Supplementary Material

**Methods**

*Meta-analytic approach*

Details of the Seed-based d Mapping with Permutation of Subject Images (SDM-PSI) method have been published previously (Albajes-Eizagirre et al., 2019c, 2019a). SDM-PSI conducts a standard permutation of subject images (PSI). In addition, it uses unbiased estimation of effect sizes based on MetaNSUE algorithms (a method for univariate meta-analysis developed to include studies from which the meta-analytic researcher knows that the analysis was not statistically significant, but he/she cannot know the actual effect size), random-effects models, Freedman-Lane-based permutations, and threshold-free cluster enhancement (TFCE) statistics (Albajes-Eizagirre et al., 2019c). In summary: (1) SDM-PSI estimates the lower and upper bounds of possible effect size images for each study within a GM mask using an a 20 mm full width half maximum (FWHM) anisotropic Gaussian kernel and 2 mm voxel size; (2) uses MetaNSUE based on multiple imputations of maximum likelihood estimation (MLE) to estimate the most likely effect size and its standard error (Albajes-Eizagirre et al., 2019b); (3) each imputed dataset is meta-analyzed and then Rubin's rules are used to combine these imputed meta-analyzed datasets; (4) SDM-PSI recreates subject images and then conducts a standard PSI, in which the maximum statistic of the combined meta-analysis image is saved. In order to allow family-wise error (FWE) rate correction for multiple comparisons, the distribution of the maximum statistic is used; (5) Hedge’s g-corrected effect sizes are calculated at the group level; (6) a random-effects model is used for the meta-analysis, in which the design matrix includes any covariate used in the MLE step and the weight of a study is the inverse of the sum of its variance and the between-study heterogeneity τ2.

Regarding the combination of reported coordinate data and statistical maps, the recreation of effect size maps from brain maps is straightforward as it only involves the transformation to Montreal Neurological Institute (MNI) stereotaxic space (in case that they were not already reported in this space) and the voxel-wise conversion of t-values (or p- or z-values) into effect sizes. For the recreation of effect size maps from peak information, effect-sizes are calculated following standard methods in those voxels containing a peak reported in the results table of the original studies, and for the remaining voxels, an effect-size is estimated depending on the correlation to close peaks using an anisotropic unnormalized Gaussian kernel. This kernel assigns higher effect-sizes to those voxels more correlated with the peak, whereas small effect-sizes are assigned to those that, even if still neighboring, show only a small correlation at the population level.

