

## A revisited neuroimaging meta-analysis

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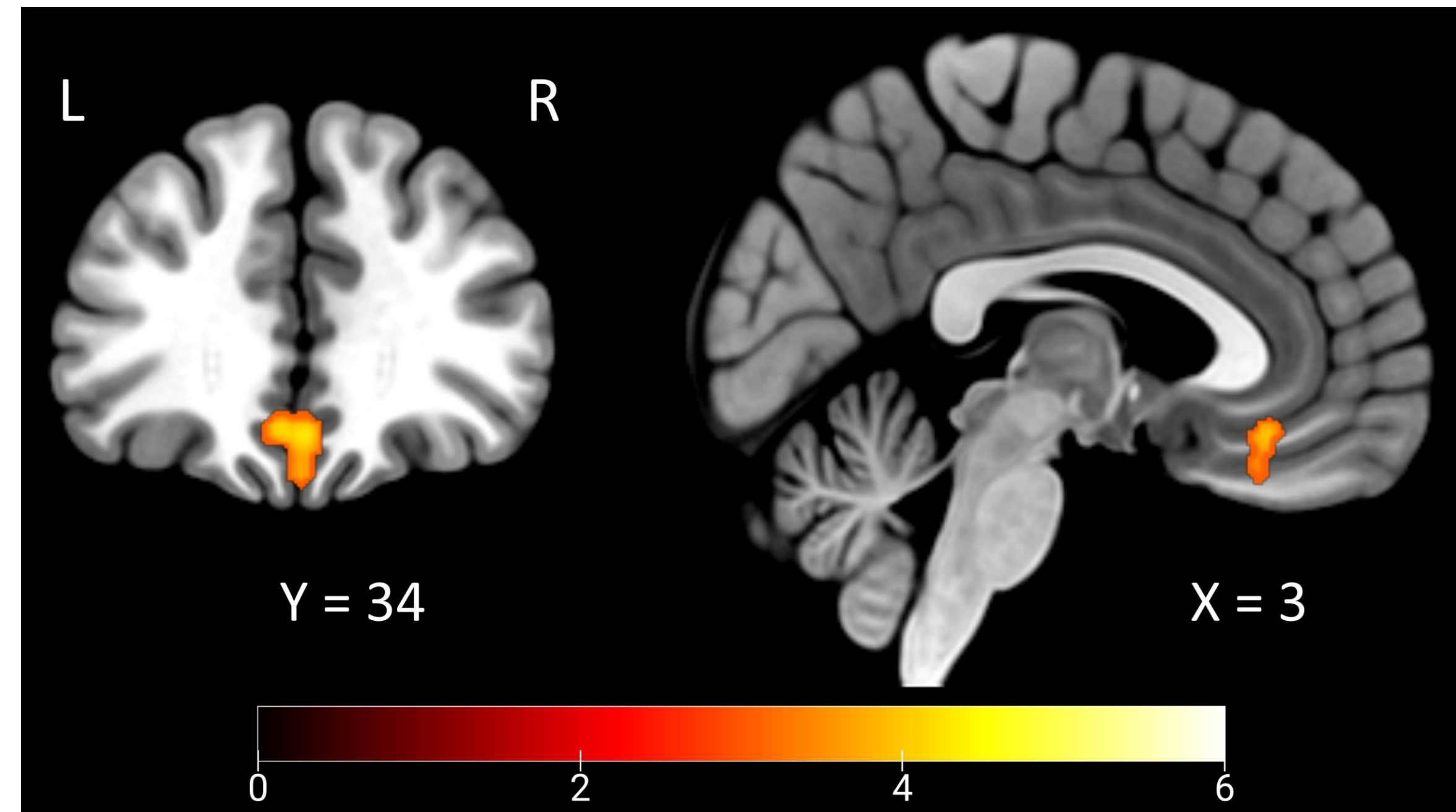
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### Introduction & Motivation

- Insomnia disorder (ID) is one of the most common sleep disorders [1].
- Previous meta-analysis (Masoud et al. 2018) showed no region of convergence [2].
- Revision of previous meta-analysis to test whether an increase of sample size yields convergence
- The meta-analysis followed the current best-practice guidelines for neuroimaging meta-analyses [3,4] and the PRISMA statement [5].
- The meta-analysis was preregistered at PROSPERO (CRD42021291597).
- We performed a coordinate-based meta-analysis (CBMA) in form of an activation likelihood estimation (ALE) analysis.
- The function of the found cluster of convergence was investigated by functional decoding
- We examined the connectivity patterns of the found cluster by meta-analytic co-activation modeling (MACM) and resting-state functional connectivity (RSFC) analysis

