Dynamics of BOLD fMRI time series: dependence on cognitive load and sensitivity to temporal pre-processing

Catie Chang[1], Biyu J. He[2], and Jeff H. Duyn[1]
[1]*Advanced MRI section, NINDS, National Institutes of Health, Bethesda, MD, United States,* [2]*NINDS, National Institutes of Health, Bethesda, MD, United States*

Introduction: It was recently demonstrated that spontaneous fluctuations in the BOLD fMRI signal resemble scale-free temporal dynamics [1], and that both the variance and Hurst exponent of the BOLD signal decrease during task activation relative to a task-free resting state. A decrease in the Hurst exponent, indicating decreased long-range temporal autocorrelation, was posited to reflect a greater efficiency in the information processing of neural systems during the task. Such findings inspire questions pertaining to the interpretation and underpinnings of the spectral characteristics of BOLD fMRI. For example, the observed changes in the previous comparison between rest and task may be attributed to spectral changes resulting from task-evoked activity, rather than from task-induced changes in brain state. Furthermore, non-neuronal fluctuations (e.g. physiological noise) may affect estimates of both absolute and relative (condition-dependent) values. Quantifying sensitivity to various sources of noise and pre-processing steps is critical if one is to confidently interpret scale-free parameters of the BOLD signal in terms of neuronal dynamics.

Here, we examine the dependence of BOLD signal variance and Hurst exponent on cognitive load and non-neuronal fluctuations using continuous n-back verbal working-memory (WM) tasks. By using tasks that are identical with respect to stimulus presentation, differing only in terms of cognitive load (low = 1-back, high = 2-back), we may more closely isolate the effect of mental effort on BOLD signal dynamics. The sensitivity of the Hurst exponent and variance to the removal of low-order trends, motion, and physiological noise is characterized, and the magnitude of variation in these parameters due to such pre-processing steps is compared to the magnitude of variation across working memory loads.

Methods: Functional MRI data were acquired at 3T (TR=2s, voxel size 3.4x3.4x4 mm^3) with concurrent respiratory and cardiac monitoring. Eleven subjects each performed one 12-min continuous 1-back task and one 12-min continuous 2-back task in counterbalanced order. Trials were presented sequentially with an inter-stimulus interval (ISI) of 3.5s; importantly, the stimulus presentation is aliased to high frequencies (0.217 Hz) of the BOLD signal by the 2-sec TR, and the short ISI induces minimal task-driven BOLD contrast, yielding primarily spontaneous activity under task conditions. In order to identify activated regions, subjects also performed a block-design task consisting of alternating 2-back and 0-back blocks (28 sec/block, 14 blocks total). Ten ROIs were defined as 6mm-radius spheres centered on selected activated and deactivated foci from the block-design analysis, and an additional 28 ROIs were defined based on multiple intrinsic networks using coordinates defined in [1]. The Hurst exponent and BOLD signal variance were computed for ROI time series in both 1-back and 2-back tasks, and were compared across datasets from which the following combinations of nuisance regressors were projected out: (1) linear and quadratic trends ('*trends*'), (2) trends and 6 affine motion parameters ('*trends+mot*'), (3) trends and physiological (cardiac, respiration) noise regressors [2,3] *('trends+phys'*), and (4) trends, motion, and physiological signals *('trends+mot+phys')*. The Hurst exponent was computed using Detrended Fluctuation Analysis [4], and BOLD signal variance was computed as the standard deviation of the percent signal change time series.

