The Bleeding Artifact of Spatially Constrained Canonical Correlation Analysis in Functional MRI

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Introduction

Local canonical correlation analysis (CCA) is a novel data analysis technique, where instead of looking at the single voxel time course, the joint time courses of a group of neighboring voxels are investigated in a 3x3 in-plane pixel region[1,2]. The value of a suitable test statistic is used as a measure of activation. It is customary to assign the value to the center voxel. However, this choice can result in false activations especially in regions of localized strong activation. The reason for the increase in false activations close to localized strong activation is due to smoothing properties of CCA. In the following we refer to this artifact as "bleeding artifact": This artifact can be reduced by using spatial dominance constraints in CCA (the larger the dominance, the smaller is this artifact). In the following we investigate if mixture modeling can be applied as a post-processing tool to eliminate the bleeding artifact for real fMRI data from a motor and a memory paradigm.

Theory

Let α specify the vector of the spatial weights of local CCA. We consider the following four scenarios for the components α_i of α where α_1 is the weight for the center voxel and the other $\alpha_i's$ represent the weights for the s neighborhood voxels.

#1. $\alpha_i > 0\ \forall\ i$ # 2. $\alpha_1 \geq \frac{1}{s-1}\sum_{i=2}^{s}\alpha_i > 0$ and $\alpha_i > 0\ \forall\ i$ #3. $\alpha_1 \geq \sum_{i=2}^{s}\alpha_i > 0$ and $\alpha_i > 0\ \forall\ i$ #4. $\alpha_1 \geq \max(\alpha_i) > 0$ and $\alpha_i > 0\ \forall\ i$.

All of these constraints lead to spatial low pass filtering, and constraints #3 and #4 provide different magnitude of dominance of the center voxel (i.e. dominance for #3 is maximum, for #4 is minimum; constraints #1 and #2 do not guarantee dominance). The bleeding artifact, B_A, is defined as the probability that the center voxel of a configuration of size s (number of pixels in local neighborhood) is declared active given that the center voxel is not active, i.e. $B_A = p(\omega > \omega_0|\text{center voxel is not active})$ where ω is the test statistic of the configuration with inactive center voxel and ω_0 is a threshold (corresponding to p=0.05 corrected). For multivariate methods this artifact is obviously a function of the analysis method applied, the CNR of the center voxel, the CNR of the whole configuration, the size of the configuration, and the statistical threshold employed. The bleeding artifact can be estimated using re-sampled resting-state data as null data and adding simulated activations with specified CNR to all voxels of the configuration except the center voxel. With this procedure simulated voxel time courses $y_i(t)$ for s voxels in a 3x3 grid are obtained by $y_i(t) = \begin{cases} y_1^{(0)}(t) & \text{for } i = 1 \\ \beta\, x(t) + y_i^{(0)}(t) & \text{for } i\,\epsilon\{2,\dots,s\} \end{cases}$

where $i = 1$ refers to the center voxel and all other i to the surrounding voxels of the configuration of size s. All $y_i^{(0)}(t)$ correspond to wavelet re-sampled resting-state time courses and represent spatially and temporally correlated null (noise) data. The activation is determined by the HRF regressor function $x(t)$ of interest multiplied by factor β so that the configuration has a given CNR. From simulated data, it is possible to determine the bleeding artifact function $B_A^{(0)}$ with $B_A^{(0)} = B_A^{(0)}(M, CNR, s, \omega_0)$ where M labels the method of data analysis, CNR the CNR of the whole configuration, s the size of the configuration, and ω_0 the statistical threshold. The bleeding artifact in real data can then be estimated by $B_A(x) = B_A^{(0)}(M, CNR, s, \omega_0)\ p(\text{x}|\text{center voxel is not active})$ where x is the CNR of the center voxel. The second factor can be determined by density estimation techniques applied to activation data and null data. Specifically, using null data first, the density function of single voxel CNR is determined nonparametrically using kernel density estimation. This will give the pdf of $f(x)$. For activation data we model the pdf as having a density $h(x)$ composed of $f(x)$ (with minor modification allowing for dilation) to represent the inactive voxels, and a Gaussian density $G_{\mu,\sigma}(x)$ with mean μ and standard deviation σ to represent the active voxels. Then, $h(x)$ can be written as $h(x) = a\frac{1}{d}f\left(\frac{x}{d}\right) + (1-a)\,G_{\mu,\sigma}(x)$ where the unknown parameters a, d, μ, σ are obtained by least square fitting. Note that we incorporated a dilation parameter d for the function $f(x)$ to allow for the fact that in activation data the distribution of the inactive voxels appears to have the same shape but is slightly broader than in null data. To correct for the bleeding artifact we propose the rule: *Voxel is assigned to be null if* $B_A > 0.5$, i.e. the measure of activation is assigned as zero if this statement is true. If this statement is not true, the measure of activation is unchanged.