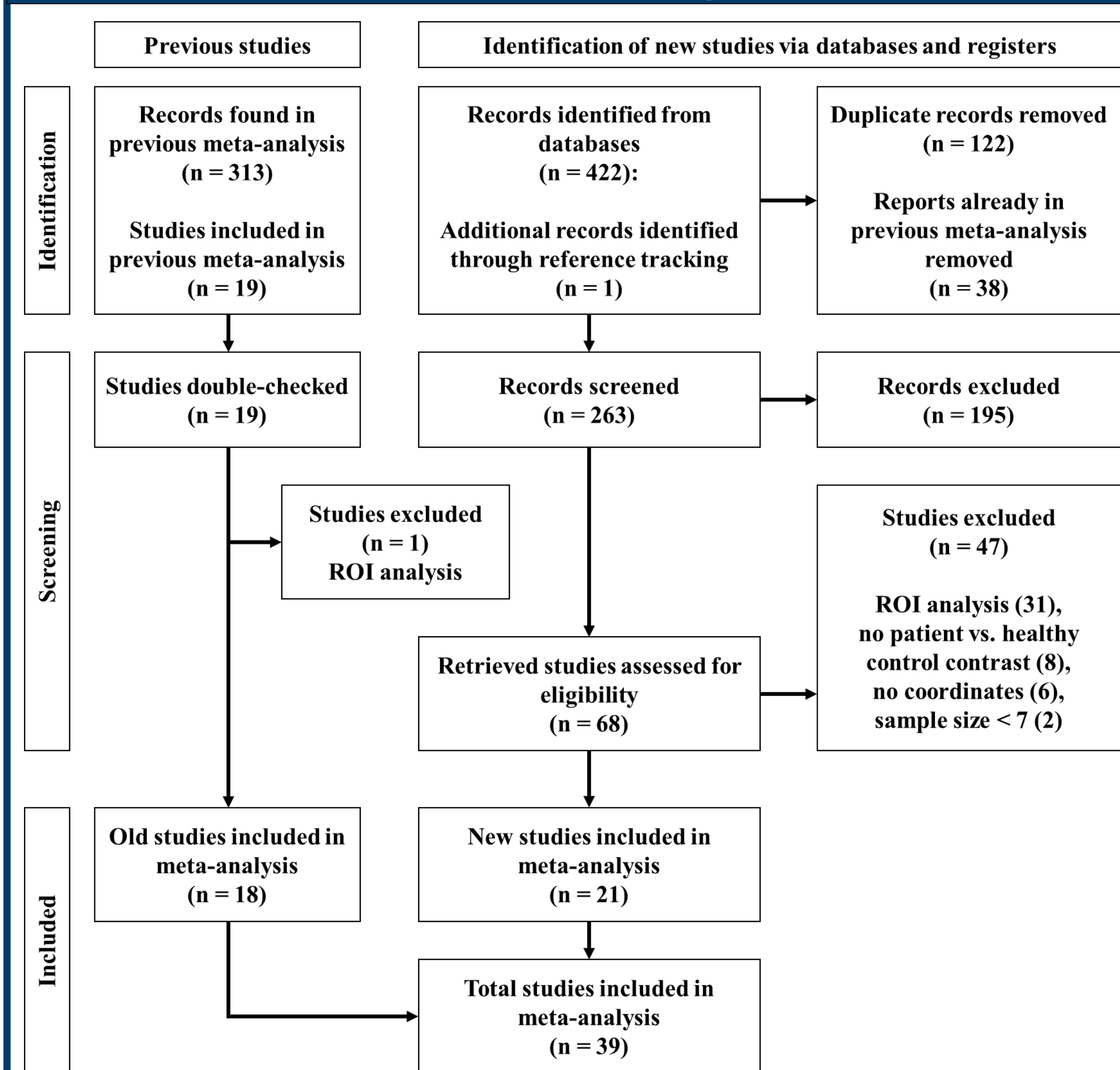
### Activation Likelihood Estimation

To identify potential brain area(s) that show convergent regional abnormality across the existing literature, the analyses were performed using the revised version of ALE.



