Fixed versus random effects models for fMRI meta-analysis

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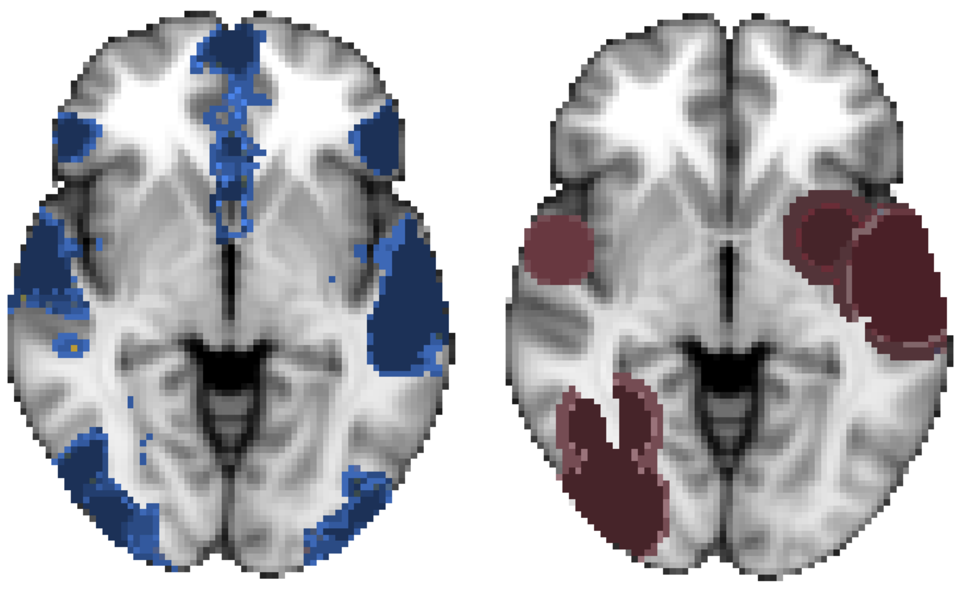
1. Detecting brain activation using fMRI

- Functional magnetic resonance imaging (fMRI) enables to detect brain regions that become activated during specific cognitive tasks such as reading or solving equations.
- The number of fMRI studies on different cognitive functions has increased substantially. However:
  - Sample sizes are typically small
  - **Reproducibility** is often limited
- Understanding the brain functioning requires integration of data across studies and labs.
- Meta-analysis is promising tool to achieve this goal.

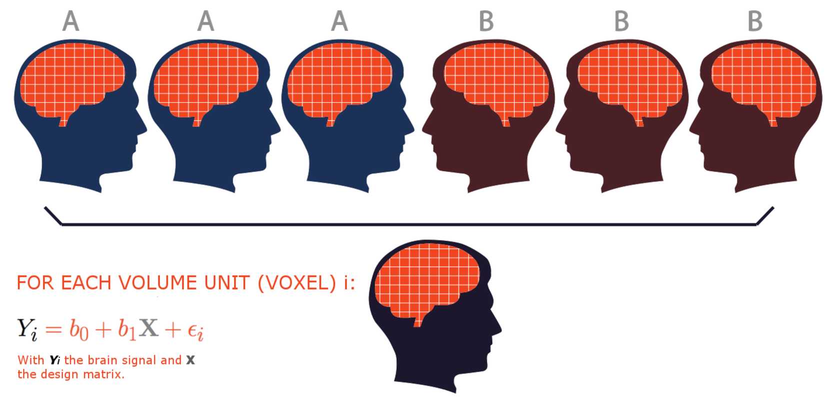
Two studies with same research question, *different results?*



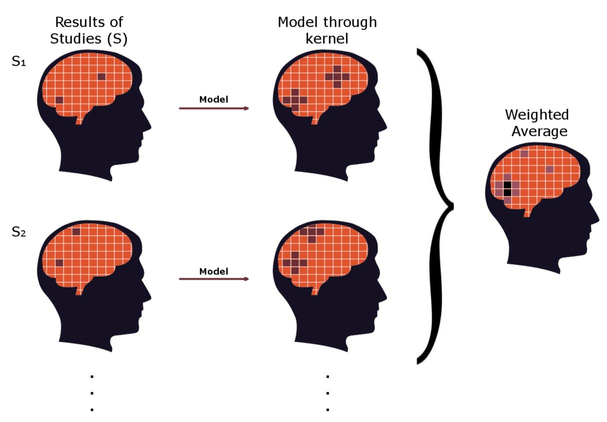
2. Aggregating *within* and *over* studies

- At study level, estimates for the degree of activation in each brain region need to be pooled over subjects.
- These pooled estimates are further investigated in a second level group analysis.
- **Fixed pooling of subjects**: second level is ordinary average of all first level estimates (no between subject variance).
- **Mixed pooling of subjects**: second level estimates are obtained within a full Bayesian framework with non-informative priors.

Pooling 6 subjects in one study.



