Which denoising for resting-state based parcellation?: Reliability & reproducibility in hippocampus

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Introduction

- **Connectivity-Based Parcellation** (CBP) reveals brain organization [1]
- **Different markers of functional connectivity** can be used for CBP: task-(in)dependent functional connectivity (RSFC, MACM) and structural (SC)
- **RSFC-CBP** most widely used to examine brain organization but **denoising** and its effects on CBP has not yet been investigated
- Recent methods developments focused on cortical partitions, hence neglecting crucial subcortical structures [2,3]
- We examined **stability and reproducibility of RSFC-CBP** as a function of different denoising approaches in the hippocampus

Methods

- RSFC-CBP and SC-CBP performed on functional and structural MRI data of **two cohorts**:
  HCP (n = 323) 1000BRAINS (n = 671)
- Hippocampus **VOI** from SPM Anatomy Toolbox & Harvard-Oxford Atlas
- **RSFC**: task-independent functional connectivity at rest
- **MACM**: task-dependent functional connectivity across BrainMap experiments
- **SC**: proxy for coplasticity, Voxel Based Morphometry (VBM) for grey matter probabilities modulated for non-linear transformations only

RSFC denoising approaches:
- 24 Motion regressors (no denoising)
- Global Signal Regression (GSR)
- White Matter and CSF signal regression (WM/CSF)
- FMRIB's ICAbased X-noisifier (FIX)
- Combination of FIX and GSR (FIX+GSR)
- FIX and WM/CSF regression (FIX+WM/CSF)

Clustering:
- k-means for k=2-7, 500 repetitions, 255 iterations

Reliability assessment:
- Internal stability: 10 000 split-half resampling
- Reproducibility: across cohorts and modalities with 10 000 bootstrap resampling
- Consistency measure: adjusted Rand Index (aRI)

Statistics:
- Analysis of Variance (ANOVA) performed on split-half-, bootstrap samples, RSFC voxels' time-course similarity, voxels' connectivity profile dissimilarity

Results

- High stability with **GSR, WM/CSF and FIX+WM/CSF** (.79-.84 aRI; p < .0001)
- **Highest reproducibility** across samples (.52 aRI) and modalities (< .45 aRI) likewise with **FIX+WM/CSF** (p < .0001, Fig. 1A)
- FIX+GSR and FIX+WM/CSF significantly **reduced** the similarity between the **time-courses of the seed voxels** (p < .0001), and additionally **enhanced the dissimilarity of their connectivity profiles** (p < .0001, Fig. 1B,C)

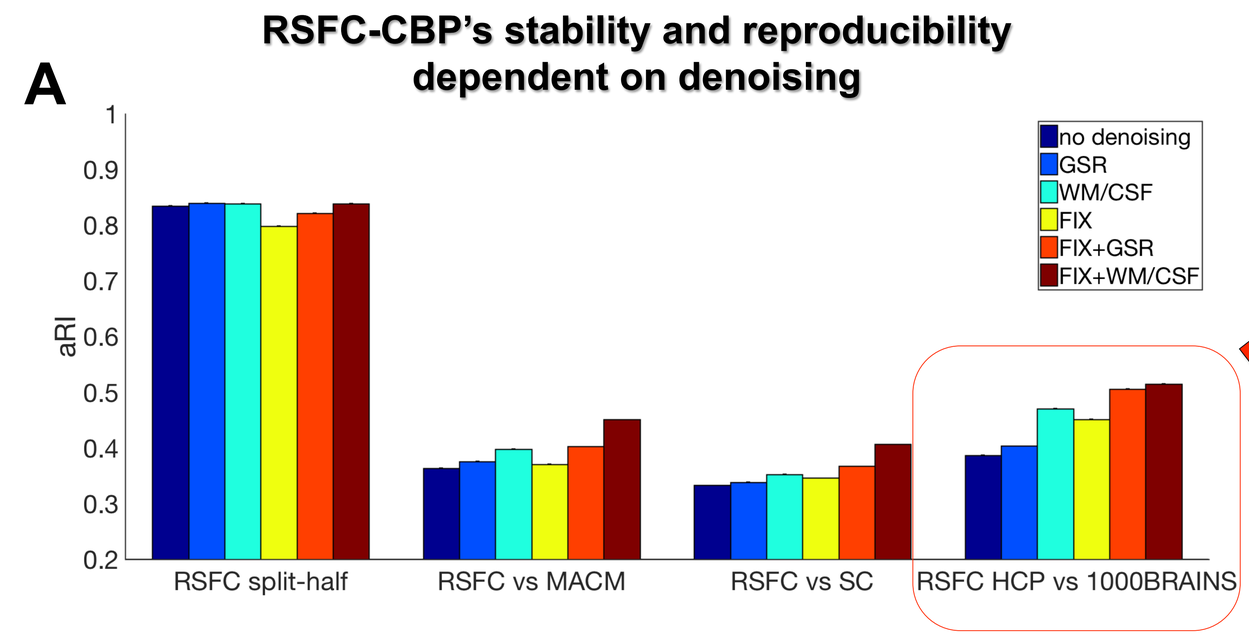

Figure 1.Note: bars represent mean and +/-standard error.

