

Supplementary Information for “No replicable morphometry variations and limited morphometry-phenotype associations for cortical neuroimaging in irritable bowel syndrome”

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* Supplementary Table 1,4, 6-12 are presented in Supplementary Excel.

Supplementary Table 2. **The exclusion criteria applied to IBS cases.** Excluded conditions included inflammatory bowel disease, GI malignancy, malabsorption, celiac or gluten sensitivity based on blood test or endoscopy, and several abdominal surgeries.

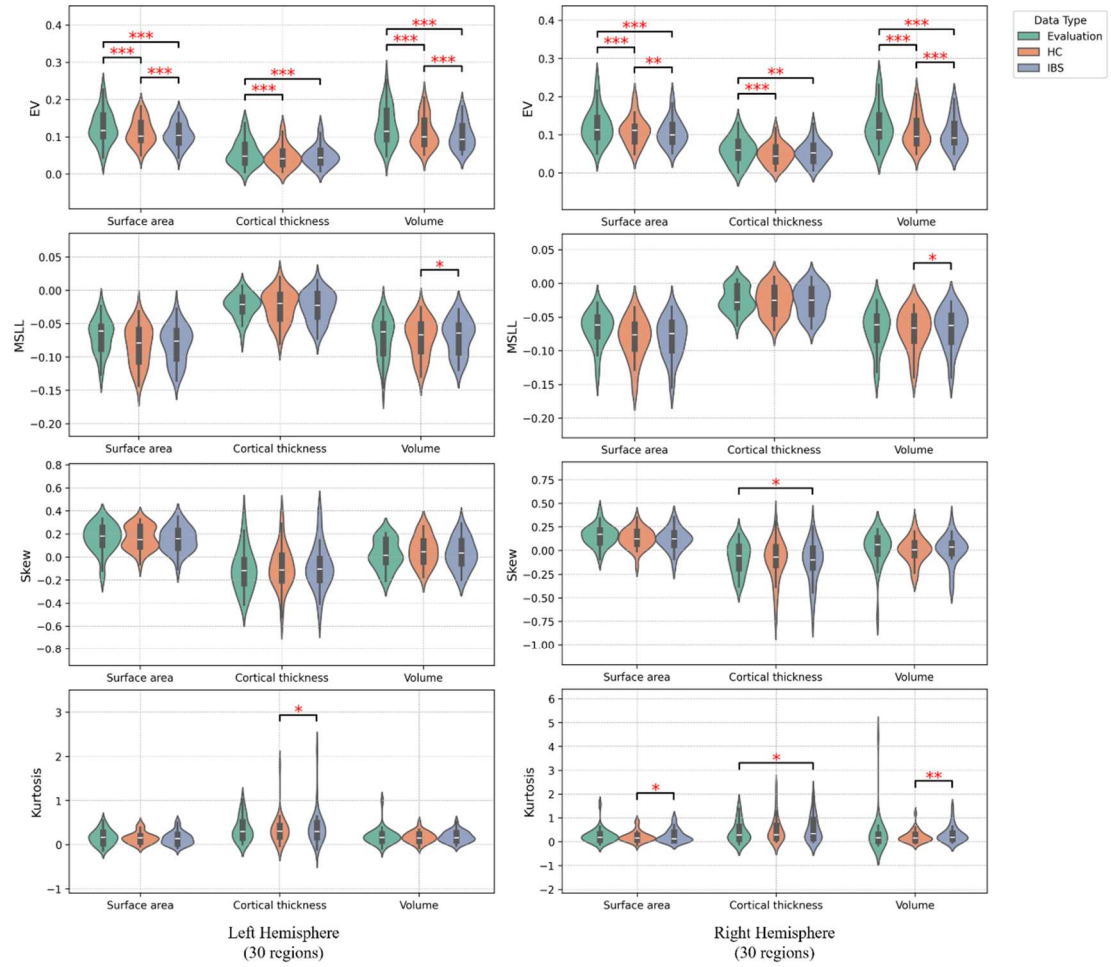
Criteria	Prompt	Positive answer	UK Biobank field
ICD-10	-	F01, F02, F03, F10, F11, F12, F13, F14, F15, F16, F17, F18, F19, F20, F21, F22, F25, F31, F33, F70, F71, F72, F73, F78, F79, K50, K500, K501, K508, K509, K51, K510, K511, K512, K513, K514, K515, K518, K519, K52, K520, K521, K523, K528, K529, K550, K551, K627, K86, K860, K861, K862, K863, K868, K869, K90, K900, K901, K903, K904, K908, K909, C15, C16, C17, C18, C19, C20, C21, C22, C23, C24, C25, C26C71, D330, I10, I60, I61, I63, S060, S061, S062, S063, S064, S065, S066, S067, S068, S069, G00, G01, G02, G03, G04, G05, G06, G07, G08, G09, G10, G11, G12, G13, G14, G20, G21, G22, G23, G24, G25, G26, G30, G31, G32, G35, G36, G37, G40, G41, G42, G43, G44, G45, G46, G47, G50, G51, G52, G53, G54, G55, G56, G57, G58, G59, G60, G61, G62, G63, G64, G70, G71, G72, G73, G80, G81, G82, G83, G90, G91, G92, G93, G94, G95, G96, G97, G98, G99	41270
OPCS-4	-	G01, G02, G03, G05, G06, G08, G27, G28, G31, G32, G33, G34, G49, G51, G58, G60, G61, G69, G71, G72, G73, G74, G75, H04, H05, H06, H07, H08, H09, H10, H11, H13, H14, H29, H33, H47, H57, H68, H69, H70	41272
Self-reported non-cancer illness code	-	1135, 1164, 1165, 1191, 1456, 1459, 1461, 1462, 1463, 1509, 1600, 1601, 1602	20002
Coeliac/Gluten sensitivity	Method of coeliac disease/gluten sensitivity diagnosis	Except 'self-diagnosis from symptoms'	21069

