

1 **Supplementary Material for Brandl, Weise et al.:**
2 **Common and specific large-scale brain changes in major depressive disorder,**
3 **anxiety disorders, and chronic pain**
4 ***A transdiagnostic multimodal meta-analysis of structural and functional MRI***
5 ***studies***

6
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81 **Supplementary Methods**

82 **1. Details of literature search**

83 The meta-analysis was registered at PROSPERO (registration number: CRD42019119709;
84 https://www.crd.york.ac.uk/PROSPERO/display_record.php?RecordID=119709). Studies
85 were searched until January 01, 2020 in PubMed, Web of Science, EMBASE, and reference lists
86 of reviews and eligible articles, using the keywords (*rest* OR intrinsic*) AND *connect* AND*
87 *seed* AND [disorder name]* for the intrinsic functional connectivity (iFC) meta-analysis and
88 (*"VBM" OR "voxel-based morphometry"*) AND *[disorder name]* for the gray matter volume
89 (GMV) meta-analysis. Detailed search terms (i.e., disorder name) for each disorder are given
90 in **Table S1**. The following diseases/conditions were eligible for inclusion:

- 91 - *Major depressive disorder (MDD)*: diagnosis of major depressive disorder/major depression
92 (including late-life depression and geriatric depression).
- 93 - *Anxiety disorders (ANX)*: generalized anxiety disorder, generalized social anxiety disorder,
94 panic disorder, phobias (e.g., social phobia), post-traumatic stress disorder, social anxiety
95 disorder.
- 96 - *Chronic pain (CP)*: chronic back pain, fibromyalgia, chronic widespread pain,
97 temporomandibular pain/disorder, osteoarthritis, irritable bowel syndrome, chronic pelvic
98 pain, dysmenorrhea, neuropathic pain, phantom pain, complex regional pain syndrome,
99 rheumatoid arthritis, central pain, migraine, tension type headache, postherpetic neuralgia,
100 post-thoracotomy pain syndrome, chronic pancreatitis, ankylosing spondylitis.

101

102 All English-language publications of whole-brain voxel-based morphometry (VBM) and seed-
103 based whole-brain iFC comparing patients with MDD, ANX, or CP to healthy subjects were
104 included. Studies were selected jointly by researchers F.B. and B.W. in a multi-step procedure

105 in line with MOOSE guidelines for meta-analyses of observational studies (**Figure 1**; MOOSE
106 checklist is provided in **Table S2**) (1). We systematically checked study quality concerning
107 design, demographic/clinical characteristics (e.g., overlap of study samples), dropout rates,
108 and precision of seed and result coordinates. Only studies including patients with explicit
109 diagnosis of the respective disorder (e.g., using DSM-5) were selected. Exclusion criteria were
110 (i) methods other than VBM or seed-based iFC, e.g., graph analysis or independent component
111 analysis, which yield different outcome measures; (ii) no whole-brain analysis; (iii)
112 neurological (other than CP) or severe medical comorbidity (psychiatric comorbidity was no
113 exclusion criterion); (iv) no peak-coordinates reported in standard space. In longitudinal or
114 intervention/challenge studies, only baseline results were considered. Task-fMRI data were
115 not considered since they reflect reactions to specific tasks instead of stable/long-term
116 changes. We made no restrictions concerning age, illness duration, symptom severity, or
117 medication status to ensure maximal study coverage, but we conducted several control
118 analyses later on.

119

120 **2. Details of data extraction**

121 Peak-coordinates of between-group effects were extracted from included GMV- and iFC-
122 studies (**Tables S3-S8**) and, if necessary, converted to Montreal Neurological Institute (MNI)
123 standard space. IFC peak-coordinates were assigned to 'seed-networks' according to the
124 location of the center-coordinate of their respective seed (which had been used in the
125 included study to calculate seed-based iFC) within a parcellation of brain-networks (2,3). We
126 selected a widely-used parcellation based on iFC-data from 1000 healthy subjects, covering
127 cortex, striatum, and cerebellum. It contained 7 seed-networks: visual (VIS), primary-
128 sensorimotor (PSM), dorsal attention (DAN), salience (SAL), limbic (LIM), frontoparietal

129 (FPN), default-mode (DMN) (**Figure S1**) (4-6). SAL refers to Yeo's 'ventral-attention network',
130 PSM to Yeo's 'somatomotor network' – they were renamed to better fit the existing
131 literature and reflect their constituent regions. As a general limitation, these
132 neurocognitively motivated network names do not claim to describe an exclusive function of
133 the network, but reflect research conventions and enable links to other papers. No similar
134 network-parcellation was available for thalamus, so studies using only thalamus seeds were
135 excluded (2).

136

137 **3. Details of meta-analysis**

138 MKDA meta-analysis of both GMV and network-iFC maps was conducted (2,3,7,8). For iFC,
139 meta-analyses were only conducted for networks with at least three studies in each disorder
140 to ensure sufficient power. MKDA-analysis followed our previous work on transdiagnostic
141 multimodal meta-analysis of structural and resting-state fMRI-studies across
142 neuropsychiatric disorders (2) and comprised the following steps: smoothing of peak-
143 coordinates with spherical kernels (radius=15mm), weighting of input studies by sample size
144 and finally averaging over the smoothed, weighted study maps (8). The resulting 'density
145 maps' (one for each meta-analytic contrast; see below for contrast details) indicated for
146 each voxel the weighted proportion of input studies that reported a group-difference peak
147 within 15mm of this voxel (=density statistic). Clusters with significantly aberrant GMV or iFC
148 at $p < 0.05$ (FWER-corrected for false-positive results from multiple testing) were then
149 identified using Monte-Carlo simulations (15,000 iterations). Clusters significant both based
150 on density statistic (height-based threshold) and based on cluster size (extent-based
151 threshold) were reported, for these thresholds convey complementary information (2,3).
152 Thus, significant results reflect regional brain clusters in which patient-versus-control

153 differences regarding GMV and network-iFC were reported by a higher proportion of studies
154 than expected by chance (8). The density statistic of each cluster reflects an effect size, i.e.,
155 the higher the density statistic, the more studies reported a peak at this location.

156

157 In particular, we tested for *common* (i.e., observed in all three disorders) and *specific* (i.e.,
158 more pronounced in one than in the other two disorders) changes in MDD, ANX, and CP.

159 1. *GMV- and iFC-changes common to MDD, ANX, and CP*, consisting of two sub-analyses:

160 a. Consistent GMV-increase/decrease and iFC-hyper/hypoconnectivity of one
161 seed-network (within-network-dysconnectivity if the result-cluster overlapped
162 with the seed-network, between-network-dysconnectivity if it overlapped with
163 another seed-network) in MDD, ANX, and CP, respectively, compared to
164 healthy controls (using MKDA-meta-analysis, $p < 0.05$ FWER-corrected).

165 b. GMV-increase/decrease and iFC-hyper/hypoconnectivity common across
166 MDD, ANX, and CP was then identified via conjunction analysis (for details, see
167 **Supplementary Methods - Details of conjunction analyses**): briefly, we
168 computed the intersection between meta-analytic result-maps and adjusted
169 the significance threshold to account for potential noise in meta-analytic p-
170 value estimations. This well-established procedure takes the already FWE-
171 corrected p-values from meta-analyses as input and leads to an even stricter
172 significance threshold than in the original meta-analysis, depending on the
173 input p-values and the number of input contrasts. In this case, the significance
174 threshold of this three-way-conjunction was $p < 0.0015$; details in
175 **Supplementary Methods - Details of conjunction analyses**) (2,9,10).

176 2. *GMV- and iFC-changes specific to MDD, ANX, and CP*, consisting of two sub-analyses:

- 177 a. Pairwise contrasts, e.g., more pronounced iFC-hyperconnectivity in MDD
178 compared to ANX (i.e., MDD>ANX), calculated via MKDA-meta-analysis and
179 subsequent conjunction ($p < 0.005$; details in **Supplementary Methods - Details**
180 **of conjunction analyses**) (9).
- 181 b. Contrasts between one disorder and the other two disorders, e.g., specific iFC-
182 hyperconnectivity in MDD compared to *both* ANX and CP, calculated via
183 conjunction across pairwise contrasts ($p < 0.00005$; details in **Supplementary**
184 **Methods - Details of conjunction analyses**) (2,9).
- 185 3. *Regional overlap between specific GMV-changes and specific iFC-changes*: to
186 investigate whether specific dysconnectivity was associated with specific changes in
187 underlying brain structure, we followed previous work (2) and conjuncted result-maps
188 of specific iFC-changes with result-maps of specific GMV-changes ($p < 3 \times 10^{-9}$ adjusted
189 for four-tailed testing; details in **Supplementary Methods - Details of conjunction**
190 **analyses**) (2,9).

191

192 **4. Details of conjunction analyses**

193 We computed the intersection between meta-analysis results by multiplying the meta-
194 analytic p-value maps (e.g., "MDD>HC", "ANX>HC", and "CP>HC"; HC refers to healthy
195 controls). Subsequently, we determined the voxel-wise significance threshold in a widely-used
196 manner that accounts for potential noise in p-value estimation during individual meta-
197 analyses (9).

198 In detail, the following conjunction analyses were conducted (for clarity, we only describe
199 analyses for GMV-increase/iFC-hyperconnectivity; procedures for GMV-decrease/iFC-

200 hypoconnectivity were identical) – the numbering corresponds to the numbering of analyses
201 in the preceding paragraph:

202 1.b. *Common GMV- and iFC-changes*. First, p-value maps of the meta-analytic contrasts
203 "MDD>HC", "ANX>HC", and "CP>HC" were multiplied. Second, the union of meta-analytic p-
204 values in each voxel was calculated with the following formula (9):

$$205 \quad U = p_{\text{Meta-analysis 1}} + p_{\text{Meta-analysis 2}} - p_{\text{Meta-analysis 1}} \times p_{\text{Meta-analysis 2}}$$

206 As we combined three meta-analytic results, this had to be done in a two-step procedure (9):

$$207 \quad U_{(MDD>HC) \cap (ANX>HC)} = p_{MDD>HC} + p_{ANX>HC} - p_{MDD>HC} \times p_{ANX>HC}$$

$$208 \quad U = U_{(MDD>HC) \cap (ANX>HC)} + p_{CP>HC} - U_{(MDD>HC) \cap (ANX>HC)} \times p_{CP>HC}$$

209 Third, the threshold was adjusted since U statistics might be too conservative (9):

$$210 \quad P = U + (1 - U) \times \ln(1 - U)$$

211 With meta-analytic significance thresholds of p=0.05 as inputs to these calculations, this
212 yielded a conjunction significance threshold of P=0.0015.

213 2.a. *Pairwise contrasts of GMV- and iFC-changes*. When calculating greater hyperconnectivity
214 in MDD than in ANX (i.e., "MDD>ANX"), for example, we first conducted an MKDA meta-
215 analysis for the contrast "(MDD>HC) > (ANX>HC)". Subsequently, we conjuncted the meta-
216 analytic result map with the result map for the contrast "MDD>HC" to restrict pairwise results
217 to 'true' changes in MDD (compared with healthy controls (HC)). Since both result maps used
218 as inputs for the conjunction employed significance thresholds of p=0.05, the procedure
219 specified above resulted in a conjunction significance threshold of P=0.005.

220 2.b. *Specific GMV- and iFC-changes*. When calculating specific hyperconnectivity in MDD (i.e.,
221 "(MDD>ANX) \cap (MDD>CP)"), for example, the hyperconnectivity map "MDD>ANX" was
222 conjuncted with the hyperconnectivity map "MDD>CP". As the significance thresholds of

223 these maps were $p=0.005$ (see above), this gave a conjunction significance threshold of
224 $P=0.00005$.

225 *3. Overlap between specific GMV- and iFC-changes.* To investigate whether specific GMV-
226 changes and specific iFC-changes overlapped, we followed previous work (2) and conjuncted
227 the result maps of specific GMV-changes with the result maps of specific iFC-changes (e.g.,
228 “ $(MDD>ANX) \cap (MDD>CP)$ ”). With input significance thresholds of $p=0.00005$ (see above), this
229 yielded a conjunction significance level of $P=5 \times 10^{-9}$. As this conjunction combined GMV-
230 increase, GMV-decrease, hyperconnectivity, and hypoconnectivity, we had to account for
231 four-tailed testing (9). Therefore, the conjunction significance threshold was further divided
232 by 2, resulting in $P=3 \times 10^{-9}$.

233

234 **5. Details of control analyses**

235 *Jackknife analyses.* We controlled for disproportionate influences of single studies via
236 jackknife analyses: we iteratively left out one study, recalculated the density statistic of each
237 significant cluster of the original analyses (contrasts “disorder vs. HC”), and compared it to the
238 original density statistic (i.e., with all studies) via χ^2 -test (2,11).

239 *Post-hoc analyses for comorbidity and further demographic and clinical variables.* Following
240 an established approach using sub-group analyses (2,3,10), we grouped studies by
241 comorbidity with one or both of the other two disorders, age (<18 years = teen, 18-35 years =
242 young adult, 35-60 years = middle aged, 60 years = senior), gender ($\geq 50\%$ male subjects vs.
243 $< 50\%$ male subjects), and use of medication (yes vs. no) (**Table S3-Table S8**). For each
244 demographic/clinical variable (e.g., age), the density statistic of each significant cluster was
245 recalculated for each sub-group (e.g., young adult) and then compared to the other sub-
246 groups via χ^2 -tests (2,3,10).

247 *Post-hoc analyses for methodological factors.* GMV-studies were grouped by whether or not
248 they had employed modulation during voxel-based morphometry (**Table S3-Table S5**), and
249 iFC-studies were grouped by whether or not they had used global signal regression during
250 fMRI-analysis (**Table S6-Table S8**). For each methodological factor (e.g., modulation), the
251 density statistic of each significant cluster was recalculated separately for each sub-group
252 (e.g., modulation used) and then compared to the other sub-group (e.g., modulation not used)
253 via χ^2 -test (2,3,10).

254 *Post-hoc analyses for posttraumatic stress disorder (PTSD)-studies.* We excluded all PTSD-
255 studies, recalculated the density statistic of each cluster that had been significant in the
256 original analysis of ANX vs. HC (both GMV and iFC), and compared it to the original density
257 statistic (i.e., with all studies) via χ^2 -test (11).

258

259 **6. Control analysis for studies without significant results**

260 Since such an analysis is not feasible within the MKDA framework, we utilized another widely-
261 used toolbox for coordinate-based meta-analysis, namely “Seed-based d-Mapping with
262 Permutation of Subject Images (SDM-PSI)” (12,13). In brief, this method estimates effect sizes
263 of input peaks and performs a meta-analysis to identify effects which are consistent across
264 studies. Significant clusters are then detected via permutation tests (providing family-wise
265 error correction for multiple comparisons) and subsequent threshold-free cluster
266 enhancement (TFCE) statistics. Crucially, the estimation of effect sizes is achieved by
267 MetaNSUE algorithms which allow for the inclusion of studies that did not report any
268 significant peaks.

269 This control analysis was conducted only for GMV – for iFC, there were maximally 2 non-
270 significant studies per disorder, and apart from one study, all employed seeds that were

271 located in seed-networks without significant meta-analytic results. A detailed list of studies
272 with no significant results can be found in **Table S10**. The results of this control analysis were
273 visually compared to the original results (i.e., without non-significant studies) and are shown
274 in **Figure S13**.

275 **Supplementary Results**

276 **1. GMV-changes**

277 **1.1 GMV-changes in MDD, ANX, and CP compared to healthy controls**

278 **Major depressive disorder.** Gray matter volume was increased in the right lateral occipital
279 cortex, mostly located within the default-mode network (DMN) and to a lesser degree within
280 visual (VIS) and dorsal attention network (DAN) (**Figure S2, Table S12**). Decreased GMV was
281 found in the medial and lateral prefrontal cortex, insula, superior temporal gyrus,
282 hippocampus, and striatum. GMV-decreases overlapped with several intrinsic brain networks,
283 but mostly with DMN.

284 **Anxiety disorders.** Increased gray matter volume was found in the right occipital cortex,
285 located mainly within DMN (**Figure S2, Table S12**). GMV was decreased in bilateral
286 hypothalamus, thalamus, striatum (putamen, Ncl. accumbens), and insula (left: whole, right:
287 posterior), right centromedial amygdala, and left hippocampus (anterior and posterior),
288 parahippocampal gyrus, temporal pole, and ventrolateral prefrontal cortex. GMV-decreases
289 lay mostly within the DMN (and to a lesser degree within other networks).

290 **Chronic pain.** Increased GMV was found for bilateral hippocampus (left: whole, right:
291 posterior), parahippocampal gyrus, and Ncl. accumbens, left amygdala (basolateral and
292 centromedial) and putamen, and right cerebellar hemisphere (**Figure S2, Table S12**). GMV-
293 increase was located mostly in DMN and limbic network (LIM). GMV-decrease was observed
294 for right anterior insula, prefrontal cortex, paracingulate gyrus, and frontal pole. GMV-
295 decrease was located mostly in DMN and primary-sensorimotor network (PSM).

296

297 **1.2 Pairwise contrasts of GMV-changes**

298 **Major depressive disorder.** We identified significantly more pronounced GMV-decrease in
299 MDD compared with CP for right parahippocampal gyrus and left superior temporal gyrus
300 (**Figure S3, Table S14**). These clusters were located mostly within DAN.

301 Compared with ANX, distinct GMV-decrease in MDD was found for left premotor cortex,
302 overlapping mainly with LIM, DMN, and frontoparietal network (FPN).

303 **Anxiety disorders.** Significantly more pronounced GMV-decrease in ANX than in CP was found
304 for bilateral temporal pole and right parahippocampal gyrus, overlapping predominantly with
305 DMN (**Figure S3, Table S14**).

306 Pairwise GMV-decrease in ANX compared with MDD was observed for left inferior frontal
307 gyrus, left thalamus, right parahippocampal gyrus, right temporal pole and right amygdala.
308 GMV-decrease was located mainly in DMN, PSM, and SAL.

309 **Chronic pain.** Distinct GMV-decrease in CP compared to MDD was identified for frontal pole,
310 prefrontal cortex, right amygdala and paracingulate gyrus (overlapping mainly with DMN), and
311 distinct GMV-increase for left insula, right putamen, right thalamus, right parahippocampal
312 gyrus and cerebellar hemisphere (located mostly in LIM and DMN) (**Figure S3, Table S14**).

313 Compared to ANX, pairwise GMV-decrease in CP was shown for right insula (overlapping
314 mostly with the salience network (SAL)), as well as GMV-increase in bilateral amygdala, right
315 thalamus and right parahippocampal gyrus (predominantly located in LIM and DMN).

316

317 **2. iFC-changes**

318 **2.1 iFC-changes in MDD, ANX, and CP compared to healthy controls**

319 **Major depressive disorder.** Regarding PSM, iFC with right lateral occipital cortex was
320 enhanced (**Figure S4, Table S16**). Concerning LIM, connectivity with right ventral putamen,
321 amygdala, and anterior insula was decreased. FPN showed decreased iFC with right angular

322 gyrus. For DMN, we found increased connectivity with left precuneus and left dorsolateral
323 prefrontal cortex. In summary, we found mainly hypoconnectivity within FPN, between FPN
324 and DAN and between LIM and SAL, as well as hyperconnectivity between DMN and FPN.

325 **Anxiety disorders.** For LIM, iFC with right angular/supramarginal gyrus, right occipital cortex
326 and right cerebellar hemisphere was enhanced, whereas with right posterior cingulate cortex,
327 connectivity was reduced (**Figure S4, Table S16**). In summary, we found both hyper- and
328 hypoconnectivity of LIM (within itself and with other networks).

329 **Chronic pain.** Concerning PSM, we found decreased iFC with right posterior insula, putamen,
330 superior temporal gyrus, ventroateral prefrontal cortex, and fusiform gyrus (**Figure S4, Table**
331 **S16**). SAL showed hypoconnectivity with bilateral dorsomedial prefrontal cortex, anterior and
332 posterior cingulate cortices, precuneus, and occipital cortex, as well as hyperconnectivity with
333 left pre- and postcentral gyrus and precuneus. LIM showed hypoconnectivity with left medial
334 prefrontal cortex. For FPN, connectivity with left superior temporal gyrus was reduced. In
335 summary, we found mainly hypoconnectivity between SAL and DMN and hyperconnectivity
336 between SAL and PSM.

337

338 **2.2 Pairwise contrasts of iFC-changes**

339 These analyses were conducted for PSM, SAL, LIM, FPN, and DMN, because common GMV-
340 decrease overlapped with these networks and at least three studies per disorder were
341 available for them (**Table S11**).

342 **Major depressive disorder.** For MDD compared to CP, distinct (i.e., more pronounced)
343 hyperconnectivity was shown for PSM in right lateral occipital cortex (**Figure S5, Table S18**).

