Group-level data-driven phMRI analysis

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Introduction: A key issue in phMRI data analysis is that the response is not always precisely known a priori, while the experimental paradigm (acute injection point) under-informs the design of a temporal signal model. "Boxcar" windows can capture major signal changes but do not always provide a close match to the temporal response, in particular for intravenous (IV) injection. Moreover, the phMRI signal sometimes has a different temporal profile in different brain regions. Recently, group-level ICA analysis has been applied to human fMRI data [1]. Here we present a group-level data-driven approach for phMRI, evaluated on three representative rodent studies, and demonstrate that this approach provides (a) an efficient study-level overview of spatiotemporal response, and (b) regressors that provide a more accurate description of the signal for subsequent hypothesis-based time course analysis.

Methods: ***Processing algorithm***: (1) Study phMRI time series' concatenated spatially; (2) Optional pre-processing (spatial rebinning, variance normalisation); (3) Group level data-driven analysis using Principal Component Analysis (PCA; 3dpc, AFNI) or Wavelet Cluster Analysis (WCA) [2,3] to estimate a single set of components for the cohort; (4) Selection of components of interest; (5) Derivation of regressor set; (6) General Linear Model (GLM) analysis using selected regressor set. ***Evaluation***: We evaluated this approach on three representative rCBV phMRI studies in the rat: (1) acute 1mg/kg IV amphetamine challenge (strong widespread response) using the data set from ref. [4] (*N=16*); (2) acute 1mg/kg IV nicotine challenge (strong but localised response, *N=10*); (3) acute 3mg/kg IV challenge with the NK1 antagonist GR-205171-A (variable response, *N=17*). Regressor sets were compared quantitatively in each case using the residual signal following GLM analysis (3dDeconvolve, AFNI) of time courses from selected ROIs for all animals in each cohort.

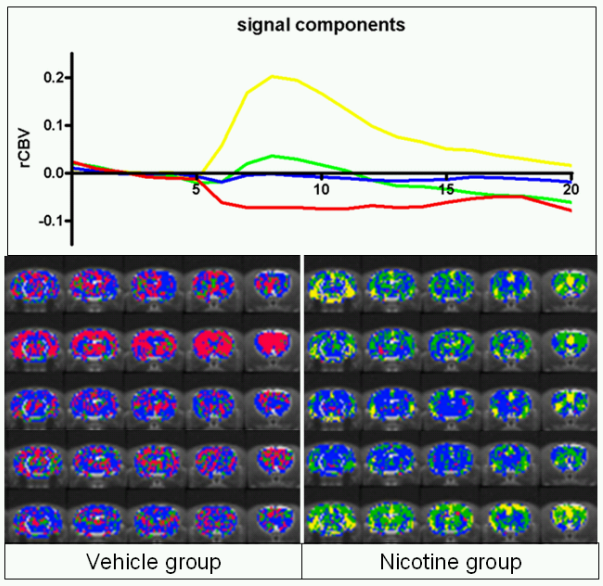
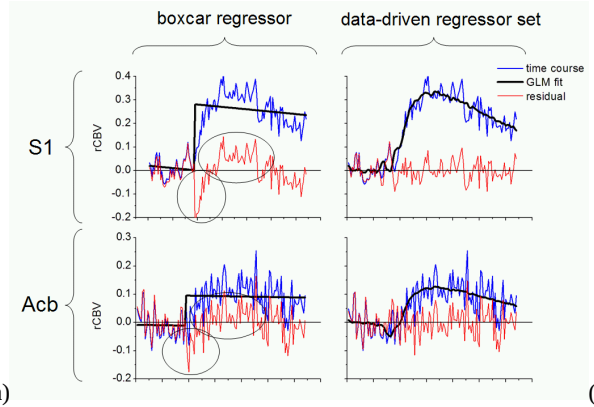


Figure 1*: Group-level WCA decomposition of nicotine study (injection at timepoint 5). Note that the* yellow *and* green *components are localised almost exclusively to the treatment group and represent potential signals of interest, while the blue component captures a flat signal pixels across both groups of subjects.*

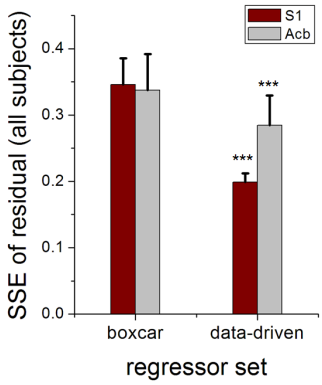
Results: Viewing spatiotemporal response components across the cohort, illustrated in Fig. 1, proved an extremely efficient way of conveying the reproducibility/variability of the response between subjects and the spatiotemporal patterns involved. PCA analysis on the time series' directly was useful only for the amphetamine study, where the first component captured the representative form of the temporal response and could be used directly as a signal model. When combined with temporal and dispersion derivatives (Fig. 2(a)) or additional PCA components (not shown), the response was modelled accurately including brain regions exhibiting slightly different temporal profiles. For the other two studies examined, direct PCA was susceptible to background drift and other uninteresting components. Here, WCA proved more useful, discriminating localised responses of interest in the nicotine (Fig. 1) and NK1 antagonist studies. Regressor sets based on selected components also provided accurate signal models, reducing residual signal features including sum-squared error, autocorrelation and kurtosis.

Discussion: Data-driven analysis of phMRI data at the group level provides an efficient overview of all data within time series study cohorts. In particular, we found this a rapid way to identify common interesting features across subjects, which could then be used to construct regressor sets for more formal analyses. Evaluation of this approach on three representative data sets demonstrated its utility in providing more accurate signal models, helping the residual noise to adhere more closely to assumptions inherent in statistical time course analysis, rendering subsequent inference more robust. WCA was useful in identifying interesting signal changes across all studies evaluated, although a reliable method to determine the optimal number of components remains outstanding [3]. Direct PCA group decomposition identified readily interpretable signals only when a strong widespread response dominated background drifts.

References: [1] Calhoun VD *et al*. 2001 Hum Brain Mapp **14** 140. [2] Whitcher B *et al*. 2004 Proc ISMRM **12** 1100. [3] Whitcher B *et al*. 2004 NeuroImage, In Press. [4] Schwarz AJ *et al*. 2004 Synapse **54**(1) 1-10.



(a)



(b)

Figure 2*: Illustration of improved time course modelling for* individual *subject time courses and across the* group *(amphetamine study). (a) Raw time course, model fit and residual signal traces for ROIs in the somatosensory cortex (S1) and nucleus accumbens (Acb). (b) Reduced residual signal across all subjects in the study using the data-driven regressor set (first direct PCA component plus first and second derivatives and a linear term). Residual sum-squared error (SSE) was significantly reduced in both ROIs, *** indicating p<0.001, Wilcoxon matched pairs test.*