



Methodological choices in Coordinate-Based Meta-Analysis: do we need a meta-meta level?

Jordi Manuella, PhD



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Who we are


Ospedale Koelliker
Prima la persona



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What's next!

How do we run CBMA nowadays?

What about replication in CBMA?

Can CBMA keep the pace of constantly increasing publication rate?



What's next!

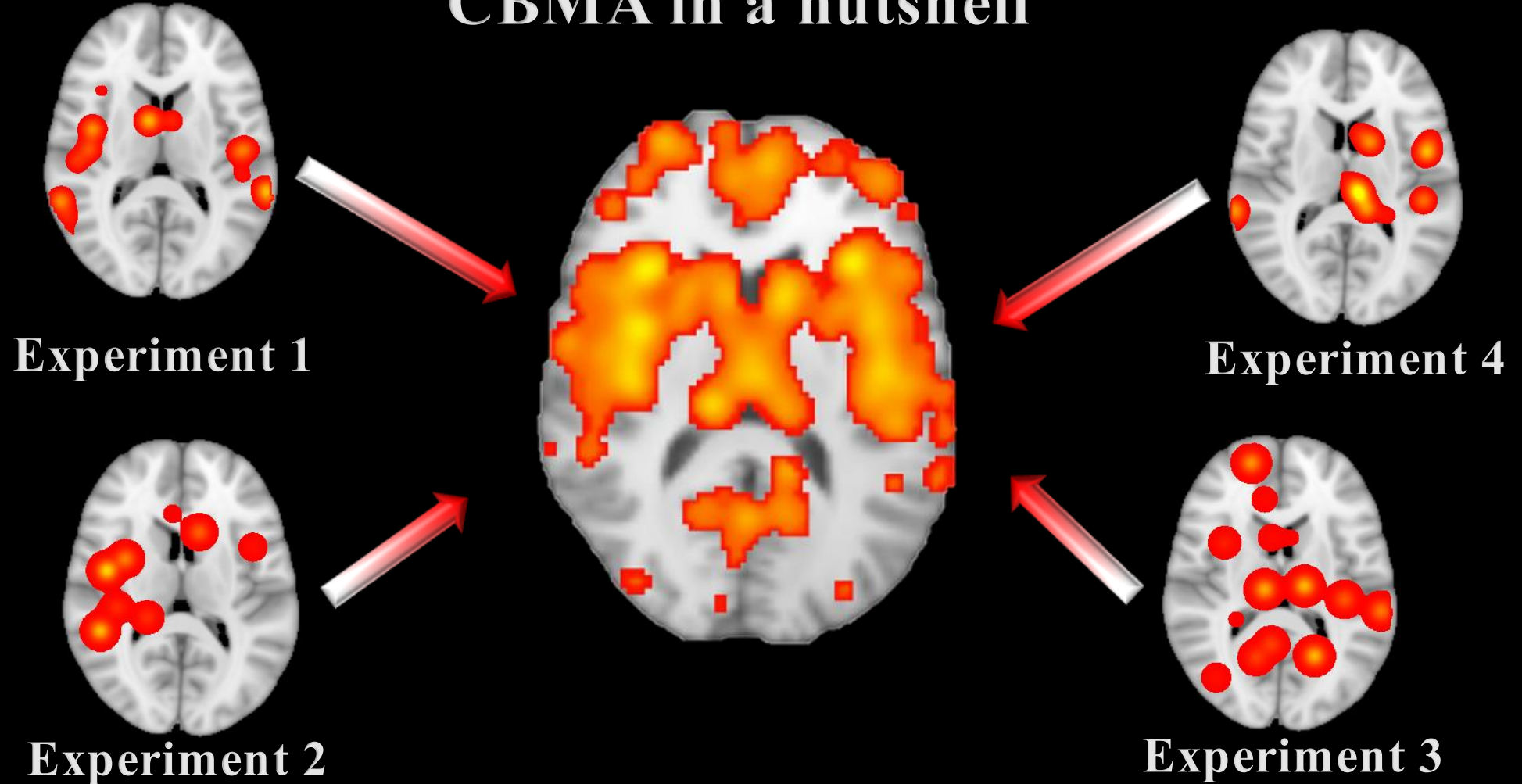
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CBMA in a nutshell

