On Current Imaging Biomarkers for Alzheimer's Disease detected by Machine Learning Techniques

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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**

- Prediction of disease onset
- Discriminant features
  - 'Empirical ROI' analysis
  - Whole-brain analyses

ISMCRM Workshop, Montabaur, Oct. 2011
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

Statistical inference effects-findings vs. Discriminant regions for machine learning
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 (Talairach) 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