**Results**

**Supplementary Table 1.** Regions showing positive correlations between baseline BOLD response and clinical response in anxiety-related disorders; uncorrected p<0.005, cluster size >10 voxels.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Region** | **Ke** | **SDM-Z** | **Voxel P** | **MNI coordinates** | **I2** | **Bias test P** |
| Frontostriatal cluster\* (bilateral dmPFC/dACC, IFG, AIC, striatum, among others) | 20650 | 5.581 | <0.001 | 6,38,22 | 0.56% | 0.217 |
| Left fusiform gyrus\* | 935 | 4.168 | <0.001 | -16,-46,-12 | 0.01% | 0.506 |
| Cerebellum, vermic lobule VI\* | 698 | 3.775 | <0.001 | 2,-64,-24 | 0% | 0.907 |
| Left thalamus | 160 | 3.434 | <0.001 | -4,-22,8 | 0% | 0.841 |
| Left supplementary motor area\* | 153 | 3.439 | <0.001 | -6,-20,58 | 0% | 0.636 |
| Right middle temporal gyrus\* | 115 | 3.526 | <0.001 | 50,-46,12 | 0% | 0.66 |
| Right middle occipital gyrus\* | 110 | 3.682 | <0.001 | 32,-64,28 | 1.15% | 0.823 |
| Right inferior temporal gyrus | 53 | 3.112 | <0.001 | 52,-34,-16 | 0.04% | 0.981 |
| Left postcentral gyrus | 50 | 3.032 | 0.001 | -46,-16,40 | 10.56% | 0.703 |
| Left inferior parietal lobule | 43 | 3.045 | 0.001 | -36,-54,36 | 4.3% | 0.64 |
| Left middle temporal gyrus | 42 | 3.15 | <0.001 | -44,-64,0 | 0.33% | 0.623 |
| Right precuneus | 37 | 2.949 | 0.002 | 6,-54,48 | 0.19% | 0.945 |
| Right middle temporal gyrus | 37 | 2.95 | 0.002 | 64,-36,-8 | 0.42% | 0.63 |
| Right precentral gyrus | 33 | 3.169 | <0.001 | 32,-10,54 | 0% | 0.837 |
| Left middle temporal gyrus | 30 | 2.99 | 0.001 | -40,-60,20 | 0.01% | 0.945 |
| Left fusiform gyrus | 22 | 2.819 | 0.002 | -34,-64,-18 | 0.53% | 0.78 |
| Right superior frontal gyrus | 19 | 3.094 | <0.001 | 22,56,2 | 0.31% | 0.282 |
| Right thalamus | 19 | 3.029 | 0.001 | 8,-18,2 | 0.08% | 0.932 |
| Left middle occipital gyrus\* | 19 | 2.98 | 0.001 | -36,-88,18 | 6.38% | 0.614 |
| Posterior cingulate cortex | 14 | 2.763 | 0.003 | -6,-32,40 | 16.28% | 0.262 |
| Midcingulate cortex | 13 | 2.937 | 0.002 | 4,-10,32 | 5.09% | 0.569 |
| Right cuneus | 12 | 2.902 | 0.002 | 8,-80,4 | 0% | 0.574 |
| Right fusiform gyrus | 12 | 2.795 | 0.003 | 38,-12,-32 | 2% | 0.823 |
| Left middle occipital gyrus\* | 11 | 2.81 | 0.002 | -24,-66,32 | 0% | 0.745 |
| Right supramarginal gyrus | 11 | 2.775 | 0.003 | 52,-46,24 | 0.52% | 0.279 |
| Right inferior occipital gyrus\* | 10 | 2.903 | 0.002 | 40,-76,-16 | 11.59% | 0.191 |

Only one local peak per gray matter brain region is displayed. Abbreviations: Ke, cluster extent; MNI: Montreal Neurological Institute; SDM: Signed Differential Mapping; P: p-value; I2: Percentage of variance attributable to study heterogeneity; dmPFC: dorsomedial prefrontal cortex; dACC: dorsal anterior cingulate cortex; IFG: inferior frontal gyrus; AIC: anterior insular cortex. \*Results maintained when excluding Price et al. (2018).

