nature neuroscience

Article

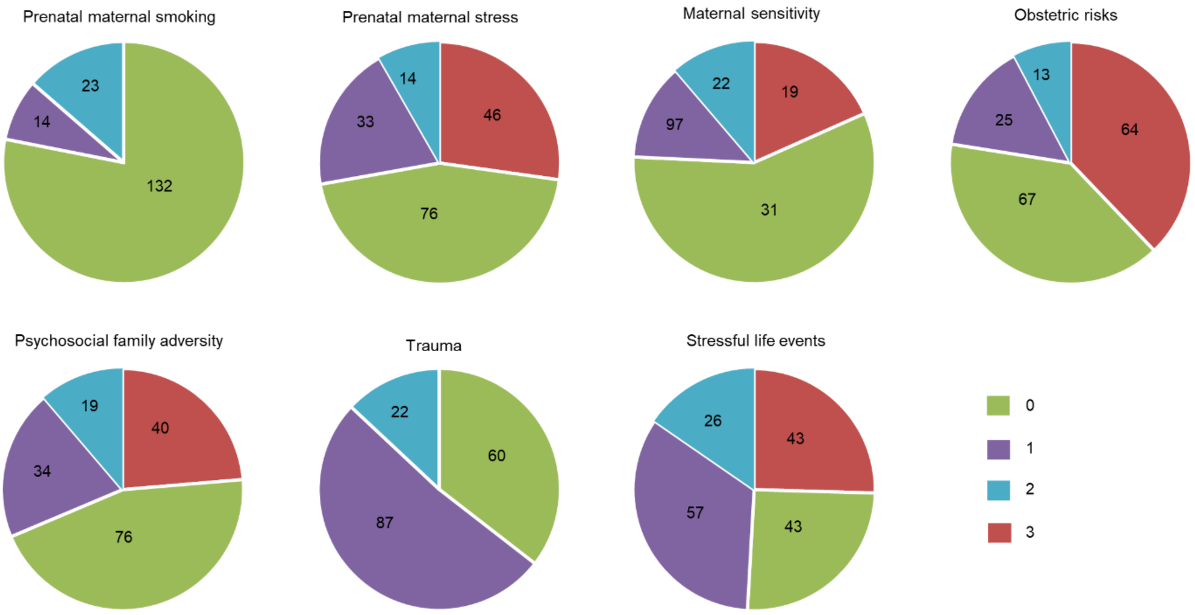
https://doi.org/10.1038/s41593-023-01410-8

# A stable and replicable neural signature of lifespan adversity in the adult brain

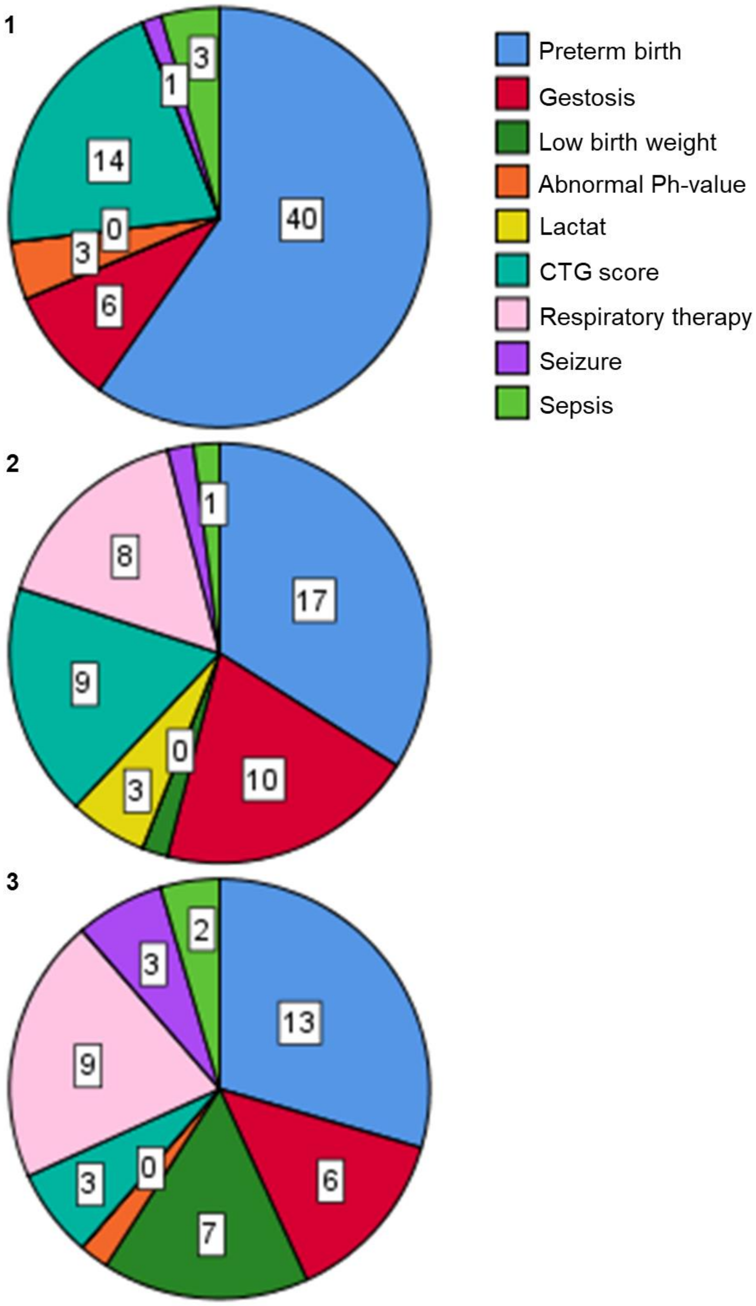
In the format provided by the authors and unedited

# SUPPLEMENTARY INFORMATION FILE

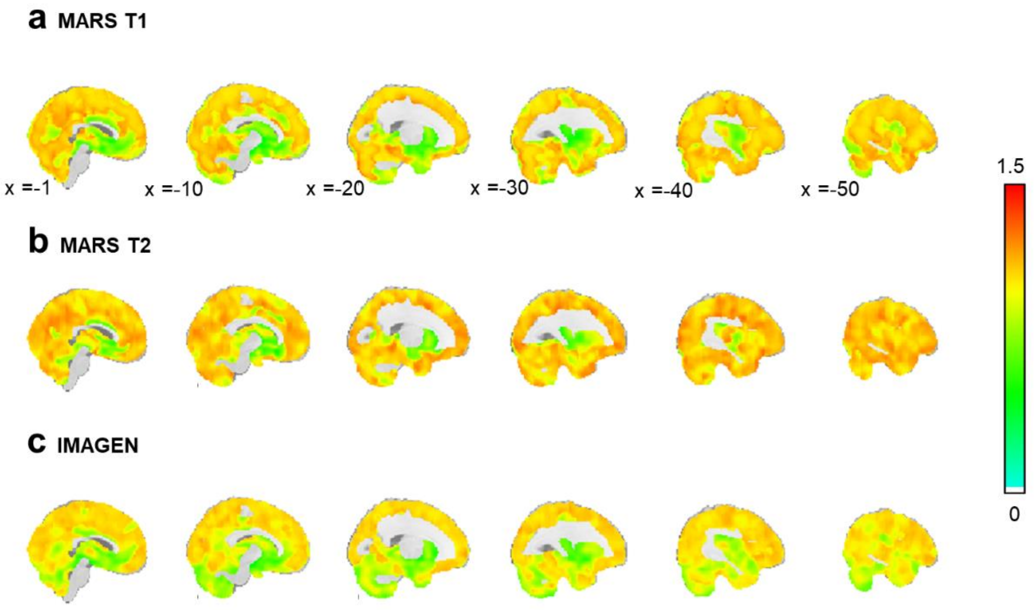
## SUPPLEMENTAL FIGURES



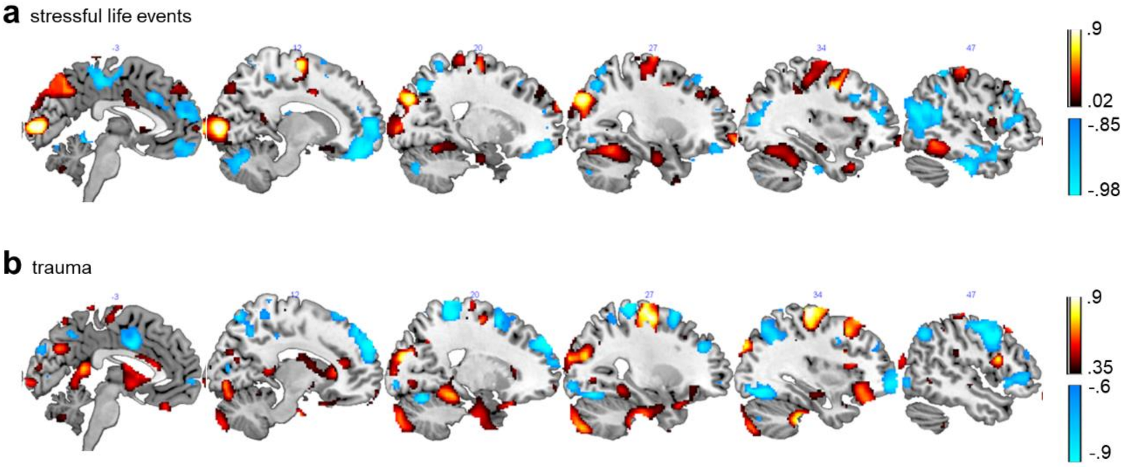

**Supplemental Figure 1.** Adversity bins. Pie charts including the number of participants for each bin of each category. 0= no adversity, 1=low adversity, 2= moderate adversity, 3= high adversity.




**Supplemental Figure 2.** Obstetric risk. Distribution of obstetric risk factors across the three exposure bins.




**Supplemental Figure 3.** Model accuracy. The figure shows the standardized mean squared error of true and predicted mean of morphometric changes as a function of adversity in a, the MARS sample at T1, b, the MARS sample at T2 and c, the IMAGEN sample. Model performance was better in subcortical than in cortical regions.




**Supplemental Figure 4.** IMAGEN structure coefficient. Spatial representation of the top 2% of the voxel-wise contribution of each adversity on predicted morphometric changes identified based on structure coefficients in the IMAGEN sample. a, stressful life events and b, trauma.

# ONLINE METHODS

## Study Design MARS

All groups had about equal size, with a slight oversampling in the high-risk combinations and with sex evenly distributed in all subgroups. A total of 384 infants born between February 1, 1986, and February 28, 1988, were recruited from 2 obstetric and 6 children's hospitals of the Rhine-Neckar region of Germany. To control confounding effects of family environment and infant medical status, only firstborn singletons of German speaking parents with no severe physical handicaps, obvious genetic defects, or metabolic diseases were selected. Participation rate at the time of recruitment was 64.5%, with a slightly lower rate in parents from psychosocially disadvantaged backgrounds. All families were Caucasians.

## MARS Assessments

*Maternal smoking during pregnancy.* Was determined by a standardized interview with the mother conducted at the 3-month assessment and classified as nonsmokers, smoking 1-5 cigarettes per day (cig./d) and more than 5 cigarettes per day for further details see [1].

*Prenatal maternal stress.* A standardized parent interview was conducted at the 3-month assessment. 11 questions were asked concerning worries, mood problems, as well as positive experiences during pregnancy. Mothers were requested to judge separately for the first and the second/third trimesters. As associations of prenatal stress in mid- and late pregnancy with behavioral outcome in the offspring have been reported to be largest [2], only prenatal stress during the second and third trimester was included.

*Early mother-child interaction*. As described in Holz et al.[3], videotapes of a 10-min standardized nursing and play situation between mothers and their three-month-olds at our lab were recorded and evaluated by trained raters (κ>0.83) using a modified version of the category system for micro-analysis of the early mother–child interaction [4, 5]. Raters were blind to parental and child risk status. Nine measures of mother–infant interaction behavior were formed by coding a behavior as present or absent in a total of 120 five-second intervals. Maternal stimulation included all attempts to attract the infant´s attention or to establish contact with him/her (vocal, facial or motor) and was coded when the baby was gazing at the mother or when the behaviors were clearly directed at the child. The scores were z-transformed and recoded such that higher scores represent lower stimulation.

*Obstetric adversity.* At the age of 3 months, an obstetric adversity score was obtained by counting the presence of 9 adverse conditions during pregnancy, delivery, and postnatal period such as preterm labor, asphyxia, or seizures. See Figure S2 for its composition. This measure of adversity was included due to the enrichment of the MARS sample with respect to obstetric risks and their well-known effects on socio-cognitive[6] and neural development[7-12].

*Psychosocial adversity*. Information on adverse characteristics of the parents (low educational level, broken home history or delinquency, poor coping skills, psychopathology), their partnership (early parenthood, one-parent family, unwanted pregnancy, marital discord) and the family environment (overcrowding, poor social integration and support, severe chronic life difficulties) was assessed according to an 'enriched' family adversity index [13] by a standardized parent interview conducted at each assessment (n=5) until the age of 11 years (range 0-9, M=2.95; SD=2.05). The score is created such that events that reflect only one possible exposure during lifetime (e.g. unwanted pregnancy) are also only counted once.

*Childhood trauma*. At the age of 23, participants completed the brief screening version of the Childhood Trauma Questionnaire (CTQ)[14]. The CTQ entails a retrospective assessment of five types of self-reported childhood maltreatment, i.e. sexual, physical, and emotional abuse, and emotional and physical neglect. The scores of all subscales were summed up.

*Life events*. To assess exposure to life stress (LS) across the life span, a semi-structured parent interview was conducted until the age of 15 years. The young adults were interviewed from the age of 19 years onwards. The interview, which was a modified and shortened version of the Munich Events List [15], evaluated the occurrence of adverse life events during a period of one year prior to the assessment. The items covered all relevant areas of children's and young adults' LS, including family, school, parents, health, legal troubles, and living conditions, such as birth of a sibling, death of a close relative or parents` separation for which the participant indicated a subjective burden. A composite score was computed by summing up the z-standardized scores from the ten assessments between the age of 3 months and 25 years.

**Anatomical image preprocessing.**

T1-weighted anatomical images with 192 slices covering the whole brain were acquired at the 25-year assessment using a 3T scanner (matrix 256x256, repetition time=2300ms, echo time=3.03ms, 50% distance factor, field of view 256x256x192mm, flip angle 9°). Preprocessing of the anatomical images entailed the following steps. First, images were reoriented to the standard (MNI) orientation [fslreorient2std], automatically cropped [robustfov] and bias-field corrected (RF/B1-inhomogeneity-correction) [FAST]. Then registered to standard space (linear and non-linear) [FLIRT and FNIRT], followed by brain-extraction [FNIRT-based or BET] as well as tissue-type segmentation [FAST] and subcortical structure segmentation [FIRST]. Data were visually inspected and evaluated by an experienced rater (NH).

As done previously[16], we selected the nonlinear Jacobian determinants as feature for the normative model given that they quantify the overall degree of tissue expansion or contraction required to match each image to the population template. Thereby, they contain all information necessary to warp the subject to template and avoid making a sometimes arbitrary distinction between what can be considered white and grey matter, and is particularly valuable in avoiding partial volume effects. Notably, these features have been shown have a stronger relationship with demographic variables than more commonly used features (e.g. modulated grey matter density[17]). The images were affine and log transformed and masked by a grey matter template.

In addition, we estimated the normative model on grey matter density, which we calculated by warping grey matter to MNI space and subsequent multiplication by the jacobian determinants and smoothing with a 6mm kernel.

