CSG Meeting:
fMRI pipelines comparison and process enhancement

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11/08/2017

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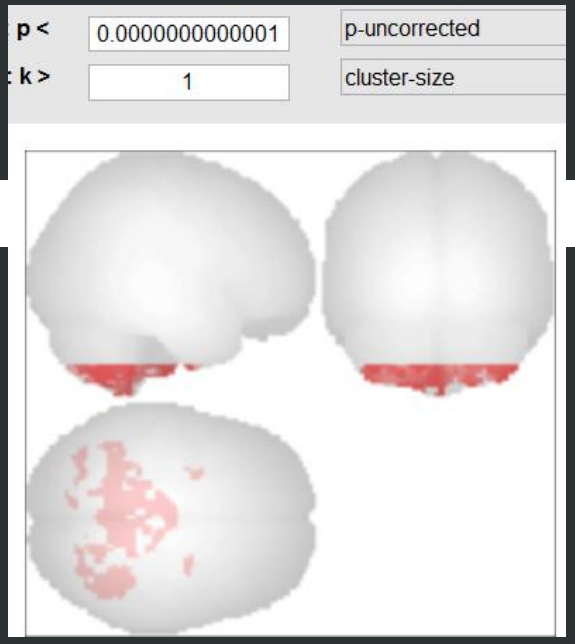
Outline

- FMRI pipeline comparison:
  - Code analysis
  - Segmentation
  - Denoising
  - First-level
  - Second-level
- Other consderations:
  - Threshold tweaking
  - Others (manips, etc)
- Conclusion

Background: Why?



Issues identified in new pipeline:

1. **Cerebellum artefact** ⟶

2. **Signal shape tampered**, only noise remains (easy to spot on CONN Denoising and 1st-level previsualizations when compared to other pipelines)
3. **Controls were preprocessed with a different pipeline** (no idea which one, can be as old as Lizette's SPM8 pipeline).
4. Current pipeline **not validated** (uses NewSeg).

fMRI pipelines: Code analysis overview

- Code & batch comparison using KDiff3 + manual inspection

- **7 packages (total: 18 pipelines scripts)** reviewed:

1. Stephen's
2. Athena's script for classifier
3. Athena's script for cosmonauts
4. Athena's from Charlène computer
5. Lizette's
6. Carol's
7. Charlène's FMRI+PET scripts (latest used as of 06/2017)

- Each package contained 1 to 6 different pipelines with an average = 3.
"Athena's only" average = 1, "rest only" average = 4.

fMRI pipelines: Code analysis results

- Analysis goal: **Isolate major differences** and ignore cosmetic changes (eg, different directories layout, non-critical parameters such as filepaths or TR due to migration)
- Significant changes included different versions of softwares (SPM8 vs SPM12, with or without VBM8/DARTEL, etc.), different modules versions (OldSeg vs NewSeg), critical parameters changes (eg, using another TPM template) and pipeline format (code+batch vs code only).

4 different scripts families were isolated:

1. SPM8 script no batch (Lizette, 2015?, Spatial_processing_Lizette*.m)
2. **SPM8+VBM8/DARTEL with batch** (Carol, 2016, script_preproc_VBM_Dartel_DEF*.m).
   Note: Charlene has a variant VBM8+PET.
3. **SPM12 OldSeg with batch** (Athena, 2016-2017, script_preproc_LIE_spm12.m)
4. **SPM12 NewSeg CRC12 tpm+PET with batch** (Charlène, 2017, script_preproc_SPM12_Charlene.m)

Note: for the rest of this presentation, only scripts 2, 3 and 4 willl be used

fMRI pipelines: Code analysis results

- **SPM12 OldSeg (Athena's)** script is the **most stable** (in terms of code): always the same in all instances analyzed.
  Pro: very fast, should fit most functional analyses + classifier.
- **3 different templates**:
  - spm8 Dartel custom patients template
  - spm12 no template (use standard)
  - spm12-NewSeg uses CRC12 custom template.
- Several **inconveniencies** :
  - difficult to migrate (all templates and software paths hardcoded or hidden in batch)
  - easily breakable (PATH with multiple software versions, no apriori check of TR, of files existence, etc.)
    → script stops in the middle of preprocess instead of before
  - accents and long filenames unsupported and no check
  - 4d nifti unsupported

fMRI pipelines: Images comparisons

- Additional technical notes with the companion .txt file (with all equivalences).

- Now the boring part is done, we can check the resulting images with each pipeline ☺

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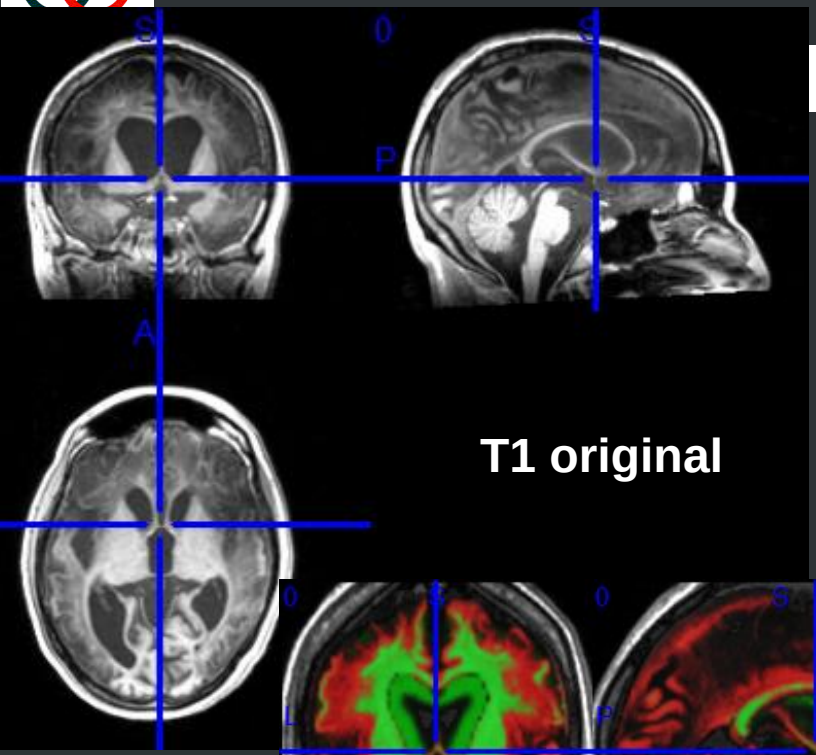
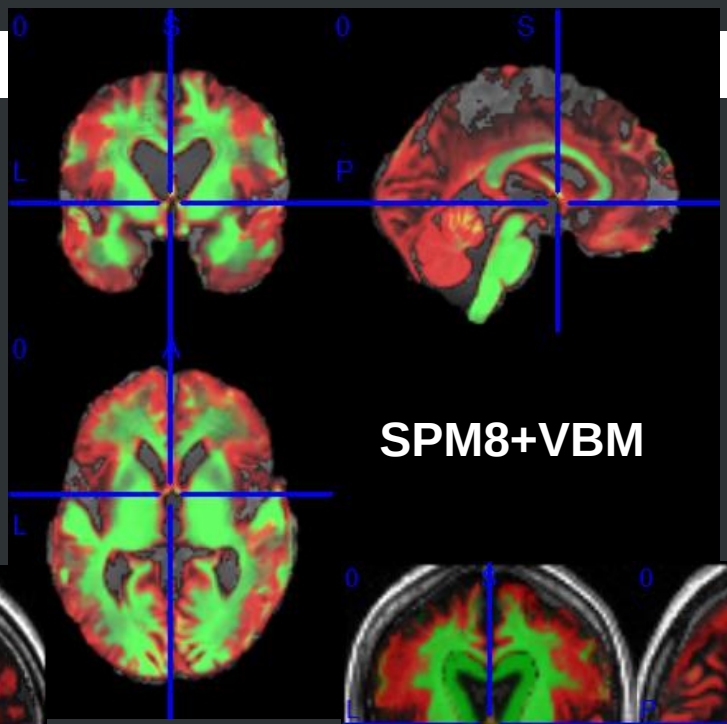
fMRI pipelines: Segmentation

