

**Supplementary Table 1**  
**Phenotypic characteristics of mothers and infants**

**Supplementary Table 1a: Summary of the phenotypic assessment of mothers and infants at two time points early in life**

	<b>Prenatal / 3<sup>rd</sup> Trimester</b>	<b>Perinatal / birth</b>
<b>Exposure to early life stress (ELS)</b>	Perceived stress (PSS <sup>1</sup> ) Prenatal distress (PDQ <sup>2</sup> ) Life events (LES <sup>3</sup> ) Social support (Soz-U. <sup>4</sup> ) Socio-demographic data Maternal health risk behavior (e.g. smoking) Psychosocial risks	Pre- and perinatal complications Perinatal stressors (e.g. asphyxia, caesarian, preterm birth) Pregnancy & obstetric history (birth weight, gestational age, birth complications)
<b>Maternal mental &amp; physical health</b>	Maternity log data semi- standardized neuropsychiatric diagnostic interview (M.I.N.I. <sup>5</sup> ) Depression screening (EPDS <sup>6</sup> ) Anxiety screening (STAI-S <sup>7</sup> , STAI-T <sup>7</sup> , ASQ <sup>8</sup> ) Anthropometry Individual & family history of metabolic and other medical disorders	

1, perceived stress scale; 2, prenatal distress questionnaire; 3, life experiences survey; 4, social support questionnaire; 5, Mini-international neuropsychiatric interview; 6, Edinburgh postnatal depression scale; 7, state- trait anxiety inventory; 8, anxiety screening questionnaire

**Supplementary Table 1**  
**Phenotypic characteristics of mothers and infants**

**Supplementary Table 1b: Summary of the information about psychopathology, socioeconomic-, psychosocial- and perceived stress of the extreme group of mothers expressed as mean  $\pm$  SD1 or percentage**

Variable	High prenatal ELS (n=10)	Low prenatal ELS (n=8)	p value
<b>Maternal psychopathology</b>			
EPDS Score <sup>3</sup>	15.40 $\pm$ 4.95	2.13 $\pm$ 1.25	0
STAI-S Score <sup>3</sup>	52.60 $\pm$ 13.32	32.62 $\pm$ 4.81	0.001
STAI-T Score <sup>3</sup>	50.90 $\pm$ 10.50	28.75 $\pm$ 4.53	0
ASQ Score <sup>3</sup>	5.40 $\pm$ 1.84	0.25 $\pm$ 0.46	0
<b>M.I.N.I. Diagnosis<sup>4</sup></b>			
none	20%	100%	0
depressive disorders	50%	0%	0.015
anxiety disorder	10%	0%	ns <sup>2</sup>
<b>Current psychiatric disorder<sup>4</sup> (%)</b>			
none	30%	100%	0.001
depressive disorder	50%	0%	0.015
anxiety disorder	10%	0%	ns <sup>2</sup>
<b>Perceived stress</b>			
PSS Score <sup>3</sup>	32.70 $\pm$ 6.93	15.25 $\pm$ 3.92	0
PDQ Score <sup>3</sup>	23.70 $\pm$ 8.06	8.63 $\pm$ 4.37	0
<b>Socioeconomic and psychosocial stress</b>			
LES-negative events Score <sup>3</sup>	8.50 $\pm$ 6.98	1.63 $\pm$ 1.06	0.013
Soz-U Score <sup>3</sup>	37.80 $\pm$ 10.68	48.00 $\pm$ 6.78	0.026
Living without a partner <sup>4</sup> (%)	40%	0%	0.037
Encouragement (Partner) <sup>4</sup> (%)	70%	100%	ns <sup>2</sup>
Separation(s) in the last year <sup>4</sup>	50%	0%	0.015
Daily arguments <sup>4</sup>	20%	0%	ns <sup>2</sup>
Physical conflicts within the preceding 12 months <sup>4</sup>	60%	0%	0.005
Composition of household >one person /room <sup>4</sup>	30%	0%	0.037
No graduation <sup>4</sup> (%)	20%	0%	ns <sup>2</sup>
No professional education <sup>4</sup> (%)	40%	0%	0.037
Monthly income per household $\leq$ 1750 Euro <sup>4</sup> (%)	70%	0%	0.001
Financial debt <sup>4</sup> (%)	50%	0%	0.015