**Supplementary Table 2.** Regions showing positive correlations between baseline BOLD response and clinical response in obsessive-compulsive disorder; uncorrected p<0.005, cluster size >10 voxels.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Region** | **Ke** | **SDM-Z** | **Voxel P** | **MNI coordinates** | **I2** |
| Left inferior frontal gyrus\* | 244 | 4.044 | <0.001 | -50,34,14 | 1.79 % |
| Right anterior insula\* | 194 | 3.769 | <0.001 | 30,26,-6 | 2.28 % |
| Left middle temporal gyrus\* | 203 | 3.329 | <0.001 | -58,-54,22 | 0.7% |
| Left cuneus | 132 | 3.772 | <0.001 | -4,-92,14 | 1.7% |
| Dorsomedial prefrontal cortex\* | 108 | 3.372 | <0.001 | -8,26,36 | 0.78% |
| Left middle temporal gyrus\* | 53 | 3.271 | <0.001 | -62,-28,-12 | 3.54% |
| Right inferior frontal gyrus | 54 | 2.957 | 0.002 | 52,32,16 | 0.37% |
| Left anterior insula\* | 53 | 3.041 | 0.001 | -28,26,-2 | 0.04% |
| Right posterior insula\* | 51 | 3.274 | <0.001 | 38,-12,-2 | 16.98% |
| Right caudate | 38 | 3.354 | <0.001 | 14,10,14 | 0.03% |
| Left caudate\* | 33 | 2.83 | 0.002 | -14,20,8 | 4.55% |
| Left ventromedial prefrontal cortex\* | 27 | 3.095 | <0.001 | -12,68,2 | 0.07% |
| Left thalamus\* | 25 | 3.084 | 0.001 | -4,-20,-4 | 0.03% |
| Right supramarginal gyrus\* | 22 | 3 | 0.001 | 66,-28,28 | 0.03% |
| Right thalamus\* | 16 | 3.067 | 0.001 | 6,-14,2 | 0.07% |
| Left inferior temporal gyrus | 14 | 2.815 | 0.002 | -58,-54,-6 | 0% |
| Right ventromedial prefrontal cortex | 12 | 3.017 | 0.001 | 8,68,16 | 0.93% |
| Left putamen\* | 12 | 2.772 | 0.003 | -30,2,2 | 4.56% |
| Left inferior frontal gyrus\* | 12 | 2.849 | 0.002 | -58,10,18 | 0.31% |
| Right middle frontal gyrus\* | 11 | 2.721 | 0.003 | 40,42,22 | 0.49% |
| Right supplementary motor area | 10 | 2.789 | 0.003 | 12,12,62 | 32.48% |
| Left posterior insula\* | 10 | 2.659 | 0.004 | -42,-2,12 | 0.7% |

Only one local peak per gray matter brain region is displayed. Abbreviations: Ke, cluster extent; MNI: Montreal Neurological Institute; SDM: Signed Differential Mapping; P: p-value; I2: Percentage of variance attributable to study heterogeneity.\*Results present in the main analysis (uncorrected p<0.005, cluster size >10 voxels).

**Supplementary Table 3.** Regions showing positive correlations between baseline BOLD response and clinical response in social anxiety disorder; uncorrected p<0.005, cluster size >10 voxels.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Region** | **Ke** | **SDM-Z** | **Voxel P** | **MNI coordinates** | **I2** |
| Right rolandic operculum\* | 171 | 3.936 | <0.001 | 52,-12,12 | 0.66 % |
| Subgenual anterior cingulate cortex\* | 72 | 3.135 | <0.001 | 4,34,-8 | 2.86 % |
| Right precentral gyrus\* | 59 | 2.928 | 0.002 | 52,-14,46 | 1.38% |
| Right posterior insula\* | 32 | 3.093 | <0.001 | 42,-2,-6 | 0.94% |
| Left rolandic operculum\* | 27 | 2.955 | 0.002 | -50,-16,12 | 0.21% |
| Right dorsolateral prefrontal cortex\* | 23 | 3.542 | <0.001 | 42,4,54 | 6.28% |
| Left supplementary motor area\* | 18 | 3.071 | 0.001 | -6,-24,60 | 2.41% |
| Posterior cingulate cortex\* | 15 | 2.925 | 0.002 | -2,-30,40 | 4.45% |
| Right middle frontal gyrus\* | 13 | 3.013 | 0.001 | 28,34,48 | 6.47% |

Only one local peak per gray matter brain region is displayed. Abbreviations: Ke, cluster extent; MNI: Montreal Neurological Institute; SDM: Signed Differential Mapping; P: p-value; I2: Percentage of variance attributable to study heterogeneity. \*Results present in the main analysis (uncorrected p<0.005, cluster size >10 voxels).

 **Supplementary Figure 1.** Regions showing positive correlations between baseline BOLD response and clinical response across anxiety-related disorders when excluding Price et al. (2018) (p<0.05 FWE-corrected).



**Supplementary Figure 2.** Regions showing positive correlations between baseline BOLD response and clinical response across anxiety-related disorders when excluding Burklund et al. (2017) (p<0.05 FWE-corrected).