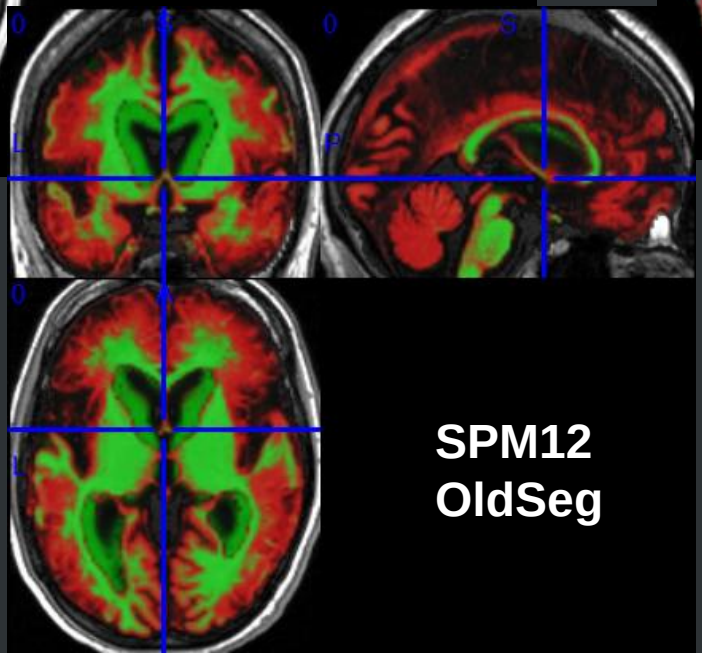


T1 original

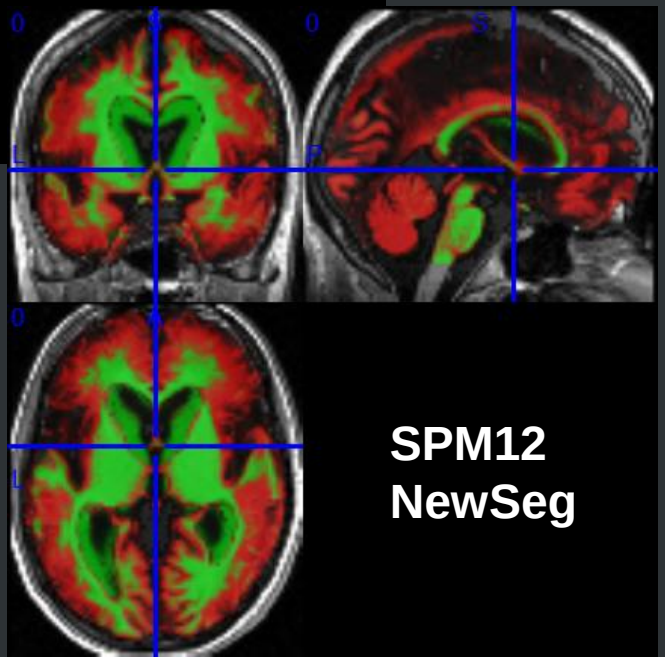


SPM8+VBM

Notice the Cerebellum Cut!

