On Current Imaging Biomarkers for

detected by Machine Learning Techniques

Alzheimer's Disease

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Outline

- Motivation
- Specification of the work
- Some on-going research results

Motivation

- What is the role of neuroimaging?
  - Prediction
  - Exploration
  - Clinical assessment
- How neuroimaging is combined with other information modalities?
  - Prediction and research
  - Clinical assessment

Motivation: materials

- Image modalities
  - Diverse image modalities
    - Is there agreement on findings/predictive power?
  - Information fusion in multi-modality
    - Combination of analyses results
    - Fusion of image information

Motivation: materials

- ML has been stressing the importance of experimental data resources
- Public vs. proprietary
  - Reproducibility
  - Independent Validation
  - Selection bias in meta-analyses?

Motivation: techniques

- Where are the current research technical trends?

Effects-finding studies

Statistical inference to confirm expected effects

Selection bias in meta-analyses?

Machine Learning

(feature extraction + classification)

Prediction of disease onset

Discriminant features

'Empirical ROI' analysis

Whole-brain analyses

Motivation: techniques

- New techniques blending with established analysis tools
  - VBM, DBM and TBM as steps for feature extraction.

Motivation: methods

- Does the application of machine learning in neuroimaging imply a change of the methodological paradigm?
  - The shift from detection to prediction
  - Effect assessment vs. statistical validation

Motivation: methods

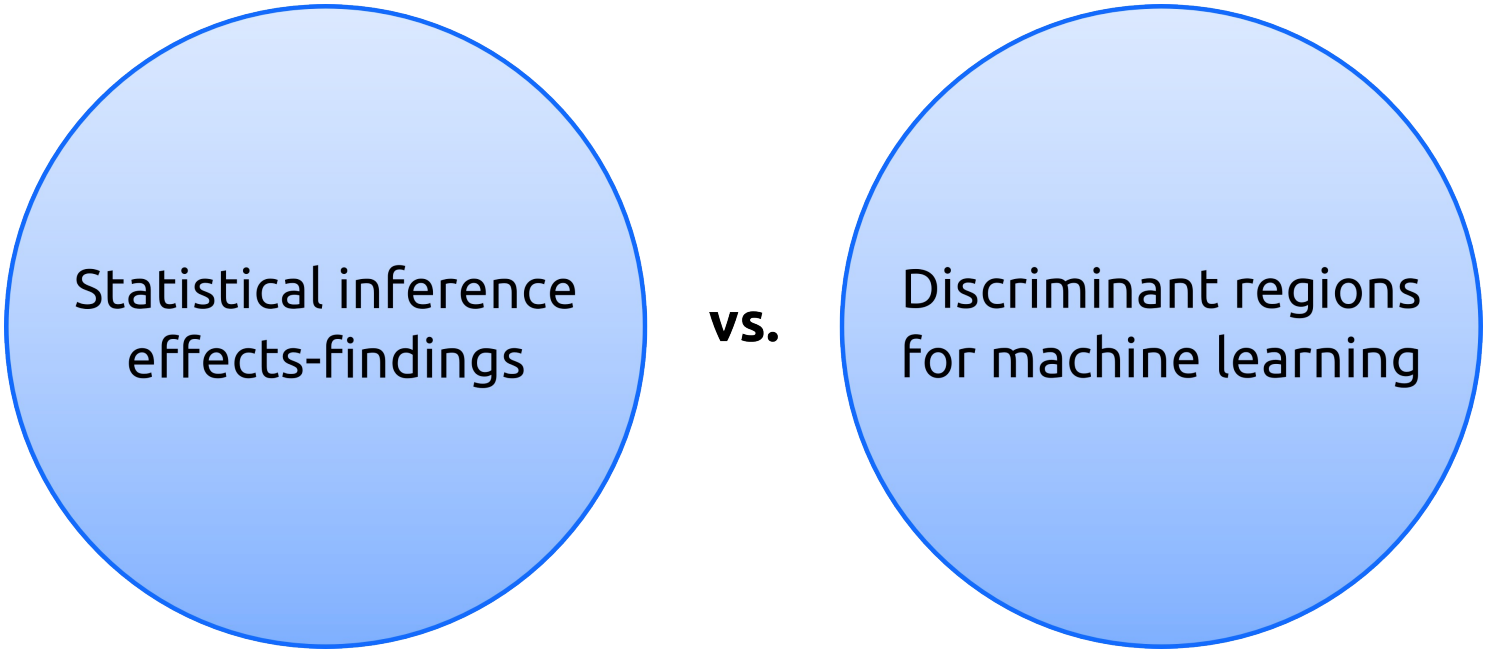
- Emphasis
  - On avoiding circularity effects and double dipping
  - Reproducibility of the results
    - Public data
    - Public code: FSL, SPM, FreeSurfer....

