

Supplementary Information

From early regulatory problems to adult psychosocial outcomes:

The role of insula morphology

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Table S1. *Unadjusted means for the gyrification index of the left insula, for both the RP and avoidant personality groups.*

RP	Avoidant personality traits under borderline level (T<65) (M, SD)	Avoidant personality traits above borderline level (T>65) (M, SD)	Combined whole RP sample (M, SD)
Control	24.81 (1.19)	24.79 (1.21)	24.81 (1.19)
Multiple and/or persistent RP	24.82 (1.21)	26.24 (1.53)	25.00 (1.33)
Multiple	24.62 (1.42)	24.54 (*)	24.61 (1.39)
Persistent	25.16 (1.10)	26.58 (1.44)	25.52 (1.31)
Multiple and persistent	24.63 (.34)	[/]**	24.63 (.34)

Notes. RPs= early regulatory problems; M = mean; SD = standard deviation; T = t-score.

*N=1.

**no participants in both multiple and persistent RPs, and avoidant personality group

Table S2. *Associations between RPs, peer relationship quality and insula morphology.*

Factor	Dependent variable	df	F	Sig.	Partial η^2
RPs	V_Ins_R	1	.284	.595	.002
	V_Ins_L	1	1.408	.237	.010
	T_Ins_R	1	.235	.629	.002
	T_Ins_L	1	.810	.370	.006
	D_Ins_R	1	.040	.841	.000
	D_Ins_L	1	.552	.459	.004
	G_Ins_R	1	.205	.652	.001
	G_Ins_L	1	.995	.320	.007
Peer relationships	V_Ins_R	10	1.217	.285	.078
	V_Ins_L	10	.848	.583	.056
	T_Ins_R	10	.288	.983	.020
	T_Ins_L	10	.735	.691	.049
	D_Ins_R	10	1.294	.239	.082
	D_Ins_L	10	1.341	.214	.085
	G_Ins_R	10	.517	.876	.035
	G_Ins_L	10	.660	.760	.044
RPs * Peer relationships	V_Ins_R	6	1.098	.366	.044
	V_Ins_L	6	.777	.589	.031
	T_Ins_R	6	1.408	.216	.055
	T_Ins_L	6	1.318	.253	.052
	D_Ins_R	6	.933	.473	.037
	D_Ins_L	6	1.807	.102	.070
	G_Ins_R	6	1.287	.267	.051
	G_Ins_L	6	.691	.657	.028

Notes: RP = early regulatory problems; V_Ins = volume of the insula; T_Ins = cortical thickness of the insula; D_Ins = sulcal depth of the insula; G_Ins = gyrification index of the insula; R = right, L = left; df = degrees of freedom; Sig. = significance.

Table S3. *Covariate/control variables definitions.*

Potential confounding variable	Definition
Gestational age	Determined based on maternal reports of the last menstrual period and ultrasound measurements during pregnancy.
Birth weight	Acquired at birth.
Sex	Biologically determined.
TIV	Determined in the preprocessing of T1 images.
SES	Collected through structured parental interviews and computed as a weighted composite score. Assessed based on the occupation of the head of the household and the highest educational qualification of either parent, categorized into low, medium, and high SES.
Scanner type	In Bonn and Munich, data acquisition transitioned from a Philips Achieva 3T TX system (Achieva, Philips, the Netherlands) to a Philips Ingenia 3T system, consistently using an 8-channel SENSE head coil. Final participant distribution: Bonn 1 – 9 participants, Bonn 2 – 5 participants, Munich 1 – 33 participants, Munich 2 – 75 participants.

Note. TIV = total intracranial volume; SES = familial socio-economic status

Table S4. *Entire adult sample group demographics.*

	Multiple/Persistent RPs	Never RPs	<i>p</i>
Participants: <i>n</i> (%)	N = 83 (24.3 %)	N = 259 (75.7 %)	
Age in years: Mean (SD)	28.14 (1.85)	27.44 (1.81)	.002
Sex: <i>n</i> (%)			.71
Female	43 (51.8 %)	128 (49.4 %)	
Male	40 (48.2 %)	131 (50.6 %)	
Gestational age in weeks: Mean (SD)	36.71 (4.39)	36.73 (4.17)	.97
Birth weight in grams: Mean (SD)	2611 (951)	2705 (960)	.44
Familial socioeconomic status: <i>n</i> (%)			.83
High	26 (31.3 %)	81 (31.3 %)	
Middle	33 (39.8 %)	111 (42.9 %)	
Low	24 (28.9 %)	67 (25.9 %)	

Note. We used χ^2 tests for sex and socioeconomic status and *t* tests for the rest of the variables. RPs = early regulatory problems; SD = standard deviation; *p* = significance level.

Table S5. *Assessment of early RPs at 5, 20 and 56 months [1].*

Regulatory problem	Item	Assessment method
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 / behavioural 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. RPs = early regulatory problems; PI = Standardized parental interview; NE = Neurological examination by the pediatrician.

^aSleeping problems at 56 months of age were diagnosed if ≥ 2 of the 4 criteria were fulfilled.

Table S6. *Items used for the peer relationship composite score [2].*

Item	Questionnaire	Definition	Scoring
No best friend	Life Course Interview	Had no best friend post school.	1
Trouble making and keeping friends	Young Adult Self Report Life Course Interview	Having somewhat or very much trouble making or keeping friends. Had none or only to 2 or 3 friends post school. Had no circle of friends post school.	1 1 1
No support	Life Course Interview	No exchange of thoughts and feelings with friends. Friends are not supportive regarding career. Friends could not be asked for help when in need of care.	1 1 1
Conflict	Life Course Interview	Having difficulties hearing uncomfortable truths from friends. Having stressful conflicts with friends.	1 1
Socializing	Life Course Interview	Not involved in social activities (e.g. dancing, music, scouts) for more than a year post school. Never gone out to bars or clubs post school.	1 1
Total score			11

Note. For analysis, the total score was standardized on the never RPs group and computed into a negative score, such that higher scores indicated better peer relationships.

References:

1. Schmid G, Schreier A, Meyer R, Wolke D (2010) A prospective study on the persistence of infant crying, sleeping and feeding problems and preschool behaviour. *Acta Paediatrica, International Journal of Paediatrics* 99:286–290. <https://doi.org/10.1111/j.1651-2227.2009.01572.x>
2. Zorjan S, Wolke D, Baumann N, Sorg C, Mulej Bratec S (2025) The association between early regulatory problems and adult peer relationship quality is mediated by the brain's allostatic-interoceptive system. *J Child Psychol Psychiatry*. <https://doi.org/10.1111/jcpp.14033>