Aberrant Brain Networks Delineation Based on Emotional Task-fMRI Studies: A neuroimaging Meta-Analysis across Multiple Psychiatric Disorders

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Introduction

State of Art

Emotional Dysfunction Across Psychiatric Disorders [1] ⟫ **Transdiagnostic ALE Meta-Analysis** *Detecting Shared Neural Alterations* [1,2] ⟪ Broad domains & task conditions ; Prior knowledge–guided

Challenges

Incomplete diagnostic scope + **Clinical Misalignment** Knowledge-driven results vs real-world psychiatry + **Lost Specificity, Limited Interpretation**

Aims

Domain-Specific Focus: **Emotion** ⟫ **Common & Specific Neural Alterations** Full-spectrum psychiatric investigation ⟪ Latent shared abnormalities via **data-driven clustering** [3]

Methods

Screening Meta-Analyses and fMRI studies

Meta-Analyses (n = 68) from which included *fMRI studies* for screening (n = 4499)

↓

Exclude duplicate *fMRI studies* (n = 1150)

↓

Exclude not qualified *fMRI studies* according to In/Exclusion criteria (n = 3047)

Inclusion

Qualified *fMRI studies* included in our transdiagnostic meta-analyses (n = 302)

Literature Screening
(*302* Studies Included)

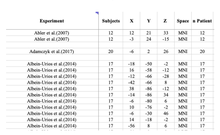
Exclusion details:
1) No adult sample (n = 374)
2) Group sample size < 7 subjects (n = 20)
3) No qualified patient (n = 190); No healthy control group for comparison (n = 46)
4) No task fMRI studies (n = 369)
5) No coordinate reported (n = 12)
6) No English journal publication (n = 8)
7) No available references (n= 17)
8) ROI studies (n = 160)
9) No significant fMRI activation results (n = 38)
10) Control condition is baseline (e.g., fixation, blank trials) condition (n = 85)
11) No qualified emotional task domain (n = 1520)
12) No qualified emotional contrasts (n = 208)

Data Collection

(x, y, z)

Conditions of Interest:
Group comparisons (emotional vs neutral; main & interaction effects)

Collected Coordinates



TAL2MNI for transforming TAL into MNI brain space [4]
Merged Overlapping samples
Activation Likelihood Estimation [5]

Between-group Data Input

JALE Toolbox ⇩ Scan Me

ALE Analyses

(threshold: cFWE $p < 0.05$, cluster-forming $p < 0.001$)

Data Analyses

An overall cross-diagnostic ALE meta-analysis

Category-driven

Diagnosis-specific ALE meta-analyses

Step1: Sort out experiments by DSM5 diagnoses

Step2: ALE meta-analyses in each diagnosis

Data-driven

ALE meta-analyses within optimal Meta-analytic groups (MAG) [2]

Step1: Correlation-Matrix-Based Clustering ➔ MAGs

Step2: MAGs Evaluation

Step3: ALE meta-analyses in each MAG

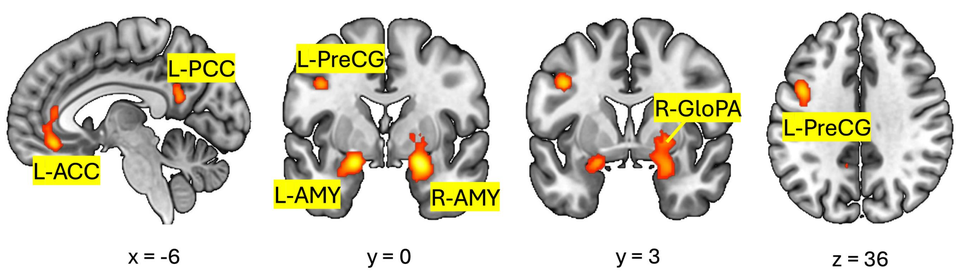
Per-Experiment Modeled Activation (MA) Map
↓
Converted each MA map to 1D feature vector
↓
Concatenated experiment-by-voxel matrix
↓
Created an experiment-by-experiment matrix to represent spatial similarity of MAs (Spearman correlation, 1-*r*)
↓
Agglomerative Clustering on this matrix (k = 2 to k = 25, average linkage)
↓
Clustering Metrics – SI score, CH score and ESD – for evaluation