**Normative Models based on adversity**

Bayesian Linear Regression was chosen based on our own reports demonstrating linear relationships between adversities and brain structure and others reporting long-term effects with respect to brain morphometry[18]. We estimated the hyper-parameters of this model (namely prior weight precision and noise precision) using an Empirical Bayes approach as we have done in prior work[19-21]. We evaluated the performance of our model by making out of sample predictions under 10-fold cross validation.

Individual-specific *Z* score[22] indicated the difference between the prediction (mean, $\hat{y}_{ij}$) at for each subject (i) at each brain location (j) and true brain structure ($y_{ij}$) scaled by the prediction variance [expected level of variation $\sigma^2_{ij}$ and variance learned from the normative distribution ($\sigma^2_{nj}$)]:

$$z_{ij} = \frac{y_{ij} - \hat{y}_{ij}}{\sqrt{\sigma_{ij}^2 - \sigma_{nj}^2}}$$

Normative modeling was run using python 3.6 and the PCNtoolkit package (version 0.19).

### Normative Models based on age

Data from 9 sites were combined to create the initial full sample. These sites are described in detail in supplementary tables 25 and 26 including the sample size, age (mean and standard deviation), and sex distribution of each site. In brief, these were derived by including data from the following publicly available sources: The Philadelphia Neurodevelopmental Cohort (PNC)[23], Cam-CAN[24], Human Connectome Project[25], UK Biobank[26, 27] and OASIS3[28] in addition to the MARS and IMAGEN data all processed using an identical pipeline. This is a subset of the data reported in our previous work[21] and we followed the same procedures reported in that manuscript with regard to quality control.

Normative modeling was run using python 3.8 and the PCNtoolkit package (version 0.26). Bayesian Linear Regression (BLR) with likelihood warping (‘sinarcsinsh’ warping function)[20, 21] was used to model voxel-wise JD development from a vector of covariates (age, sex, and site). For each voxel y is predicted as:

$y = w^T \phi(x) + \epsilon$

where $w^T$ is the estimated weight vector, $\phi(x)$ is a basis expansion of the of covariate vector x, consisting of a B-spline basis expansion (cubic spline with five evenly spaced knots) to model non-linear effects of age, and $\epsilon = N(0, \beta^{-1})$ a Gaussian noise distribution with mean zero and noise precision term $\beta$ (the inverse variance).

### Principal component analysis

The Kaiser–Meyer–Olkin measure of sampling adequacy was .69, representing a relatively good factor analysis, and Bartlett’s test of Sphericity was significant ($p < .001$), indicating that correlations between items were sufficiently large for performing a PCA. Only factors with eigenvalues $\geq 1$ were considered[29, 30]. Examination of Kaiser’s criteria and the scree-plot yielded empirical justification for retaining three factors with eigenvalues exceeding 1 which accounted for 63% of the total variance. Most adversities loaded highly on only one of the two factors (see supplemental Table 22). The predictive models were estimated for each of the three PC´s separately, based on 4 (random) sampling points of the loadings, scaled by the square root of the eigenvalue and the respective adversity mean added.

### Sensitivity analyses

First, to ensure that the results were not affected by the categorization of the adversity scores, two additional separate normative model were set up with the three principal components (not binned) and with the z-standardized (not binned) scores and, respectively. Second, to evaluate whether the stability of the patterns from T1 to T2 was not affected by the subject drop-out at T2, a further normative model at T1 was fitted including only the participants that had follow-up data. Third, to ensure that results are not affected by the inclusion of TIV, the whole analysis pipeline was repeated without this variable. Forth, to elaborate the effect of adversity only, normative models excluding sex and total intracranial volume (TIV) were created in both samples. Fifth, we excluded obstetric adversities given its qualitatively different nature of risks. Sixth, we used modulated grey matter images as outcome feature instead of JDs. Seventh, given the recent discussion on a differential impact of adversity depending on the subjective appraisal, we additionally created a normative models based on retrospectively reported trauma (CTQ) and the prospectively reported life events with the constraint that both measures cover slightly different forms of adversity.

**IMAGEN**

*Anatomical images*. MRI was performed on a 3T scanner (Siemens Trio). High-resolution anatomical MR images were obtained using a standardized 3D T1-weighted magnetisation prepared rapid acquisition gradient echo (MPRAGE) sequence based on the ADNI protocol (http://adni.loni.usc.edu/ methods/mri-analysis/mri-acquisition/). The parameters were as follows: repetition time = 2300 ms, echo time = 2.93 ms, flip angle = 9˚, 1.1x1.1x1.1 mm voxel size.

*Assessments*. During all 4 assessment waves (14, 16, 19, 22 years), the participants completed the Life Events Questionnaire (LEQ)[31] that was adapted for their age. The participants indicated the experience of an event and how they felt after the event. Negative life events were coded once if they felt “unhappy” after the event and twice if they felt very unhappy (mean=18.26, SD=8.75, range=5-40). The sum scores were z-transformed to create a composite score.

The CTQ was assessed at the age of 19 years. The total score across all scales was used (mean=31.68., SD=7.64, range=25-73).

## REFERENCES

1. Holz, N.E., *et al.* Effect of prenatal exposure to tobacco smoke on inhibitory control: neuroimaging results from a 25-year prospective study. *JAMA Psychiatry* **71**, 786-796 (2014).
2. Rice, F., *et al.* The links between prenatal stress and offspring development and psychopathology: disentangling environmental and inherited influences. *Psychological medicine* **40**, 335-345 (2010).
3. Holz, N.E., *et al.* Early maternal care may counteract familial liability for psychopathology in the reward circuitry. *Social cognitive and affective neuroscience* **13**, 1191-1201 (2018).
4. Jörg, M., *et al.* [Category system for microanalysis of early mother-child interaction]. *Z. Kinder. Jugendpsychiatr. Psychother.* **22,** , 97-106 (1994).
5. Schmid, B., *et al.* Quality of early mother-child interaction associated with depressive psychopathology in the offspring: a prospective study from infancy to adulthood. *J Psychiatr Res* **45**, 1387-1394 (2011).
6. Laucht, M., *et al.* Behavioral sequelae of perinatal insults and early family adversity at 8 years of age. *J Am Acad Child Adolesc Psychiatry* **39**, 1229-1237 (2000).
7. Nam, K.W., *et al.* Alterations in cortical thickness development in preterm-born individuals: Implications for high-order cognitive functions. *NeuroImage* **115**, 64-75 (2015).
8. Nosarti, C., *et al.* Preterm birth and structural brain alterations in early adulthood. *Neuroimage Clin* **6**, 180-191 (2014).
9. Nosarti, C., *et al.* Grey and white matter distribution in very preterm adolescents mediates neurodevelopmental outcome. *Brain* **131**, 205-217 (2008).
10. Zhou, L., *et al.* Brain gray and white matter abnormalities in preterm-born adolescents: A meta-analysis of voxel-based morphometry studies. *PLoS One* **13**, e0203498 (2018).
11. Sripada, K., *et al.* Trajectories of brain development in school-age children born preterm with very low birth weight. *Scientific reports* **8**, 15553 (2018).
12. Karolis, V.R., *et al.* Volumetric grey matter alterations in adolescents and adults born very preterm suggest accelerated brain maturation. *NeuroImage* **163**, 379-389 (2017).
13. Holz, N.E., *et al.* Ventral striatum and amygdala activity as convergence sites for early adversity and conduct disorder. *Soc Cogn Affect Neurosci* (2016).
14. Bernstein, D.P., *et al.* Development and validation of a brief screening version of the Childhood Trauma Questionnaire. *Child Abuse Negl* **27**, 169-190 (2003).
15. Maier-Diewald, W., Wittchen, H.-U., Hecht, H. & Werner-Eilert, K. *MEL - Münchner Ereignisliste* (Max Planck Institute of Psychiatry, Munich (DE), 1983).
16. Holz, N.E., *et al.* Age-related brain deviations and aggression. *Psychological medicine*, 1-10 (2022).
17. Monte-Rubio, G.C., Falcon, C., Pomarol-Clotet, E. & Ashburner, J. A comparison of various MRI feature types for characterizing whole brain anatomical differences using linear pattern recognition methods. *NeuroImage* **178**, 753-768 (2018).
18. Gehred, M.Z., *et al.* Long-term Neural Embedding of Childhood Adversity in a Population-Representative Birth Cohort Followed for 5 Decades. *Biol Psychiatry* **90**, 182-193 (2021).
19. Huertas, I., *et al.* A Bayesian spatial model for neuroimaging data based on biologically informed basis functions. *NeuroImage* **161**, 134-148 (2017).
20. Fraza, C.J., Dinga, R., Beckmann, C.F. & Marquand, A.F. Warped Bayesian linear regression for normative modelling of big data. *NeuroImage* **245**, 118715 (2021).
21. Rutherford, S., *et al.* Charting brain growth and aging at high spatial precision. *Elife* **11** (2022).

22. Marquand, A.F., Rezek, I., Buitelaar, J. & Beckmann, C.F. Understanding Heterogeneity in Clinical Cohorts Using Normative Models: Beyond Case-Control Studies. *Biological Psychiatry* **80**, 552-561 (2016).
23. Satterthwaite, T.D., *et al.* Neuroimaging of the Philadelphia neurodevelopmental cohort. *NeuroImage* **86**, 544-553 (2014).
24. Shafto, M.A., *et al.* The Cambridge Centre for Ageing and Neuroscience (Cam-CAN) study protocol: a cross-sectional, lifespan, multidisciplinary examination of healthy cognitive ageing. *BMC Neurol* **14**, 204 (2014).
25. Van Essen, D.C., *et al.* The WU-Minn Human Connectome Project: an overview. *NeuroImage* **80**, 62-79 (2013).
26. Sudlow, C., *et al.* UK biobank: an open access resource for identifying the causes of a wide range of complex diseases of middle and old age. *PLoS Med* **12**, e1001779 (2015).
27. Miller, K.L., *et al.* Multimodal population brain imaging in the UK Biobank prospective epidemiological study. *Nat Neurosci* **19**, 1523-1536 (2016).
28. Marcus, D.S., Fotenos, A.F., Csernansky, J.G., Morris, J.C. & Buckner, R.L. Open access series of imaging studies: longitudinal MRI data in nondemented and demented older adults. *Journal of cognitive neuroscience* **22**, 2677-2684 (2010).
29. Guttman, L. Some necessary conditions for common factor analysis. *Psychometrika* **19**, 149-161 (1954).
30. Kaiser, H.F. The application of electronic computers to factor analysis. *Educational and Psychological Measurement* **20**, 141-151 (1960).
31. Newcomb, M. A multidimensional assessment of stressful life events among adolescents: Derivation and correlates. *Journal of Health and Social Behavior* **22**, 400-415 (1981).

# TABLES

**Table S1. Correlation between true and predicted JDs based on adversities, sex and TIV at T1.**

| Voxels | ρ | MAX X (mm) | MAX Y (mm) | MAX Z (mm) | Region |
|---|---|---|---|---|---|
| 64594 | 0.804 | 12 | -14 | -16 | Brainstem/Hippocampus |
| 872 | 0.46 | -32 | 54 | 30 | Superior Frontal Gryus |
| 384 | 0.434 | 42 | -68 | 54 | Lateral Occipital Gyrus |
| 104 | 0.413 | 26 | -46 | 46 | Superior Parietal Lobule |
| 65 | 0.2 | -6 | 14 | 70 | Superior Frontal Gyrus |
| 41 | 0.361 | 36 | 38 | 10 | Frontal Pole |
| 32 | 0.471 | -28 | 32 | 26 | Middle Frontal Gyrus |
| 19 | 0.309 | 10 | -30 | 78 | Precentral Gyrus |
| 17 | 0.372 | 36 | -98 | -2 | Inferior Occipital Gyrus |
| 17 | 0.158 | -54 | -38 | -10 | Middle Temporal Gyrus |
| 17 | 0.21 | 2 | -14 | 66 | Precentral Gyrus |
| 17 | 0.398 | 34 | 10 | 28 | Precentral Gyrus |
| 15 | 0.153 | 14 | 58 | 38 | Frontal Pole |
| 15 | 0.241 | -20 | 16 | 68 | Superior Frontal Gyrus |
| 12 | 0.163 | -42 | -6 | 62 | Precentral Gyrus. |
| 11 | 0.158 | -56 | -10 | 46 | Postcentral Gyrus. |
| 10 | 0.189 | 42 | -52 | 54 | Superior Parietal Lobule. |

Note: ρ=correlation coefficient

**Table S2. Correlation between true and predicted JDs based on adversities, sex and TIV at T1 in limbic regions.**

| Region of Interest | hemisphere | Voxels | ρ | MAX X (mm) | MAX Y (mm) | MAX Z (mm) |
|---|---|---|---|---|---|---|
| amygdala | l | 595 | 0.71 | -12 | -10 | -14 |
| | r | 694 | 0.794 | 12 | -10 | -14 |
| hippocampus | l | 1045 | 0.76 | -10 | -12 | -18 |
| | r | 1047 | 0.8 | 12 | -12 | -16 |
| medial frontal gyrus | | 1354 | 0.684 | -8 | 30 | -12 |
| anterior cingulate gyrus | | 2450 | 0.648 | -4 | 32 | -12 |

Note: ρ=correlation coefficient, unilateral masks used for the amygdala and the hippocampus, bilateral masks used for the medial frontal gyrus and the anterior cingulate gyrus

**Table S3. Correlation between true and predicted JDs based on adversities, sex and TIV at T2.**

| Voxels | ρ | MAX X (mm) | MAX Y (mm) | MAX Z (mm) | Region |
|---|---|---|---|---|---|
| 45161 | 0.768 | 8 | -6 | 6 | Thalamus |
| 1189 | 0.393 | -8 | 28 | 56 | Superior Frontal Gyrus |
| 509 | 0.388 | -24 | -82 | 48 | Precuneus |
| 388 | 0.421 | 42 | 14 | 56 | Middle Frontal Gyrus |
| 249 | 0.327 | -34 | -54 | 48 | Inferior Parietal Lobule |
| 202 | 0.515 | 14 | 14 | 40 | Cingulate Gyrus |
| 184 | 0.211 | -20 | -52 | 66 | Superior Parietal Lobule |
| 165 | 0.272 | -8 | 62 | -8 | Medial Frontal Gyrus |
| 144 | 0.239 | 34 | -80 | 40 | Precuneus |
| 133 | 0.278 | -18 | -62 | 30 | Occipital Lobe |
| 126 | 0.388 | 28 | -44 | 40 | Parietal Lobe |
| 119 | 0.206 | 50 | -22 | 58 | Postcentral Gyrus |
| 108 | 0.228 | 14 | -60 | 40 | Precuneus |
| 108 | 0.256 | -52 | -14 | 48 | Postcentral Gyrus |
| 90 | 0.222 | 6 | 60 | 24 | Superior Frontal Gyrus |
| 87 | 0.509 | -22 | -4 | 48 | Middle Frontal Gyrus |
| 67 | 0.239 | -46 | 34 | 36 | Middle Frontal Gyrus. |
| 52 | 0.189 | -52 | -14 | -22 | Middle Temporal Gyrus |
| 50 | 0.393 | 10 | -104 | 12 | Cuneus |
| 41 | 0.156 | -44 | 4 | 46 | Middle Frontal Gyrus |
| 40 | 0.278 | -36 | -28 | 68 | Postcentral Gyrus |

| | | | | | |
|---|---|---|---|---|---|
| 35 | 0.234 | -10 | 68 | 24 | Frontal Pole |
| 32 | 0.162 | 16 | 44 | 40 | Superior Frontal Gyrus |
| 28 | 0.162 | 62 | -48 | 44 | Inferior Parietal Lobule |
| 26 | 0.399 | -46 | 40 | -20 | Middle Frontal Gyrus |
| 25 | 0.184 | -44 | 18 | -14 | Inferior Frontal Gyrus |
| 24 | 0.189 | -30 | -4 | 56 | Precentral Gyrus |
| 23 | 0.145 | -52 | 30 | -4 | Inferior Frontal Gyrus |
| 23 | 0.184 | 50 | -82 | 14 | Middle Occipital Gyrus |
| 22 | 0.355 | -22 | -28 | 52 | Postcentral Gyrus |
| 21 | 0.25 | 24 | -40 | -60 | Cerebellum |
| 20 | 0.134 | -46 | -64 | 26 | Middle Temporal Gyrus |
| 20 | 0.294 | -18 | -36 | -42 | Cerebellum |
| 19 | 0.2 | -50 | -36 | -8 | Middle Temporal Gyrus |
| 19 | 0.515 | -24 | 30 | 28 | Middle Frontal Gyrus |
| 18 | 0.151 | 12 | -90 | 18 | Cuneus |
| 17 | 0.167 | -42 | 54 | 18 | Superior Frontal Gyrus. |
| 17 | 0.156 | -28 | -76 | -22 | Declive |
| 11 | 0.189 | 40 | -46 | 50 | Inferior Parietal Lobule |
| 10 | 0.129 | 30 | 38 | 32 | Middle Frontal Gyrus |
| 10 | 0.134 | -28 | -68 | 60 | Lateral Occipital Cortex |
| 10 | 0.129 | 16 | 14 | 60 | Superior Frontal Gyrus. |