344 For LIM, hypoconnectivity was observed in right ventral putamen, amygdala and right insula,
345 and for FPN in right angular gyrus. DMN showed hyperconnectivity in left dorsolateral

346 prefrontal cortex. In summary, we found mainly DMN-FPN-hyperconnectivity, within-FPN-
347 hypoconnectivity, LIM-SAL-hypoconnectivity, and FPN-DAN-hypoconnectivity.

348 Compared to ANX, distinct hypoconnectivity in MDD was shown for LIM in right ventral
349 putamen, amygdala, and anterior insula, while for DMN, hyperconnectivity was identified for
350 left dorsolateral prefrontal cortex and left precuneus. In summary, we found mainly DMN-
351 FPN-hyperconnectivity and LIM-SAL-hypoconnectivity.

352 **Anxiety disorders.** We identified significantly more pronounced hyperconnectivity in ANX
353 compared with CP for LIM in right cerebellar hemisphere and right angular/supramarginal
354 gyrus. In summary, we found hyperconnectivity of LIM with several other networks,
355 predominantly with PSM (**Figure S5, Table S18**).

356 Compared with MDD, distinct hyperconnectivity in ANX was found for LIM in right cerebellar
357 hemisphere and right angular/supramarginal gyrus, and LIM-hypoconnectivity in right
358 posterior cingulate cortex. In summary, we found hyper- and hypoconnectivity of LIM with
359 several other networks, mainly with PSM and DMN.

360 **Chronic pain.** Significantly more pronounced hypoconnectivity in CP compared with MDD was
361 found for PSM in right posterior insula, putamen, superior temporal gyrus, and ventrolateral
362 prefrontal cortex (**Figure S5, Table S18**). SAL showed hyperconnectivity in left pre- and
363 postcentral gyrus and hypoconnectivity in bilateral dorsomedial prefrontal cortex, anterior
364 and posterior cingulate cortices, and precuneus. For LIM, hypoconnectivity was observed in
365 left medial prefrontal cortex and for FPN in left superior temporal gyrus. In summary, we
366 found mainly SAL-DMN-hypoconnectivity and SAL-PSM-hyperconnectivity.

367 Compared to ANX, pairwise hypoconnectivity was observed for PSM in right posterior insula,
368 putamen, superior temporal gyrus, ventrolateral prefrontal cortex, and fusiform gyrus, and

369 for SAL in bilateral dorsomedial prefrontal cortex, anterior and posterior cingulate cortices,
370 and precuneus. In summary, we observed mainly SAL-DMN-hypoconnectivity.

371

372 **3. Control analysis: conjunctions of GMV-changes across pairs of disorders**

373 Concerning GMV-increase, we found spatial overlap only between MDD and ANX, which
374 focused on the right parieto-occipital transition (**Figure S6**). For the pairs MDD and CP as well
375 as ANX and CP, there were no overlaps.

376 Concerning GMV-decrease, pairwise results were similar, although larger, to the three-
377 disorder conjunction results reported in the main text. All pairwise results showed rather
378 similar GMV-decrease in left insula and bilateral medial PFC and ACC. Interestingly, in the pair
379 “MDD and ANX”, GMV-decreases in bilateral hippocampus and amygdala were differentially
380 more pronounced (**Figure S7**), in the pair “MDD and CP” in the left ventral striatum (**Figure**
381 **S8**), and in the pair “ANX and CP” in the right insula (**Figure S9**).

382 **Supplementary Discussion**

383 **1. Major depressive disorder**

384 **1.1 GMV-changes compared to healthy controls**

385 Via MKDA meta-analysis, we detected consistent GMV-decrease in medial and lateral
386 prefrontal cortex, insula, superior temporal gyrus, hippocampus, and striatum, as well as
387 GMV-increase in lateral occipital cortex (**Figure S2**). These findings are well in line with
388 previous meta-analyses of GMV-changes in MDD compared to healthy subjects (14-16).

389

390 **1.2 iFC-changes compared to healthy controls**

391 We found mainly within-FPN-hypoconnectivity, LIM-SAL-hypoconnectivity, and DMN-FPN-
392 hyperconnectivity (**Figure S4**). These findings are well compatible with a previous meta-
393 analysis of aberrant network-iFC in MDD (3).

394

395 **2. Anxiety disorders**

396 **2.1 GMV-changes compared to healthy controls**

397 We identified rather localized GMV-increase in occipital cortex and more widespread GMV-
398 decrease in prefrontal, cingulate, insular cortices, and subcortical regions such as striatum,
399 amygdala, hypothalamus, thalamus, and hippocampus (**Figure S2**). These findings are
400 compatible with results from previous meta-analyses of GMV in anxiety disorders (17-19).

401

402 **2.2 iFC-changes compared to healthy controls**

403 We detected both hyper- and hypoconnectivity focused on LIM (within itself and with other
404 networks) (**Figure S4**). LIM-DMN- and LIM-FPN-hypoconnectivity, for example, are in line with
405 a recent meta-analysis of network-iFC in ANX (7).

406

407 **3. Chronic pain**

408 **3.1 GMV-changes compared to healthy controls**

409 GMV-increase was detected in hippocampus, amygdala, striatum, and cerebellum, whereas
410 GMV-decrease focused on prefrontal, cingulate, and insular cortices (**Figure S2**). These results
411 are in line with findings of previous meta-analyses of GMV comparing patients with CP to
412 healthy subjects (20-22).

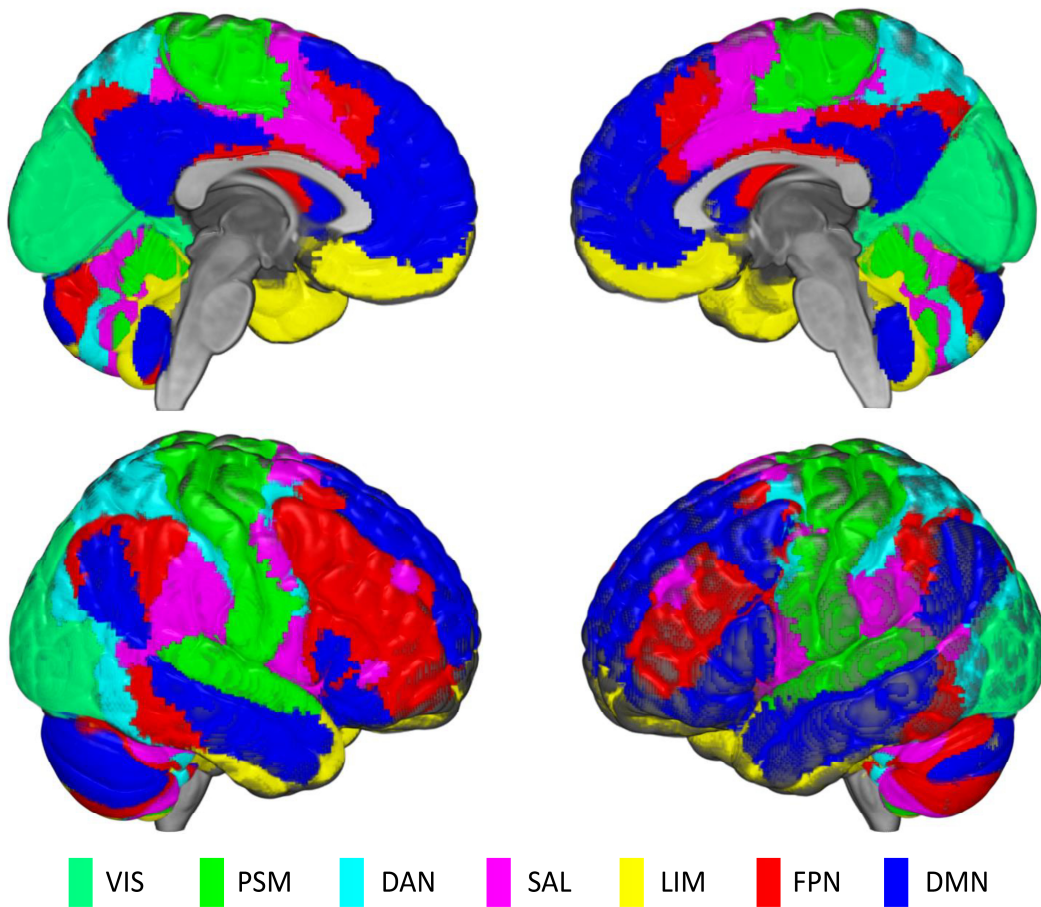
413

414 **3.2 iFC-changes compared to healthy controls**

415 We found mainly hypoconnectivity between SAL and DMN and hyperconnectivity between
416 SAL and PSM (**Figure S4**). To our knowledge, this is the first meta-analysis of network-iFC in
417 CP, so there are no previous results to compare our findings to. However, the identified
418 networks and regions are in line with previous literature reviews of CP, which highlighted
419 aberrant iFC of DMN, SAL, and PSM (23-25).

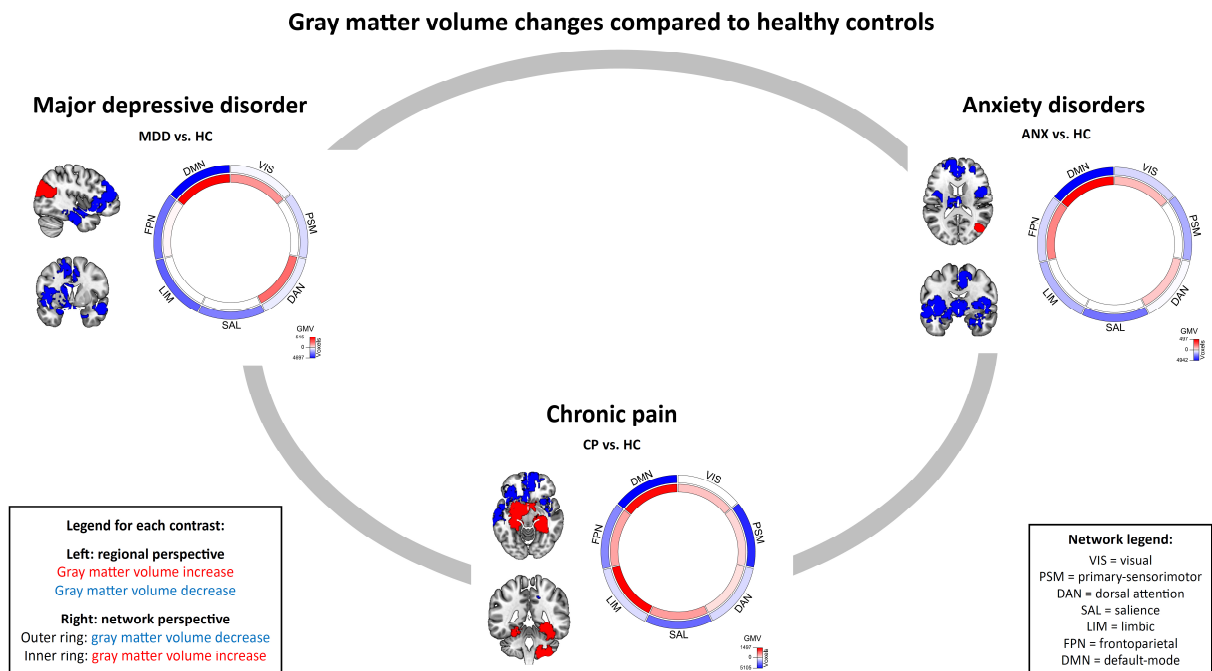
420 **Supplementary Figures**

421 **Figure S1: Intrinsic brain networks used in the analyses.**



424 **Figure S1:** Intrinsic brain networks derived from a clustering approach on iFC-data of 1000
425 healthy subjects, covering cortex, striatum, and cerebellum (4-6). DAN = dorsal attention
426 network, DMN = default-mode network, FPN = frontoparietal network, LIM = limbic network,
427 PSM = primary-sensorimotor network, SAL = salience network, VIS = visual network.

428 **Figure S2: Gray matter volume changes compared to healthy controls.**

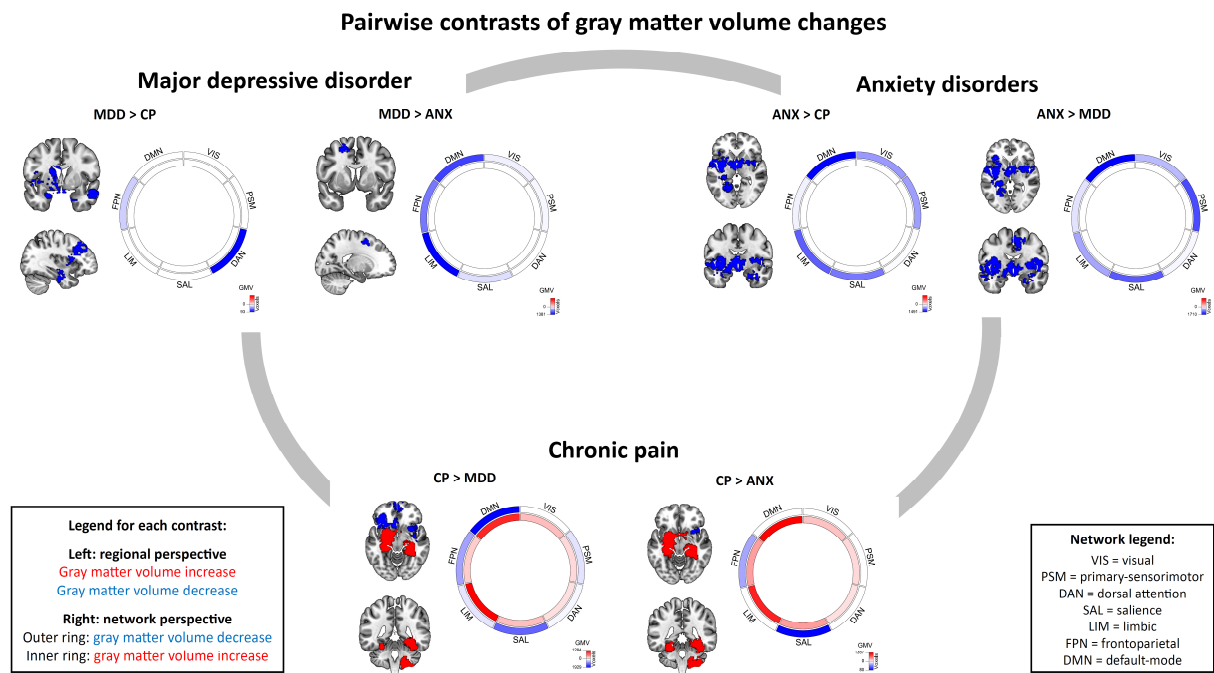


429

430

431 **Figure S2:** Gray matter volume changes were calculated by MKDA meta-analysis ($p < 0.05$
 432 FWER-corrected, height-based and extent-based threshold combined). For each contrast,
 433 meta-analytic regional result clusters are shown on the left. Their overlap with intrinsic brain
 434 networks (4-6) is displayed on the right: GMV-decrease is shown in the outer ring, GMV-
 435 increase in the inner ring of each diagram; color intensity reflects the size of spatial overlap
 436 (the more voxels, the stronger the color – a colorscale is added to each plot). ANX = anxiety
 437 disorder, CP = chronic pain, HC = healthy controls, MDD = major depressive disorder.

438 **Figure S3: Pairwise contrasts of gray matter volume changes.**

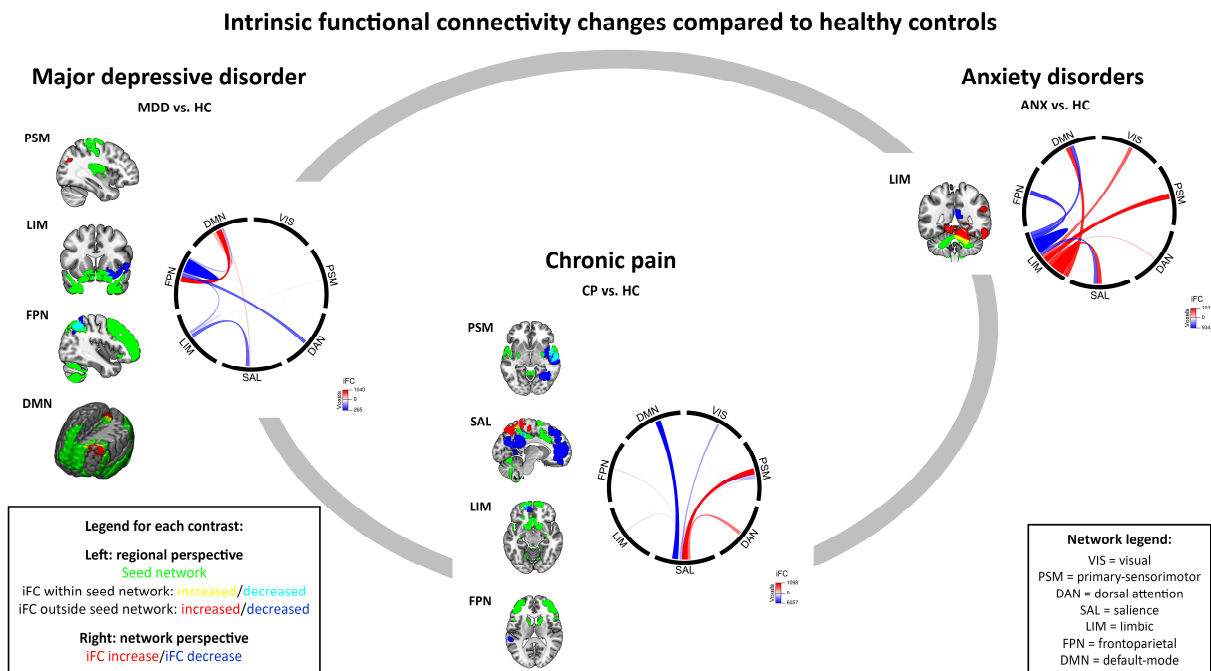


439

440

441 **Figure S3:** Pairwise contrasts of gray matter volume changes were calculated via MKDA meta-
 442 analytic contrasts between disorders (e.g., “MDD>ANX”) and subsequent conjunction with the
 443 contrast vs. healthy controls (e.g., “MDD>HC”) to restrict pairwise results to ‘true’ changes in
 444 each disorder compared with healthy subjects ($p < 0.005$). For each contrast, meta-analytic
 445 regional result clusters are shown on the left. Their overlap with intrinsic brain networks (4–6)
 446 is displayed on the right: GMV-decrease is shown in the outer ring, GMV-increase in the inner
 447 ring of each diagram; color intensity reflects the size of spatial overlap (the more voxels, the
 448 stronger the color – a colorscale is added to each plot). ANX = anxiety disorder, CP = chronic
 449 pain, HC = healthy controls, MDD = major depressive disorder.

450 **Figure S4: Intrinsic functional connectivity changes compared to healthy controls.**

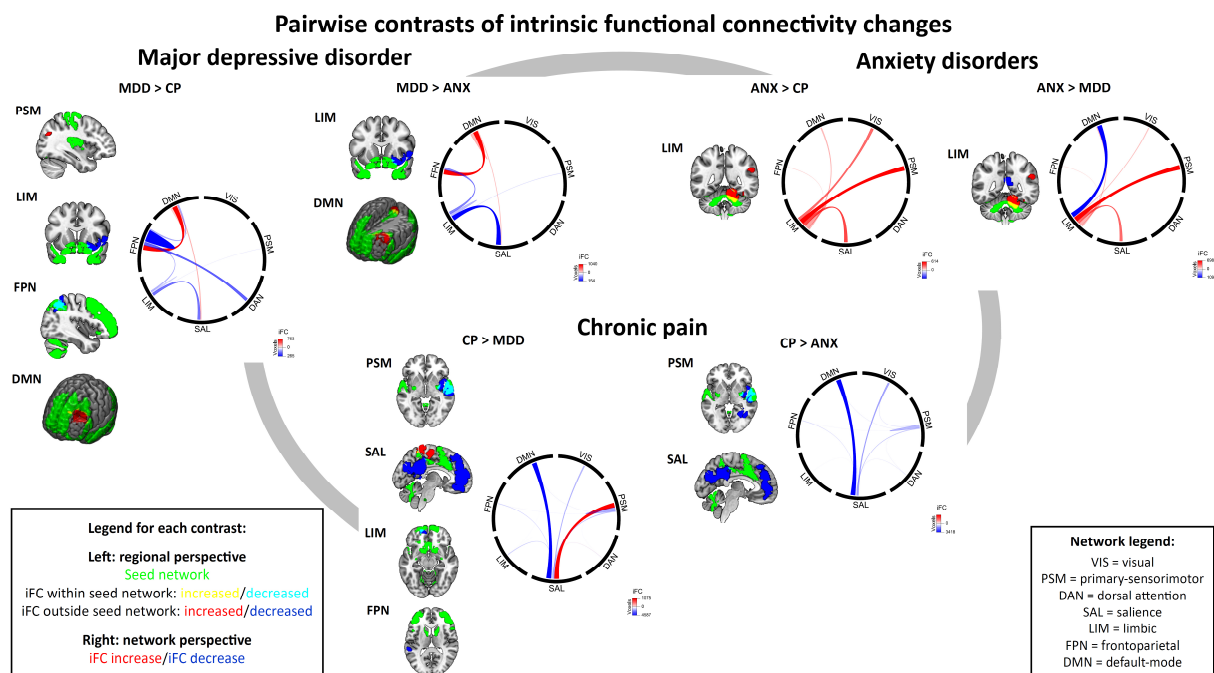


451

452

453 **Figure S4:** Intrinsic functional connectivity changes were calculated by MKDA meta-analysis
 454 ($p < 0.05$ FWER-corrected, height-based and extent-based threshold combined). For each
 455 contrast, meta-analytic regional result clusters are shown on the left. Their overlap with
 456 intrinsic brain networks (4-6) is displayed on the right in a “chord diagram” (26): between-
 457 network connectivity is shown as links, within-network connectivity as “hills”; both color
 458 intensity and link thickness reflect the size of spatial overlap (the more voxels, the stronger
 459 the color and the thicker the link – a colorscale is added to each plot). ANX = anxiety disorder,
 460 CP = chronic pain, HC = healthy controls, iFC = intrinsic functional connectivity, MDD = major
 461 depressive disorder.