The Representation Ratio (overrepresented, value > 1 or underrepresented, value < 1) of a certain category (k) in cluster *(a)* and MAG *(m),* respectively :

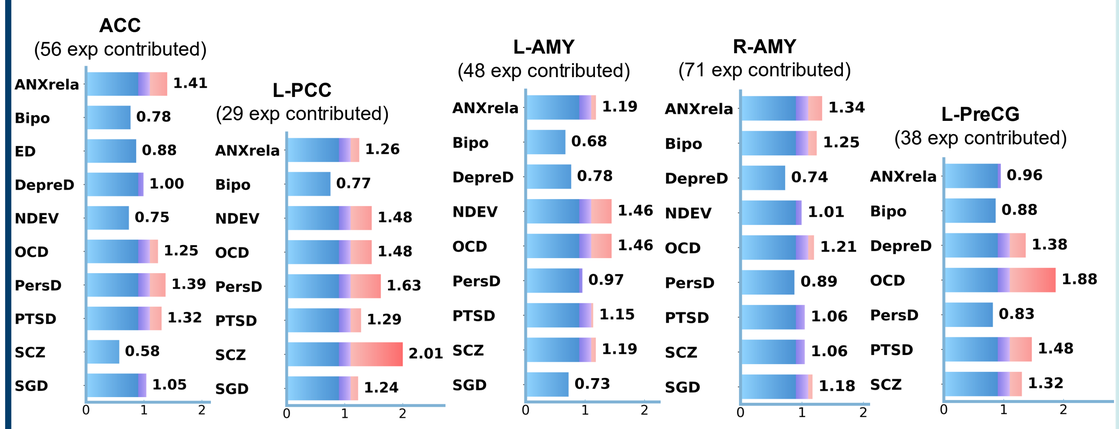
$$R_{k,a} = \left(\frac{N_{k,a}}{N_{k,\text{total}}}\right) \Big/ \left(\frac{N_a}{N_{\text{total}}}\right) \qquad R_{k,m} = \left(\frac{N_{k,m}}{N_{k,\text{total}}}\right) \Big/ \left(\frac{N_m}{N_{\text{total}}}\right)$$

Results

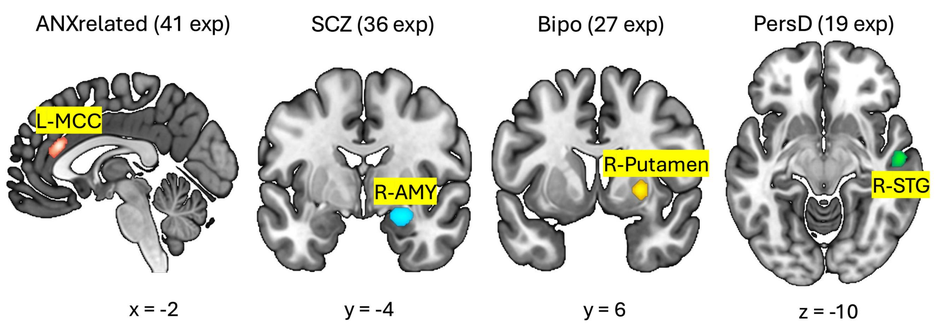
Cross-diagnostic ALE meta-analysis



L: Left; R: Right
ACC: Anterior Cingulate Cortex; PCC: Posterior Cingulate Cortex; AMY: Amygdala; GloPA: Globus Pallidus; PreCG: Precentral Gyrus