- A meta-analysis aggregates different studies.
- **ALE meta-analysis**[1] investigates the consistency of the spatial location of activation peaks in the brain.
- **ES-SDM**[2] is a random effects meta-analysis that averages effect sizes of activation peaks over studies and takes into account within and between study variance.
- **A fixed effects meta-analysis** proceeds as ES-SDM but only takes into account the within study variance.



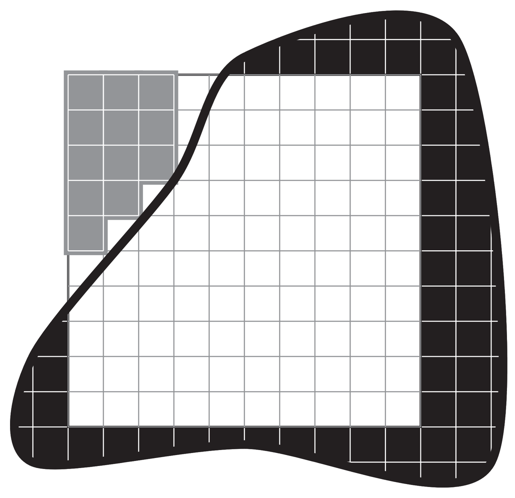
3. Goal of our study

We study the impact of
(1) the way subjects are pooled within a study and
(2) the meta-analysis method for pooling studies
on the false positive rate (FPR), power and spatial accuracy.

- Consider a benchmark (B) representing an area of true brain activation - depicted by the white square in the figure below.
- The blob represents the region of activation as detected by a meta-analysis (m).
- **Black**: false positives
- **Gray**: false negatives (i.e. lack of power)
- **Overlap** with benchmark (i.e. accuracy):

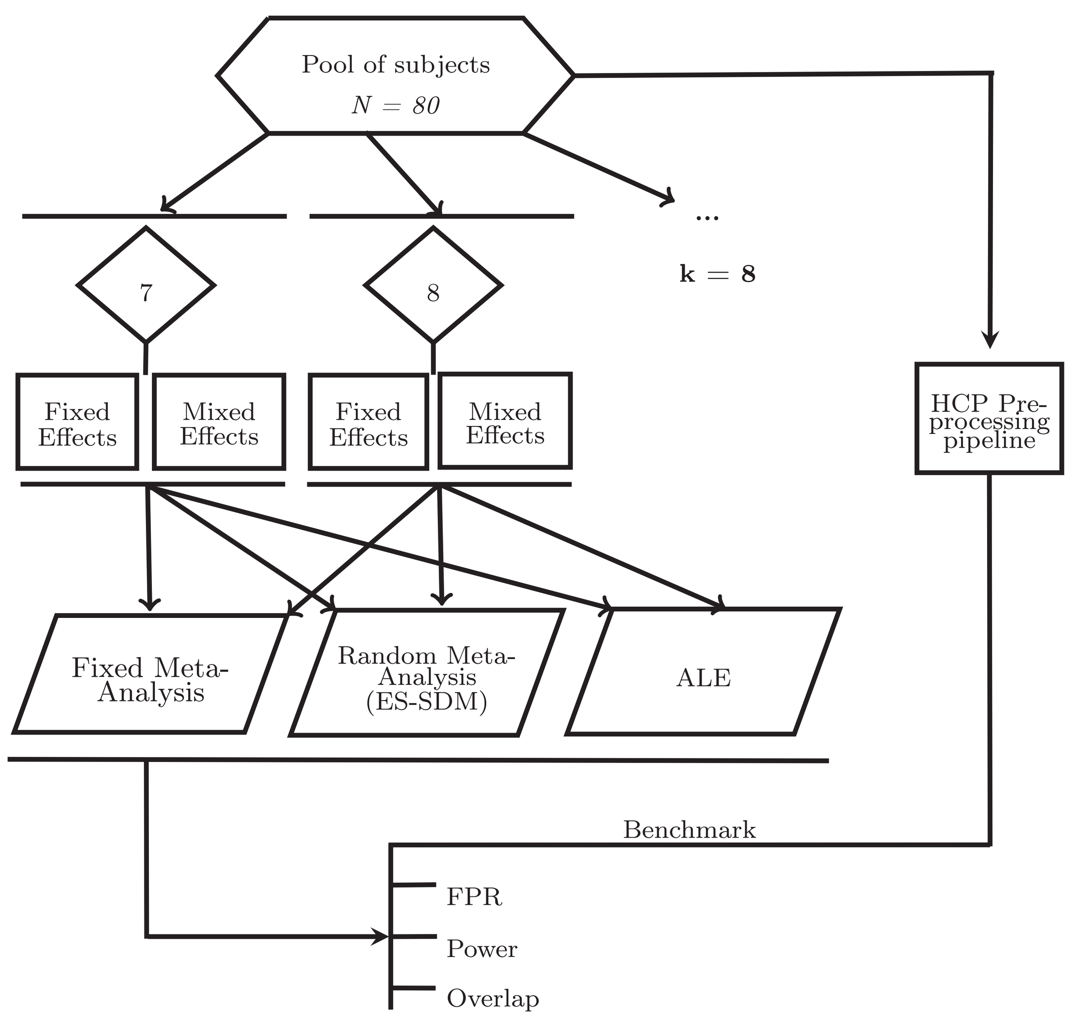
$$\frac{V_{m,B}}{V_m + V_B - V_{m,B}}$$

With V=voxels that are declared significant.

