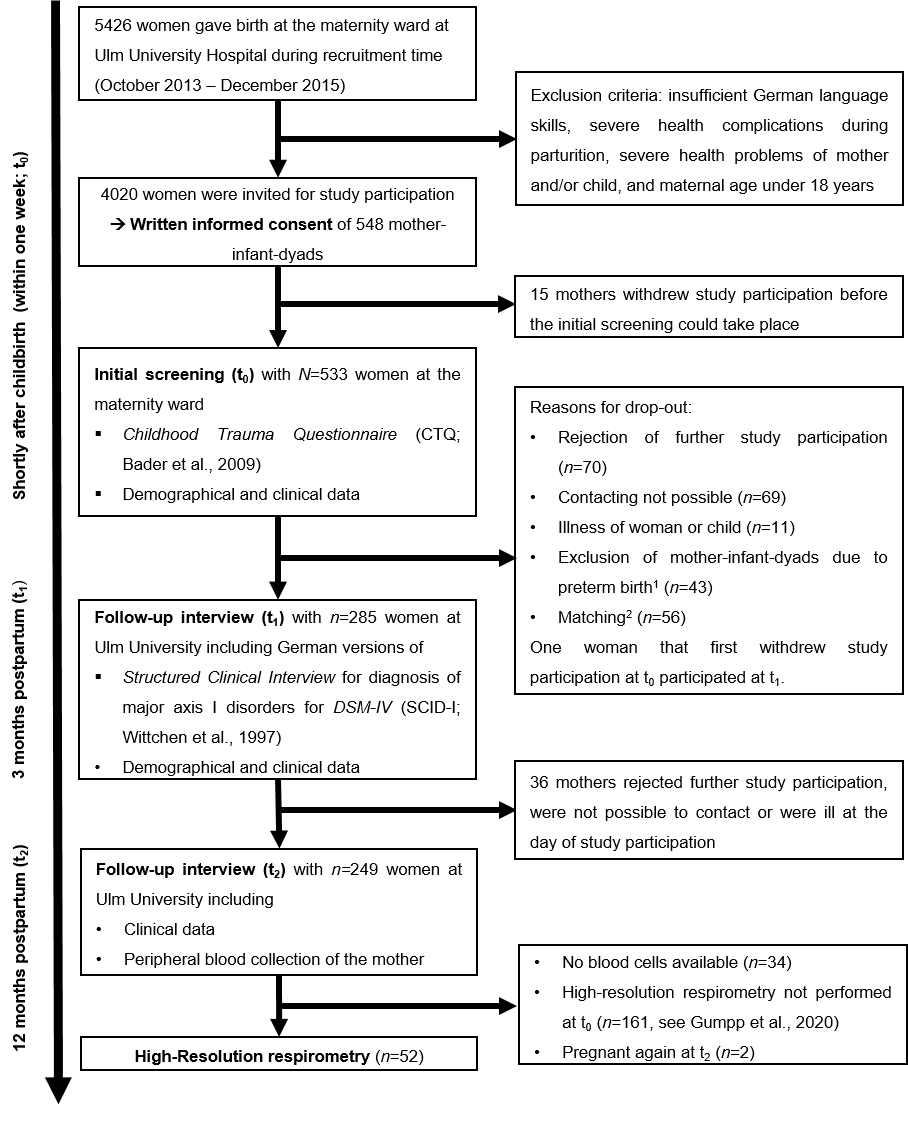
**Supplementary information**

**Investigating Mitochondrial Bioenergetics in Peripheral Blood Mononuclear Cells of Women With Childhood Maltreatment From Post-Parturition Period to One-Year Follow-up**

Anja M. Gumpp1, Alexander Behnke1, Laura Ramo-Fernández1, Peter Radermacher2, Harald Gündel3, Ute Ziegenhain4, Alexander Karabatsiakis1,5 \*, Iris-Tatjana Kolassa1 \*

\* Authors share authorship in the senior position

**Supplementary Figures**

****

**Figure S1:** Flow chart representing the procedures of recruitment, characterization and analyses of the study cohort in the project “My Childhood – Your Childhood”.

1 Another main focus of the overall project included hypotheses concerning the effects of maternal CM on the development of the child. For the purpose of testing these hypotheses in the first place, the exclusion of preterm births was chosen as further exclusion criteria at t1. 2 All women were categorized at t0 in two groups due to established CTQ cut-off criteria (Bernstein and Fink, 1998): 1) Women without any childhood maltreatment (CM) experiences (CM-) and 2) Women with at least mild to severe CM experiences (CM+). All CM+ women were contacted to participate at t1. CM- women were matched to the at t1 participating CM+ women according to the maternal age and their socioeconomic status. Thus, *n*=56 CM- women were not contacted at t1 due to this matching process.