Note: ρ=correlation coefficient

**Table S4. Correlation between true and predicted JDs based on adversities, sex and TIV at T2 in limbic regions.**

| Region of Interest | hemisphere | Voxels | ρ | MAX X (mm) | MAX Y (mm) | MAX Z (mm) |
|---|---|---|---|---|---|---|
| amygdala | l | 465 | 0.63 | -12 | -12 | -16 |
| | r | 516 | 0.669 | 14 | -12 | -16 |
| hippocampus | l | 1045 | 0.76 | -10 | -12 | -18 |
| | r | 594 | 0.686 | 14 | -14 | -16 |
| | r | 158 | 0.504 | 22 | -42 | 0 |
| medial frontal gyrus | | 428 | 0.636 | -8 | 28 | -14 |
| | | 11 | 0.167 | -6 | 50 | -24 |
| | | 10 | 0.14 | -8 | 56 | -10 |
| anterior cingulate gyrus | | 990 | 0.619 | 6 | 10 | 24 |
| | | 137 | 0.548 | 0 | 34 | -12 |
| | | 36 | 0.448 | 14 | 16 | 34 |
| | | 20 | 0.222 | 14 | -14 | 38 |
| | | 3 | 0.129 | 4 | 30 | 0 |
| | | 3 | 0.145 | 14 | 32 | 26 |

Note: ρ=correlation coefficient, unilateral masks used for the amygdala and the hippocampus, bilateral masks used for the medial frontal gyrus and the anterior cingulate gyrus

**Table S5. Correlation between true and predicted JDs based on adversities, sex and TIV in the IMAGEN cohort.**

| Voxels | ρ | MAX X (mm) | MAX Y (mm) | MAX Z (mm) | Region |
|---|---|---|---|---|---|
| 90174 | 0.762 | -10 | -12 | -16 | Brainstem/hippocampus |
| 172 | 0.238 | -34 | 18 | 38 | Middle Frontal Gyrus |
| 141 | 0.227 | 16 | -56 | 72 | Lateral Occipital Cortex |
| 93 | 0.244 | 36 | 20 | 50 | Superior Frontal Gyrus |
| 88 | 0.376 | 50 | 26 | 38 | Middle Frontal Gyrus |
| 70 | 0.161 | -10 | 8 | 74 | Superior Frontal Gyrus |
| 63 | 0.183 | -36 | 42 | -20 | Middle Frontal Gyrus |
| 51 | 0.299 | -30 | -70 | 24 | Middle Temporal Gyrus |
| 45 | 0.161 | -22 | -54 | 72 | Superior Parietal Lobule |
| 44 | 0.2 | 22 | -82 | 50 | Lateral Occipital Cortex |
| 41 | 0.172 | 38 | -60 | 20 | Middle Temporal Gyrus |
| 38 | 0.15 | -26 | -80 | 50 | Lateral Occipital Cortex |
| 38 | 0.167 | 26 | -90 | 38 | Cuneus |
| 31 | 0.139 | -18 | 26 | 58 | Middle Frontal Gyrus |
| 16 | 0.255 | 50 | 52 | 2 | Middle Frontal Gyrus |
| 15 | 0.337 | 18 | -36 | 52 | Paracentral Lobule |
| 12 | 0.134 | -46 | 46 | 20 | Middle Frontal Gyrus |

Note: ρ=correlation coefficient

**Table S6. Correlation between true and predicted JDs based on adversities, sex and TIV in limbic regions in the IMAGEN subsample.**

| Region of Interest | hemisphere | Voxels | ρ | MAX X (mm) | MAX Y (mm) | MAX Z (mm) |
|---|---|---|---|---|---|---|
| amygdala | l | 633 | 0.745 | -12 | -12 | -16 |
| | r | 728 | 0.701 | 14 | -8 | -12 |
| hippocampus | l | 1333 | 0.751 | -10 | -12 | -18 |
| | r | 1366 | 0.674 | 12 | -12 | -16 |
| medial frontal gyrus | | 755 | 0.674 | -8 | 30 | -12 |
| anterior cingulate gyrus | | 1961 | 0.602 | -8 | 34 | -10 |
| | | 3 | 0.123 | -10 | 18 | 38 |
| | | 1 | 0.1 | -6 | 24 | 36 |

Note: ρ=correlation coefficient, unilateral masks used for the amygdala and the hippocampus, bilateral masks used for the medial frontal gyrus and the anterior cingulate gyrus

**Table S7. Top 2% of the voxels of the correlation between obstetric risks and the predicted morphometric changes of the JD´s**

| Voxels | ρ | MAX X (mm) | MAX Y (mm) | MAX Z (mm) | Region |
|---|---|---|---|---|---|
| *positive association* | | | | | |
| 3865 | 0.768 | 0 | 54 | -18 | Medial Frontal Gyrus |
| 2776 | 0.73 | 62 | 4 | 18 | Precentral Gyrus |
| 1180 | 0.692 | -6 | 20 | 58 | Superior Frontal Gyrus. |
| 1175 | 0.408 | 38 | -80 | -46 | Cerebellum |
| 1085 | 0.547 | 4 | -28 | 62 | Precentral Gyrus |
| 934 | 0.49 | -46 | -48 | -36 | Cerebellum |
| 764 | 0.363 | -46 | -4 | -4 | Insula |
| 591 | 0.344 | 2 | -96 | -10 | Occipital Pole |
| 562 | 0.389 | 26 | -64 | 2 | Lingual Gyrus |
| 414 | 0.313 | -34 | -12 | 56 | Precentral Gyrus |
| 335 | 0.344 | -28 | 20 | -42 | Temporal Pole |
| 222 | 0.281 | 28 | 40 | 32 | Middle Frontal Gyrus |
| 214 | 0.54 | 36 | 36 | 16 | Frontal Pole |
| 162 | 0.325 | 0 | -46 | -40 | Brainstem |
| 139 | 0.351 | 2 | -68 | 48 | Precuneus |
| 130 | 0.231 | 32 | -54 | 42 | Superior Parietal Lobule |
| 94 | 0.262 | -42 | 20 | 46 | Middle Frontal Gyrus |
| 79 | 0.218 | -64 | 2 | 18 | Precentral Gyrus |
| 69 | 0.287 | 46 | -16 | -36 | Inferior Temporal Gyrus |
| 65 | 0.224 | 12 | -52 | 48 | Precuneus |
| 53 | 0.243 | -28 | -34 | 60 | Postcentral Gyrus |
| 50 | 0.262 | -12 | 0 | 44 | Cingulate Gyrus |
| 37 | 0.224 | -58 | -30 | -26 | Inferior Temporal Gyrus |
| 36 | 0.161 | -66 | -50 | -4 | Middle Temporal Gyrus |
| 31 | 0.117 | 56 | -40 | -14 | Middle Temporal Gyrus |
| 29 | 0.212 | 0 | -50 | 34 | Precuneus |
| 27 | 0.18 | -18 | 28 | 38 | Superior Frontal Gyrus |
| 27 | 0.205 | -36 | 62 | -2 | Middle Frontal Gyrus. |
| 26 | 0.193 | -48 | 2 | 56 | Precentral Gyrus |
| 25 | 0.224 | 46 | -42 | -40 | Cerebellum |
| 24 | 0.262 | 36 | 8 | 32 | Middle Frontal Gyrus |

| | | | | | |
|---|---|---|---|---|---|
| 23 | 0.136 | 40 | -76 | 0 | Lateral Occipital Cortex |
| 23 | 0.18 | 2 | 62 | 20 | Frontal Pole |
| 22 | 0.212 | 24 | -32 | 72 | Postcentral Gyrus |
| 21 | 0.136 | -44 | -58 | 36 | Angular Gyrus |
| 20 | 0.199 | -6 | -82 | 18 | Cuneus |
| 19 | 0.174 | -22 | 36 | 30 | Superior Frontal Gyrus |
| 19 | 0.18 | -28 | 42 | 34 | Middle Frontal Gyrus |
| 19 | 0.161 | -60 | -42 | 34 | Supramarginal Gyrus |
| 19 | 0.193 | 18 | -38 | 58 | Paracentral Lobule |
| 19 | 0.123 | 18 | -4 | 74 | Superior Frontal Gyrus |
| 18 | 0.3 | -28 | 32 | -26 | Middle Frontal Gyrus |
| 17 | 0.117 | -32 | -86 | 20 | Middle Occipital Gyrus |
| 17 | 0.123 | -26 | -78 | -16 | Cerebellum |
| 17 | 0.11 | -52 | -52 | 26 | Supramarginal Gyrus |
| 16 | 0.199 | 26 | -12 | 52 | Precentral Gyrus |
| 15 | 0.123 | 6 | -46 | -2 | Cerebellum |
| 15 | 0.123 | 16 | -80 | 48 | Precuneus |
| 15 | 0.148 | -30 | 4 | 62 | Middle Frontal Gyrus |
| 14 | 0.3 | -22 | -52 | 50 | Precuneus |
| 14 | 0.205 | -20 | -20 | 72 | Precentral Gyrus |
| 13 | 0.237 | 24 | -74 | -46 | Cerebellum |
| 13 | 0.117 | -34 | -72 | -34 | Cerebellum |
| 12 | 0.174 | 40 | 44 | -20 | Middle Frontal Gyrus |
| 11 | 0.11 | 58 | -28 | 34 | Inferior Parietal Lobule |
| 11 | 0.167 | 42 | -6 | 62 | Precentral Gyrus |
| 10 | 0.199 | 26 | -86 | 38 | Cuneus |
| 10 | 0.117 | 2 | 32 | 42 | Paracingulate Gyrus |
| 10 | 0.161 | 0 | -64 | -20 | Cerebellum |
| 10 | 0.18 | 0 | 40 | 36 | Medial Frontal Gyrus |
| 10 | 0.136 | -38 | -60 | 46 | Inferior Parietal Lobule. |
| *negative association* | | | | | |
| 13354 | 0.844 | 28 | 20 | -20 | Inferior Frontal Gyrus |
| 1053 | 0.756 | -24 | -84 | 12 | Middle Occipital Gyrus. |
| 848 | 0.781 | 2 | 34 | 0 | Anterior Cingulate Gyrus |

| | | | | | |
|---|---|---|---|---|---|
| 600 | 0.68 | 62 | -30 | 44 | Supramarginal Gyrus |
| 375 | 0.794 | -46 | 40 | 22 | Middle Frontal Gyrus |
| 272 | 0.598 | 0 | -66 | -2 | Cerebellum |
| 243 | 0.642 | 24 | -100 | -10 | Fusiform Gyrus |
| 232 | 0.61 | 14 | -46 | -58 | Cerebellum |
| 227 | 0.648 | 6 | -86 | 40 | Cuneus |
| 196 | 0.591 | -56 | -6 | 44 | Precentral Gyrus |
| 85 | 0.572 | 10 | 0 | 46 | Cingulate Gyrus |
| 76 | 0.528 | 20 | -54 | 22 | Precuneus |
| 75 | 0.655 | 30 | 62 | 22 | Superior Frontal Gyrus |
| 71 | 0.68 | -20 | -80 | -8 | Lingual Gyrus |
| 70 | 0.598 | -36 | 40 | -16 | Middle Frontal Gyrus |
| 62 | 0.541 | -64 | -28 | 44 | Supramarginal Gyrus |
| 39 | 0.604 | -56 | 34 | -4 | Inferior Frontal Gyrus |
| 35 | 0.509 | 12 | 72 | 8 | Frontal Pole |
| 19 | 0.509 | -32 | -88 | -24 | Cerebellum |
| 19 | 0.427 | -10 | 22 | -8 | Anterior Cingulate |
| 17 | 0.427 | 38 | -80 | 34 | Superior Occipital Gyrus |
| 16 | 0.452 | 16 | -30 | 38 | Cingulate Gyrus |
| 13 | 0.433 | 34 | -52 | 68 | Superior Parietal Lobule |
| 12 | 0.408 | 56 | 32 | 24 | Middle Frontal Gyrus |

Note: ρ=correlation coefficient

**Table S8. Correlation between obstetric risks and the predicted morphometric changes of the JD´s in limbic regions.**

| Region of Interest | hemisphere | Voxels | ρ | MAX X (mm) | MAX Y (mm) | MAX Z (mm) |
|---|---|---|---|---|---|---|
| amygdala | l | 137 | -0.629 | -26 | -8 | -24 |
| | l | 2 | -0.357 | -32 | 4 | -18 |
| | r | 170 | -0.73 | 30 | -12 | -16 |
| | r | 5 | -0.465 | 32 | 6 | -24 |
| | r | 3 | -0.402 | 24 | 6 | -26 |
| hippocampus | l | 69 | 0.433 | -28 | -42 | 8 |
| | l | 910 | -0.762 | -26 | -30 | -10 |
| | r | 37 | 0.199 | 22 | -40 | -8 |
| | r | 1 | 0.104 | 30 | -34 | -18 |
| | r | 671 | -0.813 | 30 | -14 | -18 |
| | r | 1 | -0.37 | 12 | -40 | 8 |
| medial frontal gyrus | | 1317 | 0.768 | 0 | 54 | 40 |
| anterior cingulate gyrus | | 205 | 0.313 | 4 | -18 | 42 |
| | | 14 | 0.25 | -12 | 0 | 22 |
| | | 2 | 0.148 | 12 | 38 | 40 |
| | | 2 | 0.199 | 4 | 22 | -10 |
| | | 1 | 0.174 | -2 | 42 | 18 |
| | | 1 | 0.104 | -2 | 18 | 32 |
| | | 1 | 0.104 | 4 | 4 | 40 |
| | | 1 | 0.104 | 8 | 12 | 40 |
| | | 1 | 0.11 | -2 | 12 | 42 |
| | | 1 | 0.104 | -2 | 0 | 46 |
| | | 1 | 0.129 | -6 | -8 | 0 |
| | | 782 | -0.781 | 2 | 34 | 46 |
| | | 52 | -0.570 | 10 | 0 | 34 |
| | | 5 | -0.376 | -10 | 4 | 8 |
| | | 1 | -0.380 | 14 | 44 | 8 |