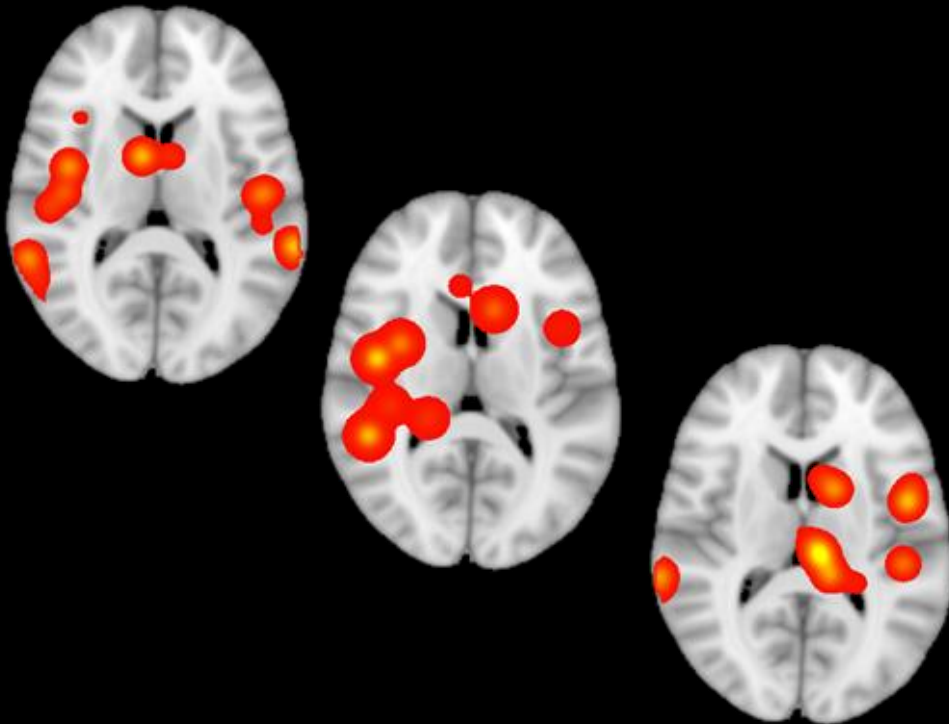


Main aim is to test convergence across previously published results



CBMA in a nutshell

Image based



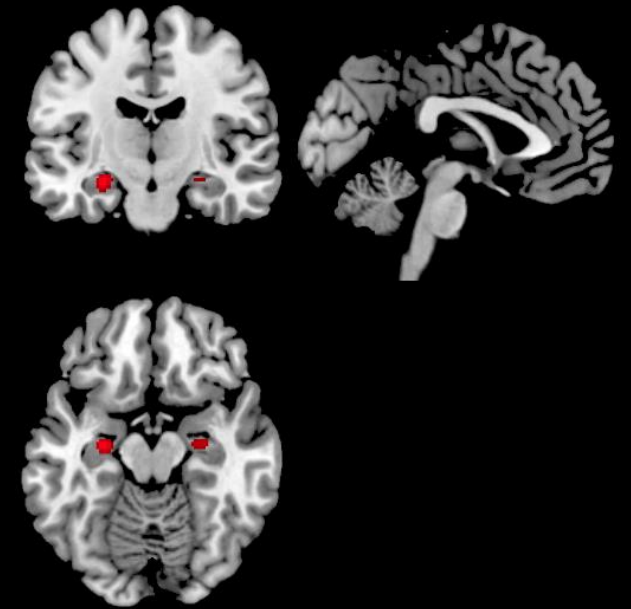
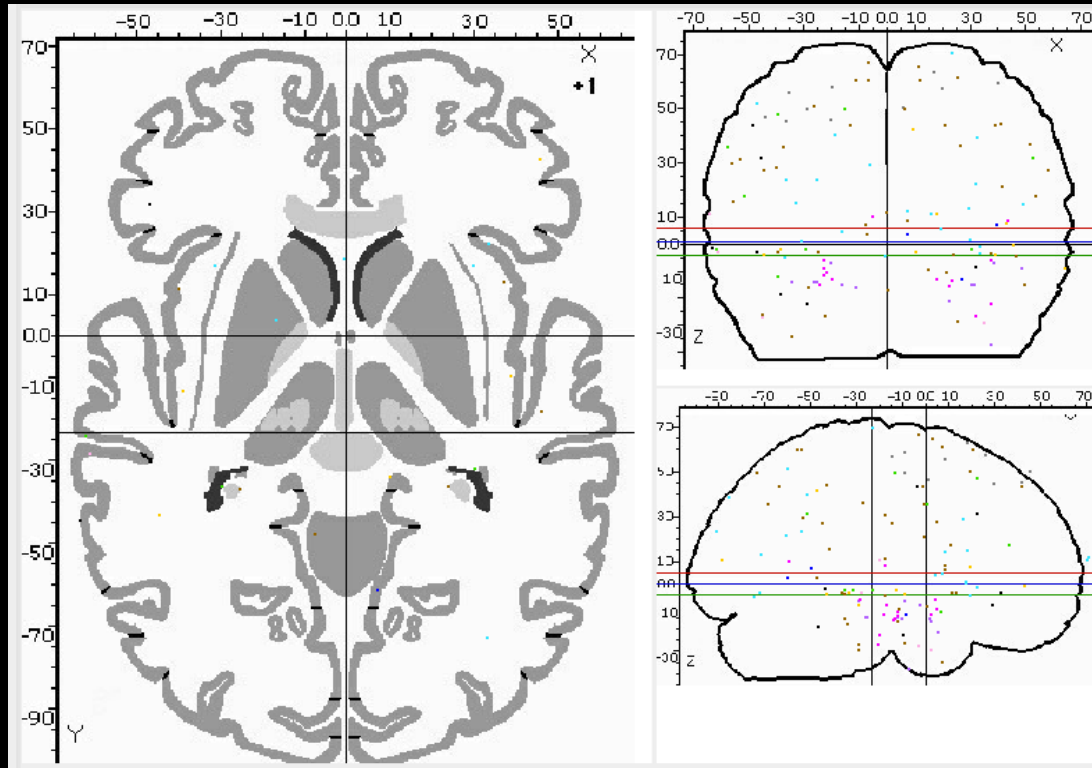
Coordinates based

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//RuschN,2004:TemporalLobeEpilepsyPatients>Normals,GrayMatter:Concentration:  
// Subjects=20  
53.00 -34.00 -12.00  
-17.00 5.00 -2.00  
17.00 51.00 17.00  
17.00 49.00 24.00  
  
//Salgado-PinedaP,2003:SchizophreniaPatients>Normals,GrayMatter:Volume:  
// Subjects=13  
-31.00 14.00 12.00  
-17.00 -27.00 -18.00  
58.00 -33.00 42.00  
-37.00 -50.00 16.00  
-23.00 0.00 10.00  
-21.00 7.00 5.00  
  
//Schmidt-WilckeT,2006:ChronicBackPainPatients>Normals,GrayMatter:  
// Subjects=18  
25.00 -18.00 5.00  
-23.00 -15.00 7.00  
-21.00 -25.00 4.00  
  