462 **Figure S5: Pairwise contrasts of intrinsic functional connectivity changes.**



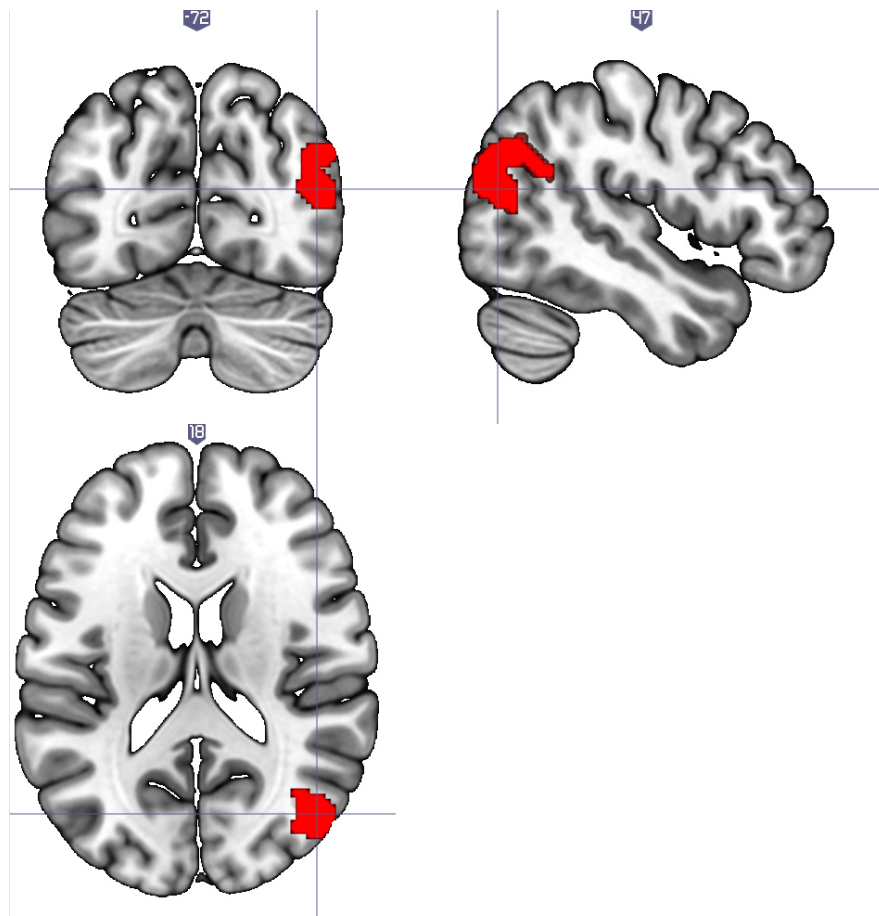
463

464

465 **Figure S5:** Pairwise contrasts of intrinsic functional connectivity changes were calculated via
 466 MKDA meta-analytic contrasts between disorders (e.g., “MDD>ANX”) and subsequent
 467 conjunction with the contrast vs. healthy controls (e.g., “MDD>HC”) to restrict pairwise results
 468 to ‘true’ changes in each disorder compared with healthy subjects (p<0.005). For each
 469 contrast, meta-analytic regional result clusters are shown on the left. Their overlap with
 470 intrinsic brain networks (4-6) is displayed on the right in a “chord diagram” (26): between-
 471 network connectivity is shown as links, within-network connectivity as “hills”; both color
 472 intensity and link thickness reflect the size of spatial overlap (the more voxels, the stronger
 473 the color and the thicker the link – a colorscale is added to each plot). ANX = anxiety disorder,
 474 CP = chronic pain, HC = healthy controls, iFC = intrinsic functional connectivity, MDD = major
 475 depressive disorder.

476 **Figure S6: Spatial overlap between GMV-increase “MDD vs. HC” and “ANX vs. HC”.**

477

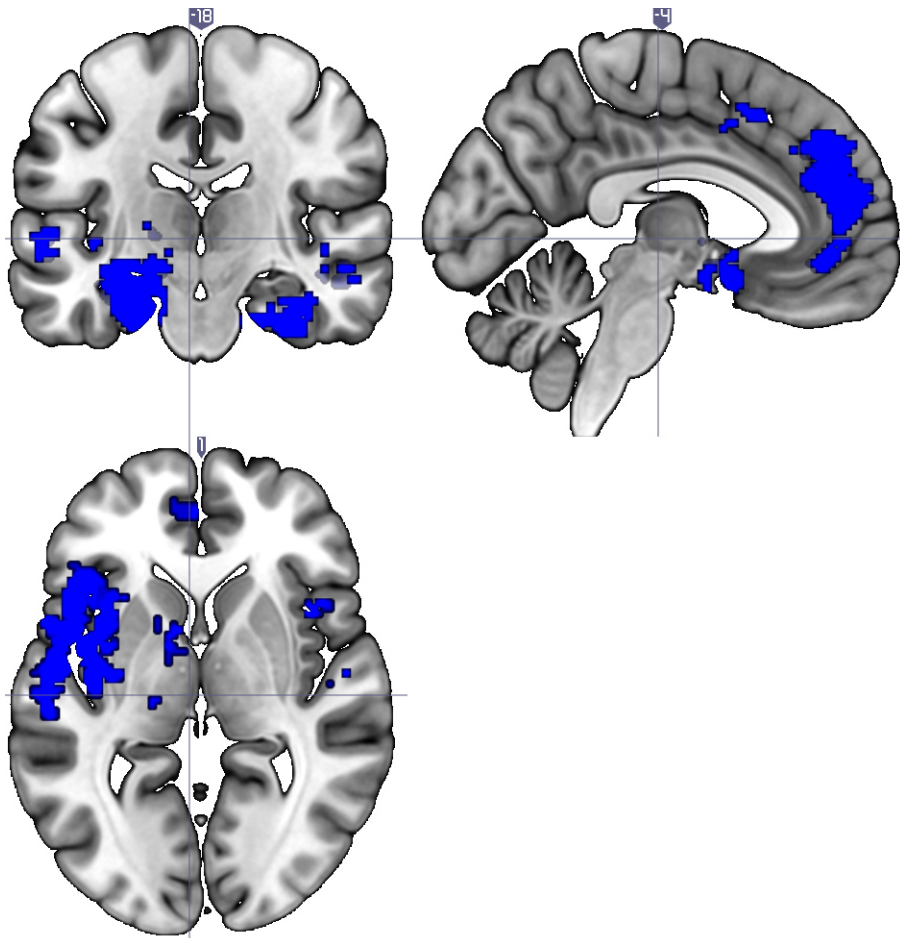


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479

480 **Figure S7: Spatial overlap between GMV-decrease “MDD vs. HC” and “ANX vs. HC”.**

481

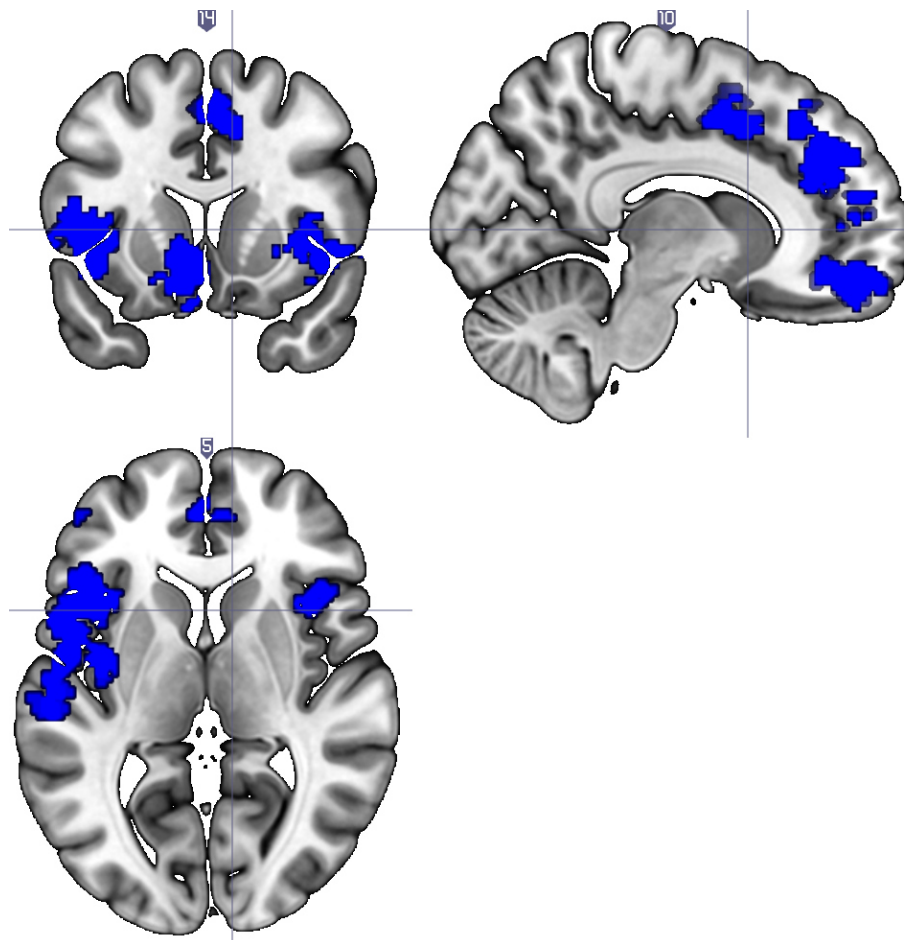


482

483

484 **Figure S8: Spatial overlap between GMV-decrease “MDD vs. HC” and “CP vs. HC”.**

485

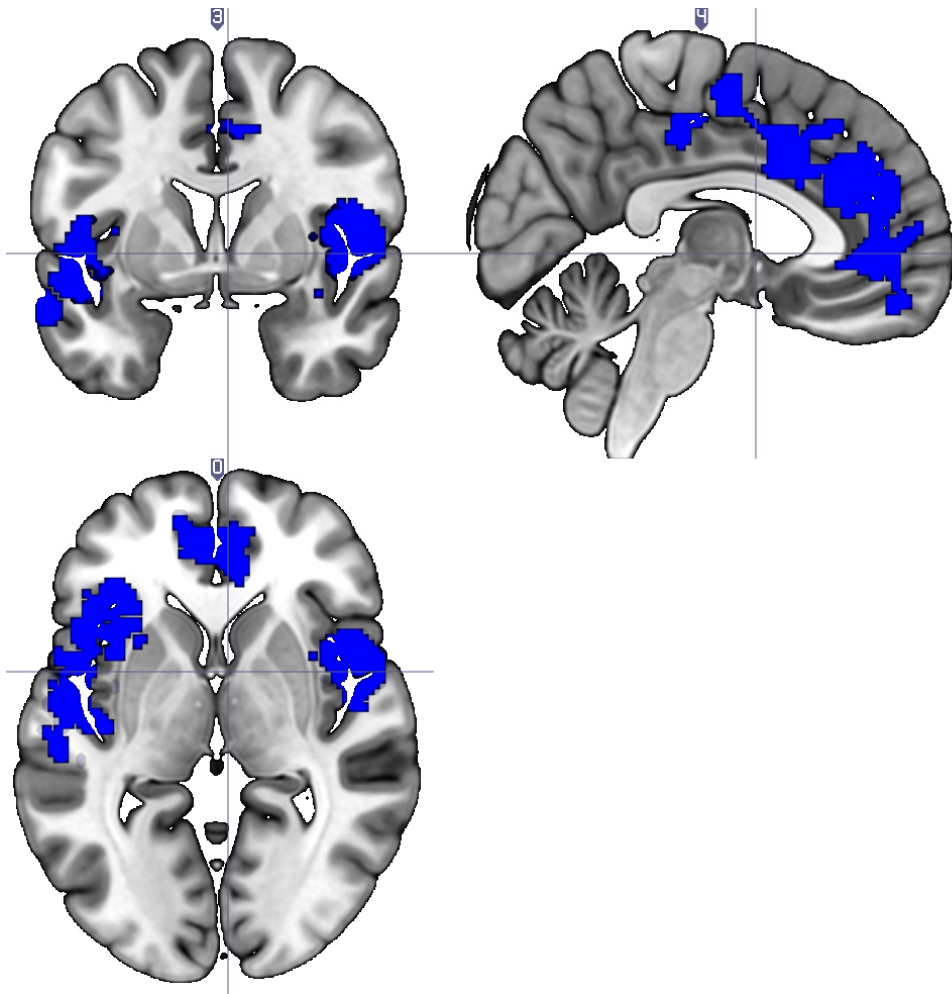


486

487

488 **Figure S9: Spatial overlap between GMV-decrease “ANX vs. HC” and “CP vs. HC”.**

489

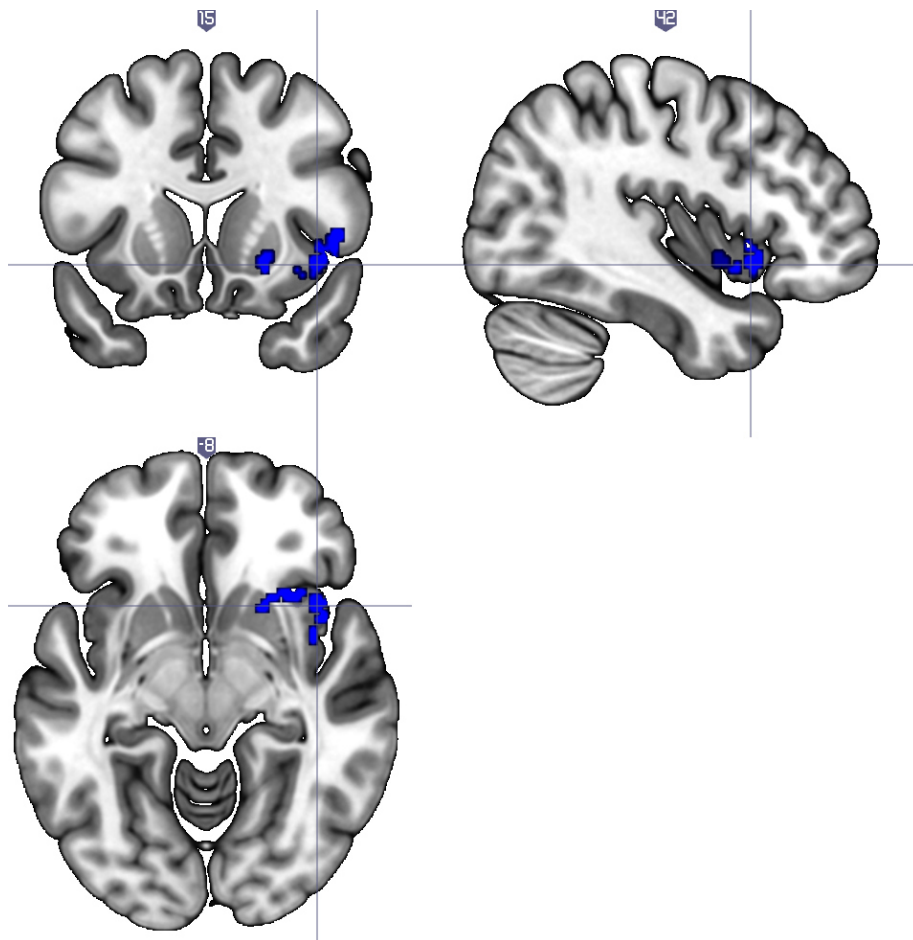


490

491

492 **Figure S10: Spatial overlap between LIM-hypoconnectivity “MDD vs. HC” and “ANX vs. HC”.**

493

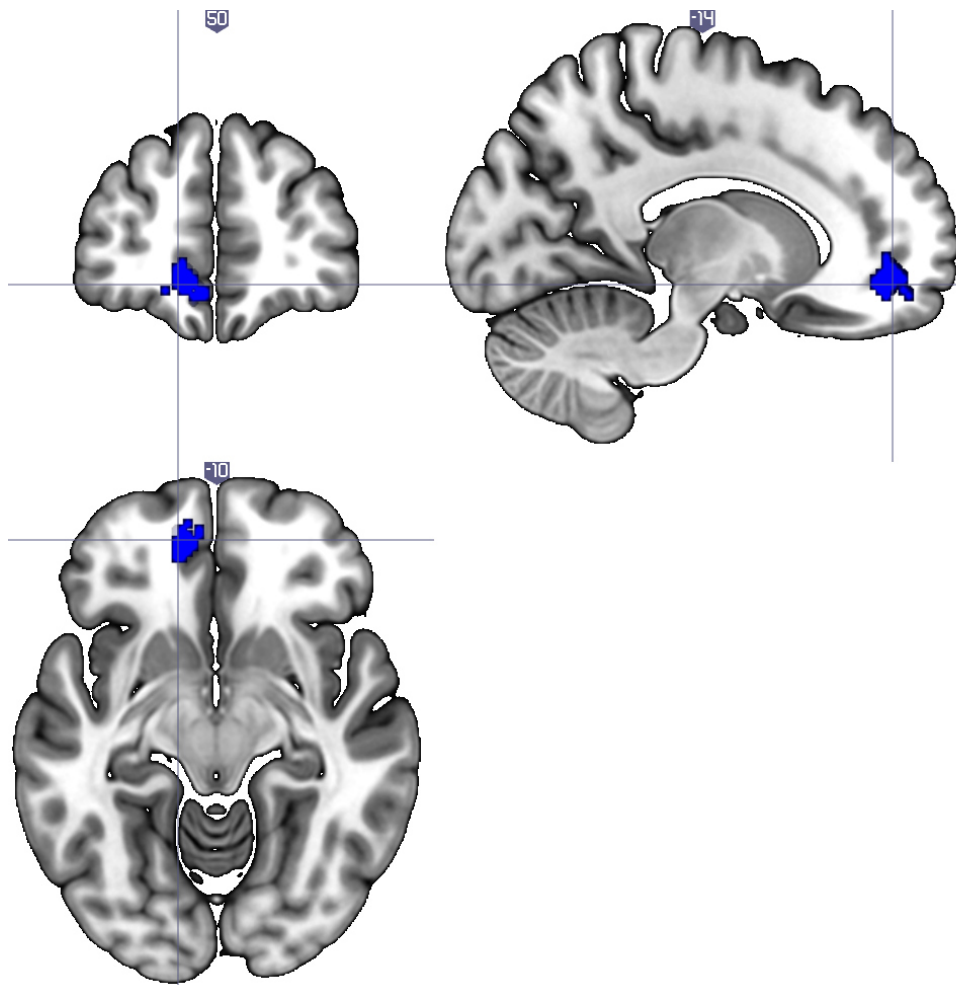


494

495

496 **Figure S11: Spatial overlap between LIM-hypoconnectivity “ANX vs. HC” and “CP vs. HC”.**

