# Bayesian Source Separation of Drug-Induced BOLD Responses with Correlated Reference Functions

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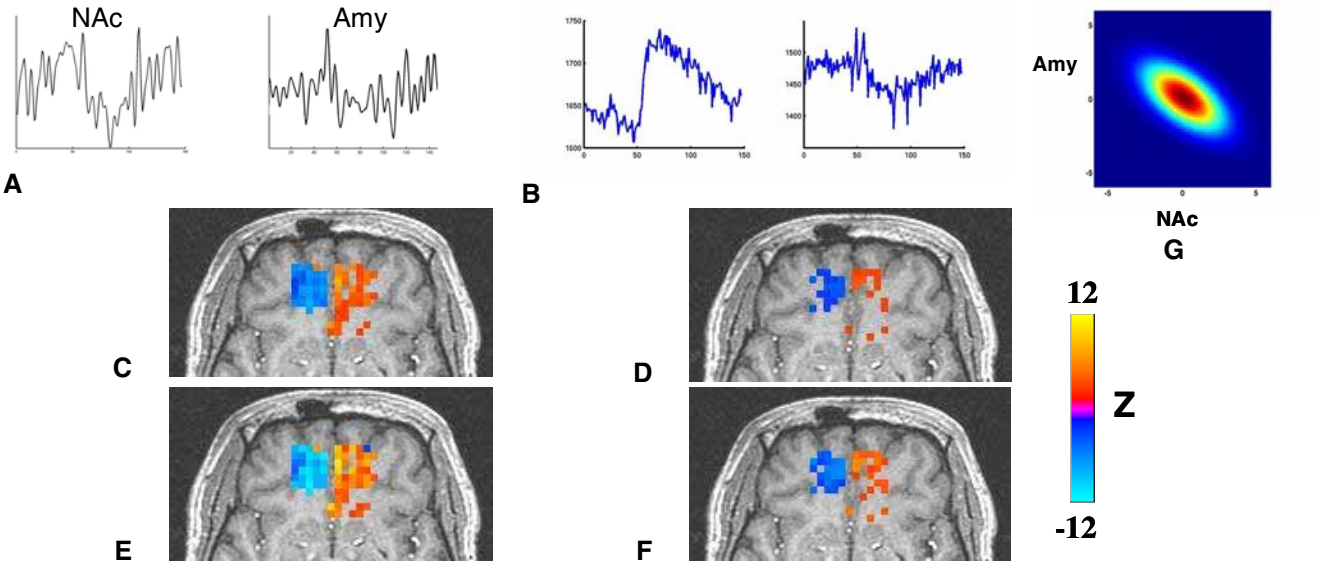
**INTRODUCTION:** Pharmacological FMRI in humans involves BOLD signal acquisition during and after the administration of a drug, and often results in a heterogeneous pattern of drug-induced hemodynamic responses in the brain. Exploratory techniques, including blind source separation, can be useful for BOLD data that contains patterns of cross-dependencies. Bayesian Source Separation (BSS) is a multivariate technique used to calculate the presence of unobserved signal sources in measured FMRI data, as well as the covariance between data voxels and between reference waveforms [1]. In this study, BOLD measurement of the acute effect of an intravenous dose of cocaine, a substance shown previously to engage multiple sites within the orbitofrontal cortex (OFC) [2], was processed with BSS. Simultaneously measured BOLD signals from the nucleus accumbens (NAc) and amygdala (Amy), both subcortical afferents to the OFC, as reference waveforms. Unlike conventional regression analysis, BSS does not assume independence between voxel time series.

**METHOD:** Acute cocaine BOLD data was collected from cocaine-dependent human subjects as described previously (1.5 Tesla, 20 min scan, 64 x 64 x 5mm, infusion after 7 min, 150 time points) [2], generating a pattern of region-specific postinfusion BOLD inflections in the NAc, Amy (**A**) and throughout the OFC (**B**). BSS was then employed on 144 voxels of BOLD data from the 2 ROIs in the medial OFC, utilizing the BOLD responses of subcortical afferents (NAc and Amy, **A**) as described previously [3]. The mechanics of BSS for systems with known (noise trends) and unobserved (neural cocaine response) are available in detail [4]. Posterior estimates for regression coefficients (following application of Bayes rule and Gibbs sampling) were converted into z-scores (**C-F**) and thresholded at $z > 3$.

**RESULTS/DISCUSSION:** Application of Bayes' rule improved the activation statistics for both NAc and Amy reference functions. The *a posteriori* NAc-activated OFC voxels (**E**) exhibited higher z-scores than the *a priori* results in the same locations (**C**). The sparse *a priori* Amy-related activation (**D**) was improved following BSS with more activated voxels and higher z-scores (**F**). The BSS analysis also revealed an inverse correlation (-0.229) between *a posteriori* reference functions, and the significant interaction was illustrated in the off-axis contour plot of the reference function covariances (**G**). These results suggest that BSS is a feasible technique for investigating the interacting subcortical-cortical communications during drug-induced brain activity.




**Results of BSS Analysis using two BOLD reference waveforms. A:** Reference waveforms representing the NAc and Amy BOLD responses. **B:** Average BOLD responses of left and right OFC regions. **C.** Prior regression *z*-scores associated with NAc. **D.** Prior regression *z*-scores associated with Amy. **E.** Posterior regression *z*-scores associated with NAc. **F.** Posterior regression *z*-scores associated with Amy. **G.** Contour plot of posterior covariance matrix of the NAc and Amy reference functions. For the parametric maps **(C-F)**, left is left and the *z*-scores shown surpass the threshold $z > 3$.

**REFERENCES: 1.** Rowe, MRM 2001. **2.** Kufahl et al., NI 2005. **3.** Kufahl et al., ISMRM 2005. 4. Rowe, C & H 2003.
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