Motivation: results

- Research frontiers
- Past:
  - Differences between pairwise matched populations of AD patients and HC
  - Cross-sectional analyses
- Current
  - Prediction of transition from MCI to AD
  - Longitudinal analyses
- Future?
  - Prediction of AD from healthy status

Motivation: results

- Is there agreement between



What happens when there are unexpected results?

Meta-analyses in neuroimaging

- Meta-analyses report statistical results over published studies to
  - identify reliable experimental effects,
  - measure the size of the effect and
  - characterize the degree of agreement across studies, detecting publication bias.
- Reported “observations” in neuroimaging:
  - Coordinate-based Meta-Analysis (CBMA)
  - Image-based Meta-Analysis (IBMA)
  - ROI-based Meta-Analysis (RBMA)

Limitation of meta-analyses: selection vs. exploration

- Meta-analyses impose/need rigorous criteria for the selection of
  - Studies to be included in the statistical analysis
  - Uniformity of observation measures and results
    - Atlas (Tailarach) coordinates
    - Same modality image results
    - ROI based observations
  - Uniformity of effect findings
- Allows for outlier detection, but not for double-dipping biased results

Selection criteria

- Journals: Neuroimage, Alzheimer's and Dementia and IEEE Trans. in Medical Image Processing.
- Search for 'Alzheimer' from 2008 to 2011.
- Inclusion criteria: Population study for inference on group differences or patient detection/prediction using T1, DTI and PET.
- 89 articles found.
- This is an ongoing work.