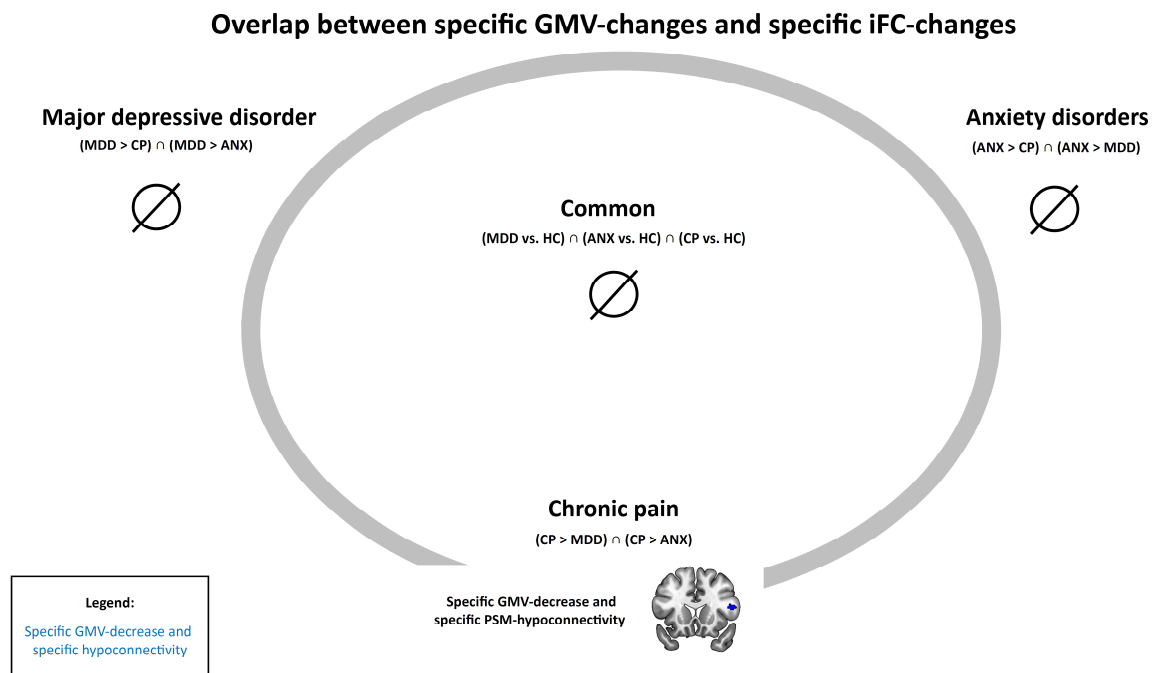
497



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499

500 **Figure S12: Regional overlap between specific GMV-changes and specific iFC-changes.**

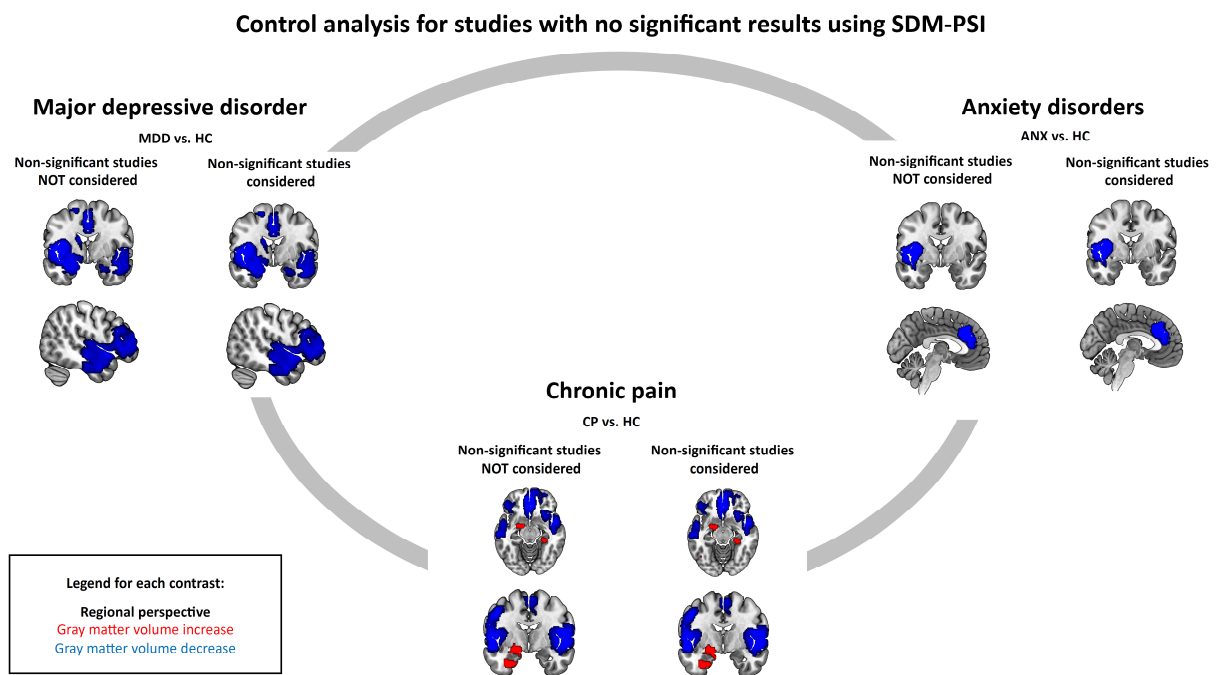


501

502

503 **Figure S12:** Overlap between result maps for specific GMV-changes (see **Figure 2** in the main
504 text) and specific iFC-changes (see **Figure 3** in the main text) calculated by inter-modality
505 conjunction analysis ($p < 3 \times 10^{-9}$).

506 **Figure S13: Control analysis for studies with no significant results.**



507

508

509 **Figure S13:** Results were calculated via “Seed-based d-Mapping with Permutation of Subject
510 Images (SDM-PSI)” (12,13) and are significant at $p < 0.05$ FWER-corrected (TFCE-based). On the
511 left of each panel, we present results for the same study sample as in the main analysis to
512 show the good comparability between MKDA and SDM-PSI toolboxes. On the right of each
513 panel, we show the results additionally including all studies with no significant peak effects
514 (**Table S10**), which are virtually identical to the results without these studies.

515

516 **Supplementary Tables**517 **Table S1: Search criteria and included studies.**

Disorder	Search terms	published until	Included studies (n)	Controls (n)	Patients (n)
Gray matter volume meta-analysis					
Major depressive disorder	("VBM" OR "voxel-based morphometry") AND depress*	July 01, 2019	63	3284	2934
Anxiety disorders	("VBM" OR "voxel-based morphometry") AND (anxiety disorder OR phobi* OR social anxiety OR posttraumatic OR panic)	July 01, 2019	41	1130	1021
Chronic pain	("VBM" OR "voxel-based morphometry") AND pain	July 01, 2019	65	2358	2185
Total			<i>169</i>	<i>6772</i>	<i>6140</i>
Intrinsic functional connectivity meta-analysis					
Major depressive disorder	(rest* OR intrinsic) AND connect* AND seed* AND depress*	July 01, 2019	68	2141	2314
Anxiety disorders	(rest* OR intrinsic) AND connect* AND seed* AND (anxiety disorder OR phobi* OR social anxiety OR posttraumatic OR panic)	July 01, 2019	41	1108	1248
Chronic pain	(rest* OR intrinsic) AND connect* AND seed* AND pain	January 01, 2020	42	1114	1229
Total			<i>151</i>	<i>4363</i>	<i>4791</i>

518

Table S2: MOOSE checklist for meta-analyses of observational studies.

Reporting criteria	Reported on page No.
Reporting of background should include	
Problem definition	7
Hypothesis statement	8
Description of study outcome(s)	8
Type of exposure or intervention used	8
Type of study designs used	7
Study population	7
Reporting of search strategy should include	
Qualifications of searchers (eg, librarians and investigators)	Supplement
Search strategy, including time period included in the synthesis and key words	9
Effort to include all available studies, including contact with authors	Supplement
Databases and registries searched	9
Search software used, name and version, including special features used (eg, explosion)	9
Use of hand searching (eg, reference lists of obtained articles)	Supplement
List of citations located and those excluded, including justification	Supplement
Method of addressing articles published in languages other than English	9
Method of handling abstracts and unpublished studies	Supplement
Description of any contact with authors	Supplement
Reporting of methods should include	
Description of relevance or appropriateness of studies assembled for assessing the hypothesis to be tested	Supplement
Rationale for the selection and coding of data (eg, sound clinical principles or convenience)	Supplement
Documentation of how data were classified and coded (eg, multiple raters, blinding and interrater reliability)	Supplement
Assessment of confounding (eg, comparability of cases and controls in studies where appropriate)	Supplement
Assessment of study quality, including blinding of quality assessors, stratification or regression on possible predictors of study results	Supplement
Assessment of heterogeneity	Supplement
Description of statistical methods (eg, complete description of fixed or random effects models, justification of whether the chosen models account for predictors of study results, dose-response models, or cumulative meta-analysis) in sufficient detail to be replicated	9-11, Supplement
Provision of appropriate tables and graphics	Figure 1, Table S1
Reporting of results should include	
Graphic summarizing individual study estimates and overall estimate	Figures 2-4
Table giving descriptive information for each study included	Table S3-Table S8
Results of sensitivity testing (eg, subgroup analysis)	16
Indication of statistical uncertainty of findings	Table S12-Table S20
Reporting of discussion should include	
Quantitative assessment of bias (eg, publication bias)	17, 22-24
Justification for exclusion (eg, exclusion of non-English language citations)	22-24
Assessment of quality of included studies	22-24
Reporting of conclusions should include	

Consideration of alternative explanations for observed results	18-19
Generalization of the conclusions (ie, appropriate for the data presented and within the domain of the literature review)	18-19
Guidelines for future research	18-19
Disclosure of funding source	25

520

521 **Table S2.** Based on Stroup et al., 2000 (1).

Table S3: Demographic and clinical characteristics of major depressive disorder studies included in the GMV meta-analysis.

Author, year	HC (n)	Male (%)	Mean age HC [years]	MDD (n)	Male (%)	Mean age MDD [years]	Illness duration	Medication	Modulation during VBM	Comorbidity
Ahn et al., 2016 (27)	26	27	31.4±7.6	34	15	32.5±7.95	-	-	no	no
Amico et al., 2011 (28) without a family history of depression	64	56	30.4±8.3	33	58	32.0±8.0	3.4±5.0 years	yes	yes	no
with a family history of depression	30	57	30.7±8.0	33	58	32.0±8.0	3.4±5.0 years	yes	yes	no
Arnone et al., 2013 (29)	66	30	32.1±9.3	39	27	36.3±8.8	-	no	yes	no
Cai et al., 2015 (30)	23	57	28.2±3.8	23	57	30.0±7.3	4,35±2.38 years	no	yes	no
Chen et al., 2016 (31)	28	50	33±11.7	27	48	33±10.8	79±86 months	no	no	no
Cheng et al., 2010 (32)	68	31	28.94±7.82	68	31	29.91±7.92	10.98±8.2 months	no	yes	no
Depping et al., 2015 (33)	22	0	31.4±11.2	22	0	33.5±8.9	5.5±4.7 years	yes	yes	no
Egger et al., 2008 (34)	20	35	72.3±7.77	14	29	71.4±7.49	-	yes	yes	no
Fang et al., 2015 (35)	18	56	59.1±7.5	20	60	59.2±3.7	3.6±1.1 years	-	no	not mentioned
Frodl et al., 2008 (36)	77	7	40.5±11.6	77	55	42.6±12.4	5.4±8.2 years	yes	yes	no
Grieve et al., 2013 (37)	34	53	31.5±12.4	102	47	33.8±13.1	11.3±11.8 years	-	yes	not mentioned
Guo et al., 2014 (38)	44	45	29.39±6.6	44	50	27.52±8.57	19.61±36.50 months	no	no	no
Harada et al., 2016 (39)	61	28	62.9±7.6	45	42	60.2±8.2	10.6±11 years	yes	no	SAD (n=1), PD (n=1)
Hwang et al., 2010 (40)	26	100	79.5±4.3	70	100	79.4±5.3	-	-	yes	not mentioned
Igata et al., 2017 (41)	44	73	41.2±11.6	27	56	45.8±12.7	-	no	yes	no
Kim et al., 2008 (42)	25	0	35.3±11.25	22	0	38.5±9.7	17.4±10.01 years	yes	no	not mentioned
Klauser et al., 2015 (43)	33	36	34.71±9.93	27	33	35.02±9.72	9.04±6.52 years	yes	yes	no
Kong et al., 2014 (44)	28	50	32.07±9.27	28	39	34.42±8.24	2.11±0.9 months	no	yes	no
Lai et al., 2010 (45)	15	27	34.3±9.87	16	31	37.91±8.76	17.5±8.98 weeks	no	yes	no
Lai et al., 2014 (46)	27	44	38.29±11.80	38	47	36.57±5.46	4.68±1.50 months	no	yes	no
Lai et al., 2015 (47)	54	46	40.38±10.51	53	47	40.07±8.99	5.03±1.62 months	no	yes	no
Lan et al., 2016 (48)	27	44	39.2±16.7	27	33	41.5±16.0	-	yes	yes	not mentioned
Lee et al., 2011 (49)	51	10	45.7±8.04	47	11	46.0±9.1	46.7±76 months	yes	no	not mentioned
Leung et al., 2009 (50)	17	0	45.8±9.8	17	0	45.5±8.5	84±49.1 months	yes	yes	not mentioned
Machino et al., 2014 (51)	29	55	38.66±8.36	29	55	39.57±8.29	52.55±57.81 months	yes	yes	no

Matsubara et al., 2016 (52)	27	37	48.3±13.0	34	35	48.65±12.95	49.5±65.1 months	yes	no	no
Matsuo et al., 2017 (53)	909	35	40.5±14.05	639	49	41.75±13.9	7.37±7.47 years	yes	no	PD (n=28), GAD (n=39), specific phobia (n=21), other ANX (n=35)
Modinos et al., 2014 (54)	46	69	25.3±4.3	23	13	44.6±5.5	-	-	no	not mentioned
Nakano et al., 2014 (55)	54	50	45.4±16.1	36	39	49.0±11.4	66.7±80.9 months	yes	no	no
Opel et al., 2016 (56)	20	50	36.3±12.1	20	50	37.9±10.9	139.4±100 months	yes	yes	not mentioned
Ozalay et al., 2016 (57)	24	0	47.3±5.6	24	0	46.2±3.9	13.3±8 months	yes	yes	no
Peng et al., 2011 (58)	30	37	45.9±9.0	22	36	46.7±8.9	8.6±6.5 months	yes	no	no
Peng et al., 2014 (59) without suicide history	28	54	28.61±5.45	18	33	31.06±7.39	-	yes	yes	no
with suicide history	28	54	28.61±5.45	20	35	27.75±7.21	-	yes	yes	no
Qi et al., 2014 (60) without anxiety disorder	28	54	28.61±5.45	18	39	31.06±7.39	-	no	yes	no
with anxiety disorder	28	54	28.61±5.45	20	55	28.65±8.18	-	no	yes	ANX (n=20)
Qiu et al., 2016 (61)	15	33	33.7±9.9	12	33	34.4±10.1	-	no	yes	no
Redlich et al., 2014 (62)	58	36	37.7±9.7	58	38	37.6±10.8	131.7±107.3 months	yes	yes	PD (n=12), social phobia (n=10), GAD (n=15), specific phobia (n=3), PTSD (n=8)
Ries et al., 2009 (63)	32	44	68.4±7.4	15	33	66.3±5.3	-	no	no	no
Salvadore et al., 2011 (64) chronic MDD	107	44	36.2±10.3	58	36	38.8±11.1	18.4±10.5 years	no	yes	no
currently-remitted MDD	107	44	36.2±10.3	27	22	40.2±12.2	15.1±12.2 years	no	yes	no
Scheuerecker et al., 2010 (65)	15	67	35.5±10.9	13	77	37.9±10.1	52.3±71.5 months	no	no	no
Serra-Blasco et al., 2013 (66)	32	28	46±8.3	22	18	49±8	-	yes	yes	no
Shad et al., 2012 (67)	22	55	16.0±2.1	22	50	15.0±2.1	-	no	yes	ANX (n=2)
Shah et al., 1998 (68)	20	65	49.3±11.8	20	65	48.9±9.8	263±133 weeks	yes	no	no

Shen et al., 2016 (69)	130	38	30.09±7.03	147	34	30.58±7.41	early onset 9.02±7.30 months / late onset 7.98±7.66 months	no	yes	no
Soriano-Mas et al., 2011 (70)	40	43	59.23±7.09	70	41	61.56±9.68	10.45±10.08 years	yes	yes	no
Sprengelmeyer et al., 2011 (71)	21	43	42.0±12.9	17	47	45.6±12.3	-	yes	yes	not mentioned
Stratmann et al., 2014 (72)	132	44	37.82±11.42	132	42	37.86±11.87	first episode: 14.66±15.73 months / recurrent episodes: 121.75±109.64 months	yes	yes	ANX (n=41)
Ueda et al., 2016 (73)	48	73	41.2±11.4	30	57	44.3±13.0	-	no	yes	no
van Tol et al., 2010 (74)	65	37	40.54±9.71	68	35	37.16±10.24	-	yes	yes	ANX (n=21)
Vasic et al., 2008 (75)	14	57	31.4±9.6	15	60	37.4±8.5	43.4±37.3 months	yes	yes	no
Vasic et al., 2015 (76)	29	38	34.5±10.7	43	40	37.1±10.9	7.2±7.1 years	yes	yes	no
Wagner et al., 2008 (77)	16	17	38.8±9.1	15	17	41.4±9.2	high risk patients: 8.9±9.4 years/ no-high risk: 3±3.2 years	-	no	no
Wagner et al., 2011 (78)	30	0	37.5±11.5	30	0	35.1±11.4	7.5±7.6 years	no	no	no
Wang et al., 2012 (79)	18	50	35±12	18	50	34±13	5±4 months	no	yes	no
Wang et al., 2014 (80)	10	0	29.8±7.5	13	0	30.9±9.1	-	no	yes	no
Wang et al., 2016 (81)	35	54	33.28±8.83	25	56	32.11±11.25	0.7±0.2 years	-	yes	no
Watanabe et al., 2015 (82)	45	73	41.05±11.15	29	55	45.5±12.7	-	no	yes	no
Wehry et al., 2015 (83)	41	34	13±2	14	21	14±3	-	-	yes	no
Yang et al., 2015 (84)	51	39	31.14±9.3	51	39	30.98±9.5	9.71±12.5 months	no	yes	no
Yang et al., 2017 (85)	23	0	39.09±14.35	35	0	44.54±11.15	32.17±45.02 months	no	yes	no
Yuan et al., 2008 (86)	16	50	67.7±3.8	19	47	67.1±7.2	3.7±2.4 years	yes	yes	no
Zhang et al., 2012 (87)	32	53	21.03±1.47	33	52	20.52±1.72	-	no	yes	no
Zhao et al., 2017 (88)	41	63	27.1±7.2	37	68	26.7±7.1	2.0±0.5 years	no	no	no
Zou et al., 2010 (89)	23	43	36.6±12.9	23	43	31.1±10.4	7.6±4.4 months	no	yes	no

524 **Table S3.** ANX = anxiety disorder, GAD = generalized anxiety disorder, GMV = gray matter volume, HC = healthy controls, MDD = major depressive
525 disorder, PD = panic disorder, PTSD = posttraumatic stress disorder, SAD = social anxiety disorder, VBM = voxel-based morphometry.