**Supplementary tables**

**Table S1**: Biological raw data of the women at t0 and t2 (*n*=52)

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **t0 (*n*=52)** | | **t2 (*n*=52)** | |
|  | **CM- group**  (*n*=29)  *Range*  *(Min – Max)* | **CM+ group**  (*n*=23)  *Range*  *(Min – Max)* | **CM- group**  (*n*=29)  *Range*  *(Min – Max)* | **CM+ group**  (*n*=23)  *Range*  *(Min – Max)* |
| **Primary mitochondrial respiration parameters (pmol O2/sec per Mio cells)** | | | | |
| Routine respiration | 2.20 – 4.22 | 2.50 – 4.86 | 2.11 – 4.62 | 2.71 – 3.83 |
| Leak respiration | 0.56 – 1.82 | 0.63 – 1.63 | 0.88 – 1.71 | 1.00 – 1.54 |
| ATP-turnover-related respiration | 1.40 – 3.19 | 1.71 – 3.35 | 1.12 – 3.54 | 1.37 – 2.52 |
| Uncoupled respiration | 3.32 – 9.56 | 4.41 – 8.64 | 3.97 – 9.77 | 3.96 – 9.68 |
| Spare respiratory capacity | 0.48 – 5.85 | 0.92 – 4.90 | 1.74 – 5.46 | 1.19 – 6.12 |
| Residual oxygen consumption (ROX) | 0 – 0.70 | 0 – 0.61 | 0.01 – 0.24 | 0.05 – 0.26 |
| **Mitochondrial density (pmol/sec per Mio cells)** | | | | |
| *Citrate-synthase* activity | 40.13 – 79.96 | 54.84 – 106.31 | 54.53 – 94.36 | 57.90 – 95.28 |
| **Flux Control Ratios (%)** |  |  |  |  |
| Routine control ratio | 39 – 89 | 39 – 82 | 33 – 68 | 37 – 70 |
| Leak control ratio | 8 – 35 | 10 – 30 | 11 – 29 | 11 – 28 |
| Net routine ratio | 24 – 68 | 27 – 59 | 18 – 40 | 22 – 42 |
| Coupling efficiency | 56 – 81 | 57 – 80 | 47 – 77 | 51 – 69 |

Primary mitochondrial respiration parameters are presented corrected for Residual oxygen consumption (ROX). CM=Childhood maltreatment. CM+=Women with at least mild to severe CM experiences. CM-=Women without CM experiences

**Table S2.** Results of linear mixed effect models for mitochondrial respiration normalized for *citrate-synthase activity* (CSA) in women (*n*=52)