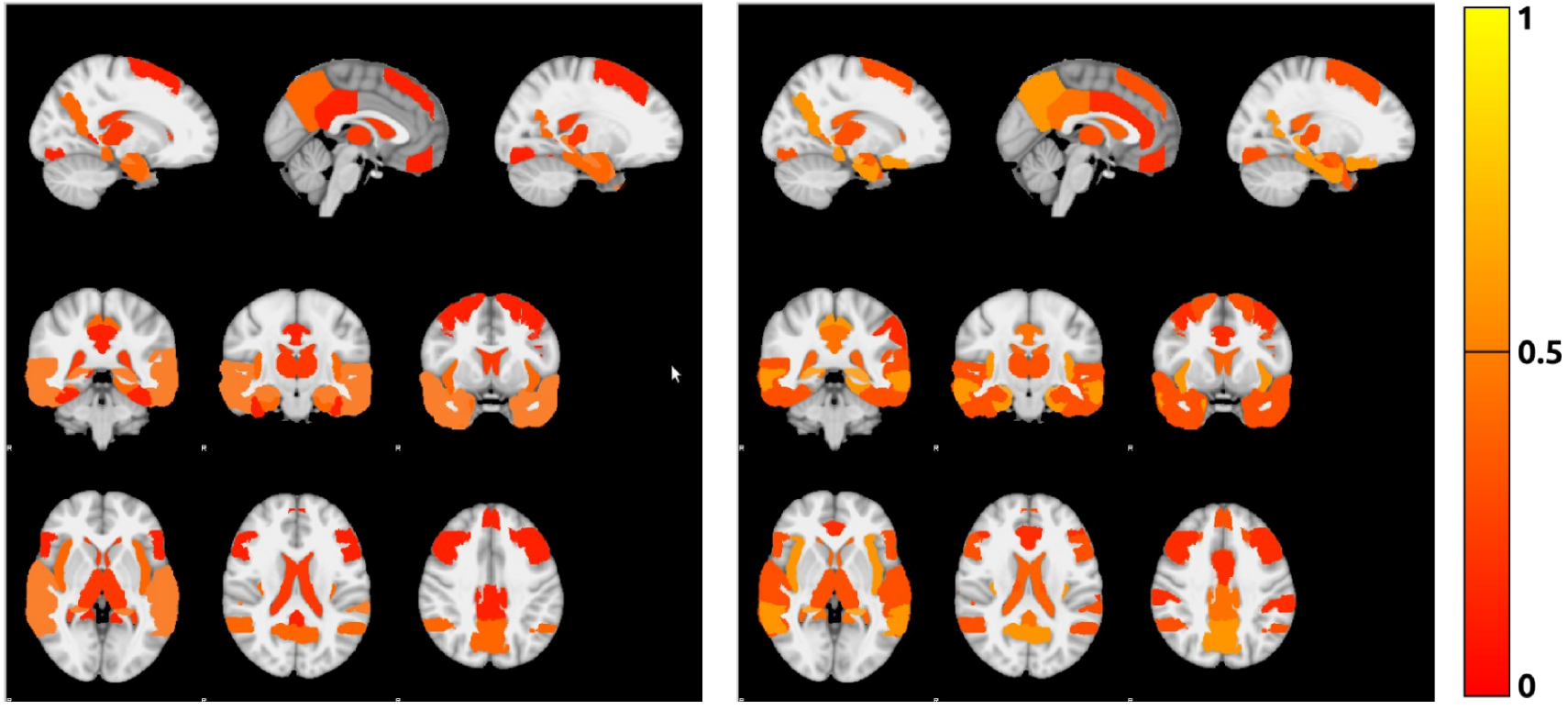
Experiment 1

- Summarized the reported regions.
- Separated the articles by modalities.
- Calculated the appearance frequency of each region in ML papers vs. Effects-finding papers.
- Plotted them in an MNI template.

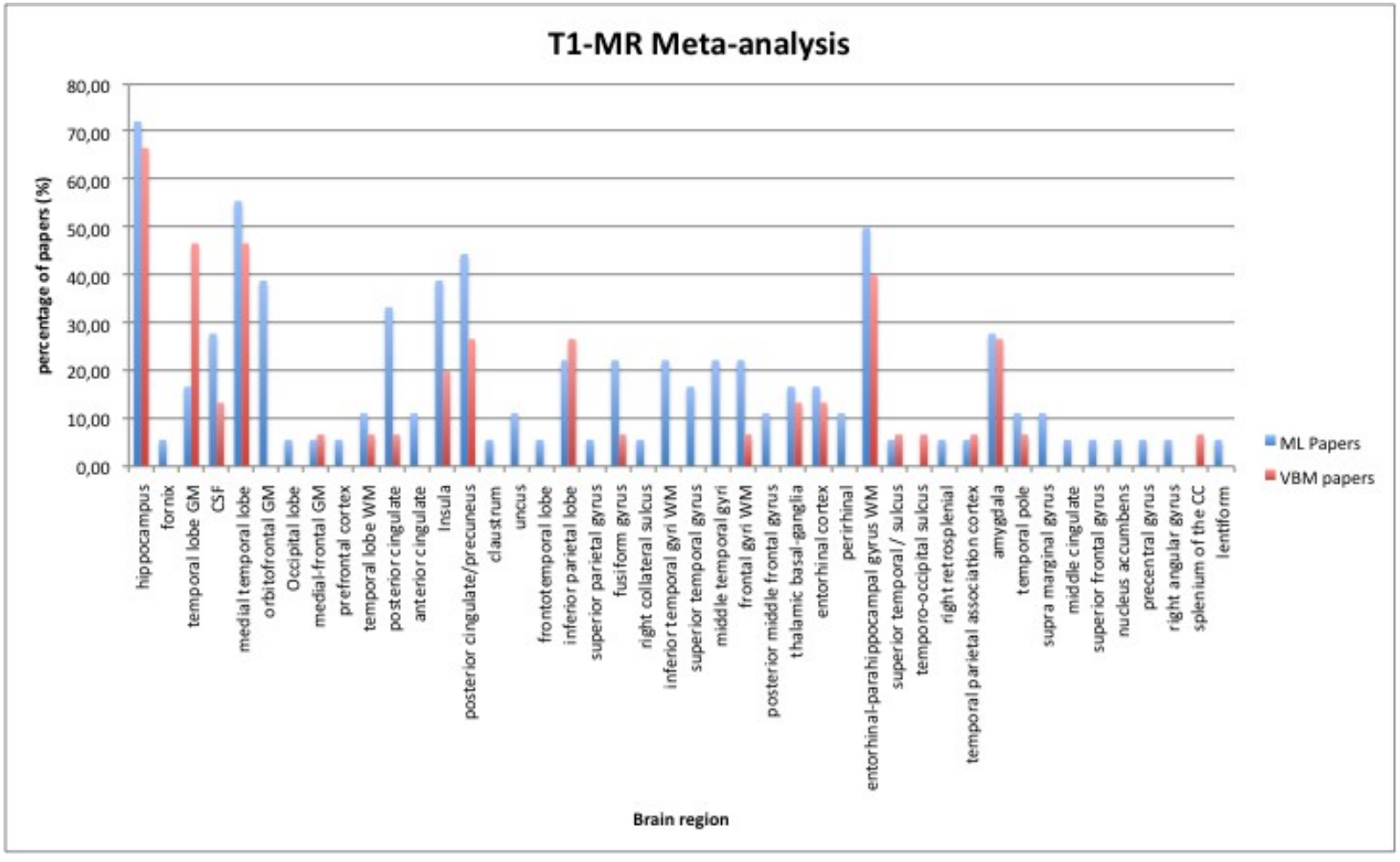
Relevant regions in anatomical MR (T1)