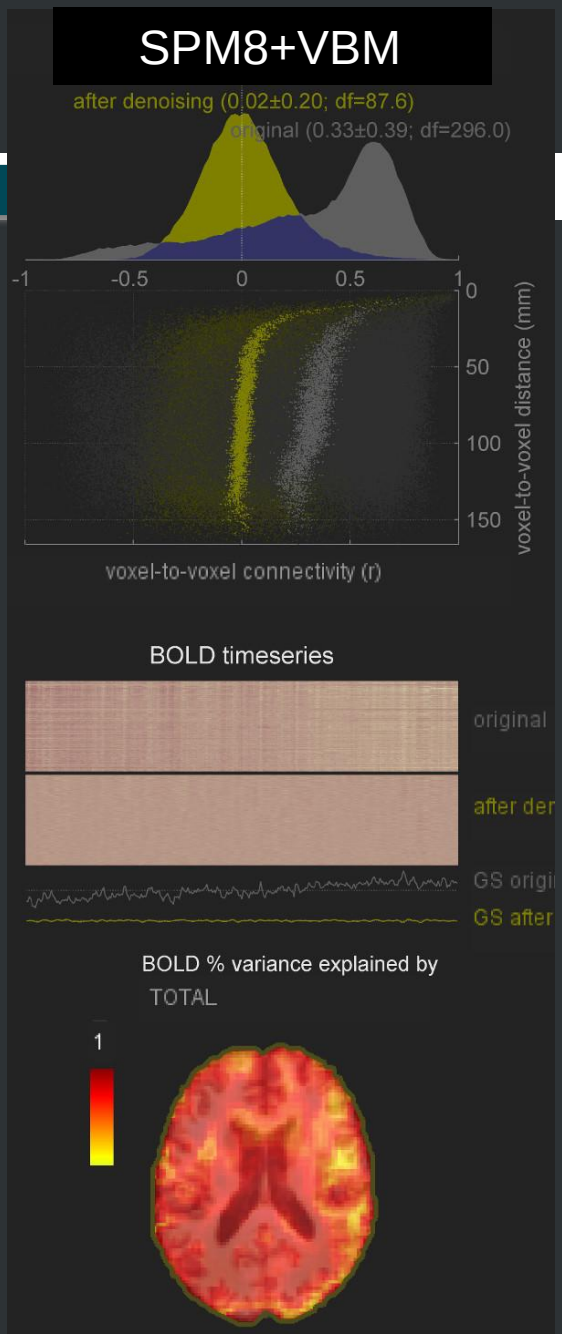


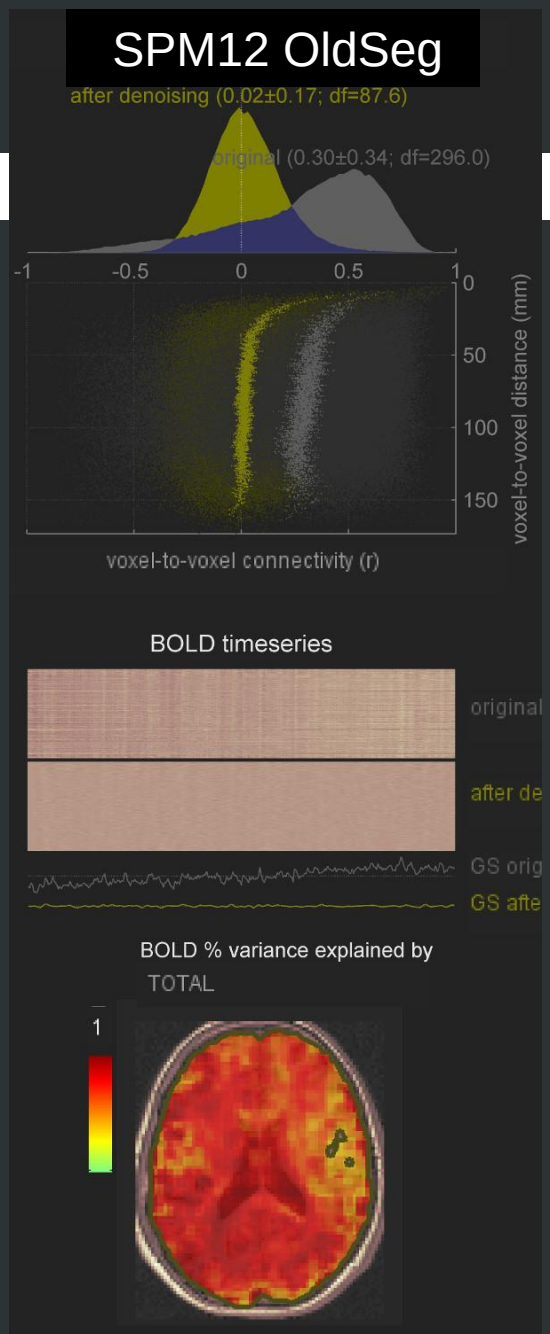
SPM12 OldSeg

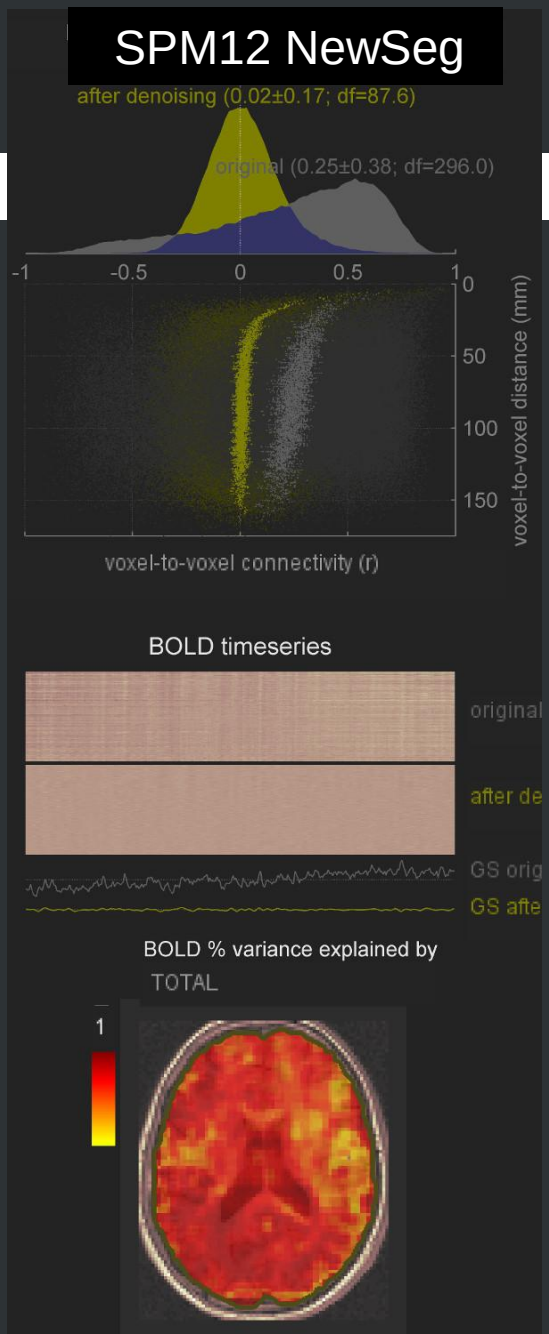


SPM12 NewSeg

fMRI pipelines: Denoising Controls

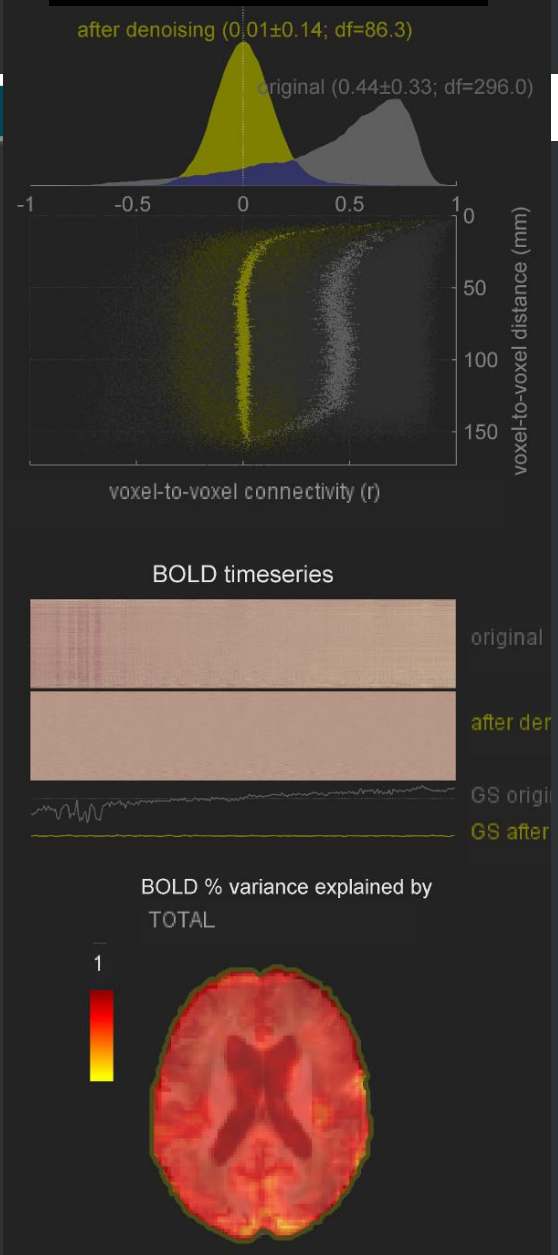




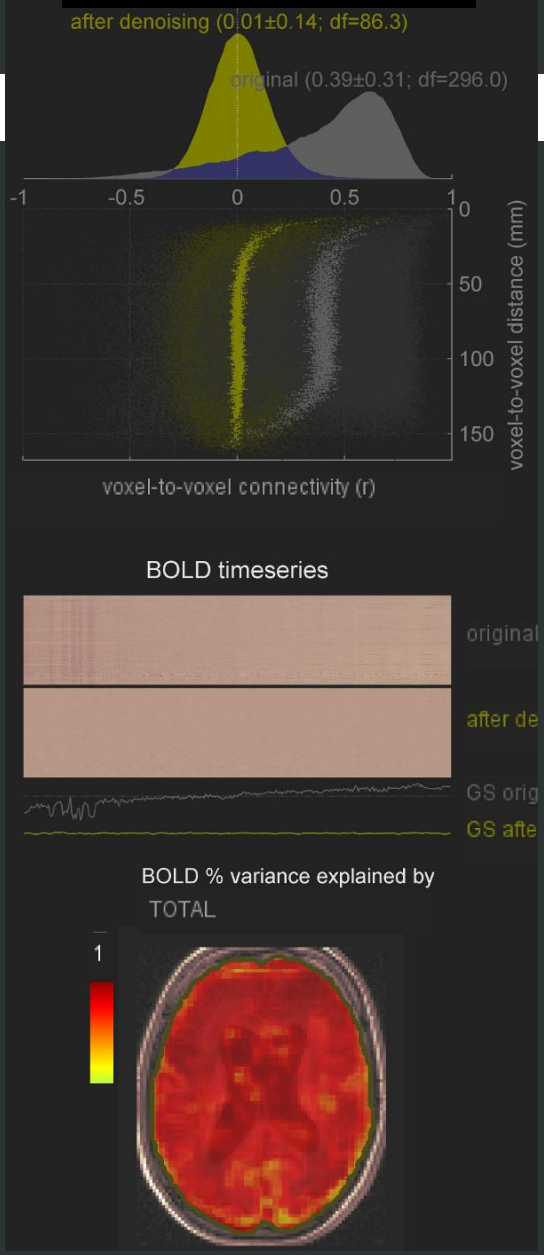


fMRI pipelines: Denoising Patient

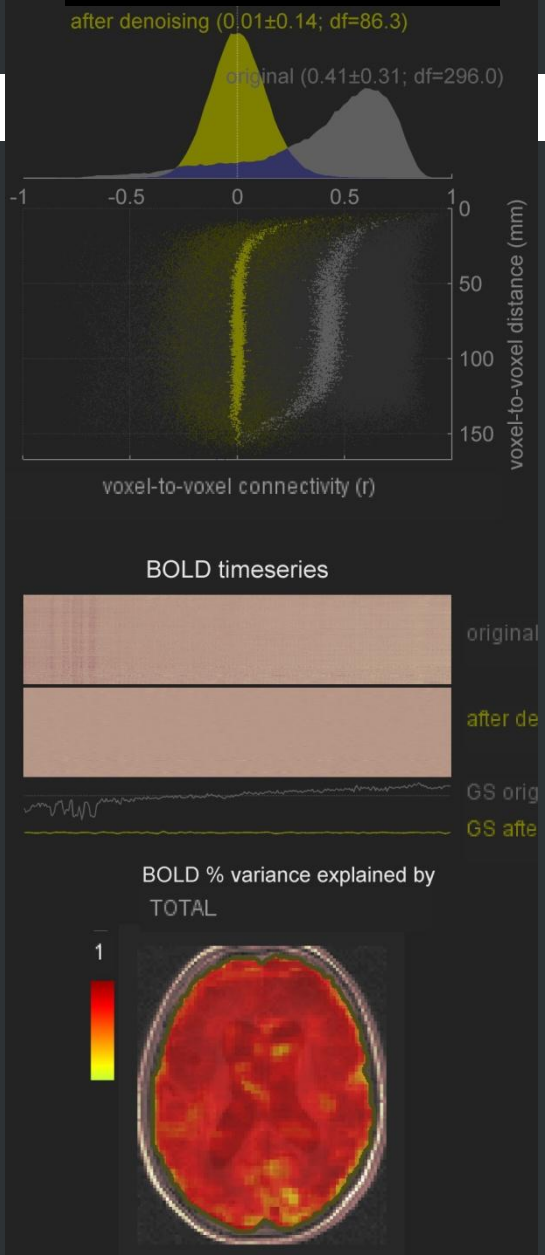
SPM8+VBM



SPM12 OldSeg



SPM12 NewSeg



