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Supplementary material

Supplementary results

Exploratory analyses of associations between prefrontal gray matter and clinical variables in the MDD sample

As stated in the main result section, analyses of potential associations between clinical variables reflecting disease course in the MDD sample and log hsCRP values yielded a significant association between log hsCRP and number of inpatient depressive episodes (beta=0.154, p=0.001) controlling for age and sex, while no significant association occurred with regard to disease duration (beta=-0.025, p=0.580) or total number of lifetime depressive episodes (beta= 0.001, p=0.985). Furthermore, no significant association between log hsCRP levels and acute depressive symptomatology as assessed via HAMD scores (beta=-0.011, p=0.810) or CES-D scores (beta=0.003, p=0.950) could be observed. No significant association between the level of atypical symptoms as measured using the IDS sum score and log hsCRP levels could be detected (beta=0.069, p=0.122). In light of these findings, hospitalization was included as a nuisance regressor in the VBM analyses as presented in the main result section.

In addition, exploratory analyses of associations between the aforementioned clinical variables and prefrontal gray matter volume related to hsCRP in the MDD sample were carried out. To this end, mean gray matter values of a sphere of 5 mm around the reported peak voxel (x= 50, y= 50, z= 8) were extracted in SPM and analysed using linear regression models in SPSS.

No significant positive or negative associations between mean prefrontal gray matter volume and disease duration (beta=-0.028, p=0.525) nor total number of depressive episodes (beta=-0.020, p=0.671), nor number of inpatient depressive episodes (beta=-0.062, p=0.169)

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emerged in these additional analyses. Furthermore, no significant association between mean prefrontal gray matter and HAMD (beta=-0.035, p=0.429) or CES-D scores (beta=-0.035, p=0.429) emerged. No significant association between mean prefrontal gray matter and atypical symptoms was detected (beta= 0.002, p=0.959).

Supplementary Table 1. Frequencies of medical comorbidities in the MDD and HC cohort, p-values derived from chi square tests.

	MDD	HC	p
Arterial hypertension	164	80	.098
Diabetes mellitus	30	8	.010
Peripheral artery disease	10	2	.082
Renal disorders	21	17	.648
Pulmonary disorders	83	21	<.001
Thyroid disorder	117	66	.114
Chronic Arthritis	33	14	.102
Peripheral Thrombosis	20	9	.259