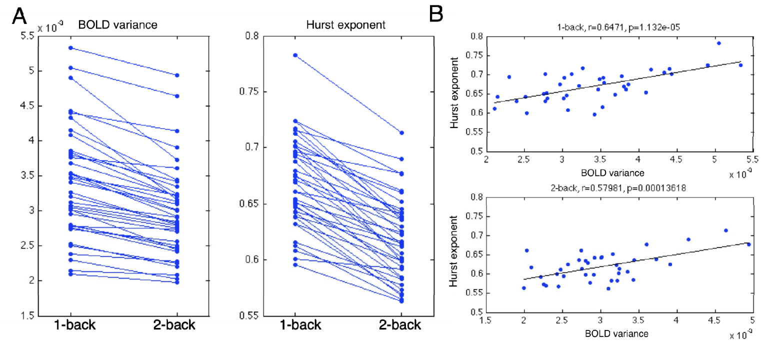

Fig. 1. (A) Decreases in BOLD variance and *H* as a function of increasing working memory load. (B) Positive correlation between variance and *H.* Each dot represents one of 38 ROIs, whose value is averaged across subjects.

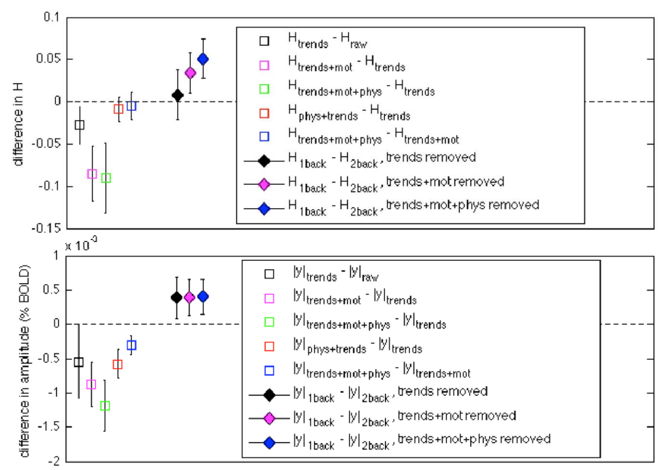

Fig. 2. *Upper:* Differences in Hurst exponent between the indicated pair of nuisance regressor sets (☐), as well as differences in the Hurst exponent between cognitive loads for data processed with the indicated nuisance regressors (◆). Bars show mean ± s.d. across 38 ROIs. *Lower:* Analogous plot for BOLD variance (|y|).

Results: (1) *Load dependence.* In the data from which all (trends, motion, and physiological) nuisance regressors were removed, the average BOLD variance and Hurst exponent (*H*) decreased from 1-back to 2-back in all ROIs (Fig. 1A). Also, consistent with [1], significant positive correlation between variance and *H* existed in both the 1-back and 2-back conditions (Fig. 1B).

(2) *Impact of pre-processing vs. cognitive load*. Figure 2 shows the degree to which *H* and variance can change when different sets of noise regressors are projected out of the data. For comparison, the amount of change due to task load, examined at selected pre-processing steps, is also shown. Note that removing motion regressors from the BOLD signal significantly *increases* the effect of cognitive load on *H* ($p<1e\text{-}6$), and that additionally removing physiological regressors leads to a significant improvement beyond motion regressors alone ($p<1e\text{-}5$). These observations run counter to the possibility that load-dependent differences in *H* are simply driven by a load-dependence of motion and physiological noise. On the other hand, differences in preprocessing did not significantly alter the effect of cognitive load on BOLD *variance* ($p>0.6$).

Conclusions:

(1) We observe decreases in BOLD signal variance and Hurst exponent as a function of increasing cognitive load, mirroring [1] and extending the findings from a 'rest v. task' comparison to the case of two tasks with different cognitive loads but identical stimulus presentation. Thus, cognitive load appears to alter dynamic properties of the BOLD signal across widespread areas of the brain.

(2) The differential effects on *H* due to the selection of nuisance regressors were found to be on the same order of magnitude as the load-dependent differences in *H.* Removal of motion and physiological regressors in addition to low-order trends produced the greatest changes in *H* compared to the removal of trends alone. Importantly, removing noise due to physiological processes and head motion was found to enhance the significance of load-dependent changes in the Hurst exponent. Results suggest the importance of appropriate data processing prior to examining and interpreting dynamic parameters.

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