Estimation of Resting State Network Activity Using Multivariate Prediction Analysis Regression (MVPA-R)

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Introduction: Analyses of resting state fMRI data have resulted in several resting state connectivity networks (RSN) that are consistent across subjects and scanning sessions [1,2]. We propose a method based on multivariate prediction analysis regression (MVPA-R) to train a classifier on resting state data that can measure the level of RSN activity from a never-before-seen dataset on an image-by-image basis. Benefits of this method include the accurate estimation of RSN activity from resting-state and task data, as well as providing a framework for evaluating trade-offs for different resting state experimental parameters [3,4,5]. We demonstrate this approach with 10 RSNs that have been previously reported in the literature [6], but any RSN can be studied with this framework.

Methods: Two 10-minute resting state fMRI scans (TE/TR/FA = 30 msec/1.75 sec/90°, 30 3.6-mm slices, 0.36 mm gap, 3.45 x 3.45 mm in-plan resolution) were acquired for 26 healthy volunteers using a Siemens 3T Tim TRIO. Preprocessing was performed in AFNI [7] and involved slice timing correction, motion correction, regressing out CSF and white matter mean time courses as well as six motion parameters, co-registration to T1, and 6-mm FWHM spatial blur. Time courses for 10 RSNs were extracted by normalizing resting state data to MNI space using a two-step procedure in FSL (flirt+fnirt) [8] followed by spatial regression (SR) to RSN templates derived from an ICA meta-analysis of resting state and task fMRI data [6].

MVPA-R training was performed in the original subject space for each RSN time course and its corresponding 10-minute resting state scan for each subject using the 3dsvm tool [9] in AFNI. The result is a spatial pattern relating fMRI data to an RSN time course. Testing was performed for each subject by applying the spatial pattern learned on one resting state scan to the independently acquired resting state scan.

Results: MVPA-R showed high prediction accuracy and high reproducibility across all RSNs (Figure 1). The prediction accuracy vs. reproducibility curves suggest three possible RSN clusters: cluster 1 includes default mode (RSN4), sensorimotor (RSN6), auditory (RSN7), medial visual (RSN1) and lateral visual (RSN3); cluster 2 includes left front parietal (RSN10), executive control (RSN8), cerebellum (RSN5) and right fronto-parietal (RSN9); and cluster 3 includes the occipital pole visual areas (RSN2). More than 2.5 minutes of training data are required to achieve high prediction accuracy and reproducibility, but more than 7.5 minutes offers no significant benefit (Figure 2). The activity of the default mode network (RSN4) can be predicted accurately one TR in the future, but beyond that it falls off substantially (Figure 3); the other networks showed a similar pattern. The spatial patterns derived from the MVPA-R training are highly consistent with what is expected from the RSN templates (Figure 4).

Conclusions: This work demonstrates that MVPA-R can be used to track activation levels of resting state networks in a never-before-seen data set. This opens up a number of exciting possibilities such as monitoring resting state network activity in real time [10] and evaluating the consistency of resting state networks in terms of reproducibility and prediction accuracy [3,4,5].

References: 1. Damoiseax, J. et. al. *PNAS* 103 (37) 2006, 2. Shehzad, Z. et. al. *Cereb Cortex*, 19(10) 2009, 3. Strother, S.C. et. al. *NeuroImage* 15(4) 2002, 4. Kjems, U.. et. al. *NeuroImage* 15(4) 2002, 5. LaConte, S.M. et. al. *NeuroImage* 18(1) 2003, 6. Smith, S.M. et. al. *PNAS* 106(13) 2009, 7. Cox, R.W. *Computers and Biomedical Research* 29 1996, 8. Smith, S.M. et. al. *NeuroImage* 23(S1) 2004, 9. LaConte, S.M. et. al. *NeuroImage* 26 2005, 10. LaConte S.M. et. al. *NeuroImage* 26(2) 2007.

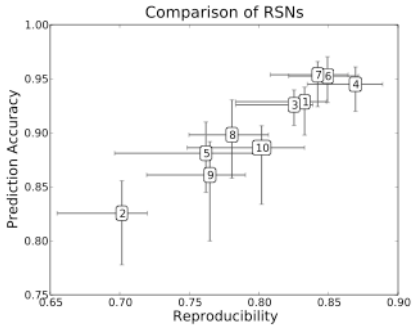

Figure 1. Comparison of RSNs. Labels correspond to RSN (see Figure 5) and error bars are quantiles.

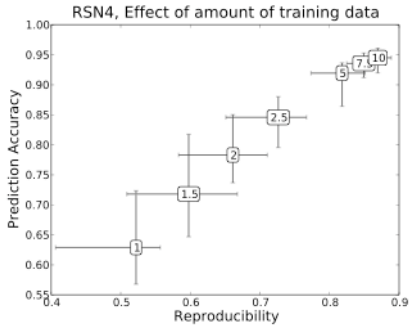

Figure 2. Effect of amount of training data. Labels correspond to amount of training data in minutes and error bars are quantiles.

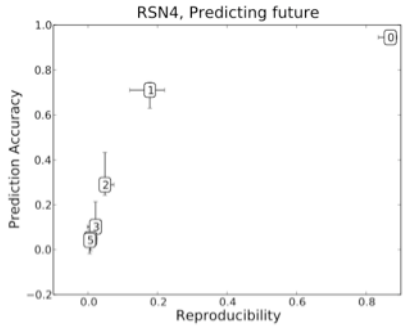

Figure 3. Ability to predict future activity of RSN 4. Labels correspond to amount of lag in TRs and error bars are quantiles.

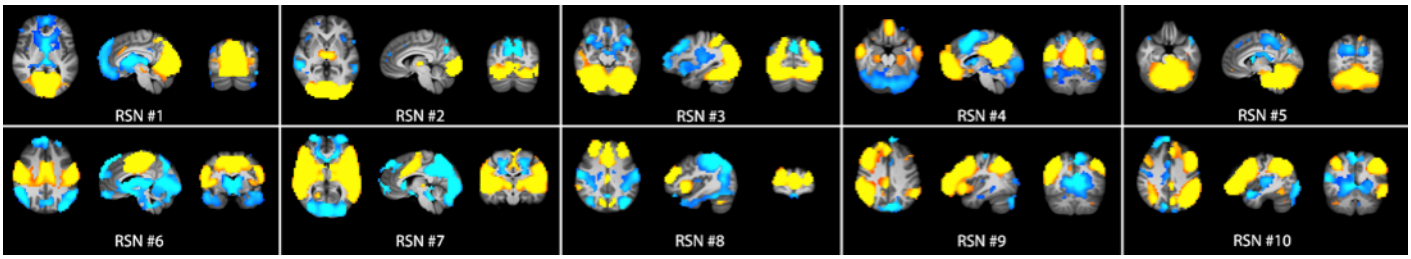

Figure 4. SVM-derived group average MVPA-R spatial patterns for each RSN. Subject-specific patterns were transformed into MNI space and combined across subjects using one-sample t tests. Statistical maps are shown using an FDR-corrected $p < 5 \times 10^{-5}$ threshold.