526 **Table S4: Demographic and clinical characteristics of anxiety disorder studies included in the GMV meta-analysis.**

Author, year	HC (n)	Male (%)	Mean age HC [years]	ANX (n)	Male (%)	Mean age ANX [years]	Type of ANX	Illness duration	Medication	Modulation during VBM	Comorbidity
Ahmed et al., 2012 (90)	32	47	14.49±2.23	21	52	16.17±1.68	PTSD	-	no	yes	MDD (n=8)
Asami et al., 2009 (91)	24	38	36.25±8	24	38	36.3±9.8	PD	3.9±3.4 years	yes	yes	MDD (n=3)
Bossini et al., 2017 (92)	18	79	41±6	19	53	40±9	PTSD	-	no	yes	no
Carrion et al. 2009 (93)	24	58	11±2.73	24	58	11±2.24	PTSD	-	no	yes	MDD (n=4)
Chen et al., 2006 (94)	12	33	33.25±5.27	12	33	34.56±4.91	PTSD	-	no	no	no
Chen et al., 2012 (95)	20	-	37.6±7.0	10	-	40.8±6.8	Recent onset PTSD	-	no	yes	no
Cheng et al., 2015 (96)	30	70	26.2±6.6	30	70	26.3±8.1	PTSD	12.5±2.7 months	no	no	no
Corbo et al., 2005 (97)	14	43	33.29±12.31	14	43	33.36±12.06	PTSD	-	no	no	MDD (n=7)
Frick et al., 2014 (98)	29	45	23.7±2.0	48	50	33.8±9.3	SAD	-	no	yes	MDD (n=3)
Gold et al., 2016 (99)	53	45	13,8±2,5	39	51	12,7±3,1	ANX	-	no	yes	no
Hakamata et al., 2007 (100)	70	0	46.0±6.9	14	0	45.6±6.2	PTSD	-	no	yes	MDD (n=7)
Herringa et al., 2012 (101)	15	93	30.1±6.3	13	85	28.9±4.2	PTSD	-	no	yes	no
Hilbert et al., 2015 (102)	24	29	32.25±9.33	19	16	33.47±8.90	GAD	-	no	yes	MDD (n=12)
Irle et al., 2014 (103)	64	52	32±10	67	48	31±10	SAD	15±9 years	yes	yes	MDD (n=16)
Kasai et al., 2008 (104)	23	-	51.8±2.3	18	-	52.8±3.4	PTSD	-	no	no	MDD (n=2)
Lai et al., 2012 (105)	21	48	41.14±11.81	30	37	47.03±10.63	late-onset PD	-	no	yes	no
Lai et al., 2015 (47)	54	46	40.38±10.51	53	47	43.283±10.11	PD	5.35±2.37 months	no	yes	no
Liao et al., 2013 (106)	25	52	16.71±0.22	26	50	16.83±0.22	GAD	-	no	yes	no
Makovac et al., 2015 (107)	19	16	29.2±9.8	19	16	30±6.9	GAD	16.78±8.01 years	yes	yes	no
Meng et al., 2013 (108)	19	68	21.58±3.72	20	70	21.80±3.68	SAD	50.50±45.82 months	no	no	no
Moon et al., 2014 (109)	22	59	33.4±9.7	22	59	37.0±10.7	GAD	4.5±6.6 years	no	yes	not mentioned
Moon et al., 2015 (110)	17	65	35.6±6.1	17	65	37.4±11.7	GAD	4.7±7.3 years	yes	yes	MDD (n=17)
Moon et al., 2017 (111)	20	65	35.0±9.3	20	65	36.9±11.3	GAD	4.3±6.8 years	yes	yes	not mentioned
Na et al., 2013 (112) with agoraphobia	22	50	40.18±12.38	12	42	43.08±9.63	PD with agoraphobia	-	-	yes	no
without agoraphobia	22	50	40.18±12.38	10	80	36.70±11.63	PD	-	-	yes	no
Nardo et al., 2010 (113)	22	73	40.8±8.9	21	71	41.7±9.4	PTSD	2.5±1.6 years	-	no	no
Nardo et al., 2013 (114)	17	65	41.59±9.04	15	80	43.33±8.35	PTSD	-	no	yes	no

O'Doherty et al., 2017 (115)	25	48	31.7±6.0	25	48	34.0±8.4	PTSD	4.61±2.57 years	yes	yes	no
Rocha-Rego et al., 2012 (116)	16	44	44.9±6.60	16	44	43.3±5.78	PTSD	3.0±4.8 years	-	yes	no
Schienze et al., 2011 (117)	15	0	23.7±3.7	16	0	22.9±4.1	GAD	3.1±4.7 years	no	yes	not mentioned
Strawn et al., 2013 (118)	28	39	13±2	15	47	13±2	GAD	-	no	yes	no
Strawn et al., 2015 (119)	27	44	14.8±3.9	38	26	14.4±3.0	GAD	-	no	yes	no
Sui et al., 2010 (120) healthy comparison	12	0	26.42±3.45	11	0	25.55±4.01	PTSD	-	no	no	no
victims of rape – non PTSD	8	0	27.50±4.00	11	0	25.55±4.01	PTSD	-	no	-	no
Talati et al., 2013 (121) SAD	37	55	31.4±9.1	33	19	31.5	SAD	-	yes	yes	MDD (n=11)
PD	20	55	31.4±7.8	16	19	34.1	PD	-	yes	-	MDD (n=3)
Tavanti et al., 2012 (122)	25	32	38.08±11.01	25	32	38.16±10.90	PTSD	7.36±8.62 years	no	yes	no
Thomaes et al., 2010 (123)	30	0	35.2±12.3	33	0	35.3±9.8	PTSD	-	yes	yes	MDD (n=21)
Tükel et al., 2015 (124)	27	44	27.70±5.83	27	44	27.70±6.67	SAD	13.76±6.99 years	no	yes	no
van Tol et al., 2010 (74)	65	37	40.54±9.71	68	26	35.96±9.45	ANX	-	yes	yes	MDD (n=37)
Yamasue et al., 2003 (125)	16	63	44.4±14	9	56	44.6±16	PTSD	-	yes	no	MDD (n=1)
Yoo et al., 2005 (126)	18	61	32.0±5.8	18	50	33.3±7.1	PD	3.6±2.2 years	no	yes	no
Zhang et al., 2011 (127)	10	100	34.40±5.37	10	100	40.8±6.83	PTSD	-	no	yes	no
Zhao et al., 2017 (88)	41	63	27.1±7.2	24	63	24.5±4.0	SAD	7.6±3.8 years	no	yes	no

527

528 **Table S4.** ANX = anxiety disorder, GAD = generalized anxiety disorder, GMV = gray matter volume, HC = healthy controls, MDD = major depressive

529 disorder, PD = panic disorder, PTSD = posttraumatic stress disorder, SAD = social anxiety disorder, SP = specific phobia, VBM = voxel-based

530 morphometry.

531 **Table S5: Demographic and clinical characteristics of chronic pain studies included in the GMV meta-analysis.**

Author, year	HC (n)	Male (%)	Mean age HC [years]	CP (n)	Male (%)	Mean age CP [years]	Type of chronic pain	Illness duration	Medication	Modulation during VBM	Comorbidity
Absinta et al., 2012 (128)	19	63	42	15	87	44	Cluster headache	10 years	no	yes	no
Apkarian et al., 2004 (129)	26	-	43.6	26	-	43.7	Chronic back pain	8.6 years	yes	no	no
Arkink et al., 2016 (130) Chronic cluster headache	48	37	47±12	23	83	48±9	Cluster headache	14±9 years	yes	yes	not mentioned
Probable cluster headache	48	37	47±12	14	43	50±10	Cluster headache	19±10 years	yes	yes	not mentioned
Chronic paroxysmal hemicrania	48	37	47±12	9	33	48±9	Chronic paroxysmal hemicrania	15±7 years	yes	yes	not mentioned
Migraine with aura	48	37	47±12	14	7	47±9	Migraine with aura	28±10 years	yes	yes	not mentioned
Episodic cluster headache	48	37	47±12	24	83	45±9	Cluster headache	16±12 years	yes	yes	not mentioned
Migraine without aura	48	37	47±12	19	5	47±8	Migraine without aura	29±15 years	yes	yes	not mentioned
As-Sanie et al., 2012 (131) endometriosis-associated	26	0	25.9±1.6	17	0	26.1±1.5	Chronic pelvic pain	5.5 years	-	yes	no
without endometriosis	26	0	24.8±1.2	6	0	24.2±1.9	Chronic pelvic pain	3.75 years	-	yes	no
Baliki et al., 2011 (132) CBP	46	43	38.77±12.5	36	64	48.20±11.38	Chronic back pain	12.3 years	yes	no	no
CRPS	46	43	38.77±12.5	28	14	40.57±7.4	CRPS	3.16 years	yes	no	no
OA	46	43	38.77±12.5	20	80	53.50±7.4	Knee osteoarthritis	11.6 years	yes	no	no
Barad et al., 2014 (133)	15	0	44.1	15	0	44.0	CRPS	2-206 months	yes	no	no
Bishop et al., 2017 (134)	31	42	44.12±13.15	74	19	45.7±13.03	Musculoskeletal pain	11±9.15 years	no	yes	no

Burgmer et al., 2009 (135)	14	0	46.9±6.8	14	0	51.0±7.3	Fibromyalgia	10±6 years	yes	yes	no
Buckalew et al., 2008 (136)	8	63	69.9±3.9	8	50	74.5±4.2	Chronic low back pain	-	no	no	no
Ceko et al., 2013 (137) older subjects	13	0	55.4±3.7	14	0	55.0±2.9	Fibromyalgia	12.1±9.0 years	yes	yes	no
younger subjects	15	0	43.1±5.3	14	0	42.4±5.9	Fibromyalgia	8.8±7.1 years	yes	yes	no
Davis et al., 2008 (138)	11	36	24-50	9	33	30-58	Irritable bowel syndrome	-	no	yes	no
Diaz-Piedra et al., 2016(139)	23	0	39.7±5.4	23	0	41.6±4.4	Fibromyalgia	102.6±75.9 months	yes	no	no
Fallon et al., 2013 (140)	15	0	39.4±8.7	16	0	38.5±8.45	Fibromyalgia	9.1±6.8 years	yes	yes	no
Fritz et al., 2016 (141)	432	57	48.92±13.96	111	30	53.12±11.77	Chronic back pain	-	yes	yes	no
Geha et al., 2008 (142)	22	-	40.5±2.3	22	14	40.7±2.3	CRPS	3.57 years	yes	yes	MDD (n=1)
Gerstner et al., 2011 (143)	9	0	24.8±1.4	9	0	25.4±2.5	Myofascial-type TMD	2.5±2.1 years	yes	yes	no
Gustin et al., 2011 (144)	30	20	53.6±3.2	21	19	54.7±2.1	Trigeminal neuropathic pain	8.5±2.1 years	yes	yes	not mentioned
Gwilym et al., 2010 (145)	16	50	68	16	50	68	Primary hip osteoarthritis	-	no	yes	no
Holle et al., 2011 (146)	14	36	65.7	14	36	65.9	Hypnic headache	-	no	no	no
Ivo et al., 2013 (147)	14	43	54	14	43	54	Chronic low back pain	10 years	-	yes	MDD (n=7)
Keltner et al., 2017 (148)	169	81	43±8	64	78	46±8	Distal neuropathic pain	-	-	yes	MDD (n=21)
Kim et al., 2008 (149)	33	12	33.8±10.5	20	15	33.7±11.3	Episodic migraine	9.8±6.0 years	yes	yes	no
Kuchinad et al., 2007 (150)	10	0	45	10	0	52	Fibromyalgia	62.6±31.9 months (homozygotes), 72.9±37.6 months (met carriers)	no	no	no
Lewis et al., 2018 (151)	18	39	71±8	29	52	68±10	Knee osteoarthritis	-	no	yes	no

Li et al., 2018 (152)	16	100	31.3±11	16	75	41.6±13.6	Chronic low back pain	10.2±9.8 years	no	yes	no
Liao et al., 2018 (153)	30	13	55.2±5.7	30	13	56.5±6.8	Knee osteoarthritis	7.3±5.1 years	yes	yes	no
Liu et al., 2015 (154)	111	0	21.3±0.9	135	0	21.7±2.1	Migraine without aura	62.6±31.9 months (homozygotes), 72.9±37.6 months (met carriers)	no	yes	no
Liu et al., 2017 (155)	50	-	22.6±0.2	80	-	22.8±0.3	Migraine without aura	59.8±4.7 months	no	yes	no
Luchtman et al., 2014 (156)	12	-	43.9±12.9	12	-	43.9±12.9	Chronic low back pain	-	-	yes	not mentioned
Marciszewski et al., 2017 (157)	57	25	28.3±1.3	25	16	30.2±2.0	Migraine	14.6±2.2 years	yes	yes	no
Martikainen et al., 2013 (158)	16	50	36±11	16	50	38±11	Chronic nonspecific back pain	5.0±3.8 years	no	yes	no
Mehnert et al., 2017 (159)	54	17	32.6±11.5	54	17	34.3±11.9	Migraine	18.1±12.3 years	-	yes	not mentioned
Mole et al., 2014 (160)	18	-	-	30	-	52.775	Spinal cord injury with neuropathic pain	11.1 years	-	no	no
Naegel et al., 2014 (161)	78	72	42.78±11.44	91	78	45.52±10.61	Cluster headache	14.42±9.39 years	yes	yes	no
Neeb et al., 2017 (162) episodic migraine	21	29	49.40±7.79	21	29	49.36±7.62	Chronic migraine	24.43±8.3 years	yes	yes	no
chronic migraine	21	29	49.40±7.79	21	29	49.04±7.46	Episodic migraine	26.71±14.42 years	yes	-	no
Obermann et al., 2013 (163)	49	43	61.8±9	60	40	62±13.2	Trigeminal neuralgia	8.3±6.7 years	yes	yes	no
Obermann et al., 2014 (164)	17	18	42.17±9.26	17	18	42.71±10.05	Vestibular migraine	6.17±4.51 years	yes	yes	no
Pleger et al., 2014 (165)	20	45	41.6±9.6	20	45	41.8±9.8	CRPS	-	-	yes	not mentioned
Pomares et al., 2017 (166)	25	0	61±7.6	26	0	61±5.4	Fibromyalgia	16±9 years	no	yes	no

Riederer et al., 2012 (167)	29	24	41.7±12.7	29	24	41.4±12.7	Medication overuse headache	15.14±11.0 years	yes	yes	no
Rocca et al., 2006 (168)	15	13	38.6	16	6	42.7	Migraine	24.8 years	yes	yes	no
Rocca et al., 2014 (169)	15	47	13.3	12	50	14.2	Episodic migraine	3.7 years	yes	yes	no
Rodriguez-Raecke et al., 2009 (170)	32	41	63.9±8.8	32	41	66.8±9.0	Unilateral primary hip osteoarthritis	7.35 years	yes	yes	MDD (n=3)
Ruscheweyh et al., 2011 (171)	31	61	63±9	45	36	66±7	Ongoing chronic pain	264±193 months	yes	no	no
Russell et al., 2018 (172)	11	18	59±7.4	28	14	62±7.7	Hand osteoarthritis	-	yes	no	no
Schmidt-Wilcke et al., 2006 (173)	18	50	49.9±8.7	18	50	50.4±6.8	Chronic back pain	176±87.6 months	yes	no	no
Schmidt-Wilcke et al., 2007 (174)	22	9	50.7±7.3	20	5	53.6±7.7	Fibromyalgia	173±86.5 months	yes	yes	not mentioned
Schmidt-Wilcke et al., 2008 (175)	31	0	32.3±12.6	35	9	32.4±9.2	Migraine	-	yes	no	no
Schmidt-Wilcke et al., 2010 (176)	11	18	51.3±8.6	11	18	52.2±8.9	Persistent idiopathic facial pain	58.3 months	-	yes	not mentioned
Schmitz et al., 2008 (177)	28	0	42.50±9.31	28	0	43.5±8.21	Migraine	30.5±11.43 years	no	no	no
Seminowicz et al., 2010 (178)	48	0	31.1±12.3	55	0	32.2±12.3	Irritable bowel syndrome	11.1±7.7 years	no	no	MDD (n=3), ANX (n=6)
Shokouhi et al., 2017 (179)	16	31	44.4±11.6	12	17	51.1±12.7	CRPS	5.9±2.9 months	no	no	no
Tu et al., 2010 (180)	32	0	23.81±2.80	32	0	23.84±2.99	Primary dysmenorrhea	10.19±3.25 years	no	yes	no
Valet et al., 2009 (181)	25	0	51.7±7.2	14	0	51.1±11.1	Chronic pain	9.8±7.2 years	no	no	MDD (n=7)
Valfrè et al., 2008 (182)	27	26	34.9±8.6	27	22	34.9±8.4	Migraine	20.6±8.9 years	-	yes	not mentioned
Vartiainen et al., 2009 (183)	28	36	32	8	13	47	Chronic widespread unilateral pain	-	-	no	not mentioned
Wang et al., 2017 (184)	40	42	55.89±8.06	41	42	55.87±8.38	Trigeminal neuralgia	7.05±5.32 years	yes	yes	no

Wilcox et al., 2015 a (185)	40	18	48.3±2.1	22	18	46.5±2.6	TMD	9.7 years	yes	yes	no
Wilcox et al., 2015 b (186)	42	19	48.6±2.0	21	19	48.7±1.7	Trigeminal neuropathy	5.5 years	yes	yes	not mentioned
Wood et al., 2009 (187)	20	0	40.05±10.01	30	0	42.03±8.43	Fibromyalgia	-	no	no	no
Yang et al., 2013 (188)	49	78	35.2±9.7	49	78	35.7±9.2	Cluster headache	8.6±6.9 years	yes	yes	no
Yoon et al., 2013 (189)	10	60	39.5±8.6	10	70	39.5±8.6	Chronic neuropathic pain	1.5 years	-	yes	no
Younger et al., 2010 (190)	15	0	38±13.7	15	0	38±13.7	Myofascial-type TMD	4.4±2.9 years	yes	no	no
Zhang et al., 2017 (191)	32	25	38.8±10.02	32	25	38.3±10.16	Migraine without aura	9.5±6.23 years	no	yes	no
Zhang et al., 2018 (192)	34	38	43.32±10.07	29	34	48.14±11.89	Trigeminal neuralgia	6.02±4.35 years	yes	yes	no

532

533 **Table S5.** CP = chronic pain, CRPS = complex regional pain syndrome, GMV = gray matter volume, HC = healthy controls, MDD = major depressive
534 disorder, OA = osteoarthritis, TMD = temporomandibular disorders, VBM = voxel-based morphometry.

Table S6: Demographic and clinical characteristics of major depressive disorder studies included in the iFC meta-analysis.

Author, year	HC (n)	Male (%)	Mean age HC [years]	MDD (n)	Male (%)	Mean age MDD [years]	Illness duration	Symptom severity	Medicated	Global signal regression	Comorbidity
Alalade et al., 2011 (193)	18	39	71.2	11	39	64.9	31,3 years	MADRS: 17.5	yes	yes	no
Alexopoulos et al., 2012 (194)	10	-	68.8	16	-	69	-	MADRS: 23.5	no	no	no
Andreescu et al., 2013 (195)	46	28	72.89	47	28	68.72	20,09 years	HAM-D: 19.06	no	no	no
Avery et al., 2014 (196)	20	40	33	20	35	36	61 months	HAM-D: 23.1	no	no	PTSD (n=3), social phobia (n=4), PD (n=1), simple phobia (n=1)
Bai et al., 2018 (197)	57	39	36.68	50	34	38.68		HAM-D: 22.78	yes	yes	no
Berman et al., 2011 (198)	15	33	23	15	33	25.7	-	BDI: 30	yes	no	not mentioned
Bessette et al., 2018 (199)	35	40	21.45	47	28	22.16	2,72 years	HAM-D: 1.64	no	no	Comorbid anxiety disorder
Cao et al., 2012 (200)	32	53	26.09	42	43	29.15	13,11 years	HAM-D: 23.60	no	no	no
Chen et al., 2018 (201)	47	21	29.70	36	56	30.70	32,1 months	HAM-D: 28.0	no	no	no
Connolly et al., 2013 (202)	45	38	16.1	30	37	16	-	BDI: 27.3	no	no	GAD (n=12), specific phobia (n=2), other anxiety disorder (n=1), PTSD (n=2)
Connolly et al., 2017 (203)	53	38	16.1	48	40	16.1	-	RADS: 64.7	no	no	GAD (n=12), specific phobia (n=4), other anxiety disorder (n=1), PTSD (n=5)
Crowther et al., 2015 (204)	20	30	31.1	23	22	33.09	32,96 months	BDI: 26.04	no	no	no
Cullen et al., 2014 (205)	29	24	16.0	41	22	15.7	10 months	BDI: 29	no	no	GAD (n=16), PTSD (n=2), SAD (n=3), PD (n=2), specific phobia (n=3), social phobia (n=4)
Davey et al., 2012 (206)	20	40	19.9	18	33	18.9	10,5 months	BDI: 35.4	yes	yes	ANX (n=6)
DelDonno et al., 2017 (207)	28	50	21	42	24	21	-	HAM-D: 4.17	no	yes	Comorbid anxiety disorder
Deng et al., 2016 (208)	29	52	26.76	29	31	28.69	-	SDS: 62.72	no	no	no

de Kwaasteniet et al., 2015 (209)	18	44	51.5	17	47	52.5	20,3 years	HAM-D: 21.8	yes	no	no
Ellard et al., 2018 (210)	39	51	25.9	35	63	42.77	-	HAM-D: 16.82	yes	yes	ANX (n=29)
Evans et al., 2018 (211)	25	40	33	33	39	36	20 years	-	no	no	not mentioned
Furman et al., 2011 (212)	19	0	33.2	21	0	39.2	-	BDI: 31.3	yes	yes	PD (n=2), PTSD (n=2), SAD (n=5)
Gabbay et al., 2013 (213)	21	43	16.3	21	43	17.1	13,6 months	BDI: 25.3	no	yes	Anxiety disorder (n=10), GAD (n=8)
Gandelman et al., 2018 (214)	21	57	68.3	79	66	66.3	-	MADRS: 27.3	yes	no	no
Gong et al., 2017 (215)	42	55	41.31	75	44	40.41	-	HAM-D: 1.1	no	yes	no
Guo et al., 2013 a, b (216) treatment-resistant depression	19	53	24.37	23	48	27.35	27,43 months	HAM-D: 24.52	no	yes	no
treatment-sensitive depression	19	53	24.37	22	55	28.09	2,95 months	HAM-D: 25.89	no	yes	no
Guo et al., 2013 c, d (217)	24	58	24.04	24	54	25.58	4,96 months	HAM-D: 25.75	no	no	no
Guo et al., 2015 a, b (218)	44	45	29.39	44	50	27.52	19,61 months	HAM-D: 25.18	no	no	no
Jacobs et al., 2016 (219)	26	46	21.15	51	29	21.49	5,23 years	HAM-D: 7.78	no	no	ANX (n=27)
Kenny et al., 2010 (220)	17	65	75.7	16	50	76.4	29 years	MADRS: 7.1	yes	no	not mentioned
Kerestes et al., 2015 (221)	21	48	19.2	21	48	19.3	-	MADRS: 33.7	no	no	no
Kim et al., 2016 (222)	20	70	14.5	22	64	13.9	-	CDI: 40.0	no	no	no
Li et al., 2015 (223)	26	42	71.19	22	18	68.14	35,19 years	GDS: 16.36	yes	no	no
Liu et al., 2018 (224)	40	45	64.68	27	37	67.33	-	HAM-D: 31.78	-	no	no
Lois et al., 2016 (225)	25	32	42.52	25	28	42.82	12,4 years	HAM-D: 0.88	yes	no	no
Lui et al., 2011 (226) nonrefractory depression	48	65	35	32	66	32	22 months	HAM-D: 23.0	no	no	no
refractory depression	48	65	35	28	64	33	193 months	HAM-D: 23.2	no	no	no
Ma et al., 2012 (227) treatment-resistant depression	17	59	24.24	18	61	27.39	35,5 months	HAM-D: 23.89	yes	yes	no
treatment-sensitive depression	17	59	24.24	17	59	26.71	2,59 months	HAM-D: 25.58	no	yes	no
Pannekoek et al., 2014 (228)	26	12	14.7	26	12	15.4	-	CDI: 18.6	no	yes	ANX (n=18)
Peng et al., 2015 (229)	16	44	33.75	16	44	34.43	8,01 weeks	HAM-D: 30.88	no	yes	no