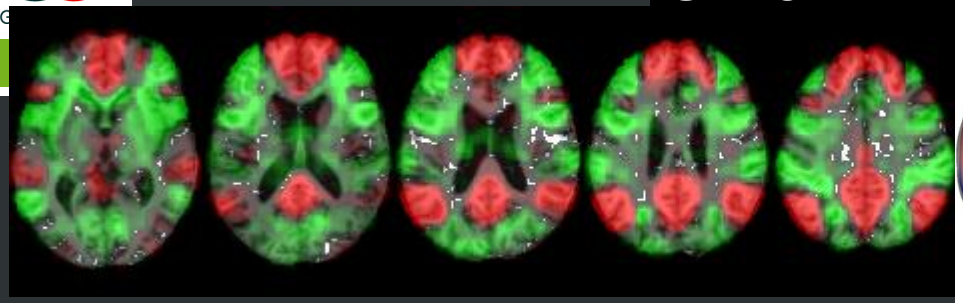
fMRI pipelines: First-Level Controls

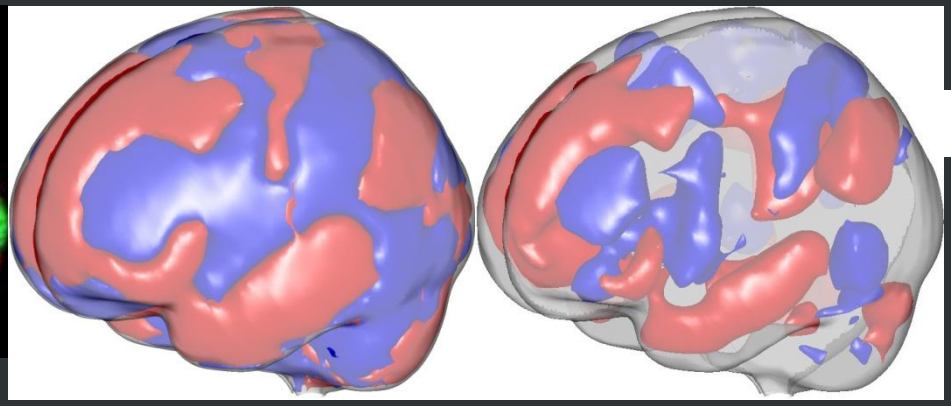
(averaged on all 8 controls)

Binarized

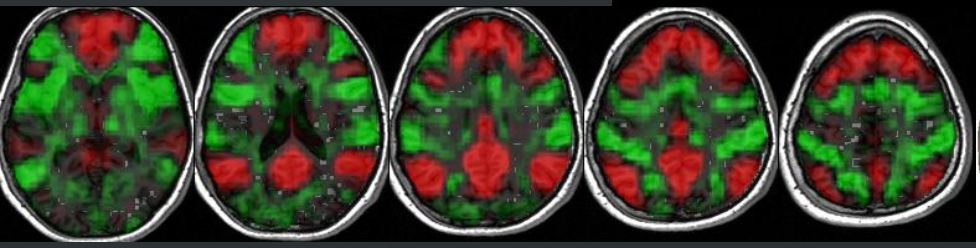
Threshold Z >= 0.1

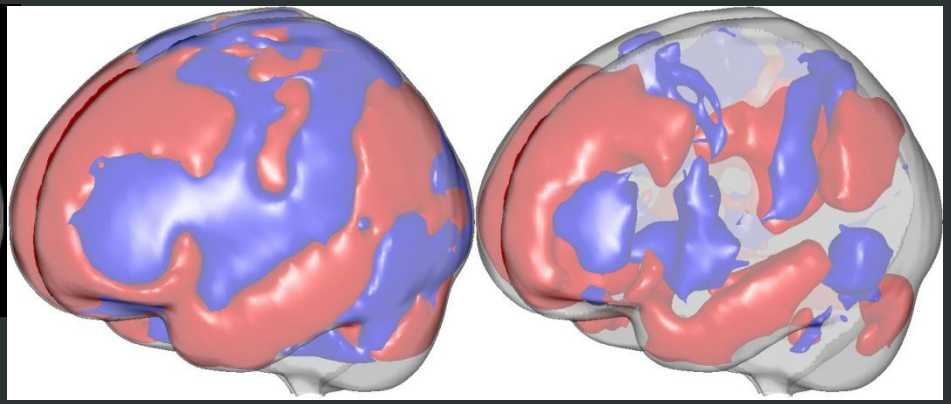
SPM8+VBM





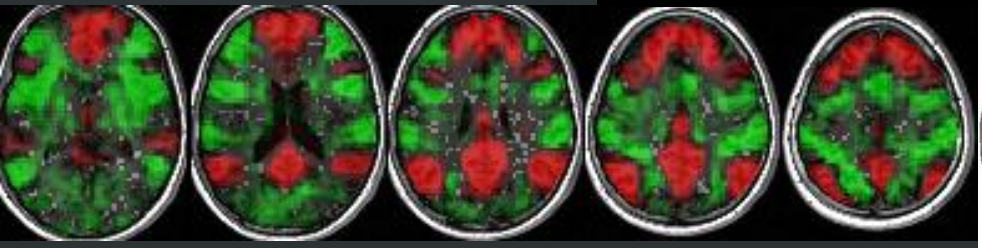
SPM12 OldSeg

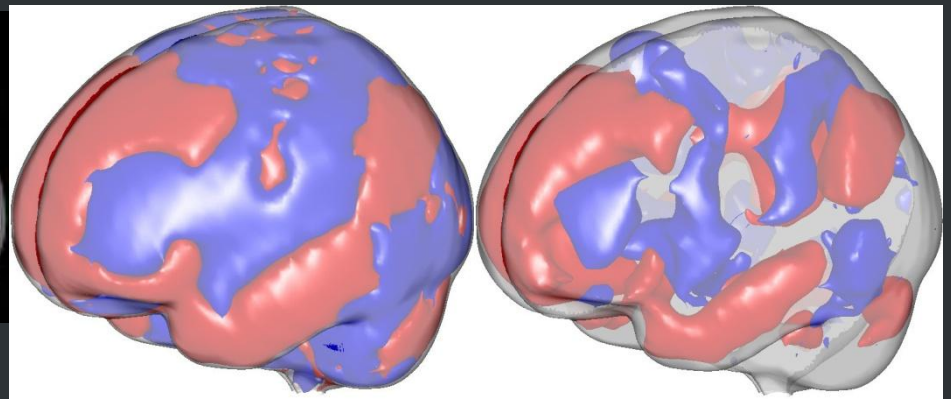




Cerebellum cut again!

