

Resting-state test-retest reliability over different preprocessing steps

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Introduction:

Resting-state (RS) functional connectivity (FC) analysis has become a widely used method for the investigation of human brain connectivity and pathology. While most of the current applications are based on data-driven analyses, the use of functionally specific, a priori defined networks provided by neuroimaging meta-analyses represent an important alternative to these, as they allow the standardized assessment of connectivity patterns. Neuronal activity as measured by functional MRI is influenced by various nuisance signals including system noise, thermal noise, and noise induced by physiological processes of the participant. The presence of these confounds in turn have an impact on the estimation of functional connectivity. Several methods exist to deal with this predicament, but little consensus has yet been reached on the most appropriate approach. Given the crucial importance of reliability for the development of clinical applications, we investigated the test-retest reliability of FC analyses in meta-analytically defined networks after removing confounding noise regressors.

Methods:

RS-fMRI data of 42 healthy subjects with an average age of 42 ± 20 years were obtained in two sessions with an average time interval of 175 ± 75 days. A seed-based FC analysis was conducted after spatial preprocessing, approach specific confound-regression, and band-pass filtering [0.01-0.08 Hz]. We focused on the effects of various commonly used confound removals in the resting state studies such as PCA de-noising, global mean signal regression, and removal of tissue-class specific mean signals (in particular, white matter (WM) + cerebrospinal fluid (CSF) and WM + CSF + grey matter (GM)) [2,3,4,5,7]. Additionally, we examined GM specific time-series extraction from seed regions. In order to compute the seed based FC, a priori defined networks were analyzed (extended socio-affective default mode [1] and working-memory [6]). Both networks show robust within network resting state connectivity as well as anti-correlation between each other. The reliability of FC was measured using two different measures Spearman correlations and the absolute differences of functional connectivity scores. The different approaches defined by the combination of different masking / confound removal approaches were compared using a non-parametric Friedman ANOVA.

Results:

The summary ranking across both indices of reliability (Spearman correlations and absolute differences) reflects the major patterns noted in the individual analyses (Fig.1). GM masking, in particular using the group-mean segmentation, improves reliability. PCA denoising in turn reduces it. Within-network connections are most reliably estimated when not using any global or tissue-class specific signal regression, with removing the global WM and CSF signals representing the next-best approach. In contrast, between-network connections are most

reliably measured by linear and second order removal of global signals of all three-tissue classes.

Fig.1: Ranking of test-retest reliability

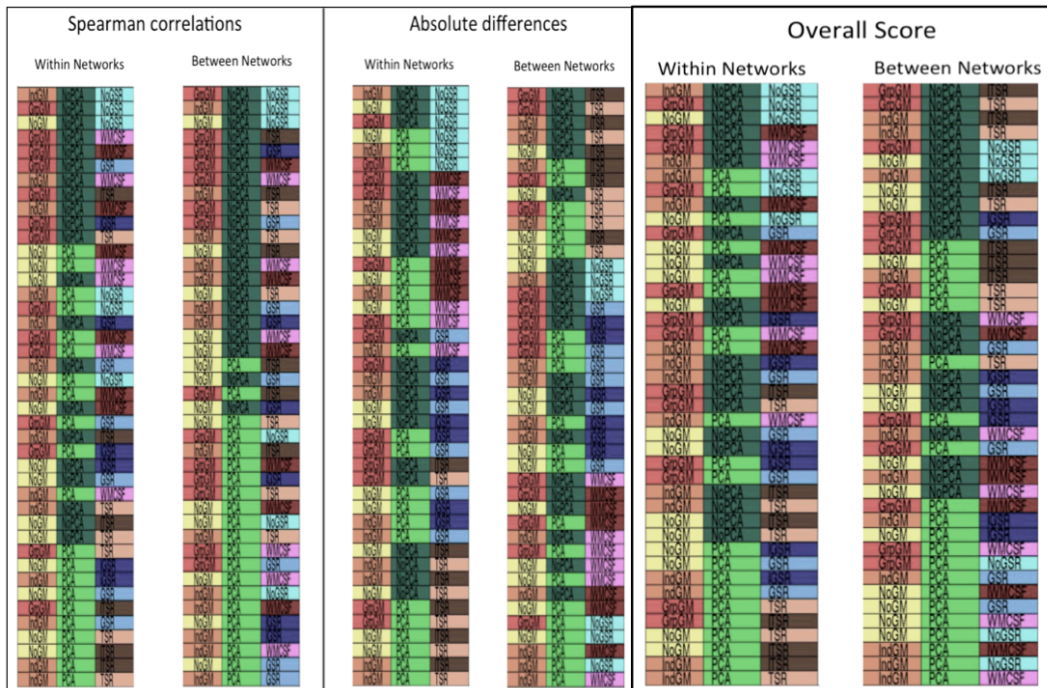


Fig.2: Combined ranking of the test-retest reliability

Variance of the time series	Combinations	% of positive correlations	
		Within Networks	Between Networks
8.86	indGM	100	100
8.86	indGM	100	100
8.86	indGM	100	100
6.07	GMGM	98.04	16.67
6.19	GMGM	99.02	15.74
5.7	GMGM	95.1	8.33
6.17	GMGM	95.1	11.11
6.17	indGM	98.04	15.74
5.55	GMGM	95.1	8.33
6.22	GMGM	95.1	8.33
6.06	indGM	98.04	15.74
5.85	GMGM	100	55.56
3.54	NGGM	96.08	12.96
3.43	NGGM	98.04	16.67
6.14	indGM	98.04	16.67
5.19	NGGM	100	61.11
5.18	NGGM	95.1	61.96
5.68	indGM	94.2	12.96
5.54	indGM	94.2	9.26
5.81	indGM	100	56.48
5.12	NGGM	94.2	9.26
4.36	NGGM	95.1	12.96
4.95	GMGM	95.1	4.81
5.54	NGGM	96.1	12.96
5.59	NGGM	96.1	12.96
4.29	NGGM	95.1	4.81
4.99	NGGM	93.4	1.11
4.86	GMGM	94.2	4.81
4.96	GMGM	92.16	4.81
4.81	GMGM	91.8	8.33
4.92	GMGM	92.16	10.18
4.91	indGM	96.08	13.89
4.87	NGGM	92.16	9.26
4.49	GMGM	91.8	8.33
3.97	NGGM	92.16	9.26
4.82	indGM	96.08	12.96
4.38	NGGM	93.4	11.11
4.59	indGM	92.16	9.26
4.34	NGGM	93.8	11.11
4.46	indGM	91.8	9.26
4.93	indGM	91.8	11.11
4.88	indGM	91.8	11.11

Conclusion:

Our results show that GM masking of the seed regions based on the group-average GM probabilities is advisable when investigating meta-analytically defined networks. In turn, PCA de-noising reduces the reliability of connectivity estimates. Finally, with respect to

global signal regression, we observe that refraining from this approach enhances reliability, but comes at the expense of potentially poorer biological validity, indicated by missing anti-correlations between what has been previously described as antagonistic networks. Here, removal of global WM and CSF signals seems to provide a good compromise, as this approach yielded reliable and meaningful estimates of within and between-network connections (Fig.2). We noted that reliability is proportional to the retained variance, presumably including structured noise. Consequently, we would argue that compromises are needed between maximizing reliability and removing variance that may be attributable to non-neuronal sources.

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