Peng et al., 2018 (230)	19	47	33.89	19	47	33.58	-	HAM-D: 24.89	no	yes	no
Penner et al., 2016 (231)	24	50	23.8	24	33	21.2	13,5 months	MADRS: 22.7	yes	no	no
Peters et al., 2016 (232)	10	30	15.8	23	43	15.61	-	RADS: 60.48	yes	no	ANX (n=8)
Philippi et al., 2018 (233)	30	0	27.1	34	0	27.9	24,2 months	BDI: 19.5	no	no	ANX (n=24)
Poeppel et al. 2016 (234)	76	47	37.34	72	47	38.43	12,31 years	BDI: 22.75	yes	no	Anxiety disorder (n=10), PTSD (n=1)
Rao et al., 2016 (235)	23	48	21.1	34	26	21.1	5,3 years	HAM-D: 2.4	no	no	not mentioned
Renner et al., 2017 (236)	18	28	42.67	18	28	41.17	-	BDI: 30.5	yes	yes	no
Sawaya et al., 2015 (237)	21	19	38.33	21	19	37.29	<24 months	HAM-D: 23.29	no	yes	no
Scheinost et al., 2018 (238)	20	40	32.6	17	29	34.3	10,2 years	MADRS: 24.1	no	no	Comorbid anxiety disorder
Schilbach et al., 2016 (239)	106	48	36.99	102	48	37.75	10,63 years	-	yes	no	not mentioned
Sheline et al., 2010 (240)	17	29	30.9	18	61	35.9	-	HAM-D: 20.2	no	no	no
Shu et al., 2014 (241)	29	45	71.41	31	35	68.13	<5 years	-	no	yes	no
Späti et al., 2015 (242)	35	43	32.7	21	52	36.6	-	BDI: 26.4	no	no	ANX (n=8)
Straub et al., 2015 (243)	19	21	16.35	19	21	16.76	-	CDRS-R: >36	-	yes	Social phobia (n=4), specific phobia (n=1)
Tadayonnejad et al., 2016 (244)	20	35	31.8	19	37	27.4	-	HAM-D: 19.1	no	no	not mentioned
Tahmasian et al., 2013 (245)	20	45	49.6	21	48	51.0	14,7 years	HAM-D: 23.8	yes	yes	GAD (n=6)
van Tol et al., 2014 (246)	20	37	33.75	20	35	38.25	57,2 months	HAM-D: 15.5	yes	yes	no
Wang et al., 2018 (247)	139	47	30.32	93	43	29.74	33.4 months	HAM-D24: 25.13	no	yes	ANX (n=35)
Workman et al., 2016 (248)	38	34	36.2	63	35	36.4	13,9 years	BDI: 3.6	no	no	PD with agoraphobia (n=1), PTSD (n=1)
Workman et al., 2017 (249) recurring episode	38	34	36.2	17	35	35.9	16,4 years	BDI: 5.2	no	no	PD with agoraphobia (n=1)
Resilient	38	34	36.2	30	40	37.6	17,4 years	BDI: 2.6	no	no	no
Wu H et al., 2016 (250)	34	44	29.71	34	40	29.88	53,41 months	HAM-D: 32.91	yes	no	no
Wu X et al., 2016 (251)	19	47	33.47	19	41	33.47	-	HAM-D: 24.89	no	yes	no
Yang et al., 2016 a (85)	23	0	39.09	35	0	44.54	32.17 months	HAM-D: 28.29	no	no	no
Yang et al., 2016 b (252)	19	42	33.8	19	42	33.3	-	HAM-D: 15.8	-	yes	no
Yang et al., 2017 (253)	36	47	29.08	40	53	28.75	6.16 months	BDI: 32.1	no	yes	no
Ye et al., 2012 (254)	30	36	45.9	22	36	46.7	8,6 months	HAM-D: 18.5	yes	no	no

Ye et al., 2017 (255) young-adult	35	49	24.8	34	50	24.15	-	HAM-D: 23.5	no	no	no
old-adult	46	22	37.22	35	26	37.14	-	HAM-D: 23.69	no	no	no
Yin et al., 2015 a (256)	39	49	65.40	32	34	67.17	-	HAM-D: 30.83	no	yes	no
Yin et al., 2015 b (257)	33	42	65.21	26	31	67.39	-	HAM-D: 30.18	no	yes	no
Yuan et al., 2014 (258)	27	19	36	27	19	36.56	-	HAM-D: 22.11	no	no	no
Zhang et al., 2015 (259) deficiency syndrome	20	15	47.75	24	4	48.42	-	HAM-D: 26.71	no	no	no
excess syndrome	20	15	47.75	21	29	41.9	-	HAM-D: 27.86	no	no	no

536

537 **Table S6.** ANX = anxiety disorder, BDI = Beck Depression Inventory, CDI = Children's Depression Inventory, CRDS-R = Children's Depression Rating

538 Scale Revised, GAD = generalized anxiety disorder, GDS = Geriatric Depression Scale, HAM-D = Hamilton Depression Rating Scale, HC = healthy

539 controls, iFC = intrinsic functional connectivity, MADRS = Montgomery-Asberg Depression Rating Scale, MDD = Major depressive disorder, PD =

540 panic disorder, PTSD = posttraumatic stress disorder, RADS = Reynolds Adolescent Depression Scale, SDS = Self-rating depression scale.

Table S7: Demographic and clinical characteristics of anxiety disorder studies included in the iFC meta-analysis.

Reference	HC (n)	Male (%)	Mean age HC [years]	ANX (n)	Male (%)	Mean age ANX [years]	Type of ANX	Illness duration	Symptom severity	Medicated	Global signal regression	Comorbidity
Aghajani et al., 2016 (260)	23	9	15.52	19	11	16.16	PTSD	5.23 years	TSCC: 50.93	yes	no	MDD (n=7)
Andreescu et al., 2014 (261)	31	42	52.18	24	21	49.54	GAD	9.5 years	HARS: 20.9	no	no	MDD (n=5)
Arnold Anteraper et al., 2014 (262)	17	47	25	17	47	24.7	SAD	-	LSAS: 77.9	no	no	MDD (n=4)
Birn et al., 2014 (263)	14	29	10.2	14	29	9.9	ANX	-	-	yes	no	MDD (n=3)
Bluhm et al., 2009 (264)	15	0	38	17	0	39	PTSD	-	CAPS: 76.9	yes	no	MDD (n=6), dysthymic disorder (n=1), depression disorder not otherwise specified (n=1)
Brown et al., 2014 (265)	22	73	44.0	20	80	44.1	PTSD	-	CAPS: 66.4	yes	no	MDD (n=9)
Chen et al., 2018 (266) trauma-exposed control	33	21	48.5	27	26	48.4	PTSD	-	CAPS: 78.2	no	no	no
healthy control	30	23	49.9	27	26	48.4	PTSD	-	CAPS: 78.2	no	no	no
Cui et al., 2017 (267)	20	70	21.65	21	74	22.05	SAD	43.81 months	LSAS: 53.9	no	no	no
Dodhia et al., 2014 (268)	18	100	29.89	18	100	29.39	GSAD	-	LSAS: 81.67	no	no	no
Dorfman et al., 2016 (269)	36	42	13	35	40	13.2	ANX	-	-	no	no	no
Geiger et al., 2016 (270)	15	47	28.47	18	39	29.56	SAD	20.5 years	LSAS: 88.6	no	no	no
Hahn et al., 2011 (271)	27	41	27.7	10	90	28.6	SAD	-	STAI: 42.1	no	no	no
Hamm et al., 2014 (272)	23	43	14.6	33	33	13.9	GAD + SP	-	PARS: 22	no	yes	no
Harricharan et al., 2016 (273) non-dissociative subtype	40	35	35.0	60	42	37.8	PTSD	-	CAPS: 67.9	no	no	MDD (n=11)
dissociative subtype	40	35	35.0	37	22	40.4	PTSD	-	CAPS: 81.6	no	no	MDD (n=23)
Harricharan et al., 2017 (274) non-dissociative subtype	40	35	35.0	60	42	37.8	PTSD	-	CAPS: 67.9	yes	no	MDD (n=11)
dissociative subtype	40	35	35.0	41	20	41.1	PTSD	-	CAPS: 81.6	yes	no	MDD (n=23)
Holmes et al., 2018 (275)	18	67	35.2	21	43	35.8	PTSD	17.8 years	MADRS: 19.0	no	yes	MDD (n=16)

Jung et al., 2018 (276)	42	45	24.7	36	47	25.4	SAD	9.3 years	LSAS: 78.3	yes	no	MDD (n=4)
Li et al., 2016 (277)	21	64	38.05	22	62	39.9	GAD	-	HAMA: 18.6	no	no	no
Liao et al., 2011 (278)	18	72	21.89	18	67	22.67	SAD	49.22 months	LSAS: 54.39	no	no	no
Liu et al., 2015 (279)	20	45	15.55	26	38	15.54	GAD	11.69 months	SCARED: 37.12	no	no	no
Makovac et al., 2015 (280)	21	14	28.67	19	11	29.58	GAD	16.78 years	SRRS: 1378.95	yes	yes	no
Manning et al., 2015 (281)	33	58	29.4	53	68	29.9	SAD	16.8 years	LSAS: 81.8	no	yes	MDD (n=18)
Misaki et al., 2017 (282)	28	100	29.0	35	100	31.9	PTSD	-	CAPS: 55.2	no	no	MDD (n=1)
Nicholson et al., 2015 (283) non-dissociative subtype	40	28	32.3	36	28	37	PTSD	-	CAPS: 69.0	no	no	MDD (n=1)
dissociative subtype	40	28	32.3	13	15	37	PTSD	-	CAPS: 79.5	no	no	MDD (n=1)
Pace-Schott et al., 2017 (284)	13	15	35.0	12	17	30.2	GAD	-	STAI: 41.7	no	yes	no
Pannekoek et al., 2013 a (285)	12	42	34.0	12	42	43.8	SAD	-	FQ: 20.8	no	no	not mentioned
Pannekoek et al., 2013 b (286)	11	9	35.0	11	9	34.5	PD	-	BAI: 14.5	yes	no	not mentioned
Patriat et al., 2016 (287)	30	40	14.0	29	38	14.6	PTSD	46 months	CAPS: 70	no	no	MDD (n=17), depressive disorder NOS (n=3)
Prater et al., 2013 (288)	17	41	25.71	20	45	25.95	GSAD	-	LSAS: 79.35	yes	yes	no
Rabellino et al., 2018 (289) non-dissociative subtype	47	32	33.81	65	38	37.58	PTSD	-	CAPS-IV: 67.39	yes	no	MDD (n=12)
dissociative subtype	47	32	33.81	37	22	40.38	PTSD	-	CAPS-IV: 81.6	yes	no	MDD (n=23)
Rabinak et al., 2011 (290)	17	100	33.71	15	100	30.12	PTSD	-	CAPS: 67.35	no	no	MDD (n=2)
Roy et al., 2013 (291)	20	35	14.8	15	33	14.9	GAD	-	SCARED: 30.3	no	no	MDD (n=3)
Sripada et al., 2012 a, b (292,293)	15	100	26.6	15	100	27.3	PTSD	-	CAPS: 75.9	yes	no	MDD (n=7)
Thome et al., 2017 (294)	41	37	37.11	57	68	33.98	PTSD	-	CAPS: 69.16	no	no	MDD (n=18)
Toazza et al., 2016 (295)	19	53	16.7	18	56	17.9	ANX	-	-	no	no	MDD (n=5)
Wang et al., 2016 (296)	28	50	33.21	28	50	32.93	GAD	29.75 weeks	SAS: 64.87	no	no	no
Yuan et al., 2016 (297)	19	68	26.26	15	67	27.07	GSAD	-	LSAS: 78.87	no	no	not mentioned
Yuan et al., 2017 a (298)	43	60	30.14	43	63	29.00	SAD	-	LSAS: 69.23	yes	no	MDD (n=10)

Yuan et al., 2017 b (299)	64	55	23.78	46	61	24.8	SAD	7.63 years	LSAS: 64.79	yes	no	MDD (n=2)
Zhang et al., 2016 (300)	33	48	48.85	33	36	52.06	PTSD	-	PCL: 43.25	-	no	not mentioned
Zhu et al., 2017 (301)	34	32	35.1	27	44	36.0	PTSD	-	CAPS: 75.7	no	no	no

542

543 **Table S7.** ANX = anxiety disorder, BAI = Beck Anxiety Inventory, CAPS = Clinician-Administered PTSD Scale, FQ = Fear Questionnaire , GAD =
544 Generalized anxiety disorder, LSAS = Liebowitz Social Anxiety Scale, GSAD = Generalized social anxiety disorder, HAMA = Hamilton Anxiety Rating
545 Scale, HARS = Hamilton Anxiety Rating Scale, HC = healthy controls, iFC = intrinsic functional connectivity, MADRS = Montgomery-Asberg Depression
546 Scale, MDD = major depressive disorder, PARS = Pediatric Anxiety Rating Scale, PCL = PTSD Checklist for DSM-5, PD = Panic disorder, PTSD =
547 Posttraumatic stress disorder, SAD = Social anxiety disorder, SAS = Social anxiety scale, SCARED = Screen for Child Anxiety Related Disorders, SP =
548 Social phobia, SRRS = Stress-Reactive Rumination Scale, STAI = Spielberger State and Trait Anxiety Inventory, TSCC = Trauma Symptom Checklist for
549 Children.

Table S8: Demographic and clinical characteristics of chronic pain studies included in the iFC meta-analysis.

Reference	HC (n)	Male (%)	Mean age HC [years]	CP (n)	Male (%)	Mean age CP [years]	Type of CP	Illness duration	Symptom severity	Medicated	Global signal regression	Comorbidity
Ayoub et al., 2019 (302)	79	56	45.4	77	43	46.2	CBP	11.5 years	VAS: 4.8	-	no	not mentioned
Baliki et al., 2011 (303)	15	67	51.67	15	67	51.87	CBP	6,73 years	VAS: 69.6	yes	no	no
Bhatt et al., 2019 (304)	26	0	10.72	32	0	11.4	IBS	-		no	no	not mentioned
Bolwerk et al., 2013 (305)	12	42	60.92	12	42	61.08	CRPS	15,5 weeks	MPQ (PRI): 11.67	yes	no	no
Case et al., 2017 (306)	15	47	28.8	15	53	24.5	SCD	-	Subjective (0-10): 0.73	yes	no	not mentioned
Cauda et al., 2009 (307)	8	50	49	8	50	61	DNP	>2 years	VAS: 5.625	no	no	not mentioned
Ceko et al., 2013 (137) older subjects	13	0	55.4	14	0	55	FM	12.1 years	VAS: 2.41	yes	no	no
younger subjects	15	0	43.1	14	0	42.4	FM	8.8 years	VAS: 2.8	yes		no
Ceko et al., 2015 (308)	16	-	-	14	-	-	CLBP	4.8 years	SF-MPQ: 17.66	yes	no	not mentioned
Chen et al., 2016 (309) episodic mirgaine	32	25	41.3	18	22	33.4	Migraine	12.4 years	VAS: 8.3	yes	no	no
chronic migraine		25		16	25	42.4	Migraine	11.3 years	VAS: 7.9	yes		no
Cottam et al., 2018 (310)	19	32	65	25	48	65	Knee OA	1-38 years	VAS: 27.8	yes	no	no
Fallon et al., 2016 (311)	15	0	39.4	16	0	38.45	FM	9.13 years	FIQ: 62.37	yes	no	not mentioned
Flodin et al., 2014 (312)	24	0	45.7	16	0	48.3	FM	7.6 years	FIQ: 61.2	yes	no	no
Flodin et al., 2016 (313)	19	16	50.4	24	17	53.8	RA	-	VAS Global: 33.7	yes	no	no
Han et al., 2013 (314)	64	17	81.6	64	27	81.3	CMP	-	-	yes	no	not mentioned
He et al., 2018 (315)	20	42	23.1	30	37	22.1	TMD	17.3 months	Pain intensity score: 41.4	no	no	no
Hong et al., 2014 (316) Male	24	100	34.33	24	100	34.71	IBS	13 years	Gracely pain scale: 5.67	no	no	no
Female	24	0	30.67	24	0	33.58	IBS	13.14 years	Gracely pain scale: 4.7	no		no
Ichesco et al., 2012 (317)	8	0	24.8	8	0	25.4	TMD	2.5 years	MPQ: 6.1	no	no	no
Ichesco et al., 2014 (318)	18	0	30.67	18	0	35.8	FM	3.9 years	SF-MPQ: 9.7	no	no	no
Jiang et al., 2016 (319)	18	61	59.2	18	61	59.67	PHN	116.78 days	VAS: 6.611	no	yes	not mentioned
Khan et al., 2014 (320)	9	0	56	9	0	54	BMS	4 years	Rating scale: 2.8	no	no	not mentioned

Kilpatrick et al., 2014 (321)	85	0	35.3	82	0	38.8	IC/PBS	10.4 years	GUPI (total): 26.2	no	no	not mentioned
Kim et al., 2017 (322)	25	56	31.7	25	48	36.1	CRPS	2,8 years	VAS: 5.0	yes	no	MDD (n=11), other mood disorders (n=7), ANX (n=1)
Kong et al., 2018 (323)	20	5	52.9	21	5	53.1	FM	-	FIQ: 45.1	yes	yes	no
Kucyi et al., 2014 (324)	17	0	32.2	17	0	33.1	TMD	>3 months	Rating scale: 4.3	no	no	no
Kutch et al., 2015 (325)	27	100	43.4	28	100	42	CPr/CPSP	8.9 years	GUPI (total): 23.5	no	no	not mentioned
Li et al., 2016 (326)	42	19	21.21	62	23	21.29	Migraine without aura	>6 months	-	no	no	no
Li et al., 2017 (327)	46	22	21.24	72	21	21.30	Migraine without aura	>6 months	-	no	no	no
Liu et al., 2017 (328)	42	36	22.95	66	36	23.09	FD	35.44 months	NDI: 50.79	no	no	no
Martucci et al., 2015 (329)	45	0	39.4	45	0	37.9	UCPPS	9.42 years	MPQ sensory: 9.34	yes	yes	no
Michels et al., 2016 (330) medication-overuse headache	16	44	42.6	11	17	44.4	MOH	16.6 years	VAS: 4.2	yes	yes	not mentioned
myofascial pain	16	44	42.6	12	27	38.3	MYO	5.5 years	VAS: 5.5	yes		not mentioned
Niddam et al., 2016 (331) migraine without aura	26	35	31.2	26	35	32.3	Migraine without aura	13.5 years	Migraine pain intensity: 8.0	no	yes	not mentioned
migraine with aura		35		26	35	28.3	Migraine with aura	13.1 years	Migraine pain intensity: 8.2	no		not mentioned
Pujol et al., 2014 (332)	36	0	44	40	0	46.4	FM	7.2 years	FIQ-total: 66.2	yes	no	no
Qi et al., 2016 (333)	32	78	27.4	31	81	29.3	IBS	32.67 months	IBS-SSS: 242.48	no	no	no
Truini et al., 2016 (334)	15	13	28-67	20	5	26-65	FM	-	-	no	no	no
Wang et al., 2017 (184)	38	33	55.89	38	42	55.87	TN	7.05 years	VAS: 5.79	yes	no	no
Wei et al., 2016 a (335)	60	0	23.9	56	0	23.1	PDM	9.5 years	PRI (recalled): 35.0	yes	yes	no

Wei et al., 2016 b (336)	49	0	23.8	46	0	23.33	PDM	9.22 years	PRI (recalled): 9.22	yes	yes	no
Wei et al., 2017 (337)	65	0	24.2	61	0	23	PDM	8.95 years	MPQ: 35.0	yes	yes	no
Wei et al., 2019 (338)	23	22	35.67	28	18	36.68	Migraine	8.95 years	VAS: 6.50	no	no	no
Yu et al., 2017 (339)	48	23	35.12	48	23	35.47	Migraine	9.38 years	VAS: 7.23	yes	no	no
Zhang et al., 2017 (340)	31	29	40.2	30	29	41	Migraine	9.6 years	VAS: 7.2	no	no	no
Zhang et al., 2019 (341)	34	38	43.32	29	34	48.14	TN	6.02 years	VAS: 6.31	no	yes	no

551

552 **Table S8.** ANX = anxiety disorder, BMS = Burning mouth syndrome, CBP = Chronic back pain, CLBP = Chronic low back pain, CMP = Chronic
553 musculoskeletal pain, CP = chronic pain, CPr = Chronic prostatitis, CPPS = Chronic pelvic pain syndrome, CRPS = Complex regional pain syndrome,
554 DNP = Diabetic neuropathic pain, FD = Functional dyspepsia, FIQ = Fibromyalgia Impact Questionnaire, FM = Fibromyalgia, GUPI = Genitourinary
555 Pain Index, HC = healthy controls, IBS = irritable bowel syndrome, IBS-SSS = IBS Symptom Severity Score, IC = interstitial cystitis, iFC = intrinsic
556 functional connectivity, MDD = major depressive disorder, MOH = medication-overuse headache, (SF-)MPQ = (Short Form) McGill Pain
557 Questionnaire Pain Rating Index, MYO = chronic myofascial pain, NDI = Nepean Dyspepsia Index, NRS = Numeric rating scale, OA = Osteoarthritis,
558 PBS = Painful bladder syndrome, PDM = Primary dysmenorrhea, PHN = Postherpetic neuralgia, PRI = Pain rating index, RA = Rheumatoid arthritis,
559 SCD = Sickle cell disease, TMD = Temporomandibular disorders, TN = Trigeminal neuralgia, UCPPS = Urologic chronic pelvic pain syndrome, VAS =
560 Visual Analogue Scale.

