Supplemental material for the manuscript "*The default mode network mediates the impact of infant regulatory problems on adult avoidant personality traits*"

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Supplemental methods

Potential confounding variables

In the present study, groups of adults with and without infant RP were matched for potential confounding variables, such as gestational age, sex, familiar socio-economic status (SES), and scanner type. Gestational age at birth was determined from maternal reports of the last menstrual period and serial ultrasounds during pregnancy. Information on family SES at birth was collected via structured parental interviews and computed as a weighted composite score derived from the occupation of the head of each family (usually the father) together with the highest educational qualification held by either parent into three categories of low, medium and high SES(1).

Ad) MRI Data Acquisition and Preprocessing

At both sites, MRI data acquisition was initially performed on Philips Achieva 3T TX systems (Achieva, Philips, the Netherlands), using an 8-channel SENSE head coil. In the course of the study, data acquisition in Bonn and Munich had to switch to a Philips Ingenia 3T system with an 8-channel SENSE head coil. The allocation of participants to each of the four scanners was as follows: Bonn I: 9 participants, Bonn II: 5 participants, Munich I: 33 participants, Munich II: 75 participants.

Resting-state data were collected for 10 min 52 s from a gradient-echo echo-planar sequence (TE = 35 ms, TR = 2608 ms, flip angle = 90°, FOV = 230 mm^2, matrix size = 64 × 63, 41 slices, thickness 3.58 and 0 mm inter-slice gap, reconstructed voxel size = 3.59 × 3.59 × 3.59 mm^3) resulting in 250 volumes of BOLD fMRI data per subject. Subsequently, a high-resolution T1-weighted 3D-MPRAGE sequence (TI = 1300 ms, TR = 7.7 ms, TE = 3.9 ms, flip angle = 15°; 180 sagittal slices, FOV = 256 × 256 × 180 mm, reconstruction matrix = 256 × 256;

reconstructed voxel size = 1 × 1 × 1 mm^3) was acquired. Immediately before undergoing the resting-state sequence, subjects were instructed to keep their eyes closed and to refrain from falling asleep.

Selection of intrinsic brain networks

Independent components reflecting intrinsic brain networks (IBN) in our data were selected based on multiple spatial cross correlations using T-map templates provided by Smith and colleagues[(2)]. For each network, the independent component with the largest correlation coefficient was chosen (Table S2). IBNs included the posterior default mode network, salience network, right and left fronto-parietal networks, the sensorimotor network, the auditory network, as well as the primary and lateral visual networks. Based on previous work[(3)] and prior anatomical knowledge, and due to a higher ICA model order (30 ICs vs. 20 ICs in Smith et al.[(2)]), we included six additional independent components in our analyses: the dorsal posterior DMN, dorsal and ventral anterior DMNs, the dorsal and ventral attention networks, as well as the basal ganglia network. In total, fourteen independent components were included in the subsequent partial correlation analysis.

ROI time course extraction

We used a voxel-wise partial correlation approach to map iFC between the time course of the posterior DMN and the time series of each other voxel in the brain, regressing out the time series of all other ROIs, the signal of white matter and cerebrospinal fluid, as well as the six head motion parameters[(4)]. For each subject the component maps (i.e. the ROIs) were thresholded at $Z > 4$, and the remaining voxels inside the mask were used to extract the first Eigen time series from the preprocessed functional data. In a second step, masks representing white matter and cerebrospinal fluid were created using FSL tissue segmentation tool FAST[(5)] and transformed into functional space. Both WM and CSF masks were thresholded at $P > 0.6$, and the remaining voxels inside each mask were used to extract the first Eigen time series from the preprocessed functional data. For every subject, these procedures resulted in fourteen component Eigen time series (i.e. one per component) and two Eigen time series representing WM and CSF. In a last step, we extracted the subject-specific 6 head motion parameters which were estimated with MCFLIRT[6]. This partial correlation procedure resulted in one partial r-map per subject that was subsequently converted to Z values using Fisher's r-to-z transformation.