**Supplementary Figure 3.** Regions showing positive correlations between baseline BOLD response and clinical response across anxiety-related disorders (uncorrected p<0.005).



**Supplementary Figure 4.** Regions showing positive correlations between baseline BOLD response and clinical response for obsessive-compulsive disorder studies (uncorrected p<0.005).



**Supplementary Figure 5.** Regions showing positive correlations between baseline BOLD response and clinical response for social anxiety disorder studies (uncorrected p<0.005).

| **Section and Topic** | **Item #** | **Checklist item** | **Location where item is reported** |
| --- | --- | --- | --- |
| **TITLE** | | |  |
| Title | 1 | Identify the report as a systematic review. | Page 1 |
| **ABSTRACT** | | |  |
| Abstract | 2 | See the PRISMA 2020 for Abstracts checklist. | Page 2 |
| **INTRODUCTION** | | |  |
| Rationale | 3 | Describe the rationale for the review in the context of existing knowledge. | Page 3 |
| Objectives | 4 | Provide an explicit statement of the objective(s) or question(s) the review addresses. | Pages 4-5 |
| **METHODS** | | |  |
| Eligibility criteria | 5 | Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses. | Pages 5-6 |
| Information sources | 6 | Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted. | Page 5 |
| Search strategy | 7 | Present the full search strategies for all databases, registers and websites, including any filters and limits used. | Page 5 |
| Selection process | 8 | Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process. | Page 6 |
| Data collection process | 9 | Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process. | Page 6 |
| Data items | 10a | List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect. | Pages 6-7 |
| 10b | List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information. | Page 7 |
| Study risk of bias assessment | 11 | Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process. | NA |
| Effect measures | 12 | Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results. | Page 7 |
| Synthesis methods | 13a | Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)). | NA |
| 13b | Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions. | Page 7 |
| 13c | Describe any methods used to tabulate or visually display results of individual studies and syntheses. | NA |
| 13d | Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used. | Page 7. Supplementary Material |
| 13e | Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression). | Page 8 |
| 13f | Describe any sensitivity analyses conducted to assess robustness of the synthesized results. | Page 8 |
| Reporting bias assessment | 14 | Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases). | Page 8 |
| Certainty assessment | 15 | Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome. | Page 8 |
| **RESULTS** | | |  |
| Study selection | 16a | Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram. | Figure 1 |
| 16b | Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded. | NA |
| Study characteristics | 17 | Cite each included study and present its characteristics. | Table 1 |
| Risk of bias in studies | 18 | Present assessments of risk of bias for each included study. | NA |
| Results of individual studies | 19 | For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots. | NA |
| Results of syntheses | 20a | For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies. | NA |
| 20b | Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect. | Page 9 |
| 20c | Present results of all investigations of possible causes of heterogeneity among study results. | Pages 10-11 |
| 20d | Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results. | Pages 9-10 |
| Reporting biases | 21 | Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed. | Pages 9-10. |
| Certainty of evidence | 22 | Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed. | Pages 9-10. Supplementary Tables 1-3. |
| **DISCUSSION** | | |  |
| Discussion | 23a | Provide a general interpretation of the results in the context of other evidence. | Pages 11-15 |
| 23b | Discuss any limitations of the evidence included in the review. | Pages 15-16 |
| 23c | Discuss any limitations of the review processes used. | Pages 15-16 |
| 23d | Discuss implications of the results for practice, policy, and future research. | Page 16 |
| **OTHER INFORMATION** | | |  |
| Registration and protocol | 24a | Provide registration information for the review, including register name and registration number, or state that the review was not registered. | Page 5 |
| 24b | Indicate where the review protocol can be accessed, or state that a protocol was not prepared. | Page 5 |
| 24c | Describe and explain any amendments to information provided at registration or in the protocol. | Page 5 |
| Support | 25 | Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review. | Page 17 |
| Competing interests | 26 | Declare any competing interests of review authors. | Page 17 |
| Availability of data, code and other materials | 27 | Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review. | NA |

*From:*  Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71

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