Note: ρ=correlation coefficient, unilateral masks used for the amygdala and the hippocampus, bilateral masks used for the medial frontal gyrus and the anterior cingulate gyrus

**Table S9. Top 2% of the voxels of the correlation between prenatal maternal stress and the predicted morphometric changes of the JD´s**

| Voxels | ρ | MAX X (mm) | MAX Y (mm) | MAX Z (mm) | Region |
|---|---|---|---|---|---|
| *positive association* | | | | | |
| 3267 | 0.594 | -22 | 54 | -14 | Superior Frontal Gyrus. |
| 1309 | 0.726 | -10 | 24 | 50 | Superior Frontal Gyrus. |
| 1074 | 0.508 | -66 | -50 | 6 | Middle Temporal Gyrus. |
| 980 | 0.346 | 68 | -42 | -12 | Middle Temporal Gyrus. |
| 581 | 0.364 | -30 | 2 | 46 | Middle Frontal Gyrus |
| 579 | 0.283 | -48 | -80 | -8 | Middle Occipital Gyrus. |
| 491 | 0.513 | 30 | -38 | -14 | Parahippocampal Gyrus |
| 491 | 0.462 | 32 | -50 | 44 | Superior Parietal Lobule |
| 479 | 0.341 | -44 | 6 | -22 | Superior Temporal Gyrus. |
| 431 | 0.243 | -4 | 8 | 6 | Caudate |
| 269 | 0.346 | -26 | -46 | -18 | Culmen |
| 250 | 0.295 | -68 | -8 | 18 | Postcentral Gyrus |
| 218 | 0.49 | -38 | -48 | 64 | Superior Parietal Lobule |
| 207 | 0.358 | 54 | -18 | -32 | Fusiform Gyrus |
| 172 | 0.272 | 6 | -42 | 38 | Cingulate Gyrus |
| 154 | 0.306 | 32 | -88 | -18 | Declive |
| 135 | 0.289 | 50 | -2 | 52 | Precentral Gyrus |
| 98 | 0.427 | -46 | -46 | 8 | Middle Temporal Gyrus |
| 91 | 0.197 | 12 | -62 | 32 | Precuneus |
| 90 | 0.243 | -4 | -76 | -2 | Lingual Gyrus |
| 90 | 0.295 | 2 | -50 | -60 | Brain Stem |
| 86 | 0.352 | -18 | -72 | -58 | Cerebellum |
| 81 | 0.231 | 44 | 4 | -12 | Planum Polare |
| 78 | 0.208 | -16 | -24 | 14 | .Thalamus |
| 73 | 0.272 | -4 | 66 | 18 | Superior Frontal Gyrus |
| 69 | 0.231 | 32 | 18 | -14 | Insula |
| 68 | 0.289 | 40 | 0 | 34 | Precentral Gyrus |
| 59 | 0.335 | -22 | -66 | 64 | Superior Parietal Lobule |
| 56 | 0.306 | 66 | -2 | 30 | Precentral Gyrus |
| 53 | 0.185 | 10 | -76 | 10 | Cuneus |

| | | | | | |
|---|---|---|---|---|---|
| 52 | 0.162 | 54 | -76 | -8 | Middle Occipital Gyrus |
| 50 | 0.237 | -12 | -98 | 22 | Middle Occipital Gyrus |
| 36 | 0.272 | 40 | 24 | -38 | Temporal Pole |
| 36 | 0.168 | 18 | -32 | 68 | Postcentral Gyrus |
| 34 | 0.266 | 52 | -10 | 24 | Postcentral Gyrus |
| 33 | 0.179 | -50 | -52 | -44 | Cerebellum |
| 30 | 0.179 | 10 | -60 | -46 | Cerebellum |
| 29 | 0.139 | 24 | 8 | 62 | Middle Frontal Gyrus |
| 28 | 0.214 | -16 | -74 | 60 | Lateral Occipital Cortex |
| 28 | 0.145 | -22 | -40 | 70 | Postcentral Gyrus |
| 24 | 0.145 | 8 | -10 | 74 | Superior Frontal Gyrus |
| 20 | 0.139 | 42 | -32 | 64 | Postcentral Gyrus |
| 18 | 0.128 | -42 | -70 | 2 | Inferior Temporal Gyrus. |
| 18 | 0.122 | -24 | 48 | 22 | Superior Frontal Gyrus. |
| 18 | 0.174 | -28 | 2 | -46 | Superior Temporal Gyrus |
| 18 | 0.191 | -10 | -84 | 16 | Cuneus |
| 18 | 0.116 | 38 | -78 | -8 | Middle Occipital Gyrus |
| 17 | 0.179 | 8 | 8 | 30 | Cingulate Gyrus |
| 17 | 0.197 | 0 | -64 | -28 | Cerebellum |
| 16 | 0.139 | -12 | 44 | 34 | Medial Frontal Gyrus |
| 14 | 0.139 | 12 | -10 | 70 | Superior Frontal Gyrus. |
| 14 | 0.11 | -42 | -58 | 32 | Superior Temporal Gyrus |
| 11 | 0.122 | 6 | -42 | 68 | Paracentral Lobule |
| 10 | 0.151 | -54 | 28 | -12 | Inferior Frontal Gyrus |
| *negative association* | | | | | |
| 11952 | 0.742 | 70 | -20 | -20 | Inferior Temporal Gyrus |
| 1437 | 0.736 | -52 | -60 | 38 | Supramarginal Gyrus |
| 1333 | 0.69 | -10 | -22 | 40 | Cingulate Gyrus |
| 470 | 0.742 | -16 | -56 | 0 | Lingual Gyrus |
| 318 | 0.609 | 2 | -82 | 34 | Cuneus |
| 220 | 0.517 | -58 | 8 | 36 | Precentral Gyrus |
| 177 | 0.54 | -44 | 14 | 14 | Inferior Frontal Gyrus |
| 148 | 0.598 | -12 | 54 | 36 | Superior Frontal Gyrus |
| 146 | 0.54 | 64 | -28 | 42 | Inferior Parietal Lobule |
| 133 | 0.558 | -12 | 40 | 30 | Medial Frontal Gyrus |

| | | | | | |
|---|---|---|---|---|---|
| 101 | 0.575 | -40 | 46 | 28 | Superior Frontal Gyrus |
| 100 | 0.523 | 38 | -16 | 64 | Precentral Gyrus |
| 94 | 0.465 | 4 | 40 | -30 | Orbital Gyrus |
| 83 | 0.569 | 20 | -52 | 56 | Precuneus |
| 74 | 0.529 | -8 | 72 | 2 | Superior Frontal Gyrus |
| 66 | 0.477 | -38 | -30 | -16 | Parahippocampal Gyrus |
| 65 | 0.46 | -34 | -62 | -60 | Cerebellum |
| 59 | 0.465 | -8 | -44 | 20 | Corpus Callosum |
| 57 | 0.437 | 8 | -74 | -54 | Cerebellum |
| 56 | 0.437 | 40 | 18 | 56 | Middle Frontal Gyrus |
| 49 | 0.442 | 8 | -78 | -10 | Lingual Gyrus |
| 44 | 0.402 | -16 | 20 | -8 | Accumbens |
| 38 | 0.534 | 26 | -56 | 68 | Superior Parietal Lobule |
| 35 | 0.511 | 60 | 24 | 22 | Inferior Frontal Gyrus |
| 31 | 0.465 | -6 | 10 | 68 | Superior Frontal Gyrus |
| 28 | 0.396 | -26 | -86 | 36 | Cuneus |
| 27 | 0.632 | -32 | 56 | 16 | Middle Frontal Gyrus |
| 20 | 0.494 | 20 | -46 | 58 | Precuneus |
| 19 | 0.46 | 8 | 30 | 34 | Cingulate Gyrus |
| 18 | 0.425 | 4 | -8 | 68 | Medial Frontal Gyrus |
| 18 | 0.517 | 6 | -28 | 26 | Posterior Cingulate |
| 17 | 0.517 | -26 | -32 | 60 | Postcentral Gyrus |
| 16 | 0.442 | -37 | -18 | 40 | Precentral Gyrus |
| 12 | 0.396 | 10 | 8 | 10 | Caudate Body |
| 12 | 0.35 | 6 | -74 | 52 | Precuneus |

Note: ρ=correlation coefficient

**Table S10. Correlation between prenatal maternal stress and the predicted morphometric changes of the JD´s in limbic regions.**

| Region of Interest | hemisphere | Voxels | ρ | MAX X (mm) | MAX Y (mm) | MAX Z (mm) |
|---|---|---|---|---|---|---|
| amygdala | l | 55 | -0.575 | -24 | -6 | -28 |
| | r | 50 | -0.448 | 26 | -6 | -26 |
| | r | 32 | -0.529 | 20 | 6 | -24 |
| hippocampus | l | 1 | 0.105 | -28 | -40 | -6 |
| | l | 161 | -0.575 | -24 | -6 | -28 |
| | l | 12 | -0.373 | -36 | -28 | -16 |
| | l | 6 | -0.373 | -16 | -36 | 4 |
| | l | 2 | -0.344 | -34 | -32 | -4 |
| | l | 1 | -0.327 | -20 | -26 | -16 |
| | r | 151 | -0.352 | 28 | -34 | -10 |
| | r | 128 | -0.454 | 26 | -6 | -28 |
| | r | 2 | -0.339 | 20 | -34 | 2 |
| medial frontal gyrus | | 181 | 0.295 | -14 | 46 | -4 |
| | | 2 | 0.128 | 12 | 42 | -18 |
| | | 1 | 0.122 | 8 | 56 | -20 |
| | | 91 | -0.465 | 4 | 40 | -30 |
| | | 6 | -0.448 | 10 | 56 | -2 |
| anterior cingulate gyrus | | 331 | 0.295 | -4 | 28 | 16 |
| | | 108 | 0.358 | 0 | 18 | 40 |
| | | 16 | 0.179 | 8 | 8 | 30 |
| | | 6 | 0.243 | -10 | 28 | 18 |
| | | 5 | 0.145 | -10 | 42 | 6 |
| | | 4 | 0.128 | -12 | 22 | 28 |
| | | 2 | 0.11 | 4 | 40 | 12 |
| | | 2 | 0.11 | 2 | -12 | 42 |
| | | 1 | 0.156 | 0 | 42 | 12 |
| | | 1 | 0.128 | -10 | 24 | 22 |
| | | 1 | 0.116 | 12 | 8 | 34 |
| | | 1 | 0.243 | 6 | -14 | 36 |
| | | 1 | 0.174 | 6 | -14 | 46 |
| | | 1 | 0.105 | 0 | -4 | 50 |
| | | 1 | 0.11 | 0 | 0 | 50 |
| | | 344 | -0.644 | 8 | -2 | 44 |
| | | 30 | -0.442 | -8 | 40 | 24 |
| | | 7 | -0.46 | 8 | 30 | 34 |
| | | 2 | -0.385 | 4 | 28 | 32 |

Note: ρ=correlation coefficient, unilateral masks used for the amygdala and the hippocampus, bilateral masks used for the medial frontal gyrus and the anterior cingulate gyrus

**Table S11. Top 2% of the voxels of the correlation between prenatal maternal smoking and the predicted morphometric changes of the JD´s**

| Voxels | ρ | MAX X (mm) | MAX Y (mm) | MAX Z (mm) | Region |
|---|---|---|---|---|---|
| *positive association* | | | | | |
| 2690 | 0.586 | 36 | -28 | -7 | Hippocampus |
| 1762 | 0.462 | -16 | -70 | -50 | Cerebellum |
| 1555 | 0.5 | 30 | -24 | 52 | Precentral Gyrus |
| 1515 | 0.5 | 42 | 12 | -16 | Insula |
| 1142 | 0.327 | -12 | 24 | 42 | Cingulate Gyrus |
| 882 | 0.36 | -40 | 16 | -20 | Inferior Frontal Gyrus |
| 840 | 0.295 | 46 | -52 | -4 | Inferior Temporal Gyrus |
| 717 | 0.327 | 0 | -46 | 40 | Precuneus |
| 636 | 0.22 | 0 | -18 | 70 | Medial Frontal Gyrus |
| 610 | 0.386 | -14 | 42 | 2 | Anterior Cingulate |
| 567 | 0.22 | 18 | -62 | 28 | Precuneus |
| 525 | 0.279 | -40 | -26 | 40 | Postcentral Gyrus |
| 404 | 0.43 | -24 | 46 | -14 | Middle Frontal Gyrus |
| 354 | 0.306 | -30 | -88 | -18 | Declive |
| 287 | 0.225 | -6 | -76 | 34 | Cuneus |
| 286 | 0.241 | 8 | -84 | -36 | Cerebellum |
| 204 | 0.22 | 4 | -40 | -8 | Brain Stem |
| 185 | 0.236 | 36 | -32 | 68 | Postcentral Gyrus |
| 183 | 0.295 | 12 | -62 | 32 | Precuneus |
| 180 | 0.23 | -46 | -64 | 2 | Middle Temporal Gyrus |
| 178 | 0.22 | -62 | -58 | 4 | Middle Temporal Gyrus |
| 159 | 0.198 | -46 | 2 | 48 | Precentral Gyrus |
| 132 | 0.203 | 62 | -10 | 26 | Precentral Gyrus |
| 121 | 0.268 | -28 | -2 | 52 | Middle Frontal Gyrus |
| 119 | 0.252 | -34 | -76 | 10 | Middle Occipital Gyrus. |
| 109 | 0.209 | -42 | -64 | -38 | Cerebellum |
| 106 | 0.333 | -42 | -50 | 20 | Middle Frontal Gyrus |
| 94 | 0.273 | -14 | 34 | 38 | Medial Frontal Gyrus |
| 77 | 0.198 | -12 | -44 | 50 | Precuneus |
| 73 | 0.29 | -32 | -84 | -44 | Cerebellum |
| 72 | 0.284 | -58 | -50 | 24 | Superior Temporal Gyrus |
| 70 | 0.198 | -44 | -10 | -36 | Inferior Temporal Gyrus |
| 69 | 0.193 | -54 | -2 | -4 | Superior Temporal Gyrus |
| 67 | 0.236 | -22 | -40 | 72 | Postcentral Gyrus |