SPM12 NewSeg

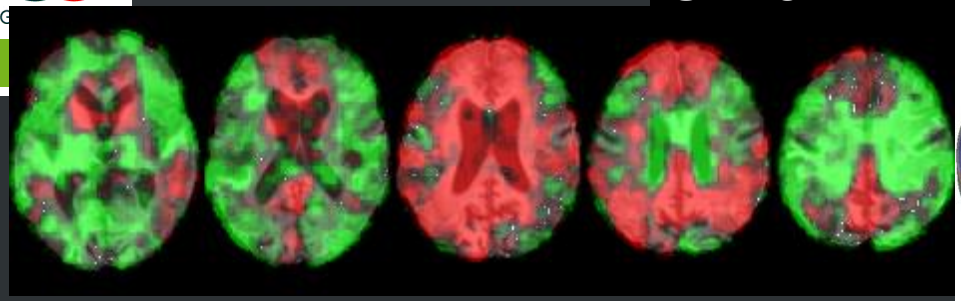


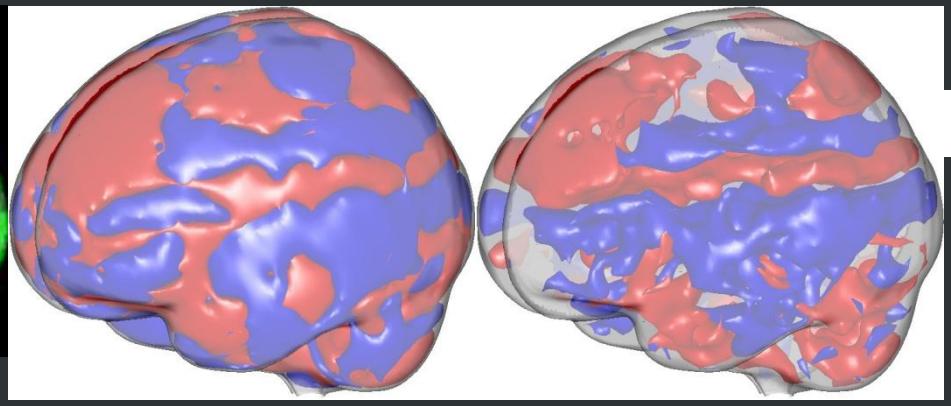


fMRI pipelines: First-Level Patient

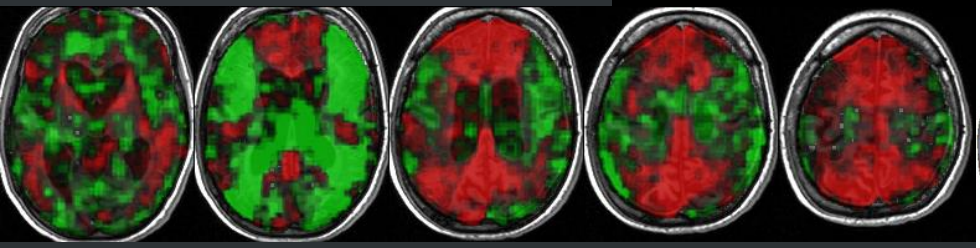
Binarized Threshold Z >= 0.1

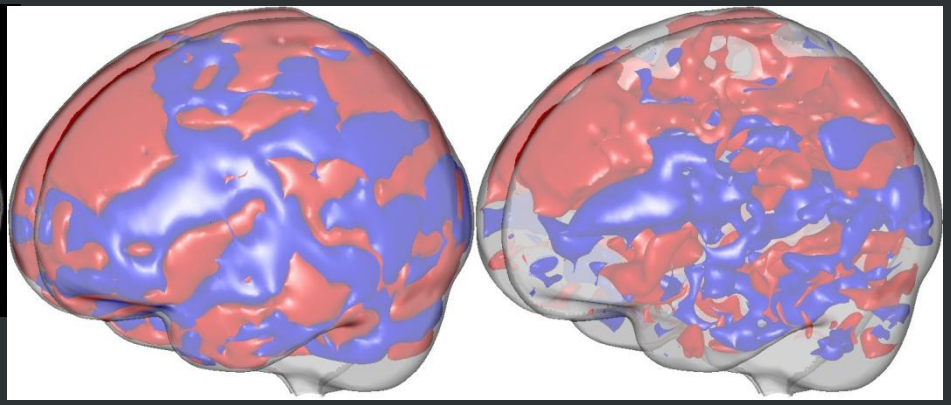
SPM8+VBM



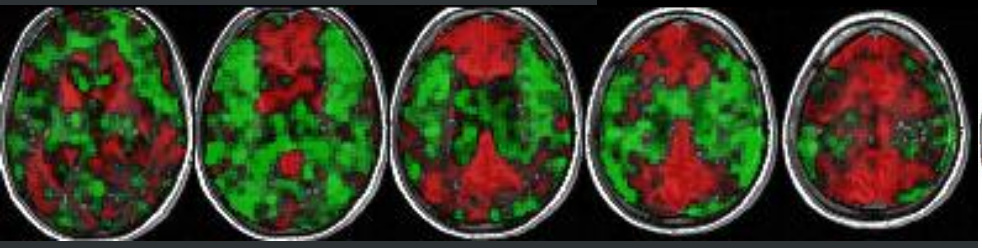


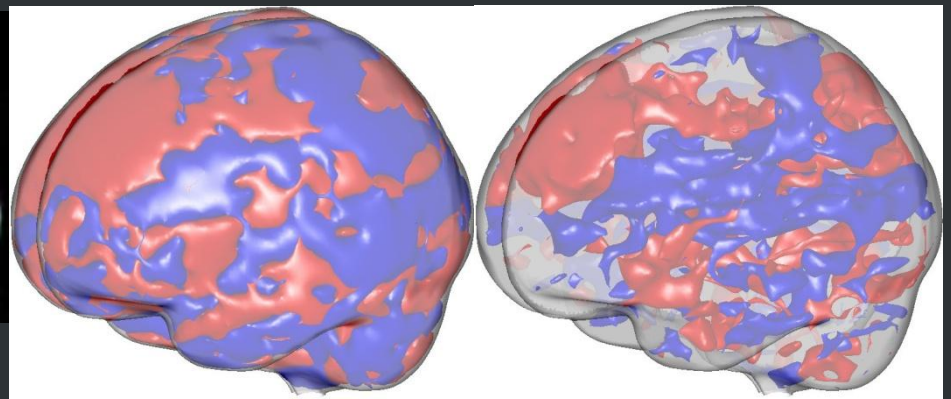
SPM12 OldSeg



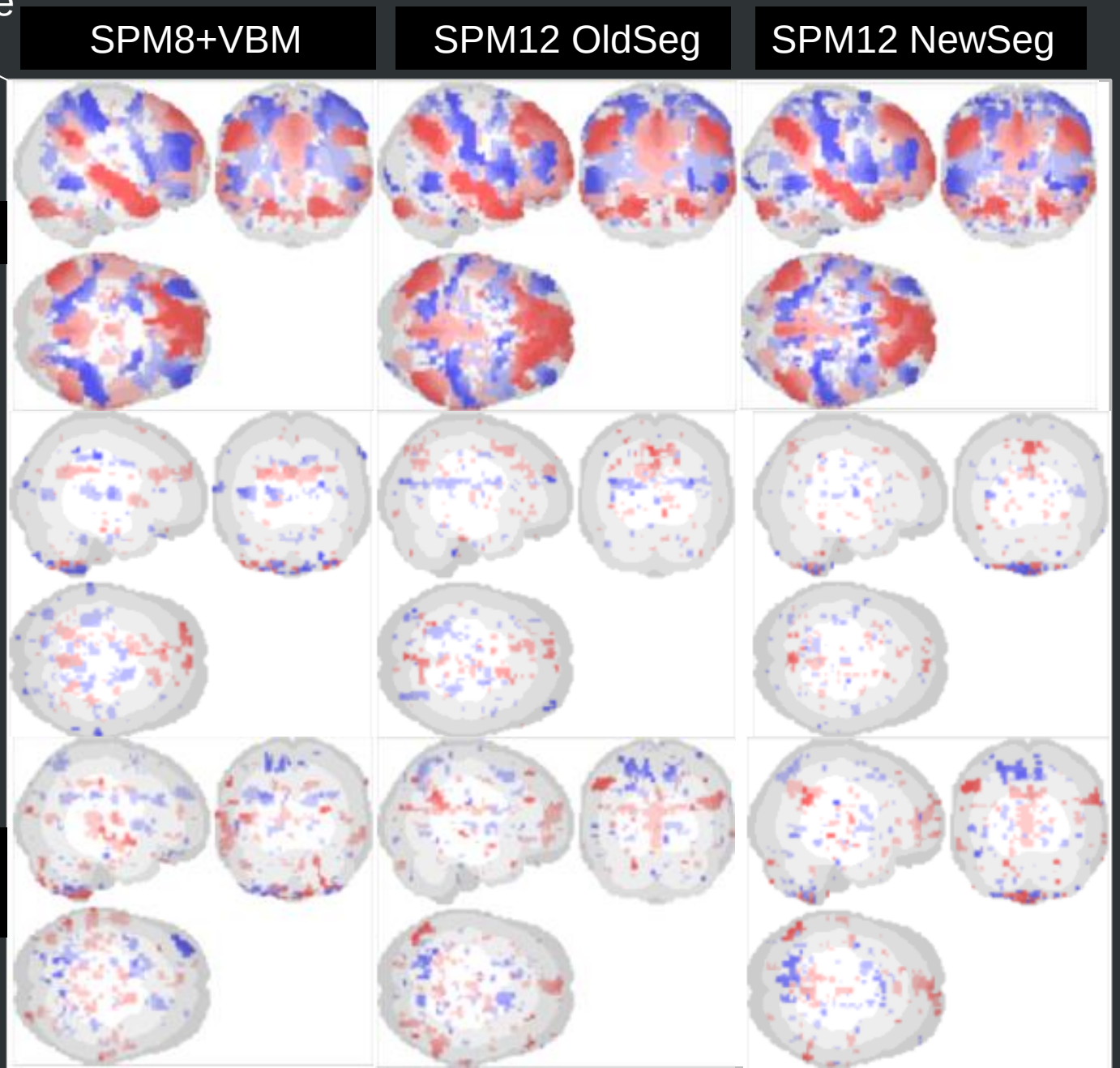


SPM12 NewSeg





fMRI pipelines: Second-Level

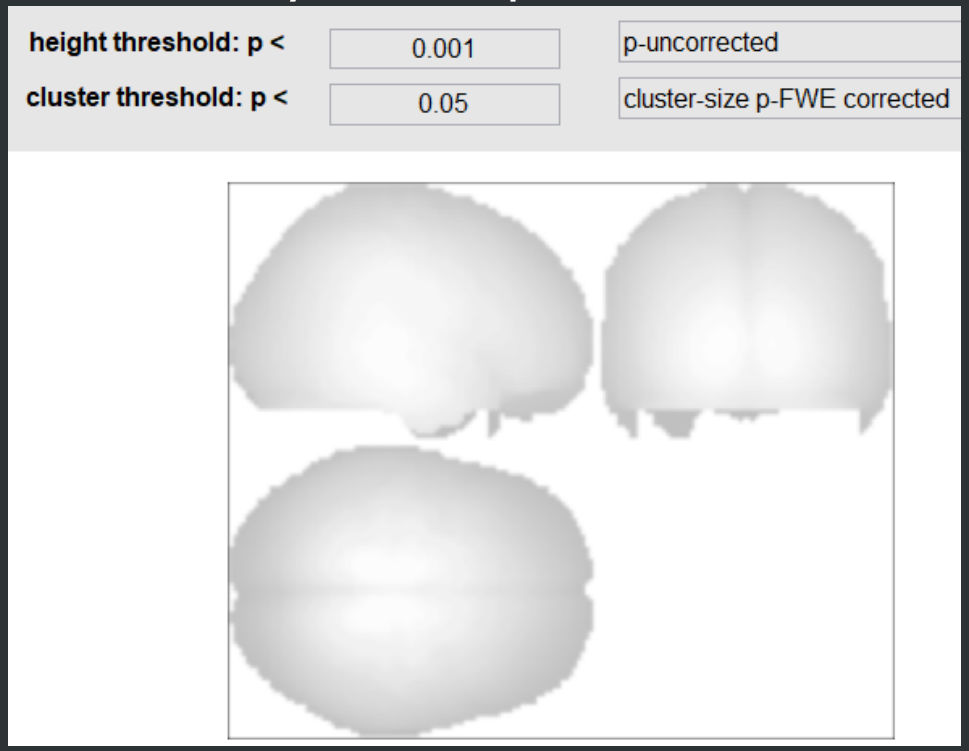


fMRI pipelines: propositions

- **Maintain 2** functional preprocessing **pipelines**:
  SPM12 OldSeg & SPM8/VBM
  (Alternative: use CONN standardized preprocessing.)
- **Unify into one script** if possible (reproducibility & maintenance, most of the code logic is the same! Only the batch change)
- **Systematic versioning** & centralized repository (petabyte "Softwares" or GitHub):
  - Versioning: ease tracking down original and compare/integrate user changes.
  - Centralized repo: code reviewing (less bugs) and easy update.
- **Validate new pipelines before** deployment: run both current and new pipeline for 1 patient and compare.
- **Freeze** version of **SPM & CONN** (& other necessary softwares) on Z:. Before updating, validate like any new pipeline.