Supplemental Tables

Table S1. Definition of Crying, Feeding, and Sleeping Problems at 5, 20, and 56 Months of Age and Assessment Mode[7]

Regulatory problems	Definition	Assessment Mode
5 months of age		
Crying problems:	1. Cry duration: ≥ 2 hours per day. AND/OR	PI
	2. Cry amount: above average. AND/OR	PI
	3. Infant is usually difficult to soothe. AND/OR	PI
	4. Infant is constantly irritable.	PI
Feeding problems:	1. Infant does not eat and drink well. AND/OR	PI
	2. Formerly and currently problems with vomiting. AND/OR	PI
	3. Disordered oral-motor functioning, i.e., problems with sucking / swallowing, disordered mouth / tongue movement.	PI
Sleeping problems:	1. Infant wakes up ≥ 2 times per night. AND/OR	PI
	2. Infant wakes up for ≥ 15 minutes at night.	PI
20 months of age		
Eating problems:	1. Occurrence of eating problems. AND/OR	PI
	2. Problems with chewing, swallowing, or not accepting solid food. AND/OR	NE
	3. Oral-motor dysfunction, i.e., uncoordinated movements, not harmonic.	NE
Sleeping problems:	Occurrence of sleeping problems.	PI
56 months of age		
Eating problems:	1. Eating problems / problems with food intake. AND/OR	PI
	2. Neurological / behavioral dysfunction (motor problems, loss of appetite, refusal to eat, or other problems).	NE
Sleeping problems[a]	1. Sleeps through during less than three nights per week.	PI
	2. Needs more than 30 minutes to fall asleep.	PI
	3. Only falls asleep when parents are around.	PI
	4. Regularly sleeps in the parental bed.	PI

Note. PI = Standardized parental interview; NE = Neurological examination by pediatrician.

[a] sleeping problems at 56 months of age were diagnosed if ≥ 2 of the 4 criteria were fulfilled.

Table S2a: Adults with RPs show decreased functional connectivity of the DMN

L/R*	Anatomical Region	cluster	Peak-voxel	Peak-voxel (MNI coordinates)			Max. T
		Size (k)	p(FWE)	x	y	z	
R	Precuneus	353	0.004	6	-66	32	4.22
L	Precuneus			-2	-52	34	3.34
L	Precuneus			-2	-60	30	3.22
R	Frontal Superior Medial	281	0.017	8	60	28	4.14
R	Frontal Superior Medial			12	54	8	3.84

Table S2b: Adult with RPs show decreased functional connectivity of the SN

L/R*	Anatomical Region	cluster	Peak-voxel	Peak-voxel (MNI coordinates)			Max. T
		Size (k)	p(FWE)	x	y	z	
L	Occipital Mid	367	0.005	-28	-84	16	4.88
R	Occipital Superior	316	0.012	26	-82	22	4.04

Table S3: Spatial cross correlation between the templates provided by Smith et al. and the IBNs identified in the present study

Template Smith et al.[2]	IBN Bäuml et al.	spatial correlation r
Visual	Visual	0.74
Latera visual	Lateral visual	0.55
DMN	posterior DMN	0.73
Salience	Salience	0.46
SMN	SMN	0.33
Auditory	Auditory	0.51
Right FPN	Right FPN	0.57
Left FPN	Left FPN	0.68

Table S4: **Differences between participants of the whole sample and the MRI sub-sample**

	Whole Sample n=229		MRI sub-sample n=113		p-value
Gestation, mean (SD)	229	36.41 (4.44)	113	37.36 (3.67)	**.037**
Birth weight, mean (SD)	229	2,655 (992)	113	2,736 (884)	.446
Small for gestational age, n (%)	229	45 (19.7)	113	32 (28.3)	.071
Multiple birth, n (%)	229	26 (11.4)	113	8 (7.1)	.214
Gender, n (%)	229		113		.730
male		113 (49.3)		58 (51.3)	
female		116 (50.7)		55 (48.7)	
Socioeconomic status at birth, n (%)	229		113		.653
High		68 (29.7)		39 (34.5)	
Middle		98 (42.8)		46 (40.7)	
Low		63 (27.5)		28 (24.8)	
Hospitalisation at birth, mean (SD	229	30.02 (33.69)	113	23.53 (28.46)	.064
Optimality, mean (SD)					
pre-pregnancy	229	1.15 (0.84)	113	1.40 (0.88)	**.015**
pregnancy	229	1.34 (1.33)	113	1.41 (1.31)	.662
birth	229	3.10 (1.86)	113	3.14 (1.82)	.862
neonatal	229	4.34 (4.28)	113	3.43 (3.28)	**.032**
Disability at 56 months, n (%)					
Cerebral palsy (grade 3 & 4)	229	3 (1.3)	113	0 (0.0)	.222
Blindness	227	1 (0.4)	113	0 (0.0)	.480
Deafness	227	0 (0.0)	113	0 (0.0)	n/a
Griffith Mental Development Scale, mean (SD)	229		113		
5 months		104.81 (15.81)		107.90	.074
20 months		103.02 (12.50)		(13.33)	**.032**