| | | | | | |
|---|---|---|---|---|---|
| 63 | 0.187 | 50 | -24 | -24 | Inferior Temporal Gyrus |
| 58 | 0.209 | -24 | 44 | 30 | Superior Frontal Gyrus |
| 57 | 0.193 | -52 | -62 | 14 | Middle Temporal Gyrus |
| 55 | 0.3 | -34 | 22 | 26 | Middle Frontal Gyrus |
| 53 | 0.182 | 48 | -70 | 28 | Middle Temporal Gyrus |
| 48 | 0.209 | -32 | 20 | 60 | Middle Frontal Gyrus |
| 47 | 0.257 | -12 | -58 | 8 | Precuneus |
| 46 | 0.214 | -46 | -14 | 52 | Postcentral Gyrus |
| 41 | 0.182 | -60 | -16 | 26 | Postcentral Gyrus |
| 40 | 0.327 | -16 | -30 | 2 | Thalamus |
| 37 | 0.203 | -56 | -24 | -26 | Inferior Temporal Gyrus |
| 37 | 0.182 | 8 | 32 | -28 | Rectal Gyrus |
| 35 | 0.193 | 16 | 66 | 10 | Superior Frontal Gyrus |
| 34 | 0.193 | 32 | 24 | -24 | Inferior Frontal Gyrus |
| 34 | 0.182 | -40 | 2 | -40 | Middle Temporal Gyrus |
| 33 | 0.203 | 14 | 48 | -18 | Medial Frontal Gyrus |
| 32 | 0.182 | -60 | 10 | -12 | Superior Temporal Gyrus |
| 32 | 0.182 | 64 | -30 | 22 | Superior Temporal Gyrus |
| 31 | 0.187 | -38 | 56 | 14 | Middle Frontal Gyrus |
| 30 | 0.22 | 42 | -66 | -4 | Lateral Occipital Cortex |
| 29 | 0.187 | -28 | 16 | 62 | Middle Frontal Gyrus |
| 27 | 0.176 | -26 | -44 | 48 | Superior Parietal Lobule |
| 27 | 0.187 | -20 | -80 | 24 | Cuneus |
| 26 | 0.225 | -22 | -10 | 74 | Precentral Gyrus |
| 26 | 0.187 | 46 | -52 | -16 | Fusiform Gyrus |
| 26 | 0.279 | 4 | 66 | 10 | Frontal Pole |
| 25 | 0.187 | 26 | 22 | -28 | Inferior Frontal Gyrus |
| 25 | 0.176 | -48 | -38 | 0 | Middle Temporal Gyrus |
| 24 | 0.176 | 12 | -58 | 60 | Precuneus |
| 24 | 0.203 | 44 | -62 | 8 | Lateral Occipital Cortex |
| 24 | 0.252 | -6 | 54 | 42 | Frontal Pole |
| 23 | 0.187 | 32 | -60 | -16 | Declive |
| 22 | 0.187 | 48 | -60 | -38 | Cerebellum |
| 21 | 0.214 | -28 | -20 | 72 | Precentral Gyrus |
| 21 | 0.193 | -34 | 46 | 26 | Middle Frontal Gyrus |

| | | | | | |
|---|---|---|---|---|---|
| 21 | 0.187 | -40 | -88 | -2 | Inferior Occipital Gyrus |
| 18 | 0.182 | -64 | -16 | 26 | Postcentral Gyrus |
| 18 | 0.209 | 6 | 44 | 8 | Anterior Cingulate |
| 18 | 0.187 | 50 | 0 | 44 | Precentral Gyrus |
| 18 | 0.225 | 6 | -42 | 22 | Posterior Cingulate |
| 18 | 0.214 | 44 | -84 | 14 | Middle Occipital Gyrus |
| 18 | 0.225 | 14 | 38 | 4 | Anterior Cingulate |
| 17 | 0.23 | 54 | -20 | -34 | Inferior Temporal Gyrus |
| 17 | 0.182 | -32 | 2 | -48 | Superior Temporal Gyrus |
| 17 | 0.193 | -6 | -76 | 28 | Cuneus |
| 17 | 0.176 | 40 | 16 | 4 | Insula |
| 17 | 0.187 | 42 | -74 | 38 | Angular Gyrus |
| 17 | 0.279 | -52 | 26 | -2 | Inferior Frontal Gyrus |
| 16 | 0.182 | -54 | 24 | 32 | Middle Frontal Gyrus |
| 16 | 0.176 | 42 | -54 | 16 | Superior Temporal Gyrus |
| 16 | 0.193 | -50 | -20 | 54 | Postcentral Gyrus |
| 15 | 0.182 | 44 | -14 | -44 | Inferior Temporal Gyrus, |
| 15 | 0.203 | -54 | -30 | 2 | Superior Temporal Gyrus |
| 15 | 0.171 | -54 | 10 | 6 | Precentral Gyrus |
| 15 | 0.193 | -4 | 32 | 38 | Medial Frontal Gyrus |
| 15 | 0.257 | 32 | -50 | 48 | Superior Parietal Lobule |
| 14 | 0.193 | -26 | 40 | -20 | Middle Frontal Gyrus |
| 13 | 0.23 | -48 | -48 | 10 | Middle Temporal Gyrus |
| 13 | 0.182 | 64 | -32 | -8 | Middle Temporal Gyrus |
| 13 | 0.203 | 54 | -6 | 14 | Central Opercular Cortex |
| 12 | 0.171 | 42 | -76 | -30 | Cerebellum |
| 12 | 0.187 | -10 | -32 | -20 | Brain Stem |
| 12 | 0.182 | 36 | 24 | 10 | Frontal Operculum Cortex |
| 11 | 0.187 | -42 | -64 | 40 | Angular Gyrus |
| 11 | 0.176 | -36 | -92 | -2 | Inferior Occipital Gyrus |
| 11 | 0.187 | 46 | -18 | -14 | Middle Temporal Gyrus |
| 11 | 0.241 | -52 | -16 | 6 | Superior Temporal Gyrus |
| 10 | 0.176 | -60 | -22 | -28 | Inferior Temporal Gyrus |

| | | | | | |
|---|---|---|---|---|---|
| 10 | 0.176 | 30 | 48 | 22 | Superior Frontal Gyrus |
| 10 | 0.22 | 24 | -84 | -40 | Cerebellum |
| 10 | 0.176 | 38 | 28 | 40 | Middle Frontal Gyrus |
| 10 | 0.284 | -20 | -24 | 58 | Postcentral Gyrus |
| *negative association* | | | | | |
| 5046 | 0.782 | -44 | -16 | 62 | Postcentral Gyrus |
| 4284 | 0.75 | -32 | -96 | 4 | Middle Occipital Gyrus |
| 1307 | 0.75 | -44 | -46 | -40 | Cerebellum |
| 601 | 0.75 | 42 | -8 | -38 | Middle Temporal Gyrus |
| 369 | 0.728 | 26 | 42 | 40 | Middle Frontal Gyrus |
| 361 | 0.594 | -24 | -50 | -6 | Parahippocampal Gyrus |
| 326 | 0.626 | -50 | -72 | -2 | Middle Occipital Gyrus |
| 299 | 0.701 | 18 | -70 | -10 | Cerebellum |
| 166 | 0.626 | 22 | -18 | -28 | Parahippocampal Gyrus |
| 137 | 0.551 | 54 | 18 | -30 | Superior Temporal Gyrus |
| 113 | 0.615 | 6 | -28 | 40 | Cingulate Gyrus |
| 101 | 0.61 | -30 | 48 | 34 | Middle Frontal Gyrus |
| 90 | 0.594 | -4 | -30 | 50 | Precuneus |
| 73 | 0.637 | 12 | -54 | 56 | Precuneus |
| 71 | 0.561 | -16 | -78 | -6 | Lingual Gyrus |
| 69 | 0.707 | -48 | 16 | 48 | Middle Frontal Gyrus |
| 65 | 0.551 | -8 | 10 | 72 | Superior Frontal Gyrus |
| 56 | 0.535 | 4 | -38 | 6 | Corpus Callosum |
| 52 | 0.524 | -14 | -14 | -34 | Cingulate Gyrus |
| 43 | 0.669 | -16 | 42 | 50 | Superior Frontal Gyrus |
| 30 | 0.658 | -22 | 16 | 66 | Superior Frontal Gyrus |
| 26 | 0.524 | -40 | -78 | -36 | Cerebellum |
| 25 | 0.491 | -4 | -6 | 40 | Cingulate Gyrus |
| 23 | 0.47 | -60 | 14 | 26 | Inferior Frontal Gyrus |
| 21 | 0.47 | -16 | -36 | -52 | Cerebellum |
| 17 | 0.486 | -52 | 30 | 24 | Middle Frontal Gyrus |
| 16 | 0.545 | 14 | 36 | 30 | Medial Frontal Gyrus |
| 11 | 0.529 | -38 | 62 | -8 | Middle Frontal Gyrus |
| 11 | 0.448 | -12 | -2 | 44 | Cingulate Gyrus |
| 10 | 0.475 | -4 | 12 | 34 | Cingulate Gyrus |
| 10 | 0.481 | 2 | -16 | 68 | Precentral Gyrus |

Note: ρ=correlation coefficient

**Table S12. Correlation between prenatal maternal smoking and the predicted morphometric changes of the JD´s in limbic regions.**

| Region of Interest | hemisphere | Voxels | ρ | MAX X (mm) | MAX Y (mm) | MAX Z (mm) |
|---|---|---|---|---|---|---|
| amygdala | l | 0 | | | | |
| | r | 0 | | | | |
| hippocampus | l | 183 | 0.392 | -32 | -30 | -8 |
| | l | 2 | 2 | 0.214 | -16 | -34 |
| | l | 1 | 1 | 0.171 | -26 | -40 |
| | l | 17 | -0.486 | -24 | -44 | 4 |
| | r | 230 | 0.564 | 32 | -28 | -4 |
| | r | 28 | -0.572 | 24 | -16 | -26 |
| | r | 12 | -0.465 | 28 | -40 | 6 |
| medial frontal gyrus | | 19 | 0.193 | 8 | 46 | -12 |
| | | 9 | 0.182 | 8 | 32 | -28 |
| | | 9 | 0.203 | -10 | 54 | 2 |
| | | 8 | 0.203 | 4 | 50 | -12 |
| | | 6 | 0.193 | 4 | 32 | -28 |
| | | 6 | 0.241 | -12 | 48 | 0 |
| | | 614 | -0.626 | 2 | 28 | -22 |
| | | 1 | -0.454 | 2 | 56 | -8 |
| anterior cingulate gyrus | | 193 | 0.386 | -14 | 42 | 4 |
| | | 62 | 0.209 | 0 | 0 | 50 |
| | | 47 | 0.252 | 6 | 20 | 40 |
| | | 18 | 0.209 | 6 | 44 | 8 |
| | | 11 | 0.198 | 14 | 40 | 4 |
| | | 9 | 0.268 | -4 | 48 | 14 |
| | | 5 | 0.203 | -10 | 22 | 24 |
| | | 4 | 0.182 | -8 | -2 | 50 |
| | | 3 | 0.176 | 10 | 38 | 4 |
| | | 2 | 0.171 | 8 | 42 | 20 |
| | | 1 | 0.193 | 8 | 40 | -2 |
| | | 1 | 0.176 | 8 | 42 | 4 |
| | | 1 | 0.176 | 8 | 28 | 18 |
| | | 25 | -0.491 | -4 | -6 | 40 |
| | | 10 | -0.475 | -4 | 12 | 34 |
| | | 9 | -0.502 | 2 | -20 | 40 |
| | | 2 | -0.411 | 10 | -8 | 40 |
| | | 1 | -0.411 | -10 | 6 | 40 |
| | | 1 | -0.443 | -4 | -20 | 42 |
| | | 1 | -0.427 | -12 | 0 | 42 |

Note: ρ=correlation coefficient, unilateral masks used for the amygdala and the hippocampus, bilateral masks used for the medial frontal gyrus and the anterior cingulate gyrus

**Table S13. Top 2% of the voxels of the correlation between maternal sensitivity and the predicted morphometric changes of the JD´s**

| Voxels | ρ | MAX X (mm) | MAX Y (mm) | MAX Z (mm) | Region |
|---|---|---|---|---|---|
| *positive association* | | | | | |
| 6660 | 0.49 | 16 | 38 | 16 | Anterior Cingulate |
| 1384 | 0.618 | -48 | 26 | 28 | Middle Frontal Gyrus |
| 1252 | 0.52 | -50 | -10 | 26 | Precentral Gyrus |
| 1029 | 0.526 | 54 | -34 | -18 | Inferior Temporal Gyrus, |
| 953 | 0.556 | -36 | -12 | 60 | Precentral Gyrus |
| 802 | 0.49 | -26 | -76 | 48 | Precuneus |
| 607 | 0.356 | 30 | 50 | 38 | Superior Frontal Gyrus |
| 589 | 0.336 | 2 | -80 | -6 | Lingual Gyrus |
| 496 | 0.474 | 42 | -82 | -32 | Cerebellum |
| 486 | 0.361 | -50 | 16 | -20 | Superior Temporal Gyrus |
| 444 | 0.51 | -42 | -82 | -30 | Cerebellum |
| 438 | 0.387 | 64 | -44 | 30 | Cingulate Gyrus |
| 414 | 0.315 | 38 | 4 | 18 | Insula |
| 370 | 0.341 | 30 | -74 | 46 | Precuneus |
| 293 | 0.32 | -8 | -62 | -54 | Cerebellum |
| 280 | 0.336 | 10 | -98 | 14 | Cuneus |
| 126 | 0.408 | 14 | -34 | 80 | Postcentral Gyrus |
| 95 | 0.274 | 14 | -50 | 28 | Posterior Cingulate |
| 86 | 0.556 | 30 | -40 | 40 | Superior Parietal Lobule |
| 86 | 0.372 | 44 | -48 | 10 | Middle Temporal Gyrus. |
| 62 | 0.295 | -54 | -32 | -20 | Inferior Temporal Gyrus |
| 60 | 0.382 | 46 | -32 | 36 | Inferior Parietal Lobule |
| 51 | 0.295 | 12 | -82 | 24 | Cuneus |
| 48 | 0.244 | -38 | -96 | 8 | Middle Occipital Gyrus |
| 45 | 0.274 | 34 | -16 | 48 | Precentral Gyrus. |
| 42 | 0.187 | -68 | -30 | -10 | Middle Temporal Gyrus |
| 42 | 0.187 | -50 | -68 | -8 | Middle Occipital Gyrus |
| 41 | 0.244 | 42 | -50 | 50 | Inferior Parietal Lobule |
| 34 | 0.438 | 4 | 12 | 70 | Superior Frontal Gyrus |

| | | | | | |
|---|---|---|---|---|---|
| 33 | 0.228 | -8 | 16 | 44 | Medial Frontal Gyrus |
| 31 | 0.29 | 64 | -6 | 32 | Precentral Gyrus |
| 30 | 0.203 | 14 | 60 | 38 | Frontal Pole |
| 27 | 0.177 | -44 | -86 | 26 | Middle Temporal Gyrus |
| 25 | 0.192 | 12 | -80 | -50 | Cerebellum |
| 23 | 0.315 | 46 | -4 | 28 | Precentral Gyrus |
| 18 | 0.187 | 10 | -64 | -36 | Cerebellum |
| 14 | 0.341 | 34 | 14 | 26 | Middle Frontal Gyrus |
| 10 | 0.177 | -42 | 32 | -8 | Inferior Frontal Gyrus |
| 10 | 0.156 | 18 | -58 | -28 | Cerebellum |
| *negative association* | | | | | |
| 8516 | 0.648 | -36 | -26 | -24 | Parahippocampal Gyrus |
| 1941 | 0.689 | -68 | -22 | 6 | Superior Temporal Gyrus |
| 1175 | 0.582 | 10 | -14 | 56 | Medial Frontal Gyrus |
| 1050 | 0.582 | 34 | -64 | -56 | Cerebellum |
| 721 | 0.535 | 52 | -72 | 20 | Middle Temporal Gyrus |
| 701 | 0.494 | 0 | -66 | 56 | Precuneus |
| 501 | 0.525 | -42 | 20 | -24 | Temporal Pole |
| 307 | 0.469 | 42 | 12 | 52 | Middle Frontal Gyrus |
| 305 | 0.551 | -6 | 8 | 36 | Cingulate Gyrus |
| 266 | 0.479 | -60 | -42 | 30 | Inferior Parietal Lobule |
| 210 | 0.407 | 30 | -100 | 6 | Middle Occipital Gyrus |
| 193 | 0.443 | 4 | 54 | -2 | Cerebellum |
| 183 | 0.484 | -2 | 40 | 36 | Medial Frontal Gyrus |
| 146 | 0.397 | -34 | -72 | 20 | Middle Occipital Gyrus |
| 132 | 0.351 | -8 | 10 | 60 | Medial Frontal Gyrus |
| 109 | 0.356 | 6 | -96 | -10 | Lingual Gyrus |
| 92 | 0.474 | 38 | 62 | 8 | Superior Frontal Gyrus |
| 88 | 0.515 | -32 | -48 | 70 | Superior Parietal Lobule |
| 75 | 0.407 | -16 | 20 | -20 | Frontal Orbital Cortex |
| 52 | 0.371 | -26 | 64 | -4 | Superior Frontal Gyrus |

| | | | | | |
|---|---|---|---|---|---|
| 35 | 0.31 | -8 | 34 | 50 | Superior Frontal Gyrus |
| 32 | 0.366 | 28 | -8 | -18 | Amygdala |
| 28 | 0.418 | 34 | 6 | 44 | Middle Frontal Gyrus |
| 27 | 0.31 | -44 | -84 | 12 | Middle Occipital Gyrus |
| 26 | 0.402 | -26 | -32 | 60 | Postcentral Gyrus |
| 25 | 0.361 | 62 | -52 | 38 | Supramarginal Gyrus |
| 24 | 0.259 | -6 | -60 | -42 | Cerebellum |
| 23 | 0.325 | 8 | 30 | 58 | Superior Frontal Gyrus |
| 21 | 0.295 | -36 | 34 | -16 | Inferior Frontal Gyrus |
| 20 | 0.284 | 26 | -62 | 66 | lateral Occipital Cortex |
| 20 | 0.387 | -8 | -18 | 78 | Precentral Gyrus |
| 19 | 0.269 | 44 | -16 | 60 | Precentral Gyrus |
| 18 | 0.284 | -22 | 24 | 62 | Superior Frontal Gyrus |
| 15 | 0.31 | 10 | 66 | 8 | Medial Frontal Gyrus |
| 13 | 0.371 | -40 | 12 | 60 | Middle Frontal Gyrus |
| 12 | 0.346 | -24 | -48 | 46 | Parietal Lobe |