//WilkeM,2001:SchizophreniaPatients>Normals,GrayMatterVolume:  
// Subjects=48  
26.00 -55.00 -14.00  
12.00 -51.00 -13.00  
28.00 -42.00 -18.00  
32.00 -6.00 -1.00  
-20.00 -73.00 -17.00
```

CBMAs bypass the lack of shared whole-brain statistical maps



CBMA in a nutshell



Whole-brain maps are estimated from peak coordinates



Main CBMA algorithms side by side



GingerALE 3.0.2



Seed-based d Mapping

formerly "*Signed Differential Mapping*"

Tests spatial convergence

Tests effect size

**Doesn't model effect direction
(e.g. increase vs decrease)**

**Do model effect direction
(e.g. increase vs decrease)**

Can't model null results

Can model null results

Doesn't allow meta-regression

Allows meta-regression

Optimized for Brainmap database

Not related with specific databases

Should we consider ALE and SDM alternative algorithms?



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Our replication attempt



Article

Seeking Overlapping Neuroanatomical Alterations between Dyslexia and Attention-Deficit/Hyperactivity Disorder: A Meta-Analytic Replication Study

Donato Liloia ^{1,2,†}, Annachiara Crocetta ^{2,†}, Franco Cauda ^{1,2,3,*}, Sergio Duca ^{1,2}, Tommaso Costa ^{1,2} and Jordi Manuella ^{1,2}

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† These authors contributed equally to this work.

Abstract: The present work is a replication article based on the paper “Are there shared neural correlates between dyslexia and ADHD? A meta-analysis of voxel-based morphometry studies” by McGrath and Stoodley (2019). In the original research, the authors used activation likelihood estimation (ALE), a technique to perform coordinate-based meta-analysis (CBMA), to investigate the existence of brain regions undergoing gray matter alteration in association with both attention-deficit/hyper-activity disorder (ADHD) and dyslexia. Here, the same voxel-based morphometry dataset was analyzed, while using the permutation-subject images version of signed differential mapping (PSI-SDM) in place of ALE. Overall, the replication converged with the original paper in showing a limited overlap between the two conditions. In particular, no significant effect was found for dyslexia, therefore precluding any form of comparison between the two disorders. The possible influences of biological sex, age, and