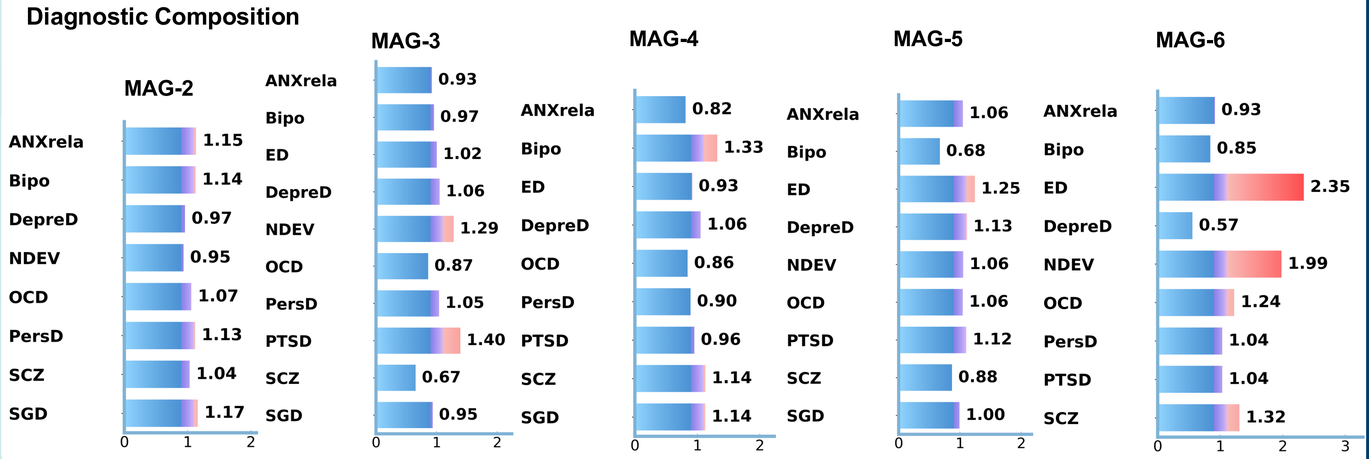
Disorder-specific ALE meta-analyses



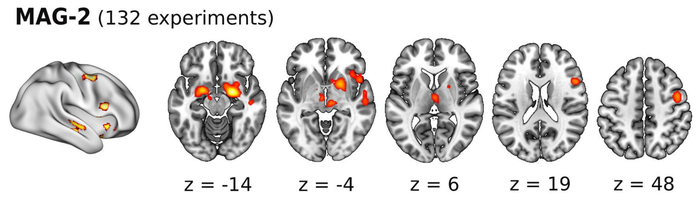
L: Left; R: Right
MCC: Middle Cingulate Cortex; AMY: Amygdala; STG: Superior Temporal Gyrus

- Five cross-diagnostic regions were identified.
- 14 categories: 4 consistent, 6 no consistent; 4 insufficient (< 17 exp).

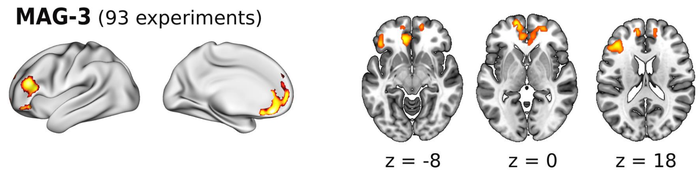
Diagnostic Composition



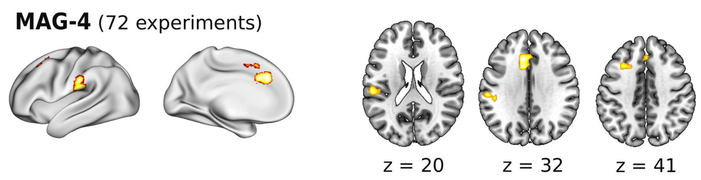
MAG-2 (132 experiments)



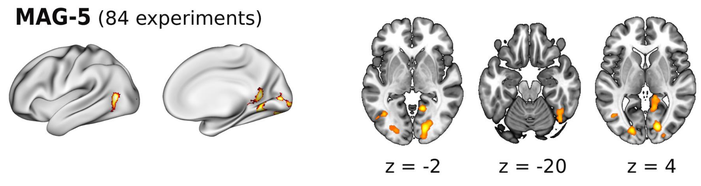
MAG-3 (93 experiments)