Note: ρ=correlation coefficient

**Table S14. Correlation between maternal sensitivity and the predicted morphometric changes of the JD´s in limbic regions.**

| Region of Interest | hemisphere | Voxels | ρ | MAX X (mm) | MAX Y (mm) | MAX Z (mm) |
|---|---|---|---|---|---|---|
| amygdala | l | 79 | 0.305 | -22 | 0 | -30 |
| | l | 14 | -0.305 | -30 | -12 | -18 |
| | l | 3 | -0.223 | -12 | -2 | -18 |
| | l | 2 | -0.238 | -16 | 0 | -16 |
| | r | 153 | 0.341 | 28 | -2 | -28 |
| | r | 22 | -0.366 | 28 | -8 | -18 |
| hippocampus | l | 122 | 0.29 | -34 | -26 | -8 |
| | l | 40 | 0.264 | -22 | -4 | -28 |
| | l | 70 | -0.412 | -16 | -34 | -8 |
| | l | 38 | -0.305 | -34 | -22 | -22 |
| | r | 285 | 0.341 | 28 | -2 | -28 |
| | r | 1 | 96 | 0.197 | 28 | -38 |
| | r | 46 | -0.402 | 20 | -32 | -4 |
| | r | 25 | -0.366 | 28 | -8 | -18 |
| | r | 5 | -0.259 | 30 | -32 | -14 |
| | r | 3 | -0.223 | 32 | -28 | -6 |
| | r | 3 | -0.254 | 8 | -40 | 6 |
| medial frontal gyrus | | 267 | 0.315 | -8 | 52 | -14 |
| | | 97 | 0.213 | 12 | 36 | -18 |
| | | 1 | 0.151 | -6 | 58 | -2 |
| | | 65 | -0.443 | 4 | 54 | -2 |
| | | 3 | -0.233 | 0 | 44 | -28 |
| | | 2 | -0.248 | 2 | 36 | -30 |
| | | 2 | -0.238 | -2 | 28 | -28 |
| | | 1 | -0.218 | 0 | 28 | -24 |
| anterior cingulate gyrus | | 1339 | 0.469 | 14 | 36 | 20 |
| | | 9 | 0.187 | -4 | 14 | 44 |
| | | 5 | 0.197 | -10 | 24 | 22 |
| | | 2 | 0.192 | 4 | 14 | 40 |
| | | 298 | -0.551 | -6 | 8 | 36 |
| | | 96 | -0.412 | -2 | 36 | 30 |
| | | 33 | -0.407 | 8 | -10 | 50 |
| | | 6 | -0.3 | 2 | -22 | 30 |
| | | 2 | -0.238 | -4 | -20 | 44 |
| | | 2 | -0.254 | 2 | -18 | 46 |

Note: ρ=correlation coefficient, unilateral masks used for the amygdala and the hippocampus, bilateral masks used for the medial frontal gyrus and the anterior cingulate gyrus

**Table S15. Top 2% of the voxels of the correlation between psychosocial family risks and the predicted morphometric changes of the JD´s**

| **Voxels** | **ρ** | **MAX X (mm)** | **MAX Y (mm)** | **MAX Z (mm)** | **Region** |
|---|---|---|---|---|---|
| *positive association* | | | | | |
| 7746 | 0.597 | 46 | 50 | 6 | Middle Frontal Gyrus |
| 7528 | 0.575 | -18 | -68 | 34 | Precuneus |
| 1319 | 0.432 | -68 | -46 | -8 | Middle Temporal Gyrus |
| 533 | 0.514 | -32 | 40 | 44 | Middle Frontal Gyrus |
| 363 | 0.602 | -34 | 0 | 58 | Middle Frontal Gyrus |
| 276 | 0.333 | 14 | -84 | 18 | Cuneus |
| 261 | 0.415 | 64 | -46 | 28 | Supramarginal Gyrus |
| 143 | 0.206 | 22 | 2 | -42 | Fusiform Gyrus |
| 118 | 0.465 | 26 | -22 | 56 | Postcentral Gyrus |
| 103 | 0.536 | -34 | -50 | 66 | Superior Parietal Lobule |
| 77 | 0.267 | 32 | 34 | 50 | Superior Frontal Gyrus |
| 43 | 0.206 | 2 | -28 | -12 | Brainstem |
| 42 | 0.233 | 16 | -40 | -44 | Cerebellum |
| 39 | 0.349 | -44 | -48 | 20 | Superior Temporal Gyrus |
| 34 | 0.377 | -28 | 28 | 30 | Middle Frontal Gyrus |
| 33 | 0.189 | 28 | -44 | 40 | Superior Parietal Lobule |
| 28 | 0.184 | -64 | -32 | 0 | Middle Temporal Gyrus |
| 27 | 0.173 | 26 | -60 | -36 | Cerebellum |
| 24 | 0.211 | 32 | -96 | -14 | Fusiform Gyrus |
| 24 | 0.228 | -38 | -34 | 68 | Postcentral Gyrus |
| 20 | 0.228 | 34 | -50 | 66 | Superior Parietal Lobule |
| 19 | 0.256 | -22 | -22 | 56 | Postcentral Gyrus |
| 16 | 0.311 | 46 | -50 | -4 | Inferior Temporal Gyrus |
| 16 | 0.305 | 62 | -34 | -20 | Inferior Temporal Gyrus |
| 15 | 0.338 | 48 | -40 | 28 | Inferior Parietal Lobule |
| 13 | 0.195 | 16 | -38 | -32 | Pons |
| 12 | 0.162 | 2 | 66 | 14 | Frontal Pole |

| | | | | | |
|---|---|---|---|---|---|
| 12 | 0.189 | 2 | 40 | 52 | Superior Frontal Gyrus |
| 10 | 0.167 | 2 | -86 | 38 | Precuneus |
| 10 | 0.189 | 28 | -68 | -24 | Cerebellum |
| *negative association* | | | | | |
| 8566 | 0.801 | -2 | -48 | -42 | Brain Stem |
| 2016 | 0.741 | 54 | -30 | 12 | Superior Temporal Gyrus |
| 1167 | 0.603 | -40 | -20 | 58 | Postcentral Gyrus |
| 900 | 0.774 | -4 | 62 | 0 | Medial Frontal Gyrus |
| 744 | 0.724 | -50 | -68 | 26 | Middle Temporal Gyrus |
| 632 | 0.641 | -12 | -46 | 48 | Precuneus |
| 504 | 0.63 | -20 | -60 | 4 | Lingual Gyrus |
| 489 | 0.746 | -36 | 12 | -38 | Superior Temporal Gyrus |
| 359 | 0.526 | 50 | -34 | -27 | Inferior Temporal Gyrus |
| 338 | 0.763 | -4 | 10 | 66 | Superior Frontal Gyrus |
| 161 | 0.57 | 20 | 50 | 44 | Superior Frontal Gyrus |
| 141 | 0.482 | -30 | -84 | -36 | Cerebellum |
| 137 | 0.531 | -10 | -64 | 68 | Lateral Occipital Cortex |
| 116 | 0.63 | 42 | -14 | -38 | Inferior Temporal Gyrus |
| 108 | 0.614 | 10 | -52 | 56 | Precuneus |
| 100 | 0.471 | 44 | 30 | -20 | Inferior Frontal Gyrus |
| 98 | 0.548 | -42 | 20 | 50 | Middle Frontal Gyrus |
| 96 | 0.438 | 56 | 16 | -26 | Superior Temporal Gyrus |
| 76 | 0.553 | -44 | 8 | 2 | Insula |
| 52 | 0.526 | 6 | -52 | 12 | Posterior Cingulate |
| 41 | 0.46 | 30 | 16 | -36 | Superior Temporal Gyrus |
| 35 | 0.438 | 40 | 42 | 30 | Superior Frontal Gyrus |
| 33 | 0.394 | 48 | 20 | 36 | Precentral Gyrus |
| 30 | 0.41 | 40 | -92 | 6 | Middle Occipital Gyrus |
| 29 | 0.421 | 2 | -18 | 66 | Precentral Gyrus |
| 28 | 0.427 | -18 | 20 | -24 | Inferior Frontal Gyrus |
| 24 | 0.399 | 8 | -70 | -28 | Cerebellum |
| 20 | 0.449 | 50 | -46 | 46 | Inferior Parietal Lobule |

| | | | | | |
|---|---|---|---|---|---|
| 17 | 0.46 | -24 | 40 | 22 | Frontal Pole |
| 16 | 0.427 | 30 | -72 | -46 | Cerebellum |
| 16 | 0.394 | 24 | -50 | -18 | Cerebellum |
| 16 | 0.311 | -58 | -64 | -8 | Inferior Temporal Gyrus |
| 13 | 0.542 | -24 | -48 | 46 | Superior Parietal Lobule |
| 12 | 0.377 | -26 | -34 | 60 | Postcentral Gyrus |
| 11 | 0.311 | 62 | -42 | 50 | Inferior Parietal Lobule |
| 10 | 0.432 | -32 | 64 | 0 | Middle Frontal Gyrus |
| 10 | 0.322 | -16 | 52 | 30 | Superior Frontal Gyrus |
| 10 | 0.399 | -28 | -10 | 72 | Precentral Gyrus |

Note: $\rho$=correlation coefficient

**Table S16. Correlation between psychosocial family risks and the predicted morphometric changes of the JD´s in limbic regions.**

| Region of Interest | hemisphere | Voxels | ρ | MAX X (mm) | MAX Y (mm) | MAX Z (mm) |
|---|---|---|---|---|---|---|
| amygdala | l | 261 | 0.305 | -32 | -2 | -26 |
| | r | 90 | 0.25 | 18 | -10 | -10 |
| | r | 3 | 0.14 | 34 | 2 | -22 |
| hippocampus | l | 404 | 0.399 | -32 | -28 | -6 |
| | l | 4 | 0.245 | -32 | -4 | -26 |
| | l | 1 | 0.156 | -26 | -2 | -28 |
| | l | 36 | -0.531 | -26 | -44 | 2 |
| | l | 1 | -0.295 | -22 | -14 | -28 |
| | r | 236 | 0.404 | 26 | -32 | -12 |
| | r | 12 | 0.344 | 14 | -40 | 8 |
| | r | 4 | 0.184 | 18 | -14 | -12 |
| | r | 1 | 96 | 0.197 | 28 | -38 |
| | r | 5 | -0.361 | 24 | -16 | -26 |
| | r | 1 | -0.289 | 26 | -42 | 4 |
| medial frontal gyrus | | 30 | 0.305 | 12 | 42 | -18 |
| | | 3 | 0.167 | -12 | 48 | 0 |
| | | 1 | 0.145 | -12 | 40 | -4 |
| | | 318 | -0.63 | -4 | 58 | -2 |
| | | 1 | -0.306 | 8 | 46 | -10 |
| anterior cingulate gyrus | | 1523 | 0.542 | -12 | 42 | 2 |
| | | 3 | 0.217 | 16 | 44 | 4 |
| | | 1 | 0.145 | 14 | 40 | 4 |
| | | 1 | 0.173 | 2 | 32 | 26 |
| | | 143 | -0.471 | -4 | -20 | 42 |
| | | 7 | -0.333 | 0 | -16 | 42 |
| | | 1 | -0.284 | 2 | -4 | 40 |

Note: ρ=correlation coefficient, unilateral masks used for the amygdala and the hippocampus, bilateral masks used for the medial frontal gyrus and the anterior cingulate gyrus