Machine Learning

Effects-finding



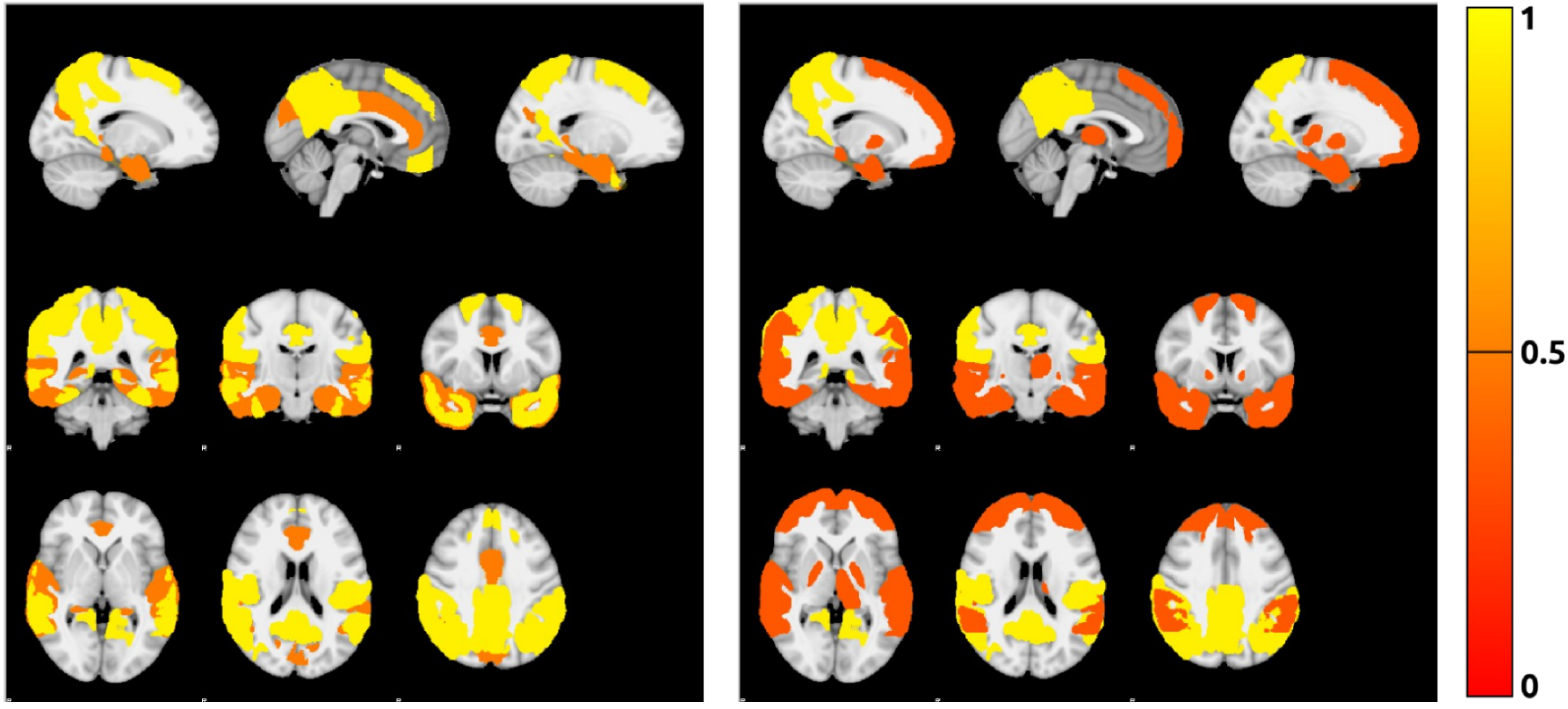
Relevant regions in anatomical MR (T1)