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Figure S1

Plots depicting the negative association between log hsCRP and gray matter volume in the MDD sample at x= 50, y= 50, z= 8 stratified for age using median split (median age: 50.31; fit line (age < 50.31): r= -.207; fit line (age > 50.31): r= -.232). *Abbreviations:* log hsCRP, logarithmic transformed high-sensitive C-reactive protein
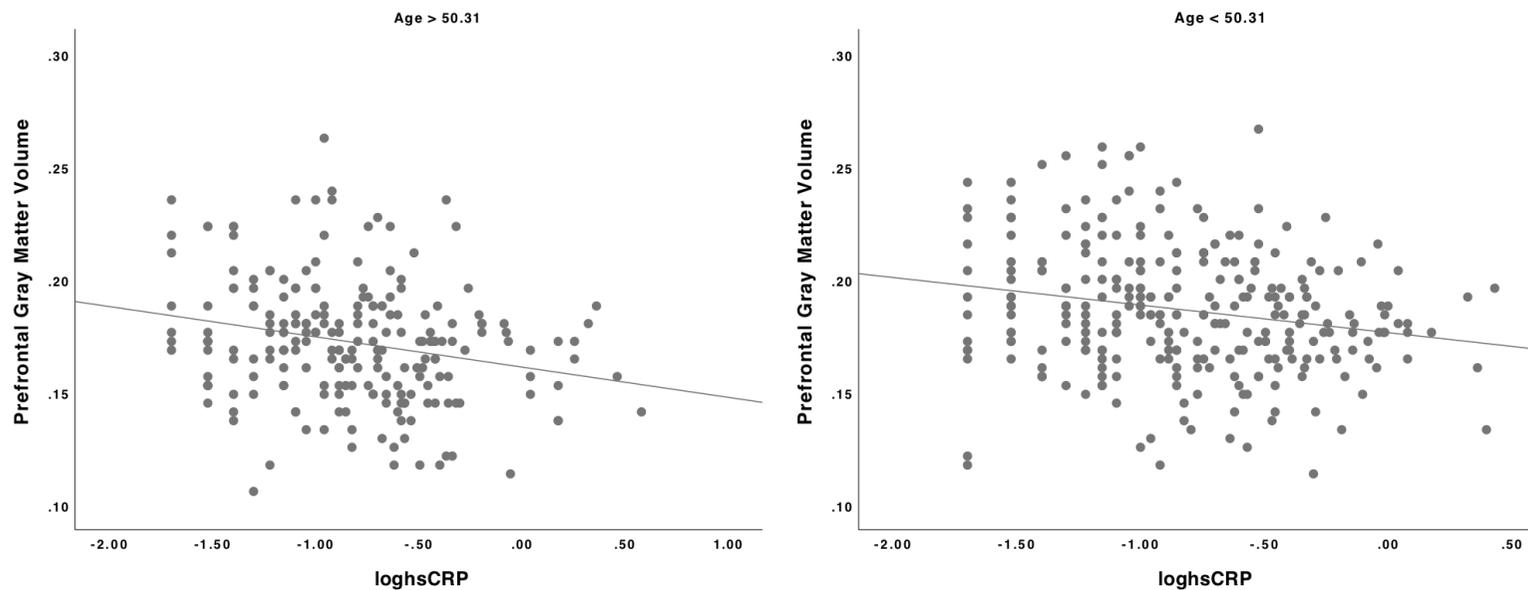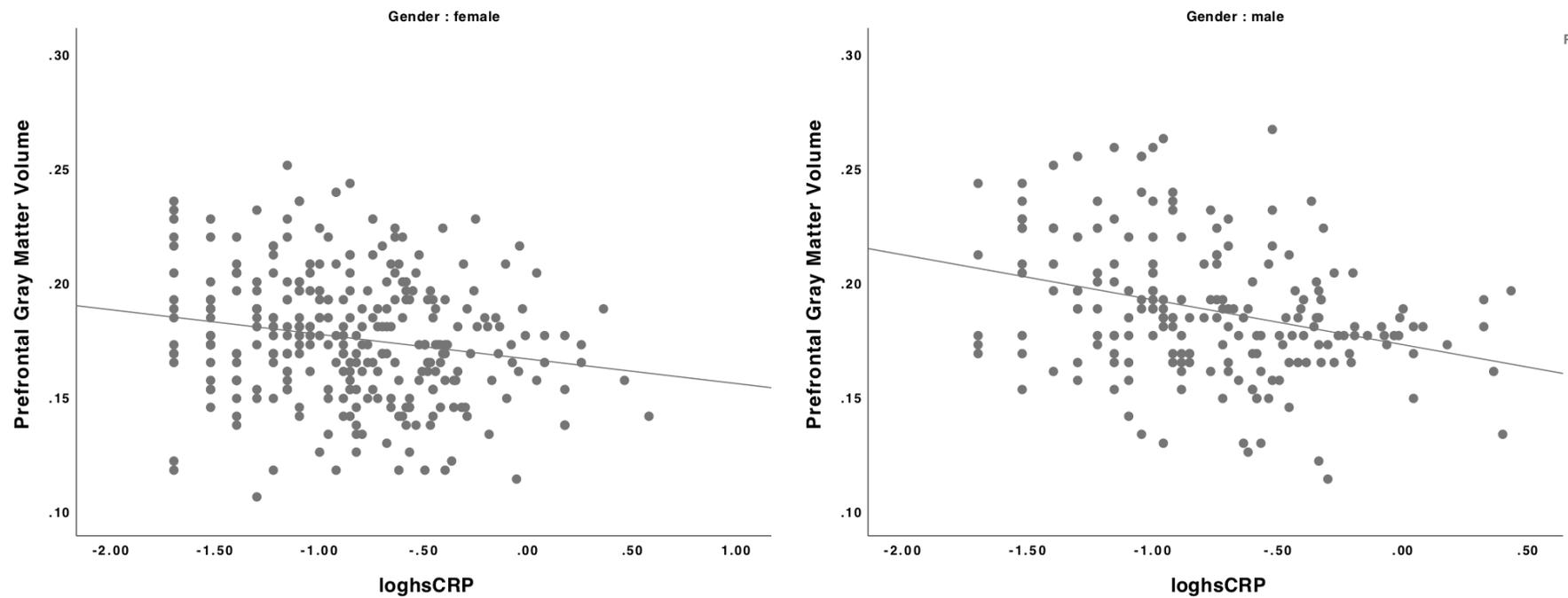
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Figure S2

Plots depicting the negative association between log hsCRP and gray matter volume in the MDD sample at x= 50, y= 50, z= 8 stratified for gender (fit line (female): r= -.190; fit line (male): r= -.311).
Abbreviations: log hsCRP, logarithmic transformed high-sensitive C-reactive protein

Figure S3

Plots depicting the negative association between log hsCRP and gray matter volume in the MDD sample at x= 50, y= 50, z= 8 stratified for BMI using median split (median BMI: 27.00; fit line (BMI > 27): r= -.252; fit line (BMI < 27): r= -.097).
Abbreviations: BMI, Body Mass Index, log hsCRP, logarithmic transformed high-sensitive C-reactive protein