				105.36 (7.52)	

Table S5. Whole sample: Adults with RPs have more behavioral and emotional problems than adults without RPs (data from term subjects only)

	Never RPs	**Multiple/Persistent RPs**	**Mann-Whitney-U-Test p-value**
	n=147	**n=49**	
YASR			
Sum scales (T-score)			
Total problems	39.34 (8.39)	43.10 (7.64)	.006
Internalizing problems	44.63 (10.56)	48.92 (11.15)	.022
Externalizing problems	43.03 (8.27)	46.00 (6.98)	.022
DSM-oriented scales (T-score)			
Depressive	52.48 (4.70)	53.14 (5.11)	.329
Anxiety	50.85 (1.93)	51.27 (2.64)	.554
Somatic	53.53 (6.05)	53.55 (5.24)	.390
Avoidant personality	52.80 (5.16)	55.78 (6.12)	<.001
Attention deficit/hyperactivity problems	50.31 (0.63)	50.43 (0.74)	.343
Antisocial personality	51.18 (2.67)	51.88 (2.81)	.010

Data are represented as mean (Standard Deviation).

Supplemental Figures

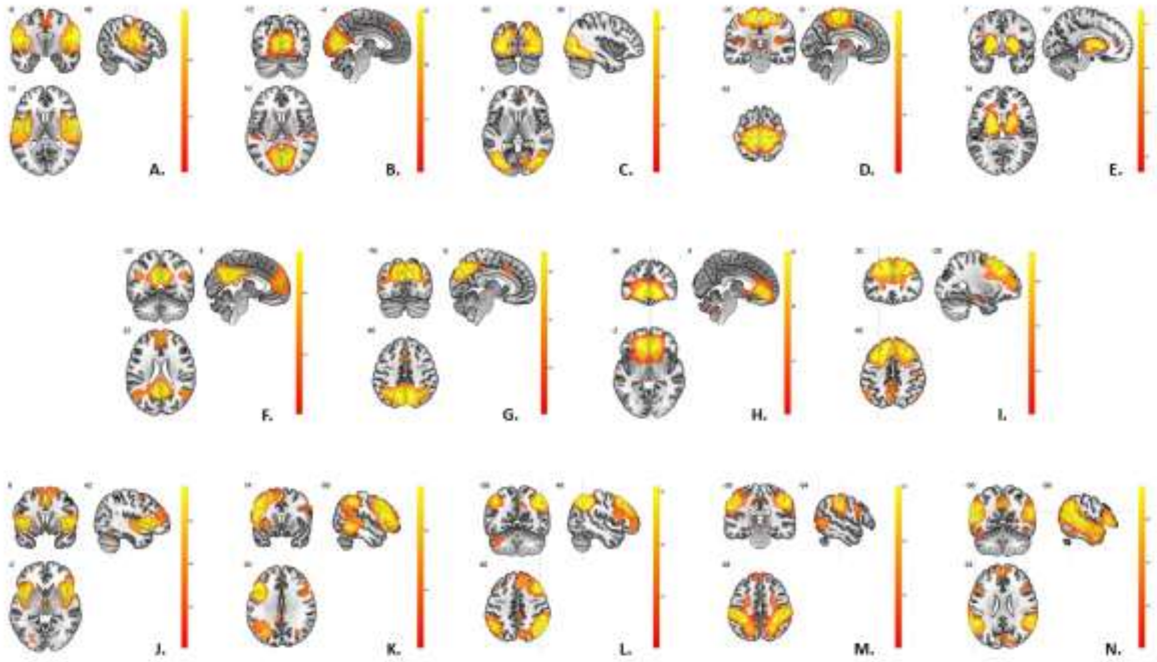

Figure S1: All fourteen IBNs included in our analysis.