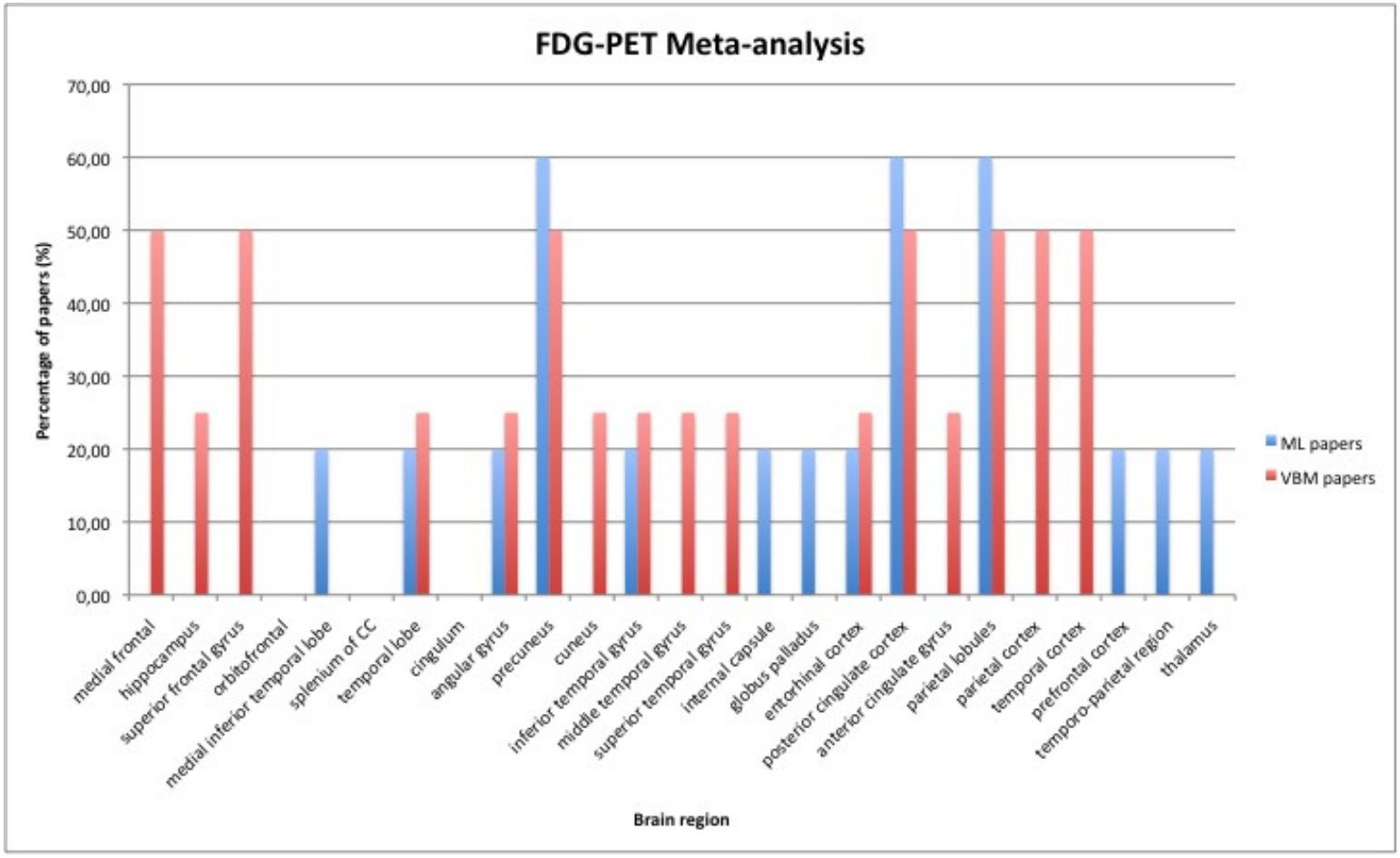
Relevant regions in FDG-PET

Machine Learning

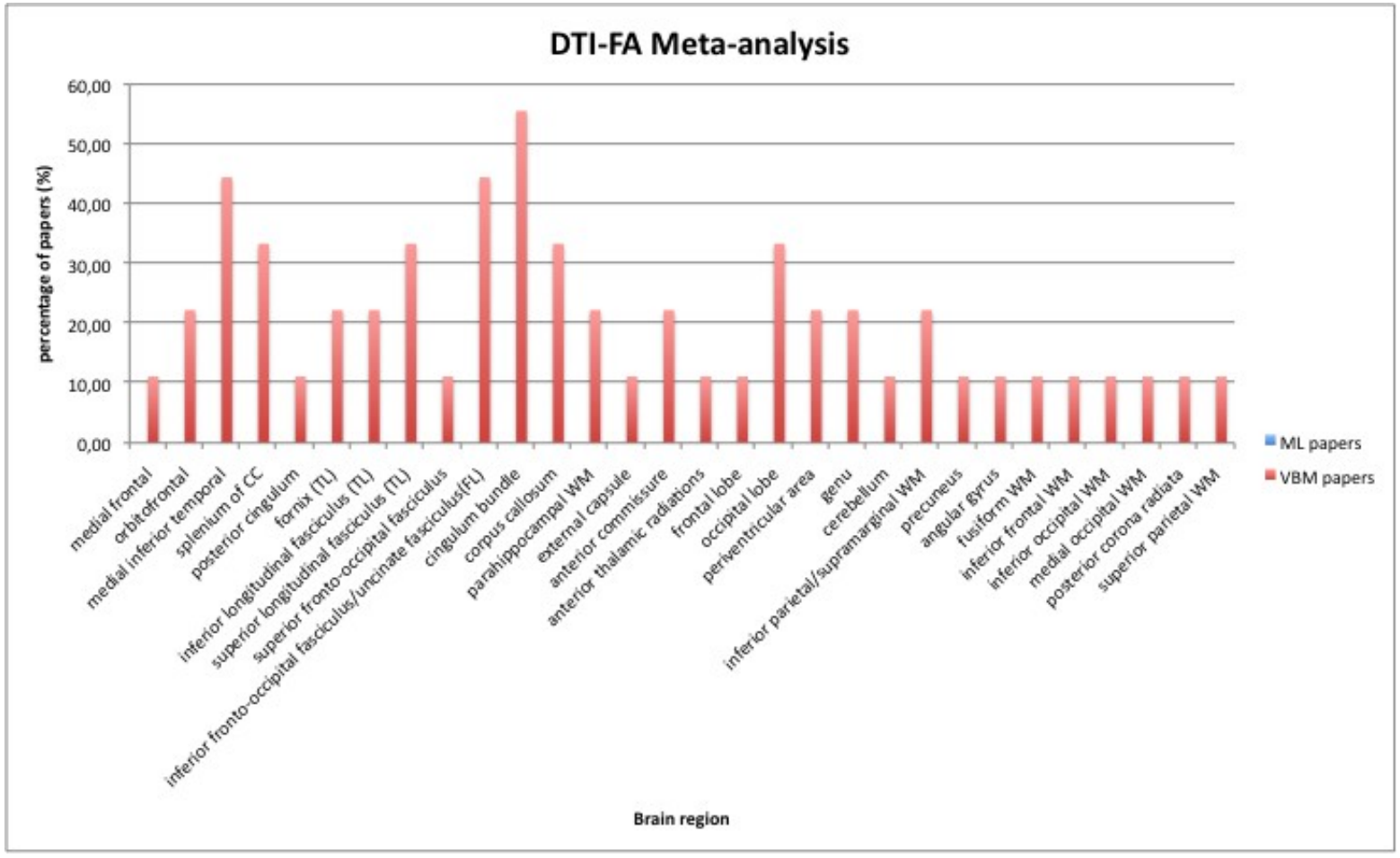
Effects-finding



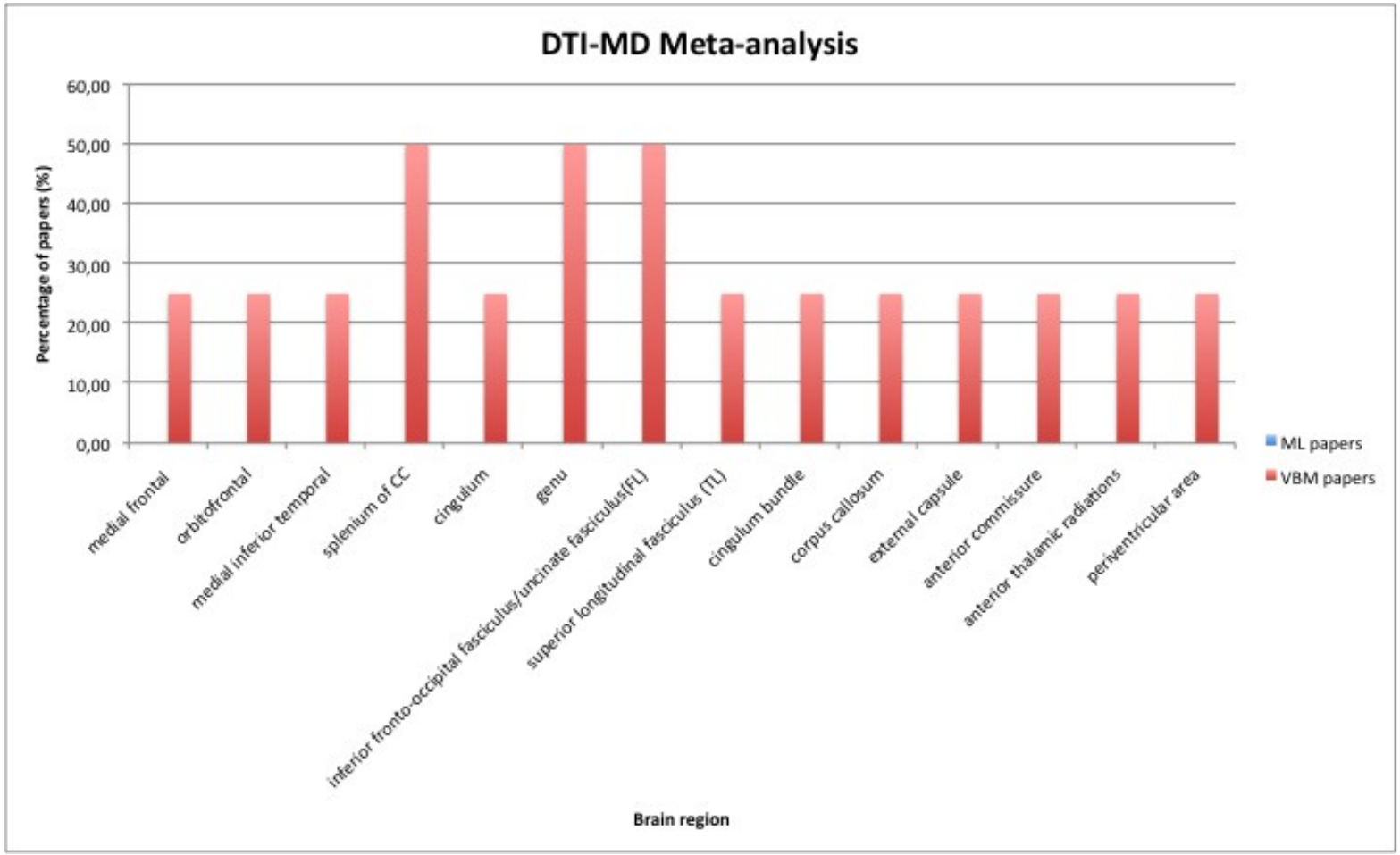
Relevant regions in FDG-PET



Relevant regions in DTI-FA



Relevant regions in DTI-MD



Observations

- Increase of AD studies applying ML algorithms for classification.
- Increased complexity in research questions for longitudinal studies make ML approaches more attractive.
  - 'Which MCI will convert to AD?'

Trends

- Reference the exact algorithm/implementation.
- Report the range of parameters values.
- Report results for all the parameters values in this range (var/stddev at least).
- Publish online feature vectors and/or statistical maps for independent validation and reproducibility of results.

Circularity effects?

- We are trying to find ways to measure double-dipping effects to show the results.

Thank you