Methods

FMRI was performed in a 3.0T GE MRI scanner (8-channel head coil, ASSET=2, TR/TE=2sec/30ms, FA= 70deg, FOV=22cmx22cm, thickness/gap=4mm/1mm, 25 slices, resolution 96x96. We acquired three fMRI data sets. The first data set was collected during resting-state where the subject tried to relax and refrain from executing any overt task with eyes closed. The second data set was collected while the subject was performing an episodic memory paradigm. Briefly, this paradigm consisted of memorization of novel faces paired with occupation, containing 6 periods of encoding, distraction, and recognition tasks (slices parallel to the long axis of hippocampus). The third data was obtained from a conventional motor task (axial slices, four 30 sec periods with on/off finger tapping). As local neighborhood for CCA we use every 3x3 in plane pixel patch and compute CCA for all 256 possible configurations involving the center voxel and its 8 neighbors.

Results

In Fig.1, we show the bleeding artifact function $B_A^{(0)}(M, CNR, s, \omega_0)$ using simulated data for CNR=0 to 1 in steps of 0.1. Note that unconstrained CCA has severe bleeding artifacts, whereas CCA with the sum constraint (high dominance constraint) has almost no bleeding artifact. Fig.2 shows activation maps obtained with different methods (A), activation maps corrected for the bleeding artifact (B), and the location of voxels that have significant bleeding artifact (C). Note that our proposed method to correct for the bleeding artifact is not limited to CCA but includes Gaussian spatial smoothing (GS) as well. Here we see that correction for the bleeding artifact leads to a separation of the left motor cortex into two activated regions(see green arrows on the magnified regions of motor cortex in Fig.3, top row are uncorrected, bottom row are corrected for B_A). This result is consistent with the activation pattern from single voxel analysis without Gaussian smoothing in Fig. 3, which does not contain any bleeding artifacts. Similar results are obtained for the memory data (not shown here).

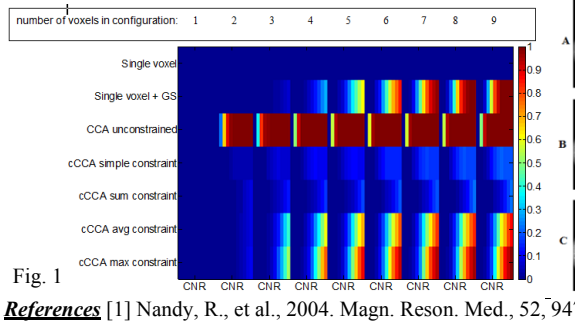

Fig. 1

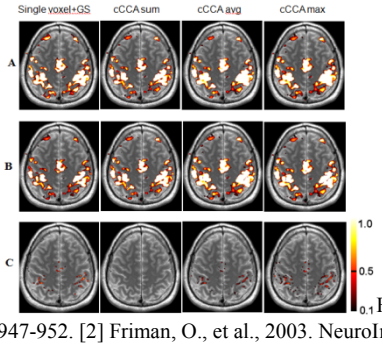

Fig. 2

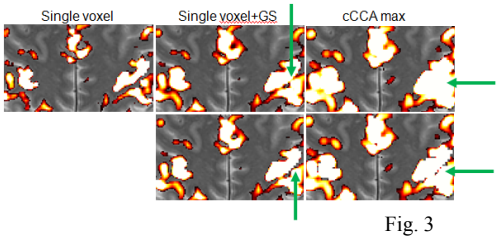

Fig. 3

References [1] Nandy, R., et al., 2004. Magn. Reson. Med., 52, 947-952. [2] Friman, O., et al., 2003. NeuroImage, 19, 837-845.