Threshold tweaking

- Necessary when only one patient, not enough power

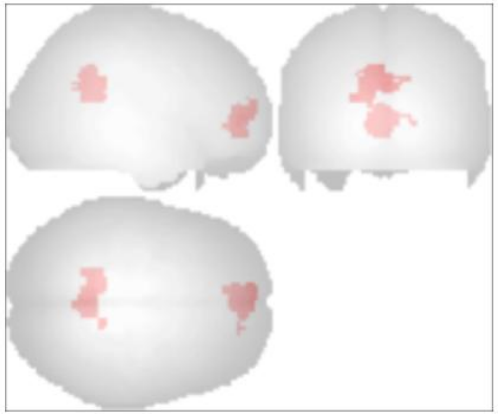


- What is acceptable for clinical?
  What is the most plausible?

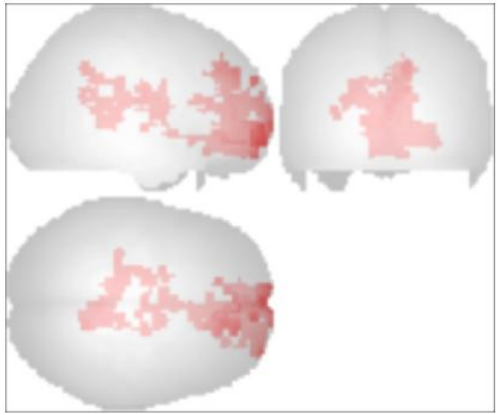
Threshold tweaking

Lower height/voxel-wise threshold

height threshold: p < 0.01 p-uncorrected
cluster threshold: p < 0.05 cluster-size p-FWE corrected

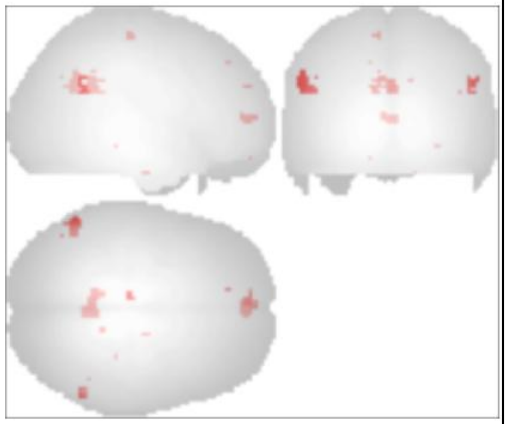


height threshold: p < 0.05 p-uncorrected
cluster threshold: p < 0.05 cluster-size p-FWE corrected

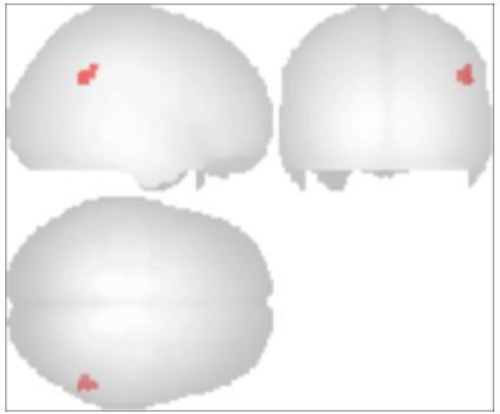


No cluster-wise correction

height threshold: p < 0.001 p-uncorrected
cluster threshold: k > 0.05 cluster-size

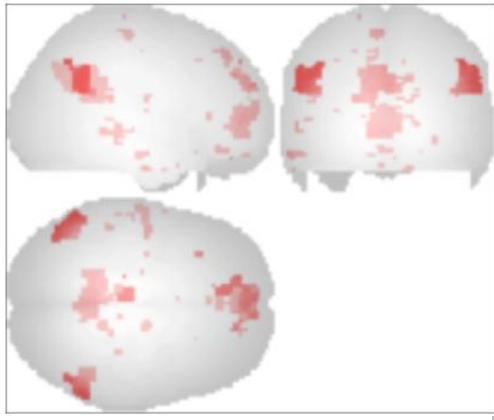


height threshold: p < 0.001 p-uncorrected
cluster threshold: p < 0.05 cluster-size p-uncorrected

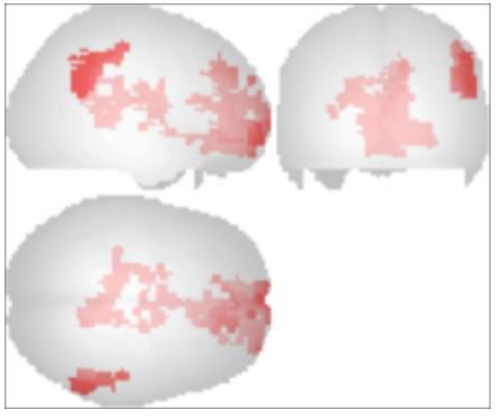


Both

t threshold: p < 0.01 p-uncorrected
r threshold: k > 0.05 cluster-size



hreshold: p < 0.05 p-uncorrected
hreshold: p < 0.05 cluster-size p-uncorrected

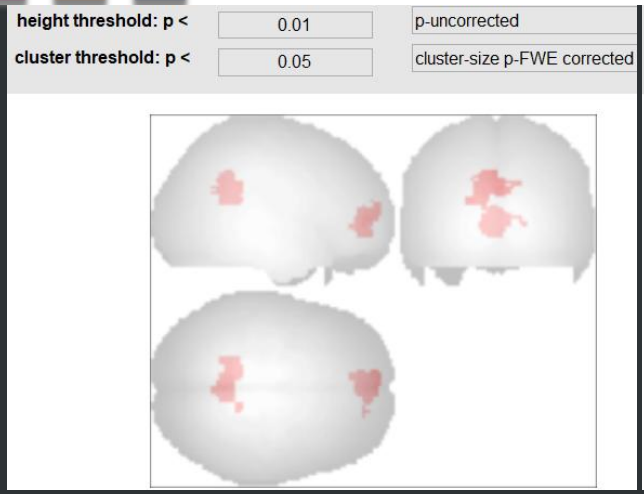


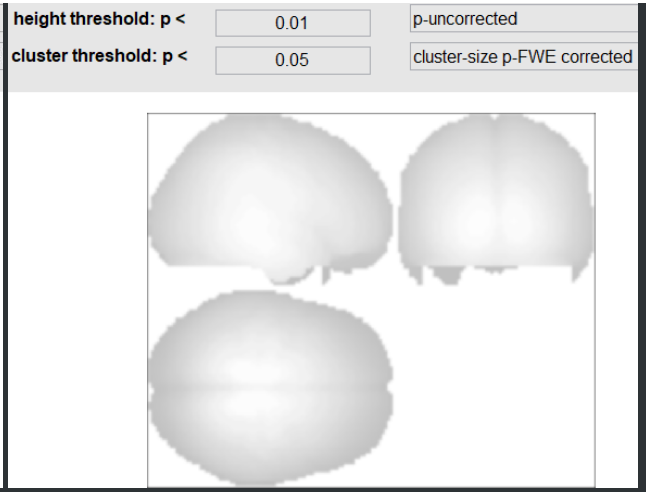
Visualization is not really two-sided

Positive

Negative

One-sided





Two-sided

Nothing to show!