Supplementary Table 3. **Definitions used for IBS group based on ROME III criteria**

Prompt	Positive answer	UK Biobank field
Frequency of discomfort/pain in abdomen in last 3 months	2-3 times per month or more	21025
For female: Discomfort/pain occurring only during menstrual bleed	No or not applicable	21026
Abdominal discomfort/pain for 6 months or longer	Yes	21027
At least two of:		
Frequency of discomfort/pain getting better or stopping after a bowel movement	At least sometimes	21028
More frequent bowel movements when abdominal discomfort/pain started / Less frequent bowel movements when abdominal discomfort/pain started	At least sometimes to at least one of these questions	21029, 21030
Stools looser when abdominal discomfort/pain started / Frequency of harder stools when abdominal discomfort/pain started	At least sometimes to at least one of these questions	21031, 21032

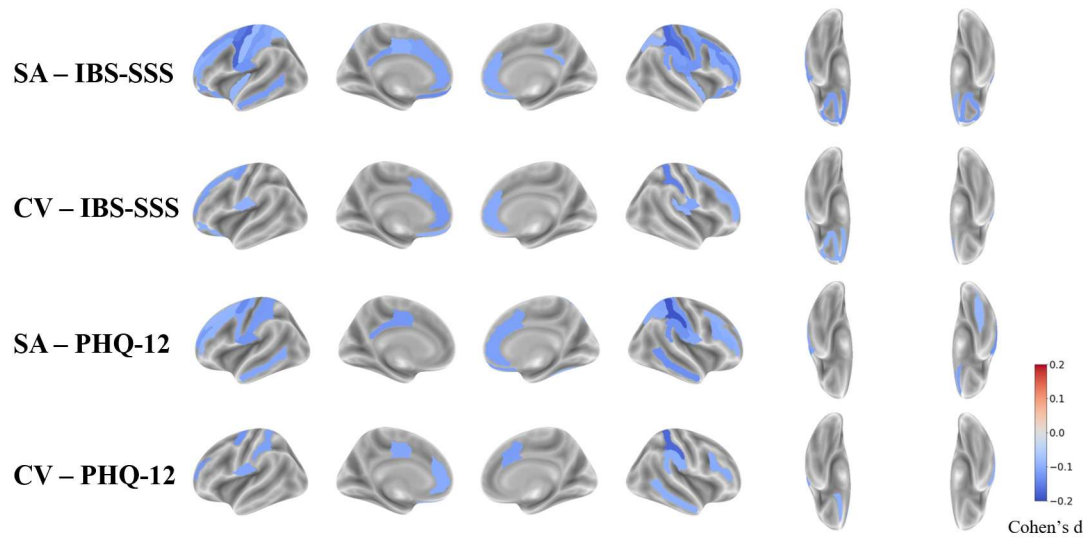
Supplementary Table 5. **Regions of interest (ROIs) related to IBS based on previous studies.** Short name stands for region's name in Destrieux parcellation. Both left and right hemispheres of listed regions were included in the current study.