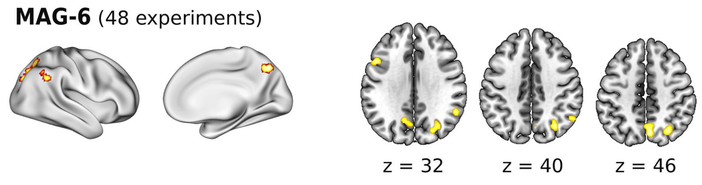
MAG-4 (72 experiments)



MAG-5 (84 experiments)



MAG-6 (48 experiments)



Cross-diagnostic ALE in each MAG

MAG-2: bilateral AMY, Putamen, Pallidum Insula, Thalamus, Inferior Frontal Gyrus (IFG), Frontal Operculum, STG/MTG, PreCG

MAG-3: (subgenual) ACC, Middle Frontal Gyrus (MFG), IFG, Insula, Frontal Pole

MAG-4: Middle Cingulate Cortex, Inferior Parietal Lobe, Parietal Operculum, MFG, Medial Superior Frontal Gyrus (preSMA)

MAG-5: Lingual Gyrus, Fusiform Gyrus, Inferior/Superior Lateral Occipital Gyrus, PCC

MAG-6: Inferior Parietal Sulcus, Precuneus, MFG, Angular Gyrus

Discussion

➢ Main contributors to cross-diagnostic regions: ANXrela, OCD, PTSD
➢ Lower contribution: Eating & Bipolar, Low emotion-related disorders
➢ DepresD-specific alteration: PreCG

Implication:
Shared stress-related processes may drive common neural deficits

➢ Minimal overlap between cross-diagnostic and disorder-specific ALE regions
➢ Interpret with caution: Limited dataset size

Implication:
Inconsistent findings may reflect clinical heterogeneity + experimental differences

➢ ALE-consistent, latent activation patterns identified
➢ MAG-2/3/4: balanced diagnostic clustering, reflecting transdiagnostic pattern
➢ MAG-5/6: more diagnosis-specific profiles

Implication:
MAG networks indicate distinct neural substrates of emotional dysfunction

[1]. McTeague, L. M., Rosenberg, B. M., Lopez, J. W., Carreon, D. M., Huemer, J., Jiang, Y., Chick, C. F., Eickhoff, S. B., & Etkin, A. (2020). Identification of Common Neural Circuit Disruptions in Emotional Processing Across Psychiatric Disorders. American Journal of Psychiatry, 177(5), 411-421. https://doi.org/10.1176/appi.ajp.2019.18111271. [2]. Boisvert, M., Dugré, J. R., & Potvin, S. (2024). Patterns of abnormal activations in severe mental disorders a transdiagnostic data-driven meta-analysis of task-based fMRI studies. Psychological Medicine, 1-12. https://doi.org/10.1017/s003329172400165x. [3]. Liu, X., Zhu, X. H., Qiu, P., & Chen, W. (2012). A correlation-matrix-based hierarchical clustering method for functional connectivity analysis. J Neurosci Methods, 211(1), 94-102. https://doi.org/10.1016/j.jneumeth.2012.08.016. [4]. Lancaster JL, Tordesillas-Gutierrez D, Martinez M, Salinas F, Evans A, Zilles K, Mazziotta JC, Fox PT. Bias between MNI and Talairach coordinates analyzed using the ICBM-152 brain template. Hum Brain Mapp. 2007;28:1194-1205. [5]. Eickhoff, S. B., Nichols, T. E., Laird, A. R., Hoffstaedter, F., Amunts, K., Fox, P. T., Bzdok, D., & Eickhoff, C. R. (2016). Behavior, sensitivity, and power of activation likelihood estimation characterized by massive empirical simulation. Neuroimage, 137, 70-85. https://doi.org/10.1016/j.neuroimage.2016.04.072

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