Because corrects for both positive and negative simultaneously!

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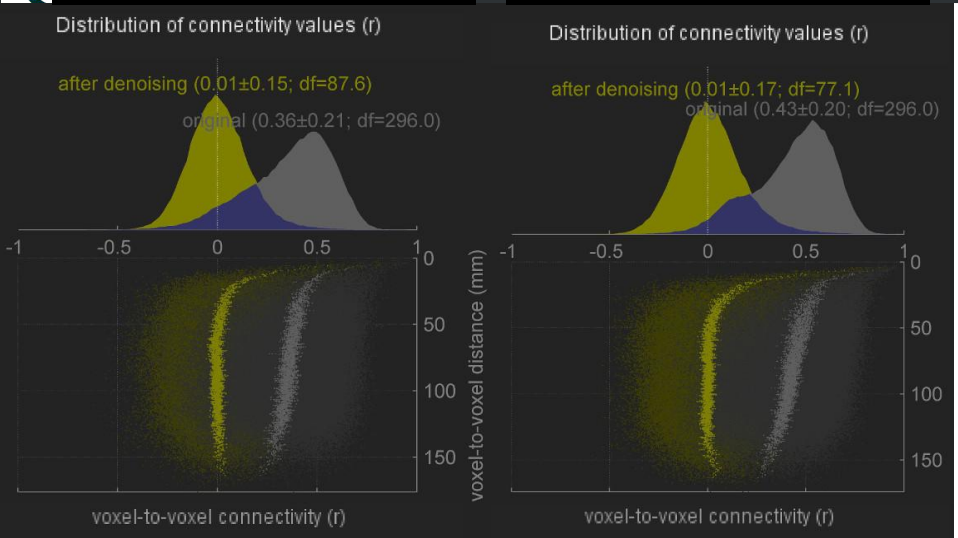
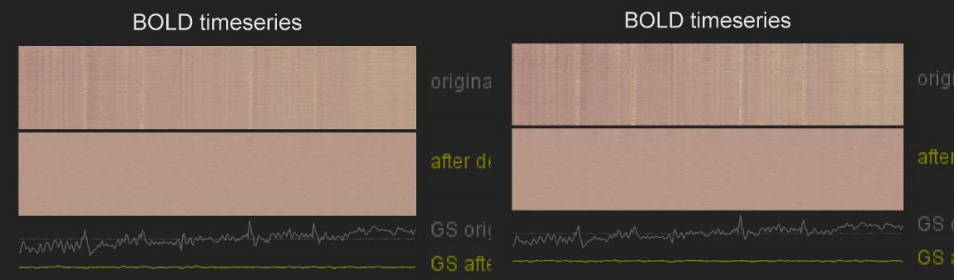
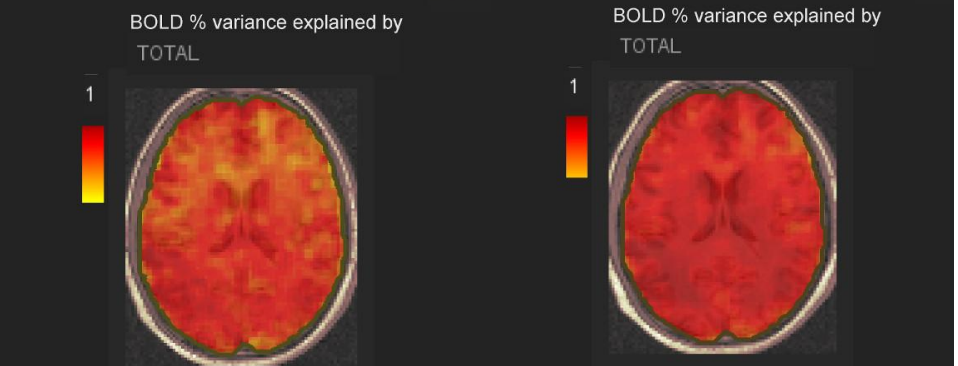
Manipulation errors & QA