Short name	Long name	Short name	Long name
S_front_sup	Superior frontal sulcus	S_intrapariet_and_P_trans	Intraparietal sulcus (intraparietal sulcus) and transverse parietal sulci
G_front_sup	Superior frontal gyrus (F1)	G_oc-temp_lat-fusifor	Lateral occipito-temporal gyrus (fusiform gyrus, O4-T4)
S_front_inf	Inferior frontal sulcus	G_temporal_middle	Middle temporal gyrus (T2)
G_front_middle	Middle frontal gyrus (F2)	G_and_S_cingul-Ant	Anterior part of the cingulate gyrus and sulcus (ACC)
S_front_middle	Middle frontal sulcus	G_and_S_cingul-Mid-Ant	Middle-anterior part of the cingulate gyrus and sulcus (aMCC)
G_front_inf-Orbital	Orbital part of the inferior frontal gyrus	G_and_S_cingul-Mid-Post	Middle-posterior part of the cingulate gyrus and sulcus (pMCC)
S_precentral-inf-part	Inferior part of the precentral sulcus	G_cingul-Post-dorsal	Posterior-dorsal part of the cingulate gyrus (dPCC)
S_precentral-sup-part	Superior part of the precentral sulcus	G_cingul-Post-ventral	Posterior-ventral part of the cingulate gyrus (vPCC, isthmus of the cingulate gyrus)
G_precentral	Precentral gyrus	S_orbital_med-olfact	Medial orbital sulcus (olfactory sulcus)
G_postcentral	Postcentral gyrus	G_orbital	Orbital gyri
S_postcentral	Postcentral sulcus	G_rectus	Straight gyrus, Gyrus rectus
G_and_S_subcentral	Subcentral gyrus (central operculum) and sulci	S_circular_insula_ant	Anterior segment of the circular sulcus of the insula
S_central	Central sulcus (Rolando's fissure)	S_circular_insula_inf	Inferior segment of the circular sulcus of the insula
G_pariet_inf-Supramar	Supramarginal gyrus	G_cuneus	Cuneus (O6)
G_parietal_sup	Superior parietal lobule (lateral part of P1)	Lat_Fis-post	Posterior ramus (or segment) of the lateral sulcus (or fissure)



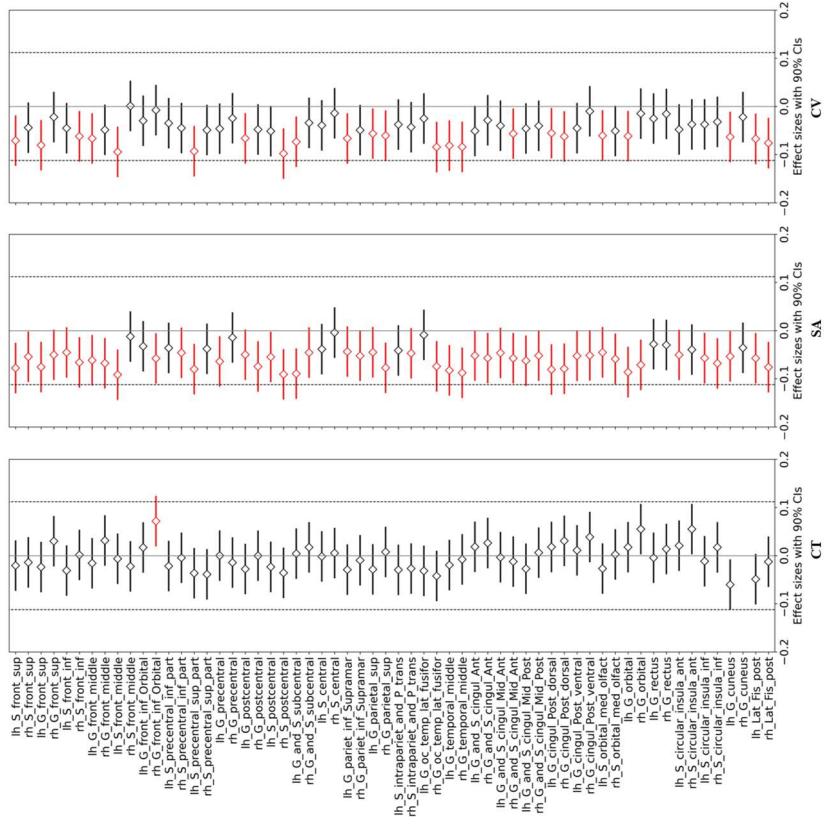
Supplementary Figure 1. **Comparison of evaluation metrics across the evaluation, healthy control (HC), and IBS datasets.**