medication status were also ruled out. Our findings are in line with literature about gray matter alteration associated with ADHD and dyslexia, often showing conflicting results. Therefore, although neuropsychological and clinical evidence suggest some convergence between ADHD and dyslexia, more future research is sorely needed to reach a consensus on the neuroimaging domain in terms of patterns of gray matter alteration.

Keywords: coordinate-based meta-analysis; voxel-based morphometry; ADHD; dyslexia; ALE; seed-based mapping; replication article; reproducibility; open science; replication crisis



Citation: Liloia, D.; Crocetta, A.; Cauda, F.; Duca, S.; Costa, T.; Manuella, J. Seeking Overlapping Neuroanatomical Alterations between Dyslexia and Attention-Deficit/Hyperactivity Disorder: A Meta-Analytic Replication Study. *Brain Sci.* **2022**, *12*, 1367. <https://doi.org/10.3390/brainsci12101367>

Academic Editor: Paul E. Engelhardt



Our replication attempt

Original study (2019)

Replication (2022)

Separate analysis for each effect direction

Both effect directions combined

Secondary analysis of the subset of studies that controlled for brain volume

Same subset analysed but with SDM instead

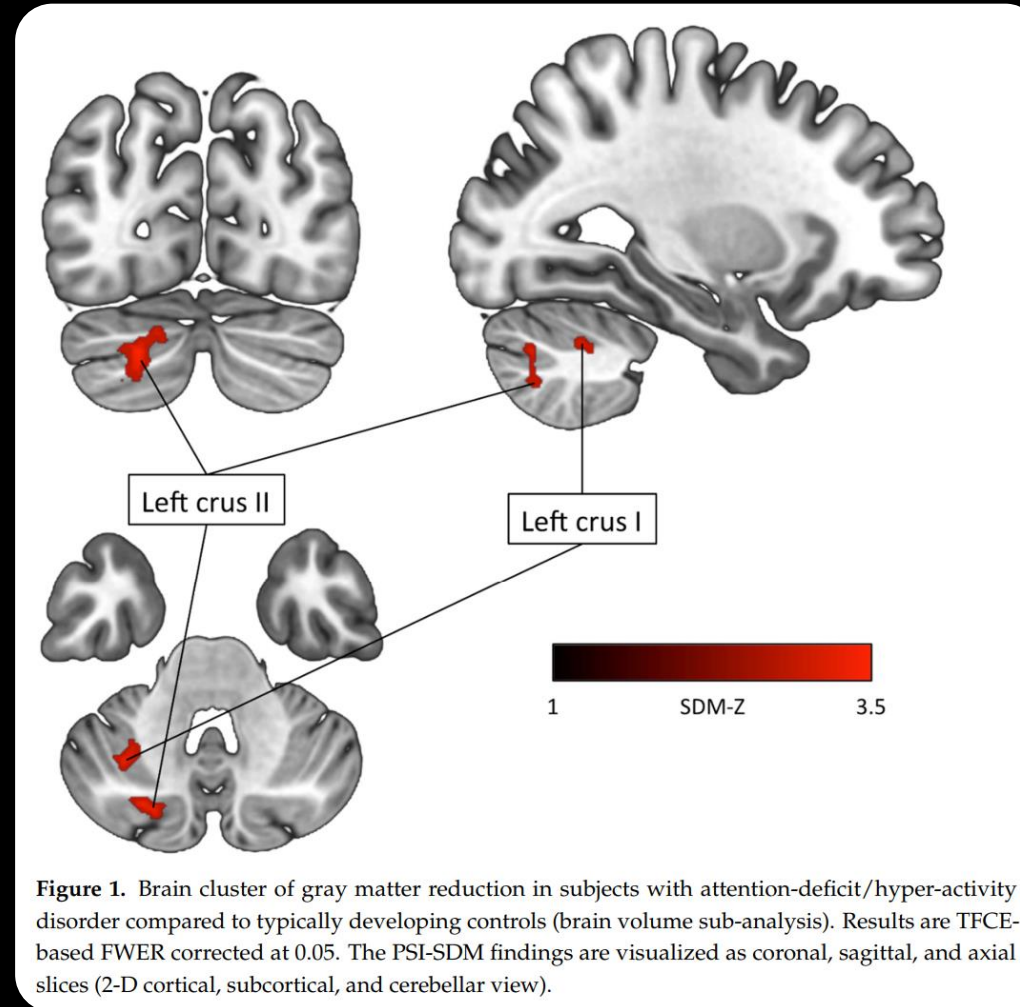
Secondary analysis of studies with participants < 12yo or >18yo

Meta-regression with mean age of the sample

Additional analysis including 9 studies reporting null results identified in the original paper



The only results of an overall failed replication



(Liloia et al., 2022)

GM reduction in ADHD patients (brain volume corrected studies only)



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A recent (scary!) real case...

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RESULTS BY YEAR

2,380 results

Page 1 of 238

1 **Aerobic Exercise Alters Brain Function and Structure in Parkinson's Disease: A Randomized Controlled Trial.**

Cite Johansson ME, Cameron IGM, Van der Kolk NM, de Vries NM, Klimars E, Toni I, Bloem BR, Helmich RC.

Ann Neurol. 2022 Feb;91(2):203-216. doi: 10.1002/ana.26291. Epub 2022 Jan 19.
PMID: 34951063 **Free PMC article.** Clinical Trial.

OBJECTIVE: Randomized clinical trials have shown that aerobic exercise attenuates motor symptom progression in **Parkinson's disease**, but the underlying neural mechanisms are unclear. Here, we investigated how aerobic exercise influences disease-related functional and ...