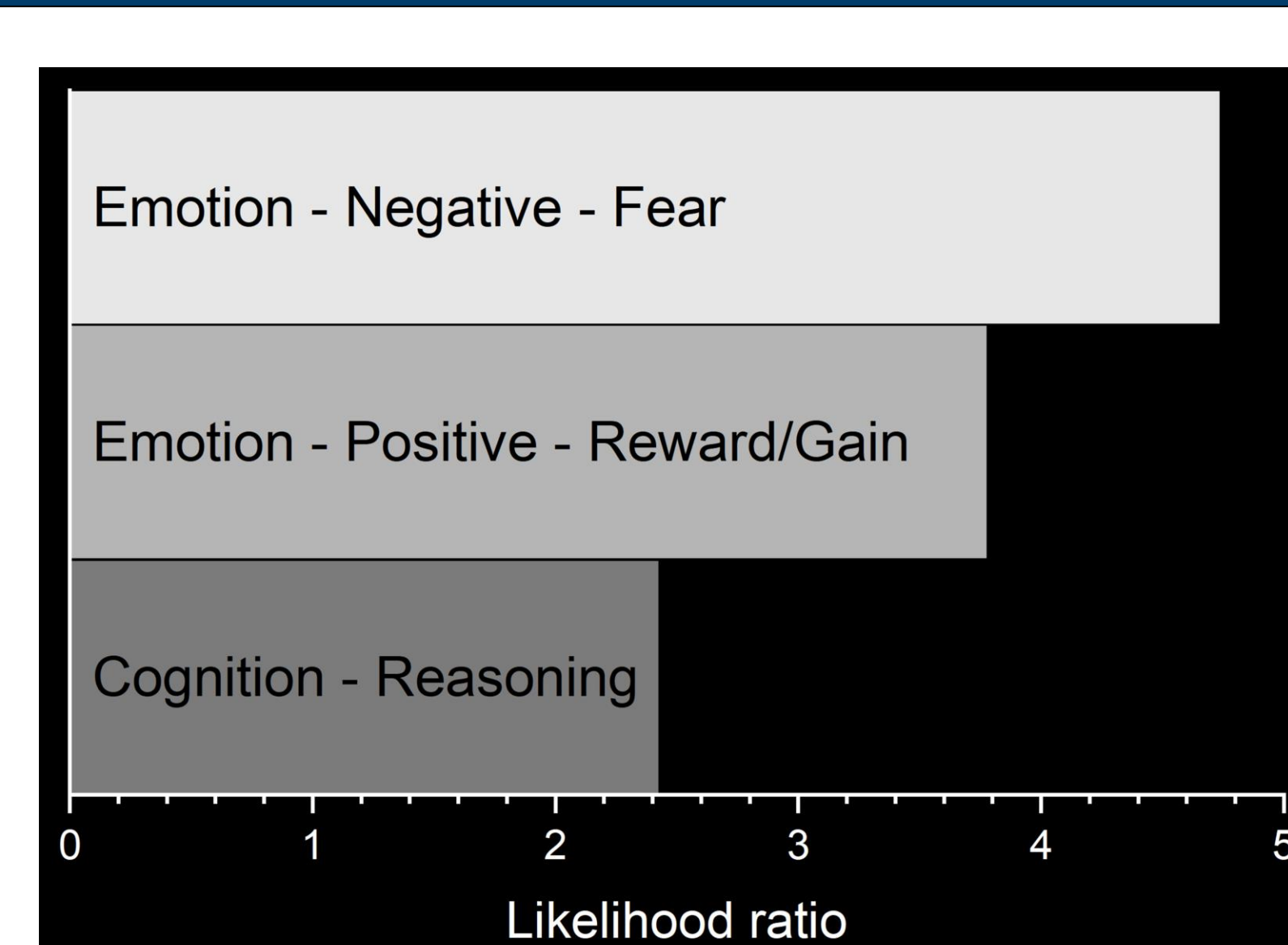
**Figure 2:** Convergent findings of the analysis on all 26 experiments. Abnormality in the subgenual anterior cingulate cortex (sgACC) (0/34/-14; 139 voxels) ( $p < 0.05$ , cFWE corrected). The coordinates are in MNI space.