**Table S17. Top 2% of the voxels of the correlation between trauma and the predicted morphometric changes of the JD´s**

| Voxels | ρ | MAX X (mm) | MAX Y (mm) | MAX Z (mm) | Region |
|---|---|---|---|---|---|
| *positive association* | | | | | |
| 4462 | 0.575 | -50 | -20 | -16 | Middle Temporal Gyrus |
| 2699 | 0.484 | -14 | 46 | 2 | Anterior Cingulate |
| 1792 | 0.489 | 46 | 26 | 32 | Precentral Gyrus |
| 1136 | 0.479 | 26 | -28 | -16 | Parahippocampal Gyrus |
| 318 | 0.371 | -26 | 16 | 42 | Middle Frontal Gyrus |
| 252 | 0.258 | 62 | -6 | 38 | Precentral Gyrus |
| 169 | 0.452 | 28 | -48 | 50 | Precuneus |
| 168 | 0.339 | -44 | 52 | 18 | Middle Frontal Gyrus |
| 132 | 0.312 | 60 | -42 | -18 | Inferior Temporal Gyrus |
| 120 | 0.29 | -60 | -64 | 0 | Middle Temporal Gyrus |
| 94 | 0.242 | -30 | -66 | 52 | Superior Parietal Lobule |
| 91 | 0.312 | 28 | -16 | 56 | Precentral Gyrus |
| 88 | 0.172 | -40 | -56 | 54 | Superior Parietal Lobule |
| 85 | 0.29 | 6 | -44 | 50 | Precuneus |
| 73 | 0.231 | -36 | 36 | 34 | Middle Frontal Gyrus |
| 72 | 0.236 | 26 | 36 | 50 | Superior Frontal Gyrus |
| 57 | 0.129 | 36 | -34 | 58 | Inferior Parietal Lobule |
| 57 | 0.161 | -16 | -84 | -18 | Declive |
| 56 | 0.188 | 44 | 10 | -4 | Insula |
| 53 | 0.156 | 0 | -2 | 60 | Medial Frontal Gyrus |
| 53 | 0.134 | -32 | -40 | 66 | Postcentral Gyrus |
| 52 | 0.226 | -32 | -24 | 46 | Postcentral Gyrus |
| 52 | 0.193 | 58 | -60 | 32 | Superior Temporal Gyrus |
| 43 | 0.156 | 22 | 58 | 0 | Superior Frontal Gyrus. |
| 40 | 0.123 | 52 | -44 | 14 | Superior Temporal Gyrus |
| 37 | 0.134 | -32 | -72 | -36 | Cerebellum |
| 36 | 0.199 | 12 | -64 | 28 | Precuneus |
| 32 | 0.161 | -6 | -62 | -2 | Cerebellum |

| | | | | | |
|---|---|---|---|---|---|
| 31 | 0.134 | -20 | -66 | 50 | Precuneus |
| 31 | 0.177 | 20 | 14 | 18 | Caudate |
| 28 | 0.226 | -40 | -30 | 34 | Inferior Parietal Lobule |
| 27 | 0.156 | 32 | 8 | -48 | Temporal Pole |
| 26 | 0.129 | -4 | -42 | 64 | Postcentral Gyrus |
| 26 | 0.193 | -52 | -34 | 32 | Inferior Parietal Lobule |
| 26 | 0.145 | -10 | -64 | 46 | Precuneus |
| 25 | 0.166 | -4 | -12 | 64 | Medial Frontal Gyrus |
| 25 | 0.177 | 32 | -54 | 62 | Superior Parietal Lobule |
| 24 | 0.231 | -18 | 12 | 20 | Caudate |
| 23 | 0.118 | 46 | -60 | 42 | Inferior Parietal Lobule |
| 23 | 0.113 | 60 | -34 | 24 | Inferior Parietal Lobule |
| 22 | 0.129 | -22 | -88 | -20 | Cerebellum |
| 22 | 0.231 | 18 | -18 | 70 | Precentral Gyrus |
| 22 | 0.183 | 42 | -8 | 36 | Precentral Gyrus |
| 21 | 0.172 | 32 | 14 | -20 | Inferior Frontal Gyrus |
| 21 | 0.22 | 28 | -30 | 72 | Postcentral Gyrus |
| 20 | 0.14 | 44 | -82 | 28 | Middle Temporal Gyrus |
| 20 | 0.145 | 52 | -36 | -6 | Middle Temporal Gyrus |
| 19 | 0.123 | 36 | 2 | 64 | Middle Frontal Gyrus |
| 19 | 0.129 | -10 | -44 | 66 | Postcentral Gyrus |
| 18 | 0.172 | 62 | -22 | 26 | Inferior Parietal Lobule |
| 18 | 0.118 | -30 | -68 | -18 | Cerebellum |
| 17 | 0.156 | 0 | -46 | 44 | Precuneus |
| 17 | 0.193 | 50 | -50 | -4 | Middle Temporal Gyrus |
| 16 | 0.15 | 46 | 16 | 40 | Middle Frontal Gyrus |
| 15 | 0.156 | -12 | -96 | -14 | Occipital Pole |
| 15 | 0.231 | 20 | 26 | 40 | Superior Frontal Gyrus |
| 15 | 0.118 | -14 | -40 | 70 | Postcentral Gyrus |
| 15 | 0.134 | -56 | 4 | 32 | Precentral Gyrus |
| 15 | 0.231 | -58 | -20 | 48 | Postcentral Gyrus |
| 15 | 0.15 | -4 | -86 | -22 | Cerebellum |
| 15 | 0.107 | -56 | 6 | -6 | Superior Temporal Gyrus |
| 15 | 0.123 | -10 | -10 | 70 | Superior Frontal Gyrus |

| | | | | | |
|---|---|---|---|---|---|
| 14 | 0.134 | -14 | 50 | 42 | Superior Frontal Gyrus |
| 13 | 0.113 | 56 | -48 | 6 | Middle Temporal Gyrus |
| 13 | 0.183 | 44 | -8 | -50 | Inferior Temporal Gyrus |
| 12 | 0.107 | 42 | -74 | -8 | Middle Occipital Gyrus |
| 12 | 0.215 | 50 | -44 | 0 | Middle Temporal Gyrus |
| 12 | 0.183 | 2 | 40 | 52 | Superior Frontal Gyrus |
| 12 | 0.118 | 38 | 24 | 2 | Insula |
| 11 | 0.134 | -68 | -50 | -8 | Middle Temporal Gyrus |
| 11 | 0.145 | -62 | -2 | 26 | Precentral Gyrus |
| 11 | 0.113 | 22 | -72 | 52 | Precuneus |
| 11 | 0.107 | 26 | 4 | 62 | Middle Frontal Gyrus |
| 11 | 0.193 | 42 | 2 | 56 | Middle Frontal Gyrus |
| 10 | 0.15 | -48 | -46 | 52 | Inferior Parietal Lobule |
| 10 | 0.123 | 48 | -26 | 58 | Postcentral Gyrus |
| 10 | 0.145 | -8 | -88 | 38 | Cuneus |
| 10 | 0.118 | -20 | 8 | -46 | Temporal Pole |
| 10 | 0.14 | 44 | -30 | 62 | Postcentral Gyrus |
| 10 | 0.102 | 34 | -74 | -12 | Fusiform Gyrus |
| 10 | 0.177 | -14 | -84 | 40 | Cuneus |
| 10 | 0.113 | 42 | -62 | -10 | Lateral Occipital Cortex |
| *negative association* | | | | | |
| 8376 | 0.797 | 8 | -50 | -46 | Brainstem |
| 1360 | 0.711 | 60 | -42 | 10 | Superior Temporal Gyrus |
| 1173 | 0.759 | -64 | -14 | 8 | Superior Temporal Gyrus |
| 1132 | 0.668 | -18 | -102 | 6 | Cuneus |
| 521 | 0.657 | 32 | 16 | -38 | Superior Temporal Gyrus |
| 507 | 0.716 | -12 | 62 | 24 | Superior Frontal Gyrus |
| 409 | 0.555 | 12 | 52 | -26 | Medial Frontal Gyrus |
| 332 | 0.732 | 38 | 44 | 30 | Superior Frontal Gyrus |
| 291 | 0.625 | -16 | 40 | 50 | Superior Frontal Gyrus |
| 290 | 0.49 | -64 | -56 | 14 | Superior Temporal Gyrus |

| | | | | | |
|---|---|---|---|---|---|
| 237 | 0.662 | -2 | -30 | 54 | Precentral Gyrus |
| 192 | 0.678 | 14 | -52 | 56 | Precuneus |
| 158 | 0.565 | -46 | -24 | 60 | Postcentral Gyrus |
| 149 | 0.522 | 50 | -42 | 52 | Inferior Parietal Lobule |
| 144 | 0.565 | 48 | -18 | 62 | Postcentral Gyrus |
| 129 | 0.533 | 28 | -84 | 42 | Cuneus |
| 126 | 0.506 | -40 | 10 | -4 | Insula |
| 113 | 0.452 | 40 | -74 | 4 | Lateral Occipital Cortex |
| 97 | 0.549 | -46 | -60 | 54 | Lateral Occipital Cortex |
| 63 | 0.485 | 8 | -66 | -6 | Lingual Gyrus |
| 52 | 0.495 | 42 | -10 | -34 | Inferior Temporal Gyrus |
| 51 | 0.463 | -30 | -74 | 46 | Precuneus |
| 47 | 0.49 | 0 | -68 | 52 | Precuneus |
| 45 | 0.555 | 4 | 66 | 24 | Frontal Pole |
| 42 | 0.442 | -56 | 12 | -24 | Superior Temporal Gyrus |
| 35 | 0.463 | 62 | -40 | 50 | nferior Parietal Lobule |
| 30 | 0.458 | -50 | -72 | -2 | Middle Occipital Gyrus |
| 29 | 0.452 | -12 | 20 | -28 | Frontal Orbital Cortex |
| 29 | 0.517 | 0 | -14 | 66 | Medial Frontal Gyrus |
| 24 | 0.517 | -12 | -48 | 48 | Precuneus |
| 19 | 0.49 | 18 | -30 | 68 | Precentral Gyrus |
| 17 | 0.452 | -34 | 40 | -8 | Frontal Pole |
| 14 | 0.538 | -16 | -66 | 66 | Lateral Occipital Cortex |
| 11 | 0.522 | -30 | -84 | -38 | Cerebellum |
| 10 | 0.425 | -46 | 18 | 48 | Middle Frontal Gyrus |

Note: ρ=correlation coefficient

**Table S18. Correlation between trauma and the predicted morphometric changes of the JD´s in limbic regions.**

| Region of Interest | hemisphere | Voxels | ρ | MAX X (mm) | MAX Y (mm) | MAX Z (mm) |
|---|---|---|---|---|---|---|
| amygdala | l | 55 | 0.161 | -30 | 2 | -20 |
| | r | 10 | 0.166 | 24 | 6 | -24 |
| | r | 2 | 0.129 | 28 | 6 | -24 |
| | r | 1 | 0.102 | 26 | 2 | -12 |
| hippocampus | l | 428 | 0.446 | -26 | -38 | -8 |
| | l | 1 | 0.102 | -38 | -24 | -12 |
| | l | 10 | -0.452 | -24 | -44 | 4 |
| | l | 2 | -0.377 | -24 | -6 | -32 |
| | r | 475 | 0.473 | 28 | -36 | -8 |
| medial frontal gyrus | | 21 | 0.29 | -12 | 48 | 0 |
| | | 3 | 0.145 | -10 | 56 | -6 |
| | | 2 | 0.113 | 12 | 50 | 0 |
| | | 1 | 0.102 | -14 | 30 | -16 |
| | | 292 | -0.544 | 4 | 42 | -30 |
| | | 4 | -0.377 | 6 | 54 | -8 |
| | | 2 | -0.361 | -2 | 50 | -10 |
| | | 2 | -0.399 | -4 | 56 | -10 |
| anterior cingulate gyrus | | 1868 | 0.425 | -12 | 48 | 2 |
| | | 5 | 0.15 | 6 | -10 | 50 |
| | | 3 | 0.134 | 2 | -4 | 46 |
| | | 2 | 0.107 | -4 | -10 | 50 |
| | | 1 | 0.113 | -2 | 38 | 10 |
| | | 1 | 0.113 | -4 | 30 | 16 |
| | | 1 | 0.102 | 0 | 30 | 18 |
| | | 1 | 0.102 | -4 | 0 | 44 |
| | | 1 | 0.118 | 6 | -8 | 46 |

Note: ρ=correlation coefficient, unilateral masks used for the amygdala and the hippocampus, bilateral masks used for the medial frontal gyrus and the anterior cingulate gyrus

**Table S19. Top 2% of the voxels of the correlation between stressful life events and the predicted morphometric changes of the JD´s**

| Voxels | ρ | MAX X (mm) | MAX Y (mm) | MAX Z (mm) | Region |
|---|---|---|---|---|---|
| *positive association* | | | | | |
| 12469 | 0.647 | -16 | -58 | 20 | Precuneus |
| 2441 | 0.653 | 2 | 20 | 40 | Cingulate Gyrus |
| 656 | 0.452 | -62 | -48 | 18 | Superior Temporal Gyrus |
| 371 | 0.452 | 40 | 14 | -46 | Temporal Pole |
| 364 | 0.47 | 14 | -34 | 58 | Postcentral Gyrus |
| 213 | 0.458 | -42 | 28 | 34 | Middle Frontal Gyrus |
| 212 | 0.33 | -26 | 4 | -50 | Superior Temporal Gyrus |
| 186 | 0.482 | 58 | -20 | -34 | Inferior Temporal Gyrus |
| 121 | 0.361 | 46 | -52 | 0 | Middle Temporal Gyrus |
| 119 | 0.385 | 18 | -60 | 34 | Precuneus |
| 104 | 0.391 | 32 | -50 | 46 | Superior Parietal Lobule |
| 93 | 0.275 | 68 | -42 | 18 | Superior Temporal Gyrus |
| 76 | 0.409 | -44 | -48 | 12 | Superior Temporal Gyrus |
| 60 | 0.294 | 60 | -36 | -22 | Fusiform Gyrus |
| 57 | 0.367 | -22 | -14 | 54 | Precentral Gyrus |
| 56 | 0.294 | 0 | -28 | 32 | Cingulate Gyrus |
| 55 | 0.342 | -6 | 30 | -28 | Rectal Gyrus |
| 51 | 0.275 | 12 | -84 | 22 | Cuneus |
| 42 | 0.251 | 18 | -66 | -46 | Cerebellum |
| 27 | 0.257 | -30 | 24 | 40 | Middle Frontal Gyrus |
| 24 | 0.269 | 46 | -14 | 32 | Postcentral Gyrus |
| 21 | 0.318 | -40 | -24 | 48 | Postcentral Gyrus |
| 21 | 0.354 | -16 | -70 | -48 | Cerebellum |
| 19 | 0.336 | -40 | 56 | 18 | Superior Frontal Gyrus |
| 19 | 0.281 | -18 | -84 | -4 | Lingual Gyrus |
| 16 | 0.251 | -14 | -44 | -42 | Cerebellum |
| 13 | 0.324 | -20 | -28 | 56 | Precentral Gyrus |
| 10 | 0.227 | -54 | -52 | -46 | Cerebellum |
| 10 | 0.227 | -34 | -50 | 66 | Superior Parietal Lobule |
| *negative association* | | | | | |
| 9710 | 0.9 | -44 | -60 | -42 | Cerebellum |
| 1406 | 0.741 | 50 | -72 | 40 | Precuneus |
| 1044 | 0.62 | 4 | 54 | -8 | Anterior Cingulate Cortex |
| 931 | 0.784 | 54 | -20 | 16 | Insula |
| 611 | 0.76 | 38 | -44 | -50 | Cerebellum |
| 519 | 0.857 | 20 | 52 | 40 | Superior Frontal Gyrus |

| | | | | | |
|---|---|---|---|---|---|
| 482 | 0.711 | -4 | -34 | 50 | Precuneus |
| 463 | 0.76 | 10 | -52 | 56 | Precuneus |
| 379 | 0.802 | 38 | -16 | 66 | Precentral Gyrus |
| 291 | 0.626 | 48 | -32 | -28 | Inferior Temporal Gyrus |
| 224 | 0.54 | -66 | -18 | -14 | Middle Temporal Gyrus |
| 118 | 0.522 | -32 | 14 | -38 | Superior Temporal Gyrus |
| 113 | 0.589 | 42 | -14 | -38 | Inferior Temporal Gyrus |
| 97 | 0.516 | -16 | 42 | 50 | Superior Frontal Gyrus |
| 91 | 0.626 | 2 | -6 | 66 | Supplementary Motor Cortex |
| 86 | 0.38 | 22 | -14 | -34 | Parahippocampal Gyrus |
| 85 | 0.41 | -16 | -40 | -54 | Cerebellum |
| 83 | 0.51 | -12 | -22 | 17 | Thalamus |
| 79 | 0.565 | -34 | 46 | 32 | Middle Frontal Gyrus |
| 57 | 0.614 | -44 | 10 | 6 | Frontal Operculum Cortex |
| 57 | 0.516 | 36 | 24 | -4 | Insula |
| 55 | 0.516 | 28 | 16 | -36 | Superior Temporal Gyrus |
| 51 | 0.467 | -4 | 10 | 62 | Medial Frontal Gyrus |
| 48 | 0.455 | -10 | 0 | 42 | Cingulate Gyrus |
| 47 | 0.42 | 39 | 14 | 14 | Frontal Operculum Cortex |
| 35 | 0.474 | -44 | 40 | -14 | Middle Frontal Gyrus |
| 26 | 0.443 | 26 | -72 | -42 | Cerebellum |
| 24 | 0.467 | 62 | 4 | 32 | Precentral Gyrus |
| 21 | 0.425 | 48 | 30 | -16 | Inferior Frontal Gyrus |
| 19 | 0.346 | 62 | -4 | 10 | Central Opercular Cortex |
| 19 | 0.394 | -28 | -36 | -40 | Cerebellum |
| 17 | 0.492 | -22 | 40 | 22 | Frontal Pole |
| 14 | 0.376 | -10 | 26 | 64 | Superior Frontal Gyrus |
| 14 | 0.431 | -22 | 52 | 34 | Superior Frontal Gyrus |
| 12 | 0.382 | 4 | -60 | 20 | Precuneus |
| 10 | 0.358 | -54 | 6 | 8 | Precentral Gyrus |