1, standard deviation; 2, not significant; 3, the first eight main variables of the principal component analysis (PCA);

4, the twelve prenatal stressors which generate the adversity score as the ninth main variable of the PCA

**Supplementary Table 1**

**Phenotypic characteristics of mothers and infants**

**Supplementary Table 1c: Summary of the demographic characteristics and general medical status of mothers and infants included in the methylome analysis expressed as mean  $\pm$  SD or percentage**

Variable	High prenatal ELS (n = 10)	Low prenatal ELS (n = 8)	p value
Maternal Age (in years)	24.10 $\pm$ 5.43	34.00 $\pm$ 3.30	0.000
Smoking during early pregnancy (4 <sup>th</sup> to 12 <sup>th</sup> wpma <sup>1</sup> ; %)	70%	12.50%	0.013
Cigarettes in total (4 <sup>th</sup> to 12 <sup>th</sup> wpma <sup>1</sup> )	297.70 $\pm$ 412.68	3.00 $\pm$ 8.50	0.050
Range of cigarettes smoked	0-1092	0-24	
Smoking during late pregnancy (3 <sup>rd</sup> trimester, %)	40%	0%	0.037
Cigarettes per day (3 <sup>rd</sup> trimester)	3.30 $\pm$ 6.31	0	ns <sup>4</sup>
Range of cigarettes smoked	0-17	0	
Alcohol intake during early pregnancy (4 <sup>th</sup> to 12 <sup>th</sup> wpma <sup>1</sup> ; %)	30%	75%	ns <sup>4</sup>
Total alcohol intake (4 <sup>th</sup> to 12 <sup>th</sup> wpma <sup>1</sup> in g <sup>5</sup> )	75.50 $\pm$ 187.18	23.50 $\pm$ 22.62	ns <sup>4</sup>
Alcohol during late pregnancy (3 <sup>rd</sup> trimester; %)	0%	0%	ns <sup>4</sup>
Primiparous	30%	37.50%	ns <sup>4</sup>
Number of risk factors in the maternity log	4.60 $\pm$ 2.38	3.17 $\pm$ 1.51	ns <sup>4</sup>
Pre-Pregnancy BMI <sup>2</sup>	25.53 $\pm$ 7.08	21.69 $\pm$ 4.57	ns <sup>4</sup>
Gestational diabetes (%)	20%	0%	ns <sup>4</sup>
Gestational age at birth (wpma <sup>1</sup> )	38.70 $\pm$ 2.00	39.63 $\pm$ 1.60	ns <sup>4</sup>
Infant's Gender (%), male	50%	37.50%	ns <sup>4</sup>

1, weeks postmenstrual age; 2, body mass index; 3, standard deviation; 4, not significant; 5, gram

**Supplementary Table 2**

**Sequences of primers used for enrichment analyses of methylated DNA and for quantitative PCR (QPCR) validation of MeDIP data.**

Human		
Gene	Forward	Reverse
<i>H19</i>	5'-GAGCCGCACCAGATCTTCAG-3'	5'-TTGGTGGAACACACTGTGATCA-3'
<i>β-actin</i>	5'-CCAACGCCAAAACCTCTCCC-3'	5'-AGCCATAAAAGGCAACTTTCG-3'
Monkey		
Gene	Forward	Reverse
<i>H19</i>	5'-TTGGTGGAACACGCTGTGATCA-3'	5'-GAGCCGCACCAGGTCTTCAG-3'
<i>Gapdh</i>	5'-TTTCTTTCCTTTCGCGCTCTG-3'	5'-CCATTCATTTCTTCCCGTT-3'
Rat		
Gene	Forward	Reverse
<i>H19</i>	5'-CCAAGACAGAAGGGGACCAT-3'	5'-TAGATTTGGGGTTCGCCTGT-3'
<i>β-actin</i>	5'-TGGGATAGTGTCCACAAGGG-3'	5'-GAAGAGTTTGGCGATGGGTG-3'
<i>Ankyrin-3</i>	5'-CAGGGGCTGTATTCTAGCAACT-3'	5'-CCCCTCCGTCTCACACTATTTT-3'