Control

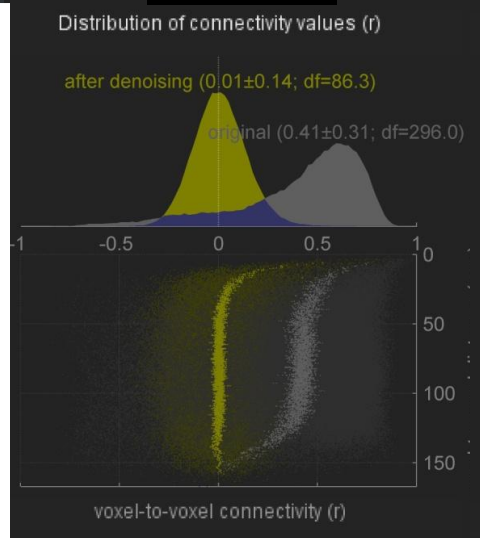


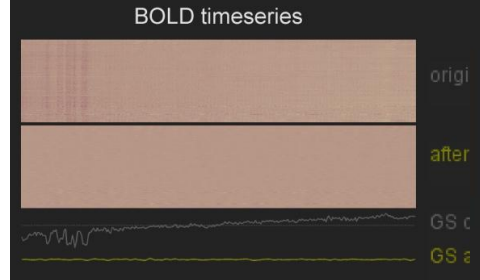


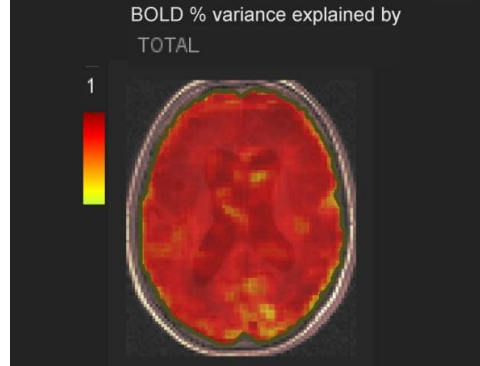


no smooth/realign

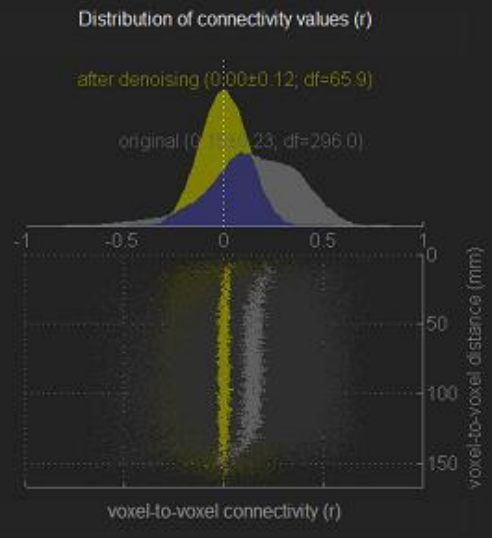
Patient

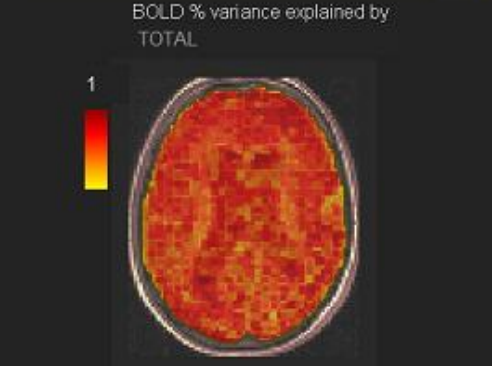






no smooth/realign





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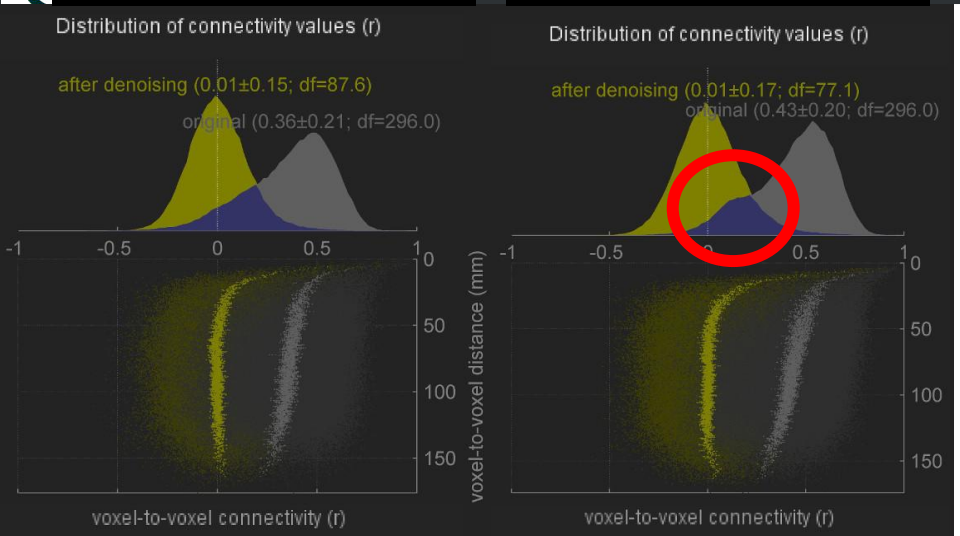
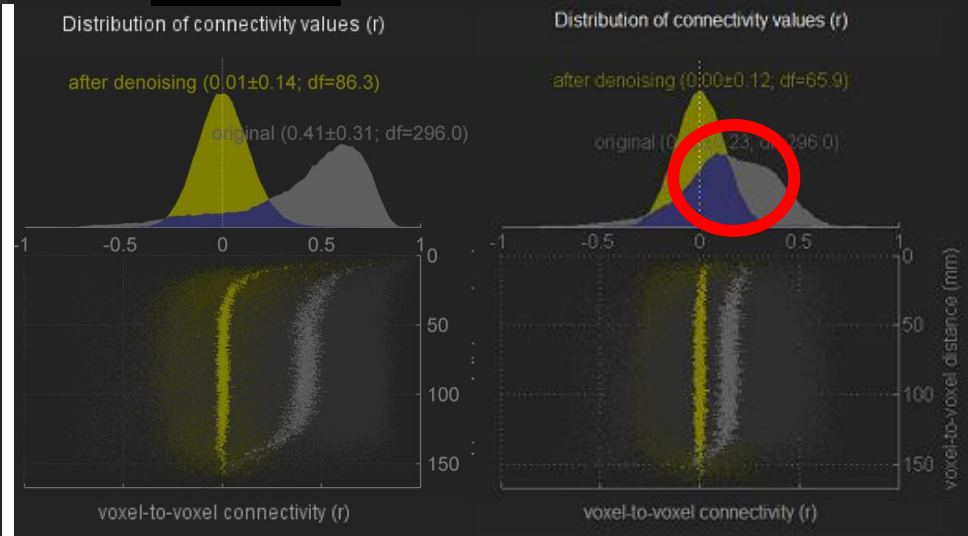
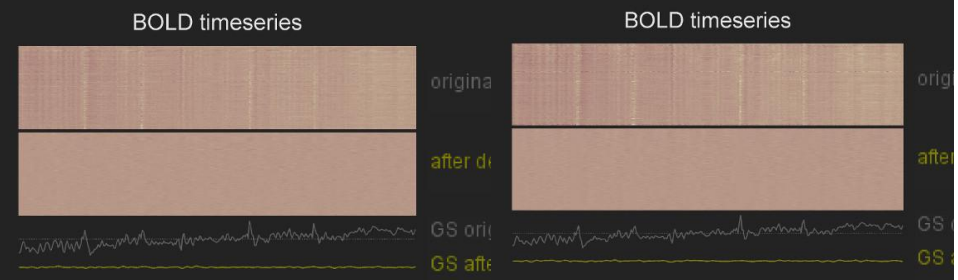
Manipulation errors & QA

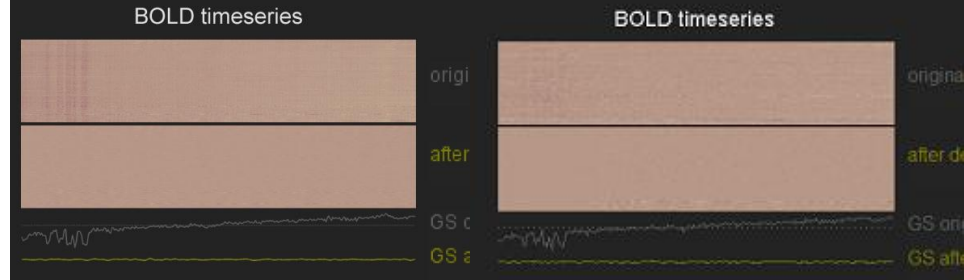
Cause of noisy signal shape!

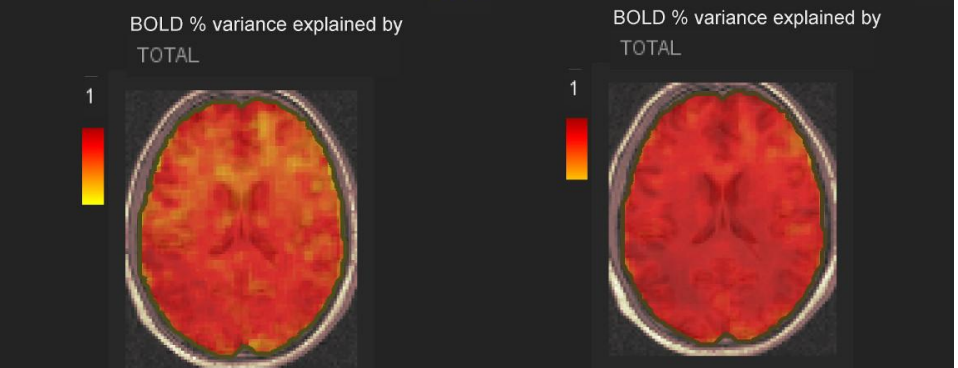
Control | no smooth/realign | Patient | no smooth/realign

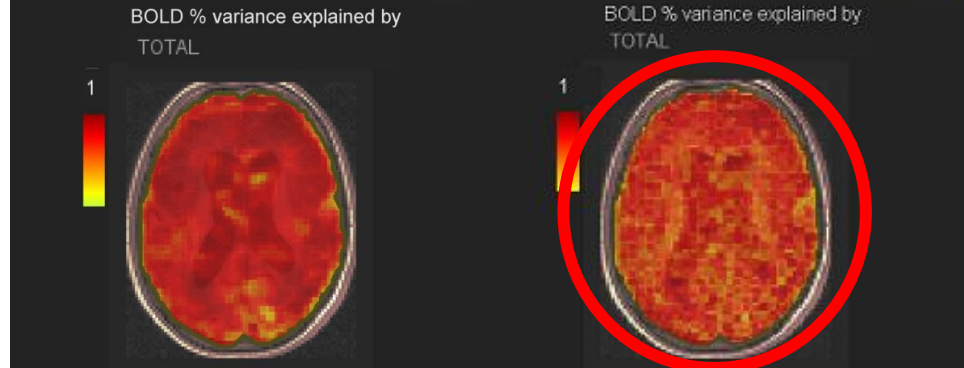












Other considerations

- **Mixed controls**: controls were not reprocessed (different normalization, smoothing kernel, modules versions, resizing, etc.)
- **Template is CRITICAL**: if bad template, the results will be totally wrong! (Use CONN overlay on MNI to QA)
- **NaN are CRITICAL**: if you include multiple patients in one CONN project, don't just set to 0, else all patients/subjects are used, including the ones you are trying to exclude! Thus artificially inflating effect size significantly! Inputing NaN instead of 0 will exclude subjects.
- Lizette mentioned that they did not use VBM/DARTEL at the time to « be able to trust the classifier » ?
- Interesting: If wrong TR and slice order (slice timing correction), MPFC seed lost all correlation, but not PCC (no change after correction).
- Ask Mohamed: why in new VBM8 script, coregister on original structural, instead of VBM bias corrected?

Propositions

- **Automate CONN** project creation: use conn subjects loader script to minimize manip errors
- **Always check Denoising** step for **very weird** artifacts
- **Reprocess controls everytime** we use a new pipeline (else not comparable! eg, normalization different, smoothing kernel can be bigger, etc.)
- Always **write threshold** used in report (voxel p and cluster p)
- For research: **save copy of scripts used on Z:** after study finished (to know version, parameters, modules used, etc.)
- Should always use cerebellum masking?

Conclusion

- **All pipelines are good**, it is just **difficult** to **migrate** (and to learn how to use them)
- One **very stable** pipeline, used for years (SPM12 OldSeg/Athena's). Should use that!
- **Version, centralize, unify & fix code** potentially useful to reduce errors or be more descriptive (parameters for easy **migration**, conn subjects loader, fix bugs or message) (also it will be faster for users ☺)
  → updated SPM12 OldSeg already done, eventually merged with Mohamed's code on GitHub? ☺
- **VBM** should be kept, but mostly for research (where segmentation matters & more conservative results).
  → Move to **CAT12**? (better report and segmentation more customizable, encouraging first results)

Thank you for your attention

References:

- N/A

BONUS SLIDES