One-side t-tests were performed under the hypothesis that normative models (NMs) would perform best on the evaluation dataset, followed by the HC dataset, and worst on the IBS dataset. Marker representation: *: $p < 0.05$; **: $p < 0.01$; *** $p < 0.001$. Abbreviation: EV, explained variance; MSLL, mean standardized log loss.

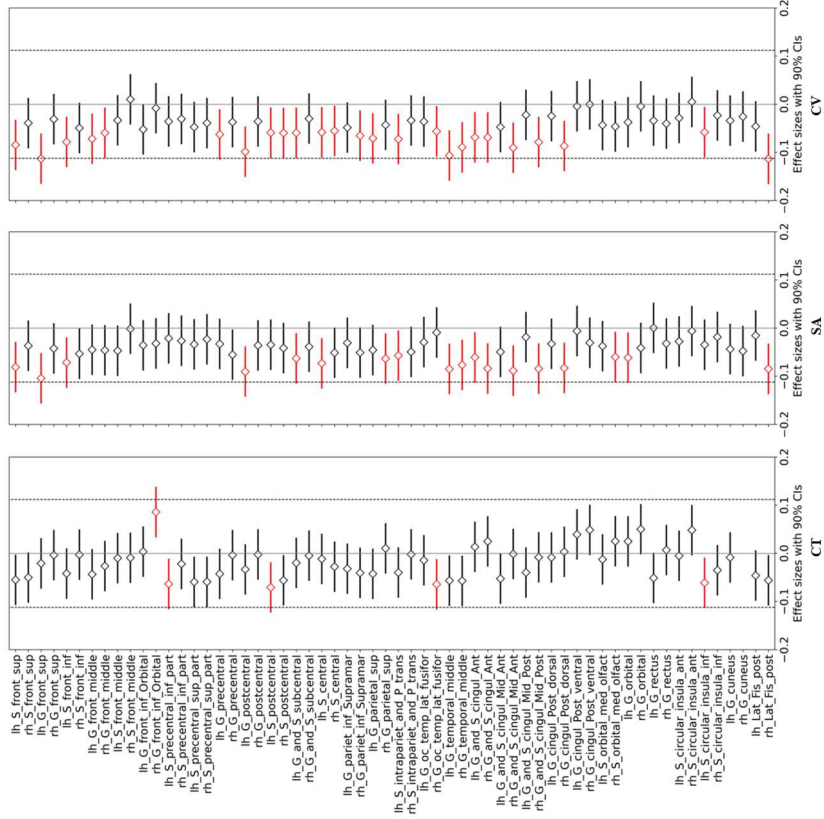


Supplementary Figure 2. **Within IBS cortical brain-phenotype associations.** Brain maps showing cortical regions in which cortical deviation scores were significantly associated with IBS symptom severity (IBS-SSS) or somatic pain severity (PHQ-12) after FDR correction. Effect sizes (Cohen's d) correspond to correlation coefficients. No significant associations were observed for depression (PHQ-9) or anxiety (GAD-7).