*H19* = methylated control; *β-actin*, *Gapdh* = un-methylated control

**Supplementary Table 3**  
**Characteristics of the Braincloud sample.**

Sample Size	Female (Male)	Age	RIN	PMI	pH
268	92 (176)	27.9 ± 22.2	8.4 ± 0.9	26.4 ± 17.1	6.5 ± 0.3

All the data are expressed as mean ± SD

**Supplementary Table 4**

**Characteristics of the samples used for the human behavioral and fMRI WM studies.**

	<b>Behavior</b>	<b>fMRI</b>
<b>N</b>	306	174
<b>Gender (M/F)</b>	138/168	81/93
<b>Age</b>	26.0±6.2	26.9±6.4
<b>Handedness</b>	0.7±0.4	0.7±0.5
<b>Parental socioeconomic status</b>	39.9±16.5	40.9±16.4
<b>IQ</b>	107.4±11.6	109.8±11.8

**Supplementary Table 5**

**Top diseases and biological functions associated with differentially methylated genes in the rat prefrontal cortex at PND62 after prenatal exposure to stress.**

<b>Diseases and Disorders</b>	<b><i>p</i> value</b>
Neurological Disease	4.22E-09
Organismal Injury and Abnormalities	3.46E-08
Cardiovascular Disease	2.67E-07
Hereditary Disorder	4.71E-07
Psychological Disorders	4.71E-07
<b>Molecular and Cellular Functions</b>	<b><i>p</i> value</b>
Molecular Transport	2.56E-08
Cell Cycle	8.28E-08
Cell-To-Cell Signaling and Interaction	4.30E-07
Cellular Development	2.82E-06
Cellular Growth and Proliferation	5.01E-06
<b>Physiological System Development and Function</b>	<b><i>p</i> value</b>
Nervous System Development and Function	2.56E-10
Organ Morphology	1.72E-05
Embryonic Development	2.40E-05
Organ Development	2.40E-05
Organismal Development	2.40E-05

**Supplementary Table 6**

List of probes showing differential methylation in the eight genes resulting from the overlap of different paradigms of early life stress exposure in different species and tissues.