How can we manage such a massive screening phase?



...and a (still unheard) proposal

Neuroscience and Biobehavioral Reviews 137 (2022) 104659

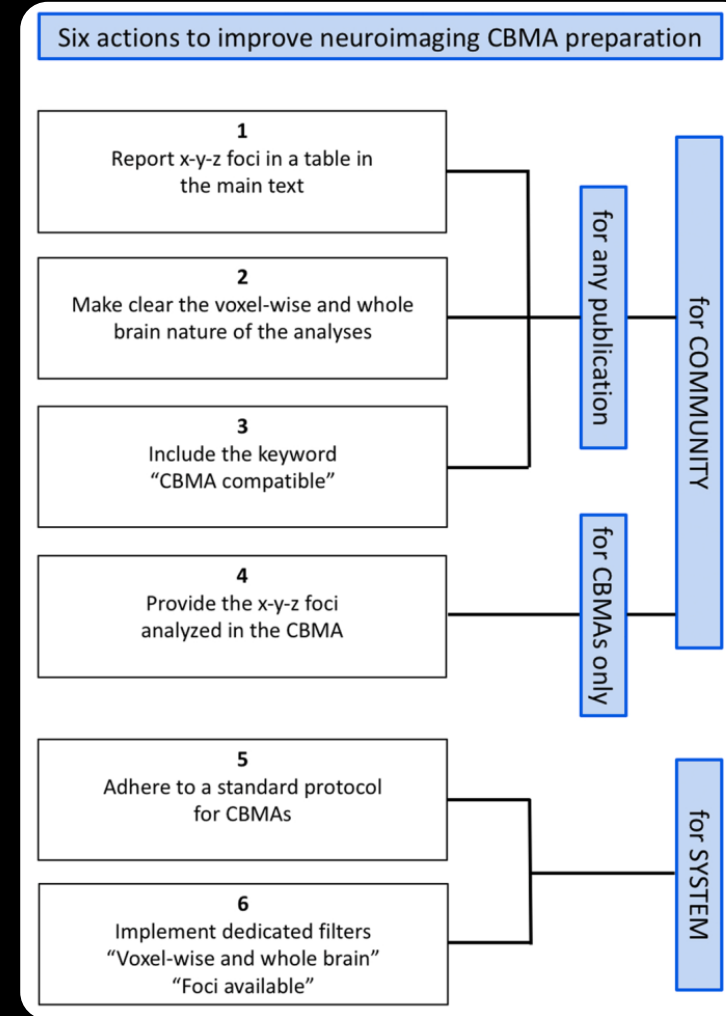


Contents lists available at [ScienceDirect](https://www.sciencedirect.com)

Neuroscience and Biobehavioral Reviews

journal homepage: www.elsevier.com/locate/neubiorev

Six actions to improve detection of critical features for neuroimaging coordinate-based meta-analysis preparation

Jordi Manuella ^{a,b}, Tommaso Costa ^{a,b,c,*}, Franco Cauda ^{a,b,c}, Donato Liloia ^{a,b}



The few available automatic tools are focused on content categorization



To sum up!

CBMAs still represent a powerfull way to test results convergence


**Available algorithms are rarely compared
(and maybe poorely comparable indeed)**

We need a practical or conceptual solution to make data selection feasible



Some meta-analytic open-source resources from our lab

Behavior Research Methods
<https://doi.org/10.3758/s13428-023-02185-3>



CBMAT: a MATLAB toolbox for data preparation and post hoc analyses in neuroimaging meta-analyses

Jordi Manuella^{1,2,3} · Donato Liloia^{1,2} · Annachiara Crocetta^{1,2} · Franco Cauda^{1,2,4} · Tommaso Costa^{1,2,4}

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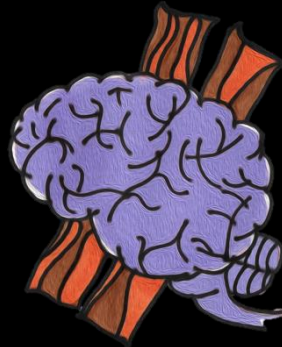


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DOI: 10.1002/hbm.25452

TECHNICAL REPORT WILEY

BACON: A tool for reverse inference in brain activation and alteration

Tommaso Costa^{1,2,3}  | Jordi Manuella^{1,2,3}  | Mario Ferraro^{3,4} | Donato Liloia^{1,2,3}  | Andrea Nani^{1,2,3}  | Peter T. Fox^{5,6}  | Jack Lancaster^{5,6} | Franco Cauda^{1,2,3} 



Neuroinformatics (2023) 21:365–374
<https://doi.org/10.1007/s12021-023-09626-6>

RESEARCH 

A Minimum Bayes Factor Based Threshold for Activation Likelihood Estimation

Tommaso Costa^{1,2,3} · Donato Liloia^{1,2} · Franco Cauda^{1,2,3} · Peter T. Fox^{4,5} · Francesca Dalla Mutta² · Sergio Duca^{1,2} · Jordi Manuella^{1,2}

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Code available on figshare
<https://doi.org/10.6084/m9.figshare.21621162>



Thanks a lot!




Ospedale Koelliker
Prima la persona



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