Note: ρ=correlation coefficient

**Table S20. Correlation between stressful life events and the predicted morphometric changes of the JD´s in limbic regions.**

| Region of Interest | hemisphere | Voxels | ρ | MAX X (mm) | MAX Y (mm) | MAX Z (mm) |
|---|---|---|---|---|---|---|
| amygdala | l | 537 | 0.555 | -32 | 4 | -18 |
| | r | 241 | 0.348 | 32 | 6 | -22 |
| hippocampus | l | 789 | 0.519 | -36 | -16 | -16 |
| | l | 11 | 0.452 | -24 | -44 | 4 |
| | l | 5 | 0.377 | -24 | -6 | -32 |
| | l | 45 | -0.687 | -24 | -44 | 4 |
| | r | 373 | 0.531 | 34 | -26 | -10 |
| | r | 6 | 0.263 | 16 | -38 | 6 |
| | r | 2 | -0.34 | 26 | -40 | 6 |
| medial frontal gyrus | | 24 | 0.342 | -6 | 30 | -28 |
| | | 21 | 0.239 | 12 | 38 | -18 |
| | | 3 | 0.19 | -12 | 48 | 0 |
| | | 1 | 0.184 | -12 | 40 | -4 |
| | | 312 | -0.62 | 4 | 54 | -8 |
| | | 3 | -0.34 | 8 | 40 | -26 |
| | | 2 | -0.352 | 2 | 32 | -22 |
| anterior cingulate gyrus | | 1521 | 0.653 | 2 | 20 | 40 |
| | | 48 | -0.455 | -10 | 0 | 42 |
| | | 3 | -0.407 | -4 | -20 | 44 |

Note: ρ=correlation coefficient, unilateral masks used for the amygdala and the hippocampus, bilateral masks used for the medial frontal gyrus and the anterior cingulate gyrus

**Table S21. Dice coefficients**

| **Dice coefficients** | ***Obstetric risks*** | ***Prenatal maternal stress*** | ***Prenatal smoke*** | ***Maternal sensitivity*** | ***Psycho-social family risks*** | ***Trauma*** | ***Stressfull life events*** |
|---|---|---|---|---|---|---|---|
| ***Obstetric risks*** | 1 | 0.26 | 0.03 | 0.15 | 0.08 | 0.07 | 0.08 |
| ***Prenatal maternal stress*** | 0.26 | 1 | 0.1 | 0.19 | 0.24 | 0.17 | 0.11 |
| ***Prenatal smoke*** | 0.03 | 0.1 | 1 | 0.02 | 0.09 | 0.19 | 0.17 |
| ***Maternal sensitivity*** | 0.15 | 0.19 | 0.02 | 1 | 0.24 | 0.15 | 0.19 |
| ***Psychosocial family risks*** | 0.08 | 0.24 | 0.09 | 0.24 | 1 | 0.32 | 0.54 |
| ***Trauma*** | 0.07 | 0.17 | 0.19 | 0.15 | 0.32 | 1 | 0.34 |
| ***Stressfull life events*** | 0.08 | 0.11 | 0.17 | 0.19 | 0.54 | 0.34 | 1 |
| **Mean Coefficient** | 0.24 | 0.30 | 0.23 | 0.28 | 0.36 | 0.32 | 0.35 |

**Table S22. Rotated component loadings.**

| | PC1 | PC2 | PC3 |
|---|---|---|---|
| Maternal smoking during pregnancy | **0.45478384** | 0.01501976 | -0.32874476 |
| Prenatal maternal stress | 0.274652 | **0.62328514** | 0.17805955 |
| Early mother-child interaction | 0.06032054 | -0.01171885 | **0.91377406** |
| Obstetric adversity | -0.09027238 | **0.74860608** | -0.10826119 |
| Psychosocial family adversity | **0.52159315** | 0.02730697 | 0.04837519 |
| Childhood trauma | **0.39768412** | -0.2098639 | 0.09292793 |
| Life events | **0.52510779** | 0.07715655 | 0.05042219 |

**Table S23. Correlation between true and predicted modulated grey matter volume based on adversities, sex and TIV at T1.**

| Voxels | ρ | MAX X (mm) | MAX Y (mm) | MAX Z (mm) | Region |
|---|---|---|---|---|---|
| 69912 | 0.628 | 20 | -32 | -18 | Parahippocampal Gyrus |
| 1318 | 0.251 | 2 | -78 | 28 | Cuneus |
| 763 | 0.256 | -50 | -52 | 6 | Middle Temporal Gyrus |
| 340 | 0.247 | -34 | -92 | 10 | Middle Occipital Gyrus |
| 294 | 0.238 | -38 | -50 | 44 | Inferior Parietal Lobule |
| 256 | 0.184 | -60 | -42 | 48 | Supramarginal Gyrus |
| 158 | 0.162 | 16 | 2 | -48 | Temporal Fusiform Cortex |
| 43 | 0.171 | 66 | -30 | 30 | Supramarginal Gyrus |
| 34 | 0.126 | -64 | -4 | -30 | Middle Temporal Gyrus |
| 28 | 0.139 | -6 | -98 | -20 | Occipital Pole |
| 25 | 0.171 | -6 | -76 | 48 | Precuneus |
| 25 | 0.144 | 46 | -44 | 12 | Superior Temporal Gyrus |
| 15 | 0.135 | -30 | -60 | 48 | Lateral Occipital Cortex |
| 14 | 0.112 | -60 | -20 | -8 | Middle Temporal Gyrus. |
| 10 | 0.126 | 32 | -34 | 72 | Postcentral Gyrus |

Note: ρ=correlation coefficient

**Table S24. Correlation between true and predicted modulated grey matter volume based on adversities, sex and TIV at T1 in limbic regions.**

| Region of Interest | hemisphere | Voxels | ρ | MAX X (mm) | MAX Y (mm) | MAX Z (mm) |
|---|---|---|---|---|---|---|
| amygdala | l | 552 | 0.516 | -26 | -16 | -14 |
| | r | 594 | 0.516 | 28 | -16 | -12 |
| hippocampus | l | 1267 | 0.566 | -18 | -34 | -4 |
| | r | 1195 | 0.624 | 34 | -24 | -12 |
| medial frontal gyrus | | 1811 | 0.476 | 12 | 40 | -18 |
| | | 1 | 0.108 | 4 | 58 | -22 |
| anterior cingulate gyrus | | 3953 | 0.404 | -12 | 48 | 8 |
| | | 6 | 0.126 | 10 | -16 | 38 |

Note: ρ=correlation coefficient, unilateral masks used for the amygdala and the hippocampus, bilateral masks used for the medial frontal gyrus and the anterior cingulate gyrus

**Table S25. Sample description and demographics.**

| | N (subjects) | N (sites) | Sex (%F/%M) | Mean age (SD) |
|---|---|---|---|---|
| **All** | 19.759 | 9 | 53.2/46.8 | 57.33 (16.96) |
| **Training set** | 9.859 | 9 | 53.7/46.3 | 57.6 (16.80) |
| **Test set** | 9.900 | 9 | 52.6/47.4 | 57.06 (17.11) |

**Table S26. Demographics across sites.**

| **Site** | **N** | **Sex (F%/M%)** | **Mean age (SD)** | **Age range** |
|---|---|---|---|---|
| Cam-CAN | 656 | 50.6/49.4 | 54.93 (18.60) | 18-89 |
| HCP | 1112 | 54.5/45.5 | 28.80 (3.70) | 22-37 |
| IMAGEN | 115 | 56.5/43.5 | 22 | 22 |
| MARS 1 | 169 | 58.6/41.4 | 25 | 25 |
| MARS 2 | 114 | 60.5/39.5 | 33 | 33 |
| OASIS 3 | 2144 | 56.8/43.2 | 70.60(9.5) | 43-97 |
| PNC | 1296 | 51.9/48.1 | 14.37(3.45) | 8-21 |
| UKB-11025.0 | 12008 | 52.1/47.9 | 62.34(7.47) | 44-88 |
| UKB-11027.0 | 2145 | 55/45 | 63.19 (7.44) | 47-88 |

**Table S27. Explained variance of normative model based on age, sex and site.**

| Voxels | EV | MAX X (mm) | MAX Y (mm) | MAX Z (mm) | Region |
|---|---|---|---|---|---|
| 77399 | 0.584 | -28 | 40 | -22 | Middle Frontal Gyrus |
| 354 | 0.262 | 28 | -36 | 44 | Postcentral Gyrus |
| 232 | 0.202 | 8 | 44 | 56 | Frontal Pole |
| 164 | 0.173 | 42 | 12 | 60 | Middle Frontal Gyrus |
| 115 | 0.154 | 18 | 20 | 68 | Superior Frontal Gyrus |
| 48 | 0.142 | -60 | -28 | 50 | Inferior Parietal Lobule |
| 45 | 0.139 | 12 | -10 | 78 | Superior Frontal Gyrus |
| 44 | 0.138 | -50 | -86 | -2 | Inferior Occipital Gyrus |
| 31 | 0.153 | 56 | 20 | 32 | Middle Frontal Gyrus |
| 29 | 0.113 | -10 | -10 | 78 | Superior Frontal Gyrus |
| 25 | 0.139 | -50 | -54 | 56 | Supramarginal Gyrus |
| 24 | 0.119 | 0 | 30 | 4 | Corpus Callosum |
| 16 | 0.114 | 16 | -16 | 40 | Cingulate Gyrus |
| 13 | 0.165 | 10 | -34 | 80 | Postcentral Gyrus |

Note: EV=explained variance

**Table S28. Explained variance of normative model based on age, sex and site in limbic regions.**

| **Region of Interest** | **hemisphere** | **Voxels** | **EV** | **MAX X (mm)** | **MAX Y (mm)** | **MAX Z (mm)** |
|---|---|---|---|---|---|---|
| amygdala | l | 641 | 0.297 | -12 | -12 | -16 |
| | r | 728 | 0.309 | 12 | -10 | -18 |
| hippocampus | l | 1374 | 0.374 | -20 | -42 | 6 |
| | r | 1381 | 0.364 | 20 | -42 | 6 |
| medial frontal gyrus | | 1920 | 0.477 | -4 | 28 | -28 |
| anterior cingulate gyrus | | 4876 | 0.301 | -6 | -14 | 28 |

Note: EV=explained variance

**Table S29. Top 2% of the voxels of the correlation between age and the predicted morphometric changes of the JD´s**

| Voxels | ρ | MAX X (mm) | MAX Y (mm) | MAX Z (mm) | Region |
|---|---|---|---|---|---|
| *positive association* | | | | | |
| 10715 | 0.927 | 2 | -84 | -26 | Cerebellum |
| 1479 | 0.905 | -58 | -12 | 42 | Precentral Gyrus |
| 1152 | 0.824 | 54 | -26 | 54 | Postcentral Gyrus |
| 896 | 0.883 | -46 | 12 | -8 | Superior Temporal Gyrus |
| 833 | 0.839 | 34 | -84 | 36 | Cuneus |
| 801 | 0.817 | -24 | -90 | 32 | Cuneus |
| 790 | 0.817 | 48 | 16 | -10 | Inferior Frontal Gyrus |
| 538 | 0.765 | 44 | -40 | -46 | Cerebellum |
| 372 | 0.707 | 20 | 16 | -40 | Temporal Pole |
| 364 | 0.817 | 56 | 18 | 30 | Middle Frontal Gyrus |
| 107 | 0.567 | -36 | -58 | 18 | Middle Temporal Gyrus |
| 89 | 0.611 | -64 | -22 | 12 | Superior Temporal Gyrus |
| 54 | 0.64 | 68 | -20 | 18 | Postcentral Gyrus |
| 36 | 0.574 | -2 | -38 | 54 | Paracentral Lobule |
| 16 | 0.442 | 28 | -92 | -34 | Cerebellum |
| 13 | 0.435 | 36 | -24 | 24 | Parietal Operculum Cortex |
| *negative association* | | | | | |
| 4051 | 0.933 | 48 | 42 | 4 | Inferior Frontal Gyrus |
| 1982 | 0.911 | -56 | -54 | 20 | Superior Temporal Gyrus |
| 1975 | 0.896 | 0 | -10 | 36 | Cingulate Gyrus |
| 1230 | 0.933 | -26 | -72 | -18 | Cerebellum |
| 1193 | 0.947 | 28 | -74 | -18 | Cerebellum |
| 825 | 0.889 | 54 | -50 | 36 | Supramarginal Gyrus |
| 351 | 0.874 | 20 | -68 | -56 | Cerebellum |
| 312 | 0.852 | 50 | -30 | -4 | Middle Temporal Gyrus |
| 263 | 0.793 | -12 | 22 | 56 | Superior Frontal Gyrus |
| 210 | 0.786 | -54 | -32 | 38 | nferior Parietal Lobule. |
| 200 | 0.815 | -18 | -68 | -56 | Cerebellum |
| 141 | 0.918 | -12 | -22 | 6 | Thalamus |
| 126 | 0.918 | 16 | -22 | 4 | Thalamus |
| 121 | 0.859 | -24 | -42 | -14 | Parahippocampal Gyrus |
| 112 | 0.771 | 48 | -18 | -32 | Fusiform Gyrus |
| 103 | 0.844 | 18 | 12 | -6 | Putamen |

| | | | | | |
|---|---|---|---|---|---|
| 87 | 0.822 | -18 | 10 | -6 | Putamen |
| 73 | 0.749 | -28 | -8 | 52 | Precentral Gyrus |
| 66 | 0.727 | -52 | -14 | -38 | Inferior Temporal Gyrus |

Note: ρ=correlation coefficient

**Table S30. Top 2% of the voxels of the correlation between age and the predicted morphometric changes of the JD´s in limbic regions.**

| Region of Interest | hemisphere | Voxels | ρ | MAX X (mm) | MAX Y (mm) | MAX Z (mm) |
|---|---|---|---|---|---|---|
| amygdala | l | 3 | 0.442 | -10 | -4 | -20 |
| | r | 3 | 0.405 | 10 | -4 | -20 |
| hippocampus | l | 205 | 0.699 | -16 | -32 | -10 |
| | l | 146 | 0.824 | -24 | -44 | 4 |
| | r | 401 | 0.817 | 24 | -40 | 8 |
| medial frontal gyrus | | 337 | -0.837 | 2 | 50 | -2 |
| | | 209 | -0.859 | -2 | 38 | -22 |
| anterior cingulate gyrus | | 223 | -0.844 | 4 | 48 | 2 |
| | | 206 | -0.896 | 0 | -10 | 36 |
| | | 7 | -0.734 | 2 | 32 | 6 |
| | | 649 | 0.868 | 0 | -6 | 26 |

Note: ρ=correlation coefficient, unilateral masks used for the amygdala and the hippocampus, bilateral masks used for the medial frontal gyrus and the anterior cingulate gyrus