Gene name	Higher methylation in	Rat PFC (postnatal day 62)		Monkey PFC (7 years old)		Monkey CD3+ (day 30 old)		Monkey CD3+ (2 years old)		Human CD34+ (cord blood)	
		diff meth probe	q value	diff meth probe	q value	diff meth probe	q value	diff meth probe	q value	diff meth probe	q value
Ank3	Stress	chr20:19580638-19580697	0.141959	chr9:76713019-76713067 0.143384 chr9:76713128-76713178 0.143384 chr9:76713244-76713294 0.143384 chr9:76713473-76713532 0.143384		chr9:76897059-76897118 0.015381 chr9:76897099-76897158 0.015381 chr9:76897139-76897198 0.015381 chr9:76897179-76897238 0.015381 chr9:76897299-76897358 0.015381 chr9:76897379-76897438 0.032022 chr9:77144454-77144513 0.015059 chr9:77144854-77144913 0.015059 chr9:77144934-77144993 0.015059		chr9:76897219-76897278 0.100842 chr9:76897299-76897358 0.100842 chr9:76899099-76899158 0.017648 chr9:76899139-76899198 0.017648		chr10:61900618-61900677 0.060659 chr10:61901941-61902000 0.185321	
	Control	chr20:19420344-19420403 0.114085 chr20:19420705-19420764 0.114085		X		X		X		chr10:62149544-62149598 0.146104 chr10:62149595-62149639 0.146104	
Cnga4	Stress	chr1:163137594-163137649 0.000065 chr1:163137327-163137372 0.000065		chr14:65936603-65936662 0.086013 chr14:65936702-65936758 0.086013 chr14:65936991-65937039 0.086013 chr14:65968017-65968072 0.191803 chr14:65968116-65968172 0.191803		X		X		chr11:6256207-6256251 0.022758 chr11:6256284-6256328 0.022758	
	Control	X		X		X		X		chr14:65967196-65967255 0.000299 chr14:65967276-65967335 0.000299 chr14:65967476-65967535 0.000054 chr14:65967516-65967575 0.000054 chr14:65967556-65967615 0.000054 chr14:65967596-65967655 0.000054 chr14:65967676-65967735 0.000054 chr14:65967716-65967775 0.000054 chr14:65967916-65967975 0.000054 chr14:65967956-65968015 0.000054 chr14:65968036-65968095 0.000054 chr14:65968076-65968135 0.000054 chr14:65967116-65967175 0.018034 chr14:65967316-65967375 0.018034 chr14:65967396-65967455 0.018034 chr14:65967476-65967535 0.018034 chr14:65967516-65967575 0.018034	
Dars2	Stress	chr13:76629115-76629165 0.005713		X		X		X		X	
	Control	X		chr1:203460771-203460815 0.135128 chr1:203460900-203460956 0.135128 chr1:203460981-203461036 0.135128		chr1:203460535-203460594 0.016604 chr1:203460615-203460674 0.016604		chr1:203460415-203460474 0.041125 chr1:203461095-203461154 0.041125		chr1:173793860-173793907 0.152082	
Gabrg2	Stress	chr10:27127411-27127470 0.186921		chr6:158458645-158458691 0.143637		chr6:158458012-158458071 0.056063 chr6:158458052-158458111 0.056063 chr6:158458412-158458471 0.001017 chr6:158458772-158458831 0.001017 chr6:158458852-158458911 0.001017 chr6:158458892-158458951 0.001017		chr6:158457932-158457991 0.161943 chr6:158458892-158458951 0.084601		chr5:161493755-161493814 0.034243 chr5:161494278-161494337 0.034243	
	Control	chr10:27130458-27130517 0.140810 chr10:27130465-27130524 0.140810 chr10:27130768-27130827 0.140810 chr10:27130966-27131025 0.140810 chr10:27131178-27131237 0.140810 chr10:27131397-27131456 0.140810 chr10:27104323-27104382 0.058220 chr10:27104987-27105046 0.164937		X		X		X		X	
Htr4	Stress	X		X		X		chr6:145085774-145085833 0.132238 chr6:145085814-145085873 0.132238 chr6:145085894-145085953 0.132238 chr6:145163181-145163240 0.124103 chr6:145163261-145163320 0.124103		chr5:148034080-148034124 0.010424 chr5:148034081-148034125 0.010424 chr5:148034081-148034125 0.010424 chr5:148034443-148034495 0.010424	
	Control	chr18:58416260-58416319 0.164027		chr6:145163771-145163827 0.149301		chr6:145163981-145164040 0.100424		X		X	
Lphn2	Stress	X		chr1:84116661-84116711 0.130892		chr1:84117017-84117076 0.077143 chr1:84117257-84117316 0.077143 chr1:84117337-84117396 0.077143 chr1:84117617-84117676 0.077143 chr1:84505713-84505772 0.179901 chr1:84505993-84506052 0.179901 chr1:84506033-84506092 0.179901 chr1:84506193-84506252 0.179901		chr1:84506033-84506092 0.184338 chr1:84506193-84506252 0.184338 chr1:84742988-84743047 0.042337 chr1:84743548-84743607 0.042337		chr1:81771325-81771384 0.176615	
	Control	chr2:247201889-247201948 0.067236 chr2:247268119-247268163 0.012587		X		X		X		X	
Slc22a2	Stress	X		X		X		chr4:157239558-157239617 0.005790 chr4:157240038-157240097 0.005790 chr4:157240078-157240137 0.005790		chr6:160699502-160699557 0.195967	
	Control	chr1:42443429-42443481 0.008736		chr4:157247817-157247861 0.198596 chr4:157248155-157248199 0.198596		chr4:157238718-157238777 0.024379		X		X	
Tiam1	Stress	chr11:30218874-30218928 0.027820 chr11:30218705-30218752 0.027820 chr11:30218643-30218689 0.027820		X		chr3:15243884-15243943 0.015329 chr3:15243964-15244023 0.015329		X		X	
	Control	X		chr3:14951518-14951562 0.123568		chr3:15241884-15241943 0.064748 chr3:15242084-15242143 0.064748 chr3:15242164-15242223 0.003634 chr3:15242524-15242583 0.003634 chr3:15242564-15242623 0.003634 chr3:15242644-15242703 0.003634 chr3:15242684-15242743 0.003634 chr3:15242724-15242783 0.003634 chr3:15242764-15242823 0.003634		chr3:15242844-15242903 0.037906		chr21:32932342-32932386 0.146465 chr21:32932167-32932211 0.146465	