561 **Table S9: Comorbidity across investigated disorders in the included studies.**

Disorder	Included studies	Studies with comorbid						Total number of studies with comorbidity	Studies that did not mention comorbidity
		MDD	ANX	CP	MDD+ANX	MDD+CP	ANX+CP		
Gray matter volume meta-analysis									
Major depressive disorder	63		7					7	10
Anxiety disorders	41	15						15	3
Chronic pain	65	5			1			6	15
Intrinsic functional connectivity meta-analysis									
Major depressive disorder	68		22					22	5
Anxiety disorders	41	26						26	4
Chronic pain	42				1			1	15

562

Table S10: Studies with no significant results.

Author, year	HC (n)	Patients (n)
Gray matter volume meta-analysis		
Major depressive disorder		
Hagan et al., 2015 (342)	36	109
Biedermann et al., 2015 (343)	35	46
Jia et al., 2010 (344)	52	52
Treadway et al., 2009 (345)	19	19
Yoshikawa et al., 2006 (346)	29	22
Colloby et al., 2011 (347)	30	28
Koolschijn et al., 2010 (348)	38	28
Anxiety disorders		
Szabó et al., 2015 (349)	60 (trauma-exposed)	75
	60 (non-exposed)	
Moon et al., 2015 (350)	15	15
Jatzko et al., 2006 (351)	15	15
Eckart et al., 2011 (352)	19 (traumatized)	20
	13 (non-traumatized)	
Chronic pain		
Yu et al., 2017 (353)	20	25
Chen et al., 2016 (354)	40	40
Hougaard et al., 2015 (355)	60	20
Tessitore et al., 2013 (356)	20	25
Dolman et al., 2014 (357)	14	28
Seminowicz et al., 2013 (358)	23	13
Russo et al., 2012 (359)	14	14
Farmer et al., 2011 (360)	16	19
Hsu et al., 2009 (361)	29	29 (with affective disorders)
	29	29 (without affective disorders)
Celle et al., 2017 (362)	39	25 (episodic migraine)
	39	37 (history of migraine)
Ung et al., 2014 (363)	47	47
Intrinsic functional connectivity meta-analysis		
Major depressive disorder		
Demenscu et al., 2016 (364)	25	25
Anxiety disorders		
Brunetti et al., 2017 (365)	20	20
Olivé et al., 2018 (366)	50	67
		41 (with dissociative subtype)
Chronic pain		
Schwedt et al., 2014 (367)	20	38

566 **Table S11: Number of studies, number of patients/controls, and mean age of**
 567 **patients/controls per seed network and disorder.**

	LIM	FPN	DMN	SAL	PSM	DAN	VIS
Total	55 1712/1580 29.88/29.05	30 787/727 37.43/37.40	76 2456/2279 36.76/36.42	47 1511/1376 35.39/34.95	18 606/541 41.78/39.93	4 115/86 37.54/39.11	5 158/129 36.86/39.11
MDD	20 695/640 29.48/28.85	15 376/350 40.57/41.64	47 1622/1479 36.95/36.69	13 368/360 32.4/30.71	5 107/111 43.15/43.73	1 23/20 33.09/31.1	2 64/39 27.61/28.09
ANX	29 803/740 29.15/27.77	6 156/163 28.92/27.70	14 403/394 28.73/28.32	10 314/266 36.23/35.7	3 158/95 32.98/28.15	1 28/28 32.93/33.21	0 - / - - / -
CP	6 214/200 35.01/35.99	9 255/214 36.75/36.21	15 431/406 43.21/42.68	24 829/750 36.81/36.95	10 341/335 44.62/41.57	2 64/38 40.56/46.06	3 94/90 46.1/46.47

568

569 **Table S11.** The first line of each cell represents the number of studies using seeds located in
 570 the respective seed network, the second line represents the number of patients/controls, and
 571 the third line the mean age of patients/controls. ANX = anxiety disorders, CP = chronic pain,
 572 DAN = dorsal attention network, DMN = default-mode network, FPN = frontoparietal network,
 573 LIM = limbic network, MDD = major depressive disorder, PSM = primary-sensorimotor
 574 network, SAL = salience network, VIS = visual network.

Table S12: Gray matter volume changes compared to healthy controls.

Effect anatomy/region	MNI peak coordinates			Voxels	Maximum P (density statistic)	p-Value p_{FWER}
	x	y	z			
MDD						
<i>MDD > HC</i>						
R lateral occipital cortex, superior division	46	-70	24	2252	0.105	0.007
<i>MDD < HC</i>						
L inferior frontal gyrus, pars opercularis	-44	16	8	13	0.151	0.007
L frontal operculum cortex	-44	12	6	577	0.135	<0.001
R frontal pole	32	44	26	563	0.131	0.001
L subcallosal cortex	-6	16	-14	3078	0.119	<0.001
R insula	42	-6	-18	1618	0.113	0.017
L central opercular cortex	-46	2	4	839	0.097	0.039
L anterior cingulate cortex	-2	18	12	18807	0.118	<0.001
ANX						
<i>ANX > HC</i>						
R lateral occipital cortex, superior division	48	-64	30	1538	0.235	0.031
<i>ANX < HC</i>						
L frontal orbital cortex	-38	22	-10	12	0.280	0.031
L insular cortex	-38	8	-12	2545	0.233	<0.001
L thalamus	-2	-8	-2	428	0.215	0.007
L paracingulate gyrus	-8	48	20	338	0.222	0.021
L pallidum	-16	-8	-4	5633	0.228	<0.001
L temporal pole	-36	22	-32	26	0.133	<0.001
L frontal operculum cortex	-38	28	4	108	0.138	<0.001
L paracingulate gyrus	-2	46	18	1614	0.205	0.005
L Thalamus	0	4	4	14413	0.155	<0.001
CP						
<i>CP > HC</i>						
L Amygdala	-22	-6	-16	459	0.273	0.002
R parahippocampal gyrus, posterior division	28	-32	-14	95	0.236	0.010
L Hippocampus	-24	-12	-18	1723	0.186	<0.001

R parahippocampal gyrus, posterior division	28	-36	-12	571	0.186	<0.001
L Hippocampus	-24	-18	-18	1920	0.129	<0.001
R lobus anterior cerebelli	20	-32	-22	6257	0.122	<0.001
L temporal fusiform cortex, anterior division	-32	-4	-42	269	0.075	<0.001
L temporal fusiform cortex, posterior division	-38	-12	-36	49	0.064	<0.001
L brainstem	-10	-36	-18	29	0.068	<0.001
L lingual gyrus	-22	-44	-14	31	0.065	<0.001
CP < HC						
L medial prefrontal cortex	0	58	0	59	0.204	0.017
L paracingulate gyrus	-2	32	34	32	0.186	0.031
R central opercular cortex	44	10	2	943	0.166	<0.001
L frontal orbital cortex	-38	28	-4	290	0.162	0.005
L frontal pole	-2	58	6	1318	0.166	<0.001
L central opercular cortex	-46	-14	14	245	0.150	0.021
L paracingulate gyrus	-2	32	32	1093	0.166	<0.001
R central opercular cortex	44	8	2	1236	0.135	<0.001
L anterior cingulate cortex	0	24	26	3072	0.124	<0.001
L premotor cortex	-44	-4	18	2436	0.147	<0.001
L anterior cingulate cortex	-10	16	28	15774	0.133	<0.001
L frontal pole	-12	70	6	112	0.078	<0.001
L medial prefrontal cortex	0	66	22	10	0.072	<0.001

576

577 **Table S12.** Aberrant gray matter volume in major depressive disorder (MDD), anxiety
578 disorders (ANX), and chronic pain (CP), based on Multilevel Kernel Density Meta-Analysis
579 ($p < 0.05$ FWER-corrected, both height- and extent-based threshold). HC = healthy controls,
580 MNI = Montreal Neurological Institute, P = weighted proportion of studies (=density statistic).

581 **Table S13: Common gray matter volume changes.**

Effect anatomy/region	MNI peak coordinates			Voxels	p-Value
	x	y	z		
Common volume increase: (MDD > HC) ∩ (ANX > HC) ∩ (CP > HC)					
-					
Common volume decrease: (MDD < HC) ∩ (ANX < HC) ∩ (CP < HC)					
Bilateral prefrontal cortex	8	50	-22	1464	<0.0015
L insula, superior temporal gyrus, and lateral prefrontal cortex	-56	-8	-14	1191	<0.0015
R lateral and medial supplementary motor area	10	10	40	87	<0.0015
R insula and inferior frontal gyrus	54	6	-4	51	<0.0015
R lateral and medial supplementary motor area	12	28	40	14	<0.0015

582

583 **Table S13.** Common gray matter volume changes in major depressive disorder (MDD), anxiety
 584 disorders (ANX), and chronic pain (CP), based on MKDA meta-analysis and subsequent
 585 conjunction ($p < 0.0015$). HC = healthy controls, MNI = Montreal Neurological Institute.

Table S14: Pairwise contrasts of gray matter volume changes.

Effect anatomy/region	MNI peak coordinates			Voxels	p-Value
	x	y	z		
MDD					
MDD > ANX					
<i>Volume increase: (MDD > controls) > (ANX > controls)</i>					
-					
<i>Volume decrease: (MDD < controls) > (ANX < controls)</i>					
L premotor cortex	-26	10	44	208	<0.001
MDD > CP					
<i>Volume increase: (MDD > controls) > (CP > controls)</i>					
-					
<i>Volume decrease: (MDD < controls) > (CP < controls)</i>					
R parahippocampal gyrus	34	-16	-34	5432	<0.001
L superior temporal gyrus	-52	8	-10	1599	<0.001
ANX					
ANX > MDD					
<i>Volume increase: (ANX > controls) > (MDD > controls)</i>					
-					
<i>Volume decrease: (ANX < controls) > (MDD < controls)</i>					
L inferior frontal gyrus	-44	28	-12	10463	0.000446
L thalamus	-14	-22	2	1124	<0.001
R parahippocampal gyrus	24	-12	-34	220	<0.001
R temporal pole	32	20	-42	123	<0.001
R amygdala	36	4	-28	68	<0.001
ANX > CP					
<i>Volume increase: (ANX > controls) > (CP > controls)</i>					
-					
<i>Volume decrease: (ANX < controls) > (CP < controls)</i>					
L temporal pole	-46	18	-18	9489	0.00052
R parahippocampal gyrus	38	-14	-38	588	<0.001
R temporal pole	38	20	-40	337	<0.001
CP					
CP > MDD					
<i>Volume increase: (CP > controls) > (MDD > controls)</i>					

L insula	-32	-6	-20	5341	0.00173
R fusiform gyrus	24	-30	-18	1520	0.000687
R lobus cerebelli posterior	30	-50	-62	1474	<0.001
R parahippocampal gyrus	30	-8	-36	214	<0.001
R putamen	26	-4	4	25	<0.001
R thalamus	18	-18	2	20	<0.001
Volume decrease: (CP < controls) > (MDD < controls)					
R frontopolar prefrontal cortex	0	66	6	4311	0.0011
R amygdala	32	8	-22	1789	0.0041
L inferior frontal gyrus	-30	40	-12	1424	0.000185
R primary motor cortex	40	-4	36	92	<0.001
L supplementary motor area	-22	28	34	11	<0.001
CP > ANX					
Volume increase: (CP > controls) > (ANX > controls)					
L amygdala	-32	-4	-24	5349	0.00164
R parahippocampal gyrus	36	-30	-14	4245	0.000684
R amygdala	14	-4	-10	31	<0.001
R thalamus	12	0	0	23	<0.001
Volume decrease: (CP < controls) > (ANX < controls)					
R insula	30	10	-16	246	0.00057

587

588 **Table S14.** Pairwise contrasts of gray matter volume changes across major depressive disorder
589 (MDD), anxiety disorders (ANX), and chronic pain (CP), based on MKDA meta-analysis and
590 subsequent conjunction ($p < 0.005$). HC = healthy controls, MNI = Montreal Neurological
591 Institute.

592 **Table S15: Specific gray matter volume changes.**

Effect anatomy/region	MNI peak coordinates			Voxels	p-Value
	x	y	z		
MDD					
<i>Specific volume increase: (MDD > ANX) ∩ (MDD > CP)</i>					
-					
<i>Specific volume decrease: (MDD > ANX) ∩ (MDD > CP)</i>					
-					
ANX					
<i>Specific volume increase: (ANX > MDD) ∩ (ANX > CP)</i>					
-					
<i>Specific volume decrease: (ANX > MDD) ∩ (ANX > CP)</i>					
L inferior temporal gyrus	-48	6	-38	7405	<0.00005
Posterior cingulate cortex	0	-28	10	236	<0.00005
R parahippocampal gyrus	24	-12	-34	117	<0.00005
R temporal pole	36	22	-40	109	<0.00005
R amygdala	36	4	-28	45	<0.00005
R superior temporal gyrus	42	-4	-18	17	<0.00005
CP					
<i>Specific volume increase: (CP > MDD) ∩ (CP > ANX)</i>					
L parahippocampal gyrus	-30	-6	-54	4875	<0.00005
R lobus cerebelli posterior	30	-50	-62	1474	<0.00005
R lobus cerebelli anterior	52	-52	-34	1455	<0.00005
R gyrus rectus	10	10	-22	38	<0.00005
R thalamus	18	-18	2	20	<0.00005
<i>Specific volume decrease: (CP > MDD) ∩ (CP > ANX)</i>					
R insula	30	10	-16	210	<0.00005

593

594 **Table S15.** Specific gray matter volume changes in major depressive disorder (MDD), anxiety
 595 disorders (ANX), and chronic pain (CP), based on conjunction across pairwise contrasts
 596 ($p < 0.00005$). MNI = Montreal Neurological Institute.

Table S16: Intrinsic functional connectivity changes compared to healthy controls.

Seed network	Effect network	Effect anatomy/region	MNI peak coordinates			Voxels	Maximum P (density statistic)	p-Value p_{FWER}
			x	y	z			
MDD								
<i>MDD > HC</i>								
PSM	DAN	R Lateral Occipital Cortex, superior division	34	-70	30	40	0.779	0.0432
DMN	FPN	L middle frontal gyrus	-44	26	32	60	0.234	0.031
DMN	-	L middle frontal gyrus	-40	28	30	699	0.200	<0.001
DMN	DMN	L precuneus cortex	-2	-66	44	395	0.190	0.029
DMN	-	L middle frontal gyrus	-36	32	28	993	0.132	0.009
<i>MDD < HC</i>								
LIM	DMN	R Insular Cortex	30	14	-12	26	0.311	0.002
LIM	SAL	R Insular Cortex	38	8	-10	811	0.246	0.016
FPN	FPN	R angular gyrus	42	-54	50	608	0.301	0.035
ANX								
<i>ANX > HC</i>								
LIM	SAL	R supramarginal gyrus, posterior division	60	-40	24	621	0.304	0.011
LIM	-	L tegmentum mesencephali	-12	-24	-14	8913	0.231	0.004
<i>ANX < HC</i>								
LIM	DMN	R cingulate gyrus, posterior division	6	-44	18	374	0.185	0.041
LIM	-	R orbitofrontal cortex	22	40	-10	5515	0.163	0.040
CP								
<i>CP > HC</i>								
SAL	PSM	L postcentral gyrus	-8	-40	60	2427	0.217	0.017
<i>CP < HC</i>								
PSM	SAL	R central opercular cortex	46	-2	4	1077	0.655	0.040
PSM	-	R fusiform gyrus	36	-58	-8	962	0.449	0.046
PSM	PSM	R central opercular cortex	54	-2	8	1138	0.452	<0.001
PSM	PSM	R primary auditory cortex	60	-4	0	1241	0.305	0.001
PSM	-	R insula	34	-12	8	163	0.275	0.001

SAL	DMN	L paracingulate gyrus	-2	46	-8	11	0.330	0.026
SAL	DMN	L paracingulate gyrus	-4	54	4	141	0.329	0.042
SAL	VIS	R cuneal cortex	12	-70	24	10	0.297	0.035
SAL	DMN	L paracingulate gyrus	-4	50	2	1461	0.286	<0.001
SAL	DMN	R precuneous cortex	8	-58	28	913	0.288	0.001
SAL	DMN	R paracingulate gyrus	2	44	26	1953	0.234	<0.001
SAL	FPN	L frontal pole	-22	58	8	28	0.172	<0.001
SAL	VIS	R cuneal cortex	20	-72	22	1008	0.176	<0.001
SAL	-	L medial prefrontal cortex	-14	38	12	11	0.159	<0.001
SAL	DMN	L cingulate gyrus, posterior division	-2	-46	32	688	0.186	<0.001
SAL	DMN	L precuneous cortex	-10	-60	20	7908	0.263	<0.001
SAL	-	R paracingulate gyrus	2	46	16	3176	0.129	0.049
SAL	DAN	R lateral occipital cortex, superior division	44	-64	22	1555	0.134	<0.001
LIM	-	L anterior prefrontal cortex	-12	52	-8	311	0.409	0.059
FPN	PSM	L planum temporale	-58	-36	12	55	0.447	0.042

598

599 **Table S16.** Intrinsic functional connectivity changes in major depressive disorder (MDD),
600 anxiety disorders (ANX), and chronic pain (CP), based on Multilevel Kernel Density Meta-
601 Analysis ($p < 0.05$ FWER-corrected, both height- and extent-based threshold). Labelling of
602 effect networks was derived from the location of the cluster's peak coordinate. - = cluster was
603 located outside of the network mask. DAN = dorsal attention network, DMN = default-mode
604 network, FPN = frontoparietal network, HC = healthy controls, LIM = limbic network, MNI =
605 Montreal Neurological Institute, P = weighted proportion of studies (=density statistic), PSM
606 = primary-sensorimotor network, SAL = salience network, VIS = visual network.