A. Auditory network; B. Visual network; C. Lateral visual network; D. Sensorimotor network; E. Basal ganglia network; F. Posterior DMN; G. Dorsal posterior DMN; H. Ventral anterior DMN; I. Dorsal anterior DMN; J. Salience network; K. Left fronto-parietal network; I. Right fronto-parietal network; M. Dorsal attention network; N. Ventral attention network

P < 0.05, FWE-cluster corrected

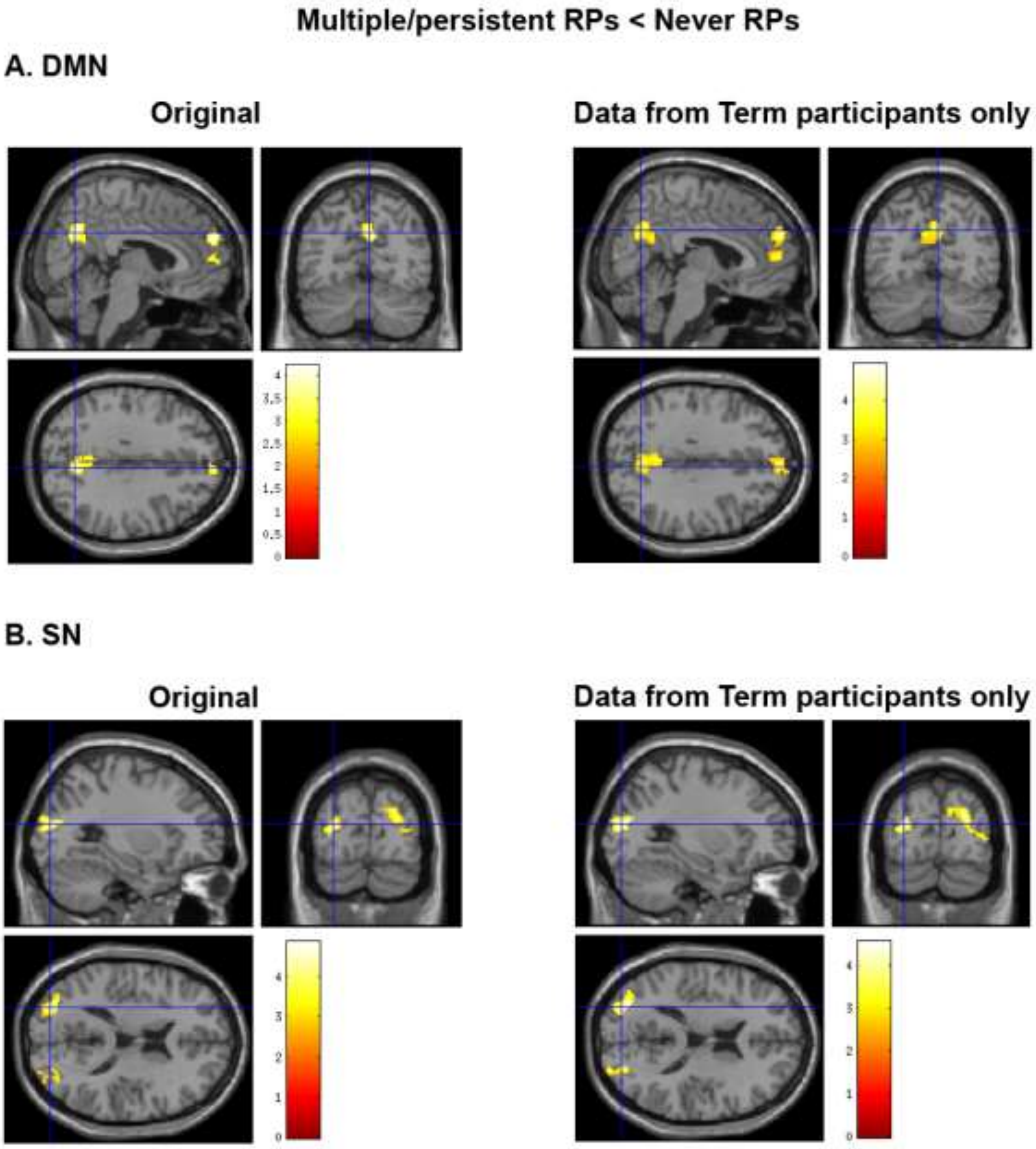

Figure S2: Two sample t-tests for both the original data and term data only, with significance threshold p < 0.05, FWE cluster-level corrected; the color bars represent T-values; for ease of visual inspection, cross hair location corresponds to the peak voxel of the original data's two sample t-tests.

References

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