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Outcome** | **Predictor** | ***b* (*SE*)** | **95% CI (*b*)** | **β** | **η2** | ***F*** | ***p*** | **Post Hoc Tests** a | | |
|  |  |  |
| **Routine respiration normalized for CSA** | Intercept | 0.08 (3.94\*10-3) | [0.07, 0.09] |  |  | 407.48 | <0.001\*\*\* |  |  |  |
| CM | 9.35\*10-4 (2.01\*10-3) | [-2.94\*10-3, 4.81\*10-3] | 0.05 | 0.009 | 0.22 | 0.643 |  |  |  |
| Time | -2.23\*10-3 (1.94\*10-3) | [-5.97\*10-3, 1.51\*10-3] | -0.12 | 0.015 | 1.32 | 0.256 |  |  |  |
| Duration of Cryopreservation | -2.61\*10-5 (3.44\*10-6) | [-3.28\*10-5, -1.95\*10-5] | -0.61 | 0.368 | 56.56 | <0.001\*\*\* |  |  |  |
| CM ⨯ Time | 8.28\*10-4 (2.83\*10-3) | [-4.64\*10-3, 6.30\*10-3] | 0.04 | 0.001 | 0.09 | 0.771 |  |  |  |
| Overall model statistics: *F*(4,74.99) = 17.00, *p* < 0.001\*\*\*, R² = 0.404 (0.404), σri = 0.000 | | | | | | |  |  |  |
| **Leak respiration normalized for CSA** | Intercept | 0.02 (2.15\*10-3) | [0.02, 0.02] |  |  | 84.16 | <0.001\*\*\* |  |  |  |
| CM | 3.14\*10-4 (1.05\*10-3) | [-1.71\*10-3, 2.34\*10-3] | 0.04 | 0.016 | 0.09 | 0.765 |  |  |  |
| Time | 3.00\*10-3 (9.38\*10-4) | [1.16\*10-3, 4.82\*10-3] | 0.37 | 0.236 | 10.19 | 0.002\*\* |  |  |  |
| Duration of Cryopreservation | -4.31\*10-6 (1.88\*10-6) | [-8.04\*10-6, -6.57\*10-7] | -0.22 | 0.058 | 5.10 | 0.027\* |  |  |  |
| CM ⨯ Time | 1.25\*10-3 (1.36\*10-3) | [-1.40\*10-3, 3.92\*10-3] | 0.13 | 0.010 | 0.85 | 0.361 |  |  |  |
| Overall model statistics: *F*(4,75.44) = 7.03, *p* < 0.001\*\*\*, R² = 0.326 (0.200), σri = 0.001 | | | | | | |  |  |  |
| **ATPturn-over-related respiration normalized for CSA** | Intercept | 0.06 (3.26\*10-3) | [0.05, 0.07] |  |  | 344.88 | <0.001\*\*\* |  |  |  |
| CM | 5.04\*10-4 (1.63\*10-3) | [-2.64\*10-3, 3.65\*10-3] | 0.03 | 0.001 | 0.10 | 0.757 |  |  |  |
| Time | -5.21\*10-3 (1.52\*10-3) | [-8.23\*10-3, -2.27\*10-3] | -0.32 | 0.192 | 11.71 | 0.001\*\* |  |  |  |
| Duration of Cryopreservation | -2.24\*10-5 (2.85\*10-6) | [-2.84\*10-5, -1.67\*10-5] | -0.58 | 0.400 | 60.57 | <0.001\*\*\* |  |  |  |
| CM ⨯ Time | -3.12\*10-4 (2.22\*10-3) | [-4.63\*10-3, 4.05\*10-3] | -0.02 | <0.001 | 0.02 | 0.889 |  |  |  |
| Overall model statistics: *F*(4,75.18) = 27.54, *p* < 0.001\*\*\*, R² = 0.553 (0.521), σri = 0.002 | | | | | | |  |  |  |
| **Uncoupled respiration normalized for CSA** | Intercept | 0.14 (0.01) | [0.12, 0.16] |  |  | 169.71 | <0.001\*\*\* |  |  |  |
| CM | 4.51\*10-3 (5.29\*10-3) | [-5.70\*10-3, 0.01] | 0.11 | 0.019 | 0.73 | 0.396 |  |  |  |
| Time | 0.01 (5.10\*10-3) | [1.73\*10-3, 0.02] | 0.28 | 0.093 | 5.14 | 0.027\* |  |  |  |
| Duration of Cryopreservation | -4.16\*10-5 (9.06\*10-6) | [-5.91\*10-5, -2.41\*10-5] | -0.43 | 0.175 | 20.66 | <0.001\*\*\* |  |  |  |
| CM ⨯ Time | 1.32\*10-3 (7.46\*10-3) | [-0.01, 0.02] | 0.03 | <0.001 | 0.03 | 0.860 |  |  |  |
| Overall model statistics: *F*(4,74.99) = 6.50, *p* < 0.001\*\*\*, R² = 0.206 (0.206), σri = 0.000 | | | | | | |  |  |  |
| **Spare respiratory capacity normalized for CSA** | Intercept | 0.06 (9.20\*10-3) | [0.04, 0.07] |  |  | 36.58 | <0.001\*\*\* |  |  |  |
| CM | 3.55\*10-3 (4.69\*10-3) | [-5.50\*10-3, 0.01] | 0.10 | 0.013 | 0.57 | 0.451 |  |  |  |
| Time | 0.01 (4.52\*10-3) | [5.00\*10-3, 0.02] | 0.39 | 0.146 | 9.20 | 0.004\*\* |  |  |  |
| Duration of Cryopreservation | -1.54\*10-5 (8.03\*10-6) | [-3.09\*10-5, 8.84\*10-8] | -0.18 | 0.036 | 3.61 | 0.062 |  |  |  |
| CM ⨯ Time | 5.18\*10-4 (6.61\*10-3) | [-0.01, 0.01] | 0.01 | <0.001 | 0.01 | 0.938 |  |  |  |
| Overall model statistics: *F*(4,74.99) = 4.63, *p* = 0.002\*\*, R² = 0.155 (0.155), σri = 0.000 | | | | | | |  |  |  |

*Note*: \* *p* < 0.050, \*\* *p* < 0.010, \*\*\* *p* < 0.001, two-tailed. All models are random intercept models (σri… standard deviation of random intercepts). Coefficients of determination (R²) present variance explanation of the total model (including random effects) and, in brackets, variance explanation by fixed effects (i.e. model predictors) only. CM- as reference group.

a Linear post-hoc tests were not performed as the CM ⨯ Time interactions were not significant.

**Supplementary references**

Bader K, Hänny C, Schäfer V, Neuckel A, Kuhl C (2009) Childhood Trauma Questionnaire – Psychometrische Eigenschaften einer deutschsprachigen Version. *Zeitschrift für Klinische Psychologie und Psychotherapie* 38, 223–230.

Bernstein D, Fink L (1998) Manual for the childhood trauma questionnaire. *New York: The Psychological Corporation*.

Gumpp AM, Boeck C, Behnke A, Bach AM, Ramo-Fernández L, Welz T, Gündel H, Kolassa I-T, Karabatsiakis A (2020) Childhood maltreatment is associated with changes in mitochondrial bioenergetics in maternal, but not in neonatal immune cells. *Proceedings of the National Academy of Sciences* 117, 24778–24784.

Wittchen H-U, Zaudig M, Fydrich T (1997) *SKID. Strukturiertes Klinisches Interview für DSM-IV.* Göttingen: Hogrefe.