607 **Table S17: Common intrinsic functional connectivity changes.**

Effect anatomy/region	MNI peak coordinates			Voxels	p-Value
	x	y	z		
Common hyperconnectivity: (MDD > HC) ∩ (ANX > HC) ∩ (CP > HC)					
-					
Common hypoconnectivity: (MDD < HC) ∩ (ANX < HC) ∩ (CP < HC)					
-					

608

609 **Table S17.** Common intrinsic functional connectivity changes in major depressive disorder
 610 (MDD), anxiety disorders (ANX), and chronic pain (CP), based on MKDA meta-analysis and
 611 subsequent conjunction ($p < 0.0015$). HC = healthy controls, MNI = Montreal Neurological
 612 Institute.

Table S18: Pairwise contrasts of intrinsic functional connectivity changes.

Seed network	Effect anatomy/region	MNI peak coordinates			Voxels	p-Value
		x	y	z		
MDD						
<i>MDD > ANX</i>						
<i>Hyperconnectivity: (MDD > controls) > (ANX > controls)</i>						
DMN	L frontal cortex (BA9)	-50	24	32	1753	0.000365
DMN	L parietal cortex (BA7)	-4	-66	52	395	0.00138
<i>Hypoconnectivity: (MDD < controls) > (ANX < controls)</i>						
LIM	R globus pallidus	18	4	-4	827	0.000471
<i>MDD > CP</i>						
<i>Hyperconnectivity: (MDD > controls) > (CP > controls)</i>						
PSM	R angular gyrus	36	-76	28	40	0.00186
DMN	L frontal cortex (BA9)	-50	24	32	1562	0.000359
<i>Hypoconnectivity: (MDD < controls) > (CP < controls)</i>						
LIM	R Insula	42	4	-16	788	0.000885
FPN	R angular gyrus	44	-50	44	609	0.001
ANX						
<i>ANX > MDD</i>						
<i>Hyperconnectivity: (ANX > controls) > (MDD > controls)</i>						
LIM	R lobus cerebelli posterior	18	-64	-40	1647	0.000145
LIM	R superior temporal gyrus	52	-40	8	621	0.000399
<i>Hypoconnectivity: (ANX < controls) > (MDD < controls)</i>						
LIM	R cingulate gyrus (isthmus/BA30)	12	-44	10	374	0.00159
<i>ANX > CP</i>						
<i>Hyperconnectivity: (ANX > controls) > (CP > controls)</i>						
LIM	R lobus cerebelli posterior	18	-64	-40	2022	0.0018
LIM	R superior temporal gyrus	52	-40	8	621	0.000269
<i>Hypoconnectivity: (ANX < controls) > (CP < controls)</i>						
-						
CP						
<i>CP > MDD</i>						

Hyperconnectivity: (CP > controls) > (MDD > controls)						
SAL	R primary motor cortex	8	-26	48	1502	0.00039
Hypoconnectivity: (CP < controls) > (MDD < controls)						
PSM	R insula	44	-4	-8	3622	0.0023
SAL	R primary visual cortex	12	-72	20	6844	0.0012
SAL	L dorsal anterior cingulate area (BA32)	-2	52	-2	5725	0.0017
SAL	L lobus anterior cerebelli	-2	-48	-4	53	<0.001
LIM	L frontopolar prefrontal cortex	-6	54	-16	116	0.0032
FPN	L superior temporal gyrus (BA22)	-52	-40	10	55	0.0015
CP > ANX						
Hyperconnectivity: (CP > controls) > (ANX > controls)						
-						
Hypoconnectivity: (CP < controls) > (ANX < controls)						
PSM	R insula	44	-4	-8	2509	0.00226
PSM	R fusiform gyrus	38	-64	-20	962	0.00222
SAL	R primary visual cortex	12	-72	20	7150	0.0014
SAL	L dorsal anterior cingulate area (BA32)	-6	50	-4	2497	0.0019

614

615 **Table S18.** Pairwise contrasts of intrinsic functional connectivity changes across major
616 depressive disorder (MDD), anxiety disorders (ANX), and chronic pain (CP), based on MKDA
617 meta-analysis and subsequent conjunction ($p < 0.005$). DMN = default-mode network, FPN =
618 frontoparietal network, HC = healthy controls, LIM = limbic network, MNI = Montreal
619 Neurological Institute, PSM = primary-sensorimotor network, SAL = salience network.

620 **Table S19: Specific intrinsic functional connectivity changes.**

Seed network	Effect anatomy/region	MNI peak coordinates			Voxels	p-Value
		x	y	z		
MDD						
<i>Specific hyperconnectivity: (MDD > ANX) ∩ (MDD > CP)</i>						
DMN	L anterior middle frontal gyrus	-40	40	2	1562	<0.00005
<i>Specific hypoconnectivity: (MDD > ANX) ∩ (MDD > CP)</i>						
LIM	R parahippocampal gyrus	30	-2	-30	781	<0.00005
ANX						
<i>Specific hyperconnectivity: (ANX > MDD) ∩ (ANX > CP)</i>						
LIM	R lobus cerebelli posterior	18	-64	-40	1541	<0.00005
LIM	R superior temporal gyrus	52	-40	8	621	<0.00005
<i>Specific hypoconnectivity: (ANX > MDD) ∩ (ANX > CP)</i>						
-						
CP						
<i>Specific hyperconnectivity: (CP > MDD) ∩ (CP > ANX)</i>						
-						
<i>Specific hypoconnectivity: (CP > MDD) ∩ (CP > ANX)</i>						
PSM	R middle temporal cortex (BA21)	60	-20	-12	2509	<0.00005
SAL	R primary visual cortex	18	-66	8	4886	<0.00005
SAL	L orbitofrontal cortex	-2	44	-22	2386	<0.00005
SAL	R secondary visual cortex	22	-46	-2	170	<0.00005

621

622 **Table S19.** Specific intrinsic functional connectivity changes in major depressive disorder
623 (MDD), anxiety disorders (ANX), and chronic pain (CP), based on conjunction across pairwise
624 contrasts ($p < 0.00005$). DMN = default-mode network, LIM = limbic network, MNI = Montreal
625 Neurological Institute, PSM = primary-sensorimotor network, SAL = salience network.

626 **Table S20: Regional overlap between specific GMV-changes and specific iFC-changes.**

Seed network	Effect anatomy/region	MNI peak coordinates			Voxels	p-Value
		x	y	z		
MDD						
-						
ANX						
-						
CP						
<i>Specific GMV-decrease and specific hypoconnectivity</i>						
PSM	Right ventrolateral prefrontal cortex	48	20	10	18	<3x10 ⁻⁹

627

628 **Table S20.** Results are based on inter-modality conjunction ($p < 3 \times 10^{-9}$). ANX = anxiety
 629 disorders, CP = chronic pain, GMV = gray matter volume, MDD = major depressive disorder,
 630 MNI = Montreal Neurological Institute, PSM = primary-sensorimotor network.

631 **Table S21: Noise correction methods (additional to global signal regression) implemented**
632 **in iFC studies.**

Author, year	Noise correction method(s)
Major depressive disorder	
Alalade et al., 2011 (193)	high-pass and temporal low-pass filtering
Alexopoulos et al., 2012 (194)	temporal band-pass filtering
Andreescu et al., 2013 (195)	not reported
Avery et al., 2014 (196)	not reported
Bai et al., 2018 (197)	temporal band-pass filtering, regression of WM, CSF, 24 head-motion parameters (Friston)
Berman et al., 2011 (198)	high-pass and low-pass filtering; detrending
Bessette et al., 2018 (199)	temporal band-pass filtering, regression of WM and CSF, time series detrending
Cao et al., 2012 (200)	removal of linear trend, temporal band-pass filtering, reduce low-frequency drift
Chen et al., 2018 (201)	temporal band-pass filtering, regression of WM, CSF, 24 head-motion parameters (Friston)
Connolly et al., 2013 (202)	temporal band-pass filtering, regression of WM and CSF
Connolly et al., 2017 (203)	temporal band-pass filtering, regression of WM and CSF, linear regression
Crowther et al., 2015 (204)	temporal band-pass filtering
Cullen et al., 2014 (205)	regression of WM, CSF and six motion parameters
Davey et al., 2012 (206)	high-pass filtering to remove low-frequency drifts, linear regression
DelDonno et al., 2017 (207)	temporal band-pass filtering, regression of WM and CSF
Deng et al., 2016 (208)	temporal band-pass filtering to reduce low-frequency drifts, detrending
de Kwaasteniet et al., 2015 (209)	temporal band-pass filtering, regression of WM, CSF and head movement
Ellard et al., 2018 (210)	not reported
Evans et al., 2018 (211)	temporal band-pass filtering, motion censoring, physiological noise correction
Furman et al., 2011 (212)	temporal band-pass filtering, regression of WM, CSF and six motion parameters
Gabbay et al., 2013 (213)	temporal band-pass filtering, linear and quadratic detrending
Gandelman et al., 2018 (214)	temporal band-pass filtering, regression of WM, CSF, realignment parameters
Gong et al., 2017 (215)	temporal band-pass filtering
Guo et al., 2013 a, b (216) treatment-resistant depression	temporal band-pass filtering to reduce low-frequency drift, regression of WM, CSF and six motion parameters
treatment-sensitive depression	
Guo et al., 2013 c, d (217)	temporal band-pass filtering, linear detrending, regression of WM, CSF ROI, six motion parameters
Guo et al., 2015 a, b (218)	temporal band-pass filtering, linear detrending, regression of WM, ventricular ROI, six motion parameters
Jacobs et al., 2016 (219)	temporal band-pass filtering, regression of WM and CSF
Kenny et al., 2010 (220)	temporal high-pass filtering
Kerestes et al., 2015 (221)	linear regression of six motion parameters, high-pass filtering to remove low-frequency drifts
Kim et al., 2016 (222)	temporal band-pass filtering, linear detrending to reduce low-frequency drifts
Li et al., 2015 (223)	temporal band-pass filtering, regression of WM, CSF, six motion vectors
Liu et al., 2018 (224)	Linear detrending, temporal band-pass filtering

Lois et al., 2016 (225)	temporal band-pass filtering, regression of WM, CSF, six parameters
Lui et al., 2011 (226) nonrefractory depression	temporal band-pass filtering, linear detrending, regression of WM and CSF
refractory depression	
Ma et al., 2012 (227) treatment-resistant depression	temporal band-pass filtering to reduce low-frequency drifts
treatment-sensitive depression	
Pannekoek et al., 2014 (228)	temporal high-pass filtering
Peng et al., 2015 (229)	temporal band-pass filtering
Peng et al., 2018 (230)	temporal band-pass filtering, regression of WM, CSF and head-motion
Penner et al., 2016 (231)	temporal band-pass filtering
Peters et al., 2016 (232)	not reported
Philippi et al., 2018 (233)	regression of WM, CSF, six motion parameters
Poepl et al. 2016 (234)	temporal band-pass filtering
Rao et al., 2016 (235)	not reported
Renner et al., 2017 (236)	not reported
Sawaya et al., 2015 (237)	temporal band-pass filtering, high-pass filtering
Scheinost et al., 2018 (238)	linear and quadratic drifts, regression of WM, CSF, six motion parameters
Schilbach et al., 2016 (239)	temporal band-pass filtering, regression of six motion parameters
Sheline et al., 2010 (240)	temporal band-pass filtering, regression of six parameters
Shu et al., 2014 (241)	temporal band-pass filtering, linear detrending, regression of WM, CSF, six motion parameters
Späti et al., 2015 (242)	temporal band-pass filtering, regression of 24 parameters
Straub et al., 2015 (243)	not reported
Tadayonnejad et al., 2016 (244)	temporal band-pass filtering, regression of WM and CSF
Tahmasian et al., 2013 (245)	temporal band-pass filtering
van Tol et al., 2014 (246)	not reported
Wang et al., 2018 (247)	temporal band-pass filtering, linear detrending, regression of 24-parameter (Friston)
Workman et al., 2016 (248)	temporal band-pass filtering, regression of WM, CSF, 24 motion parameters
Workman et al., 2017 (249) recurring episode	temporal band-pass filtering, regression of WM, CSF, 24 motion parameters
Resilient	
Wu H et al., 2016 (250)	temporal band-pass filtering, regression of WM, CSF, six motion parameters
Wu X et al., 2016 (251)	temporal band-pass filtering to reduce low-frequency drift, linear regression of WM, CSF and six motion parameters
Yang et al., 2016 a (85)	temporal band-pass filtering, regression of WM, CSF, motion-relevant parameters
Yang et al., 2016 b (252)	temporal band-pass filtering, linear detrending, regression of WM and CSF
Yang et al., 2017 (253)	temporal band-pass filtering to reduce low-frequency drift, regression of WM, CSF, six motion parameters
Ye et al., 2012 (254)	temporal band-pass filtering, linear detrending
Ye et al., 2017 (255) young-adult	temporal band-pass filtering
old-adult	
Yin et al., 2015 a (256)	temporal band-pass filtering, linear detrending
Yin et al., 2015 b (257)	temporal band-pass filtering, linear detrending
Yuan et al., 2014 (258)	temporal band-pass filtering, regression of WM, CSF, six motion parameters

Zhang et al., 2015 (259) deficiency syndrome	temporal band-pass filtering
excess syndrome	
Anxiety disorders	
Aghajani et al., 2016 (260)	temporal band-pass filtering, regression of WM and CSF
Andreescu et al., 2014 (261)	regression of motion and CSF
Arnold Anteraper et al., 2014 (262)	temporal band-pass filtering, regression of WM and CSF
Birn et al., 2014 (263)	not reported
Bluhm et al., 2009 (264)	temporal band-pass filtering
Brown et al., 2014 (265)	temporal band-pass filtering, regression of WM and CSF
Chen et al., 2018 (266) trauma-exposed control	temporal band-pass filtering to remove low-frequency drifts, regression of WM, CSF and head motion parameters
healthy control	
Cui et al., 2017 (267)	temporal band-pass filtering, linear detrending, regression of WM, CSF, six motion parameters
Dodhia et al., 2014 (268)	regression of WM, CSF and movement parameters
Dorfman et al., 2016 (269)	temporal band-pass filtering, regression of WM and 12 motion parameters, cubic detrending
Geiger et al., 2016 (270)	temporal band-pass filtering
Hahn et al., 2011 (271)	temporal band-pass filtering, linear regression of WM and CSF
Hamm et al., 2014 (272)	removal of non-neuronal sources of noise
Harricharan et al., 2016 (273) non-dissociative subtype	temporal band-pass filtering
dissociative subtype	
Harricharan et al., 2017 (274) non-dissociative subtype	temporal band-pass filtering
dissociative subtype	
Holmes et al., 2018 (275)	regression of WM, CSF, 24-parameters motion model
Jung et al., 2018 (276)	removing physiological noise
Li et al., 2016 (277)	temporal band-pass filtering, linear detrending
Liao et al., 2011 (278)	temporal band-pass filtering, regression of WM and CSF
Liu et al., 2015 (279)	temporal band-pass filtering, linear regression of WM, CSF, six motion parameters
Makovac et al., 2015 (280)	not reported
Manning et al., 2015 (281)	temporal band-pass filtering, linear regression of WM and CSF
Misaki et al., 2017 (282)	regression of WM, CSF, 12 motion parameters
Nicholson et al., 2015 (283) non-dissociative subtype	temporal band-pass filtering
dissociative subtype	
Pace-Schott et al., 2017 (284)	temporal band-pass filtering, linear regression of WM, CSF, six parameters
Pannekoek et al., 2013 a (285)	temporal high-pass filtering
Pannekoek et al., 2013 b (286)	temporal high-pass filtering
Patriat et al., 2016 (287)	temporal band-pass filtering, motion censoring
Prater et al., 2013 (288)	temporal band-pass filtering, regression of six motion parameters
Rabellino et al., 2018 (289) non-dissociative subtype	temporal band-pass filtering, regression of six motion parameters
dissociative subtype	
Rabinak et al., 2011 (290)	temporal band-pass filtering, regression of WM, CSF, six movement parameters
Roy et al., 2013 (291)	not reported
Sripada et al., 2012 a, b (292,293)	temporal band-pass filtering

Thome et al., 2017 (294)	temporal band-pass filtering
Toazza et al., 2016 (295)	temporal band-pass filtering, regression of WM, CSF, six motion parameters
Wang et al., 2016 (296)	decreasing spatial noise
Yuan et al., 2016 (297)	temporal band-pass filtering, linear and quadratic detrending, regression of WM, CSF, six motion parameters
Yuan et al., 2017 a (298)	temporal band-pass filtering
Yuan et al., 2017 b (299)	temporal band-pass filtering, linear detrending, regression of WM, CSF, 24 parameters mode (Friston)
Zhang et al., 2016 (300)	temporal band-pass filtering, linear detrending, regression of WM, CSF, six movement parameters
Zhu et al., 2017 (301)	temporal band-pass filtering, linear regression of WM, CSF, six parameters
Chronic pain	
Ayoub et al., 2019 (302)	temporal band-pass filtering, regression of WM, CSF, six dimensions
Baliki et al., 2011 (303)	temporal high-pass filtering, linear regression
Bhatt et al., 2019 (304)	temporal band-pass filtering, regression of WM, CSF, six parameters
Bolwerk et al., 2013 (305)	not reported
Case et al., 2017 (306)	temporal band-pass filtering, motion correction
Cauda et al., 2009 (307)	temporal band-pass filtering, regression of WM, CSF, six motion parameters
Ceko et al., 2013 (137)	temporal band-pass filtering, regression of WM, CSF, six motion parameters
older subjects	
younger subjects	
Ceko et al., 2015 (308)	temporal band-pass filtering, regression of WM, CSF, six motion parameters
Chen et al., 2016 (309)	temporal band-pass filtering, linear detrending
episodic migraine	
chronic migraine	
Cottam et al., 2018 (310)	regression of WM, CSF, six motion parameters
Fallon et al., 2016 (311)	temporal band-pass filtering
Flodin et al., 2014 (312)	temporal band/high-pass filtering, regression of WM and CSF
Flodin et al., 2016 (313)	temporal band-pass filtering, regression of WM and CSF
Han et al., 2013 (314)	temporal band-pass filtering
He et al., 2018 (315)	temporal band-pass filtering, linear detrending, scrubbing regression
Hong et al., 2014 (316)	temporal band-pass filtering, regression of WM, CSF, six parameters
Male	
Female	
Ichesco et al., 2012 (317)	temporal band-pass filtering, removing linear drift, regression of WM, CSF and realignment parameters
Ichesco et al., 2014 (318)	temporal band-pass filtering, removing linear drift, regression of WM, CSF and realignment parameters
Jiang et al., 2016 (319)	temporal band-pass filtering, linear detrending, regression of WM, CSF, six motion parameters
Khan et al., 2014 (320)	temporal band-pass filtering, regression of WM, CSF, six motion parameters
Kilpatrik et al., 2014 (321)	temporal band-pass filtering, regression of WM, CSF, six motion parameters
Kim et al., 2017 (322)	temporal band-pass filtering, regression of WM, CSF, six motion parameters
Kong et al., 2018 (323)	temporal band-pass filtering

Kucyi et al., 2014 (324)	temporal band-pass filtering, regression of WM, CSF, six motion parameters
Kutch et al., 2015 (325)	temporal high-pass filtering, regression of WM, CSF, six motion parameters
Li et al., 2016 (326)	temporal band-pass filtering
Li et al., 2017 (327)	temporal band-pass filtering, linear detrending
Liu et al., 2017 (328)	temporal band-pass filtering, detrending
Martucci et al., 2015 (329)	temporal high-pass filtering, regression of WM and CSF
Michels et al., 2016 (330)	removing all non-neuronal noise
medication-overuse headache	
myofascial pain	
Niddam et al., 2016 (331)	temporal band-pass filtering, linear detrending, regression of WM, CSF, six motion parameters
migraine without aura	
migraine with aura	
Pujol et al., 2014 (332)	temporal high-pass filtering, drift removal, regression of WM and CSF
Qi et al., 2016 (333)	temporal band-pass filtering, regression of WM, CSF, six motion parameters
Truini et al., 2016 (334)	not reported
Wang et al., 2017 (184)	temporal band-pass filtering
Wei et al., 2016 a (335)	temporal band-pass filtering, regression of WM, CSF, six movement parameters, linear detrending
Wei et al., 2016 b (336)	temporal band-pass filtering, regression of WM, CSF, six movement parameters, linear detrending
Wei et al., 2017 (337)	temporal band-pass filtering, regression of WM, CSF, six movement parameters, linear detrending
Wei et al., 2019 (338)	temporal band-pass filtering, detrending
Yu et al., 2017 (339)	temporal band-pass filtering, regression of WM and CSF
Zhang et al., 2017 (340)	temporal band-pass filtering
Zhang et al., 2019 (341)	temporal band-pass filtering

633

634 **Table S21:** CSF = cerebrospinal fluid, WM = white matter.

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