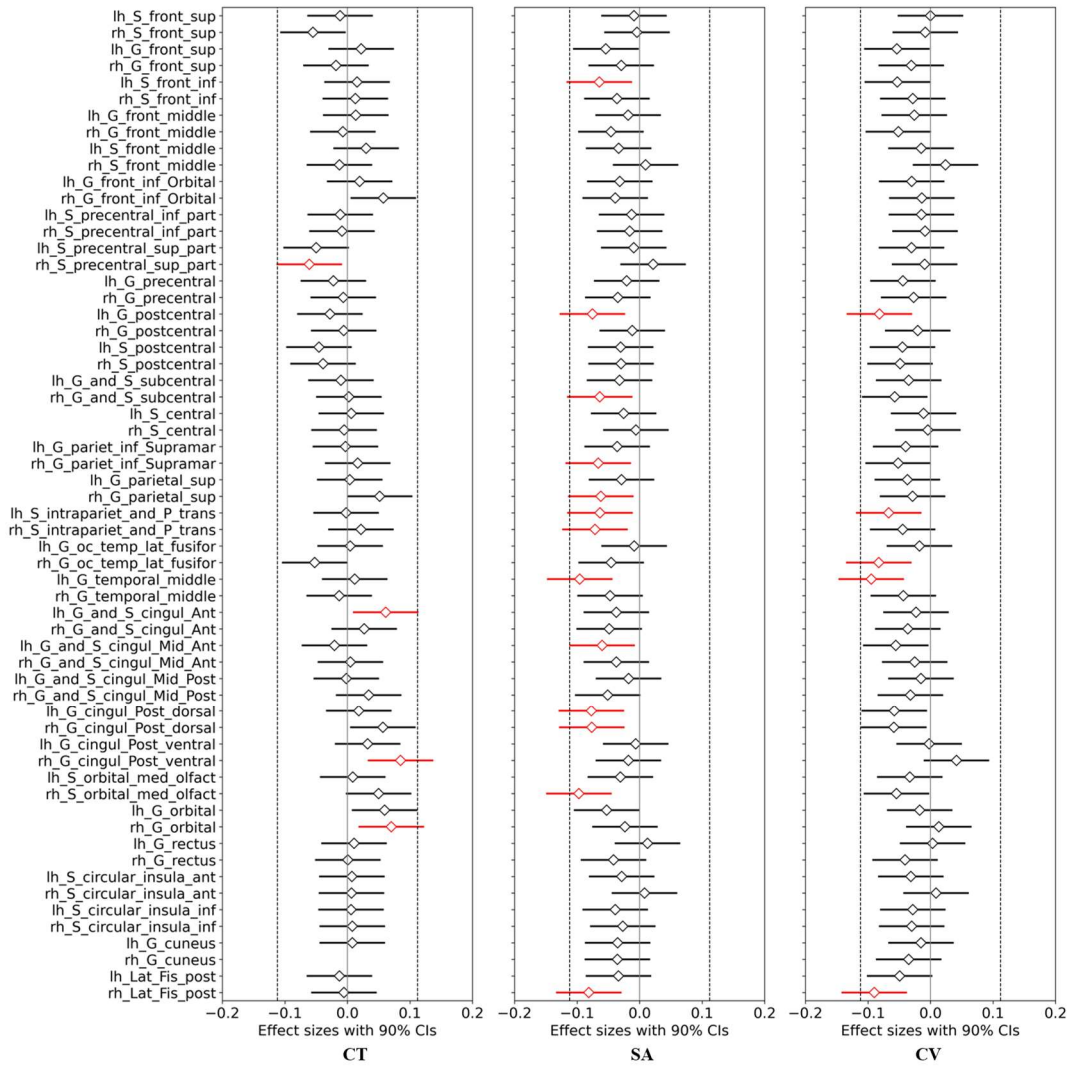
a PHQ-12



b PHQ-9

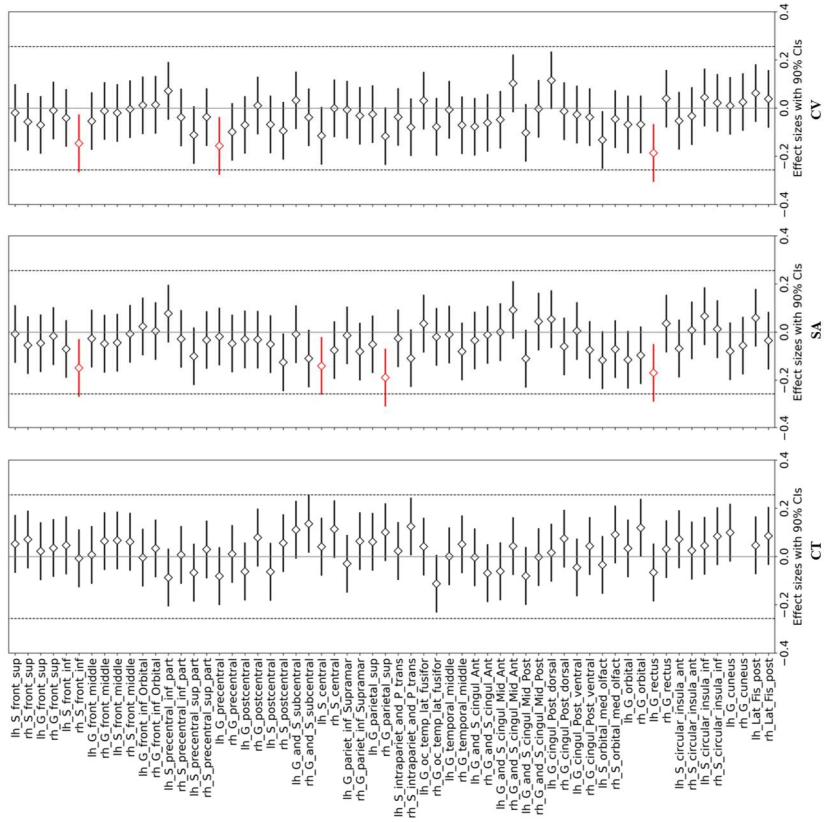


c GAD-7

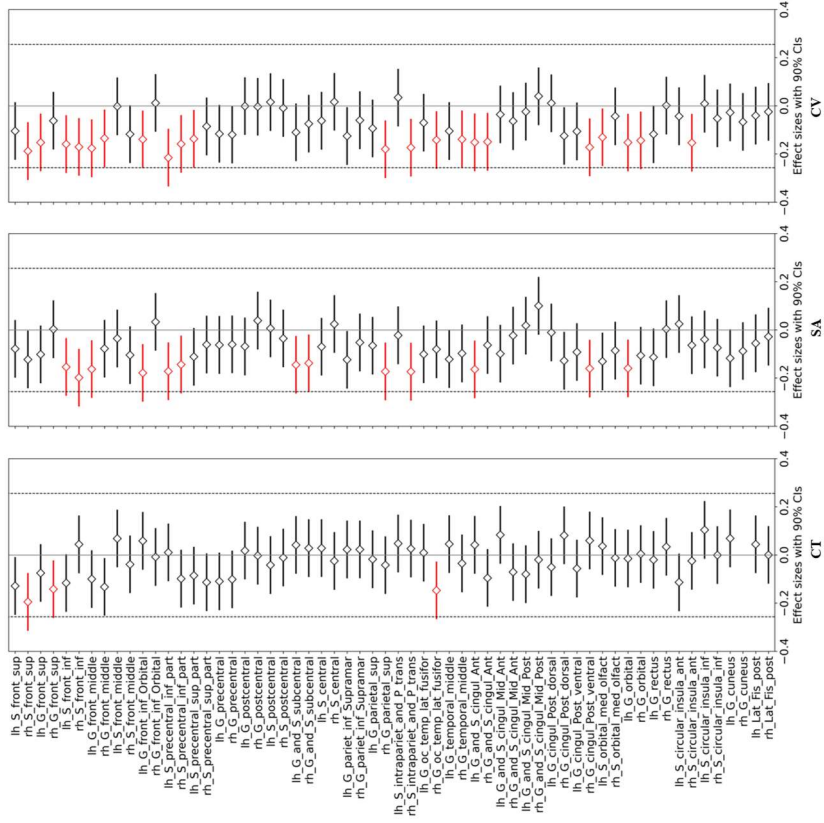


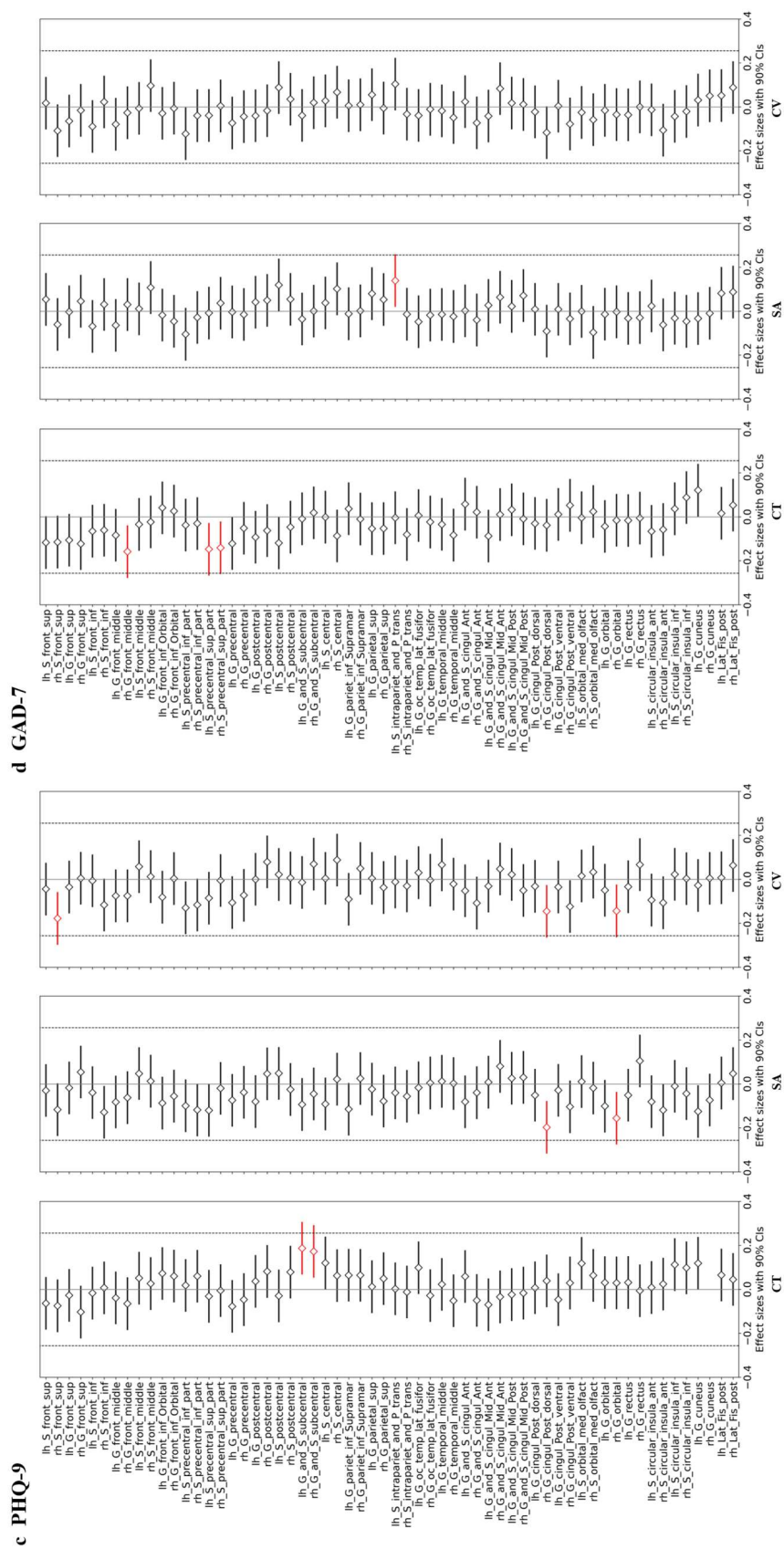
Supplementary Figure 3. **Forest plots of cortical brain-phenotype correlation differences between IBS and HCs.** Forest plots show the effect sizes (Cohen's q) and 90% CIs for group differences in cortical brain-phenotype associations across all ROIs for **a** PHQ-12, **b** PHQ-9 and **c** GAD 7. Forest plots for IBS-SSS are available in the main draft in Figure 3.b. Equivalence test was applied using a SESOI of $|0.112|$. Regions in red with CIs overlapped the equivalence bounds are marked as inconclusive.

a IBS-SSS



b PHQ-12





Supplementary Figure 4. Forest plots of difference-in-differences effect sizes for group \times sex interaction effects. Forest plots show difference-in-differences effect sizes and 90% CIs for sex moderation of brain-phenotype associations across all ROIs for **a** IBS-SSS, **b** PHQ-12, **c** PHQ-9 and **d** GAD 7. Equivalence test was applied using a SESOI of 0.256|. Regions in red with CIs overlapped the equivalence bounds are marked as inconclusive.