- With FIX-WM/CSF 2-cluster solution demonstrated highest convergence across samples and between RSFC and SC (p < .0001)
- **Highest consistency between RSFC and MACM for 5-cluster solution** (p < .0001) featuring a differentiation into tail, body and a three-way subdivision of the hippocampus head into a ventral, dorsolateral, and dorsomedial part (Fig. 2)

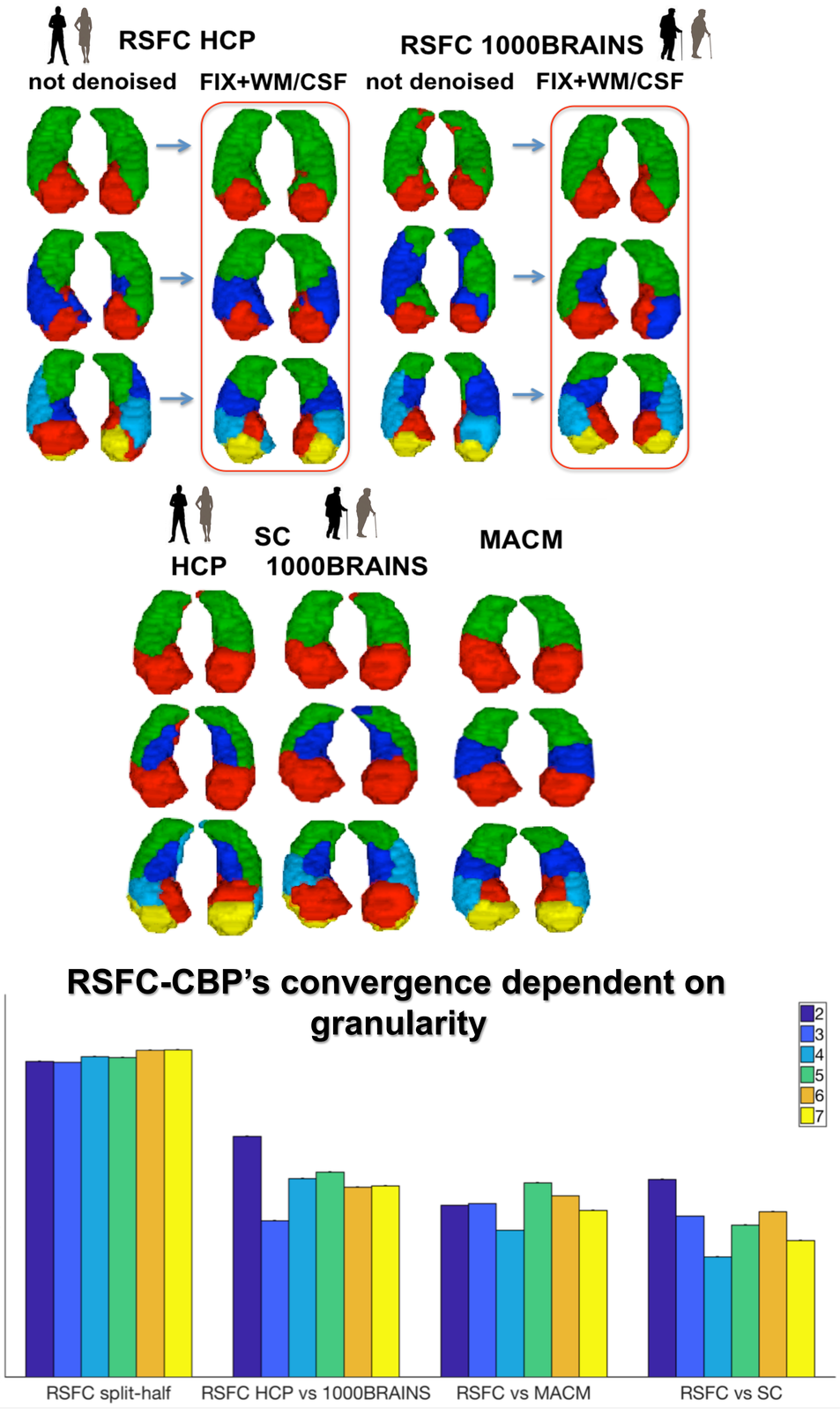

Figure 2. Note: bars represent mean and +/- standard error.

Discussion

- **Model-based and model-free denoising strategy** in combination such as FIX +WM/CSF leads to **stable clustering of the hippocampus**
- This approach successfully **eliminated structured noise** rendering the seed time-series' less inter-correlated and **enhanced the distinctiveness** of the connectivity profiles
- **FIX+WM/CSF** also yielded **most reproducible** clusterings across samples and modalities
- **Conclusion: higher biological validity of RSFC-CBP** after FIX +WM/CSF denoising, revealing a hippocampal organization confirmed by tracing, lesion and genetic studies across species [4,5,6].

References: [1] Eickhoff S B, Yeo B T, Genon, S. (in press). Nature Review Neuroscience. [2] Glasser MF, Coalson TS, Robinson EC, Hacker CD, Harwell J, Yacoub E, Ugurbil K, Andersson J, Beckmann CF, Jenkinson M, Smith SM, Van Essen DC (2016) Nature. 536(7615):171-178. [3] Schaefer A, Kong R, Gordon EM, Laumann TO, Zuo XN, Holmes AJ, Eickhoff SB, Yeo BTT (2017) Cereb Cortex. 18:1-20. [4] Fanselow M S, Dong H-W (2010) Neuron. 65(1):7-19. [5] Poppenk J, Evensmoen H R, Moscovitch M, Nadel L (2013) Trends Cogn Sci.17(5):230-40. [6] Strange B A, Witter M P, Lein E S, Moser E I (2014) Nat Rev Neurosci. 15(10):655-69.

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