In the conditions marked with X, we found no probes differentially methylated between the control and stressed groups.



**Supplementary Table 7**

**Summary of the probes associated with Ank3 and Gabrg2 which are differentially methylated between control and stressed groups.**

	Higher methylation in	Rat PFC	Monkey PFC (7 years old)	Monkey CD3+ (day 30 old)	Monkey CD3+ (2 years old)	Human CD34+ (cord blood)	Monkey Whole Blood (2 years old) diff meth probe      q value	Monkey Buccal Cells (2 years old) diff meth probe      q value
<b>Ank3</b>	Stress	✓	✓	✓	✓	✓	chr9:77074944-77075003    0.038705 chr9:77074984-77075043    0.038705	chr9:76897139-76897198    0.158048
	Control	✓	X	X	X	✓	X	X
<b>Gabrg2</b>	Stress	✓	✓	✓	✓	✓	X	X
	Control	✓	X	X	X	X	chr6:158457292-158457351    0.001338	chr6:158457612-158457671    0.044732
							chr6:158457372-158457431    0.001338	chr6:158457772-158457831    0.094282
							chr6:158457852-158457911    0.001338	chr6:158458332-158458391    0.102620
							chr6:158458092-158458151    0.001338	chr6:158458372-158458431    0.102620
						chr6:158458132-158458191    0.001338		

In the conditions marked with X, we found no probes differentially methylated between the control and stressed groups, while in the conditions marked with ✓ we found probes differentially methylated between the control and stressed groups.

**Supplementary Table 8**

**List of the p values and effect size estimates ('differential') associated with probes, mapping Ank3, which were more methylated in the stressed group compared to the controls.**

Samples	diff meth probe	p value	differential (log2)
Rat PFC (postnatal day 62)	chr20:19580638-19580697	0.049	0.913
Monkey PFC (7 years old)	chr9:76713019-76713067	0.014	1.360
	chr9:76713128-76713178	0.011	1.160
	chr9:76713244-76713294	0.037	1.090
	chr9:76713473-76713532	0.024	1.590
Monkey CD3+ (day 30 old)	chr9:76897059-76897118	0.010	0.966
	chr9:76897099-76897158	0.017	1.038
	chr9:76897139-76897198	0.009	1.072
	chr9:76897179-76897238	0.043	0.827
	chr9:76897299-76897358	0.024	0.871
	chr9:76897379-76897438	0.034	0.768
	chr9:77144454-77144513	0.012	0.926
	chr9:77144854-77144913	0.039	1.085
Monkey CD3+ (2 years old)	chr9:77144934-77144993	0.022	0.948
	chr9:76897219-76897278	0.040	0.551
	chr9:76897299-76897358	0.022	0.846
	chr9:76899099-76899158	0.047	0.562
Human CD34+ (cord blood)	chr9:76899139-76899198	0.046	0.615
	chr10:61900618-61900677	0.007	0.519
Monkey Whole Blood (2 years old)	chr10:61901941-61902000	0.026	0.894
	chr9:77074944-77075003	0.027	0.552
Monkey Buccal Cells (2 years old)	chr9:77074984-77075043	0.038	1.482
	chr9:76897139-76897198	0.007	1.651