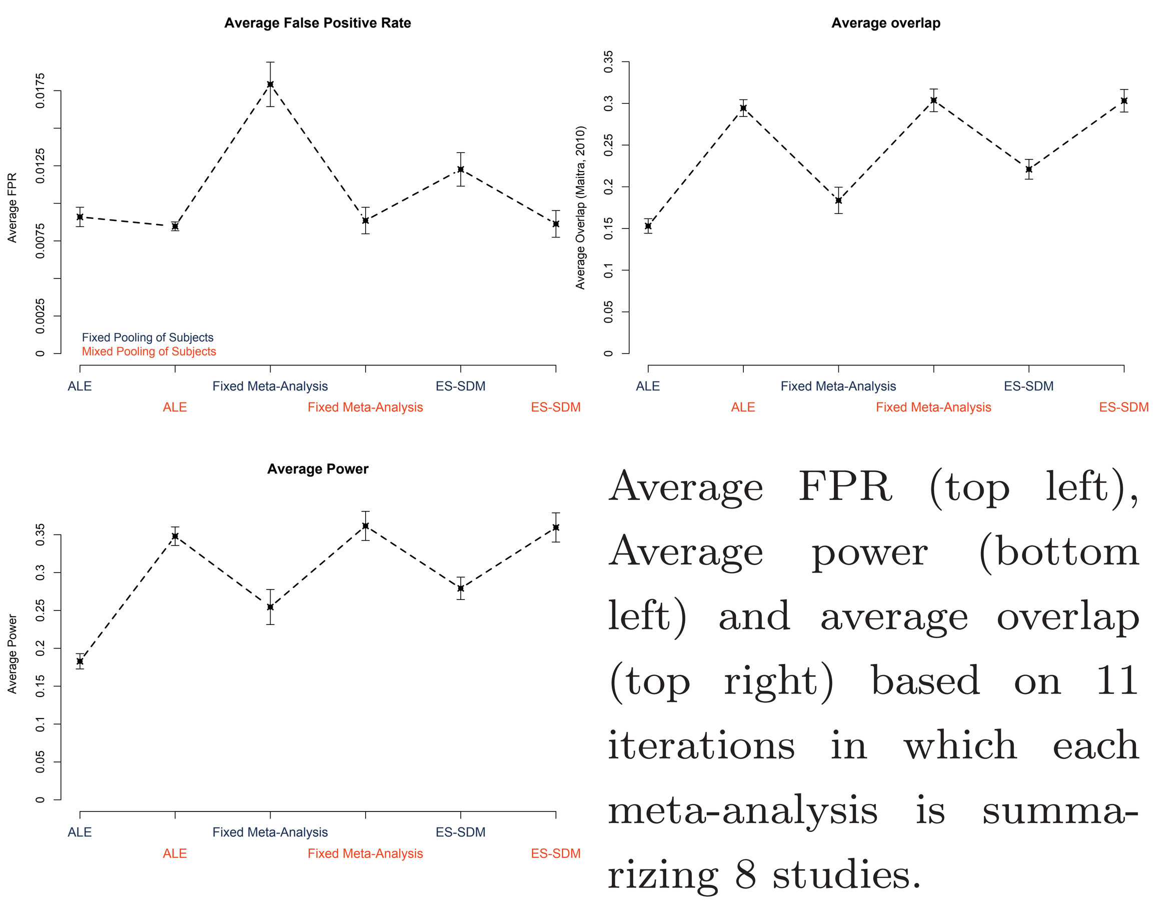


4. Method and design

- Real data from the Human Connectome Project[3]: 80 subjects scanned doing a language and math task.
- We create 8 studies with respectively 7, 8, 9, 10, 10, 11, 12 & 13 subjects by random subsampling (without replacement) from the total pool of subjects.
- Different methods for aggregating within and over studies are combined.
- Group analysis on all 80 subjects ⇒ benchmark.
- FPR, power and overlap are calculated on the result of each meta-analysis with the benchmark image.
- Subsampling is repeated 11 times.



5. Results



Average FPR (top left), Average power (bottom left) and average overlap (top right) based on 11 iterations in which each meta-analysis is summarizing 8 studies.

6. Conclusion

Overall, the power and overlap is highest and FPR lowest for:

1. All meta-analyses based on pooling subjects through a mixed effects analysis.

When pooling subjects using fixed effects, the order from best to worst performance is:

1. Random effects meta-analysis
2. Fixed effects meta-analysis
3. ALE meta-analysis

Depending on the way subjects are pooled within study, there is an effect on the level of aggregating studies.
In general we advise **not to use fixed effects pooling of subjects** unless for the purpose of pooling scanning sessions within subjects.

7. References

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[3] Van Essen et al. The WU-Minn Human Connectome Project: an overview. *NeuroImage*, 80:62–79, October 2013.