### PRISMA flow diagram



**Figure 1:** PRISMA study selection strategy flow chart. The search was conducted in October 2021.

### Functional Decoding

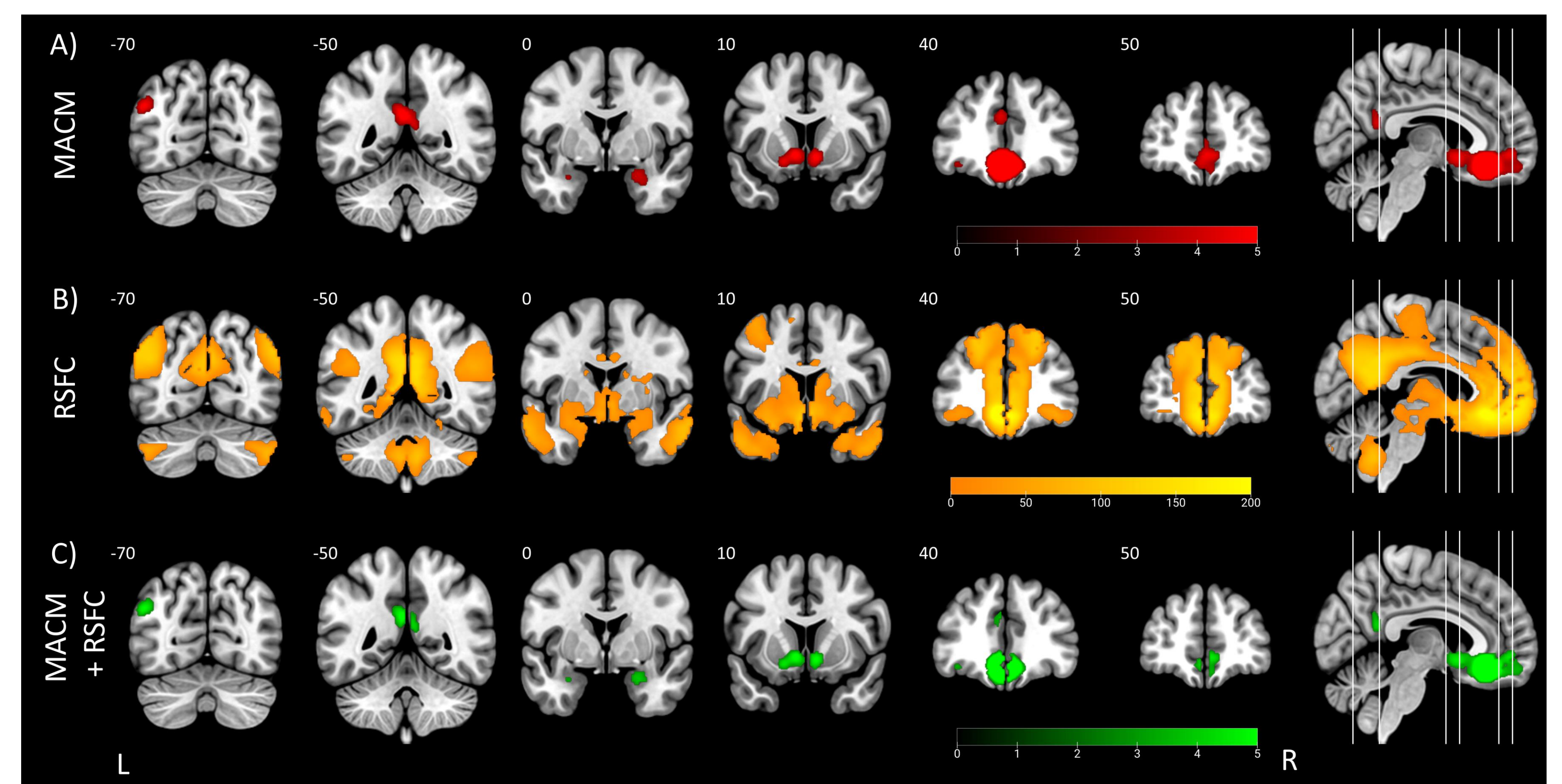


We identified the functional role of the sgACC cluster by using Functional Decoding based on t-fMRI meta-data of the BrainMap database. The cluster was used as seed to find types of tasks that activate the seed more likely than by chance, implicating the functional role of the seed region.

**Figure 3:** Functional decoding of the convergent cluster in the subgenual anterior cingulate cortex ( $p < 0.05$ , FDR corrected).

### Connectivity Patterns

- Task-based functional connectivity (FC) of the found cluster was obtained by performing an MACM on t-fMRI experiments of the BrainMap database. An ALE was conducted on t-fMRI experiments, that activated the seed regions, to find convergence over all their foci, including foci outside the seed, so that robustly coactivated regions can be identified.
- Task-free FC was acquired by applying RSFC on 192 healthy adults of the eNKI dataset, with the cluster of convergence as seed.
- Both resulting connectivity maps were overlapped to find robust FC of the seed.



**Figure 4:** Results of the connectivity analyses of the cluster of found convergence. A) MACM ( $p < 0.05$ , cFWE corrected). B) RSFC ( $p < 0.05$ , cFWE). C) Conjunction of both analyses. The coordinates are in MNI space.

### Search, selection and included studies

- Databases:** PubMed, Web of Science and BrainMap up to October 2021
- Inclusion criteria:**
  - "Insomnia patient vs healthy control" contrast
  - VBM, PET, rs-fMRI, t-fMRI analysis
  - Whole brain analysis
  - Group size  $> 6$
  - Reported coordinates of significant differences

**Table 1:** Summary of the included studies with number of studies, experiments, participants, foci, and portion of modalities. Shown are the original meta-analysis of 2018 and the revision of 2022.

Meta-analysis	Found reports	Included studies	Experiment number	ID patients	Healthy control	Peak foci
2018	313	19	19	404	395	115
2022	576	39	26	909	969	252

### Conclusion

Convergent structural and functional abnormalities were found in the sgACC in ID patients compared to healthy controls. Moreover, the cluster is associated with emotional processing and reasoning and showed functional connectivity to various regions of the salience and default-mode networks. The sgACC is a promising target for future studies to characterize the pathophysiology of insomnia.