uNBIASED - A fully automated model-free fMRI analysis method based on response reproducibility

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Introduction: Crucial brain function can be localized via activation maps derived from fMRI. This approach is increasingly being used in presurgical planning in patients with brain tumors and epilepsy to facilitate resection of affected tissue without harming essential functional areas, minimizing the risk of post-surgical deficit [1]. The aim of this study was to develop an analysis method sensitive to activation in regions of pathology, where responses might deviate from predictions due to modified HRF [2] and implement a means to automatically identify and exclude runs affected by poor performance or artifacts ("bad" runs) from the analysis. The suggested method, which we call uNBIASED, is an extension of the BIASLESS method of Levin et al. (2001) [3] to N runs (N>=2) and is tested on 7 T clinical data.

Materials and Methods: Ten patients (with brain tumors and epilepsy) performed 7 to 10 runs of a hand task, consisting of 4 rest and 3 task phases (of 20 s each) presented in a block design. To assess the method's reproducibility, data were acquired from 3 healthy volunteers, who performed 20 runs of a hand, chin and foot task, respectively. EPI data were acquired with a 7 T scanner with a 32-channel head coil, with 34 ACPC slices, a resolution of 1.8x1.8x3 mm and TE/TR=21/2500 ms.

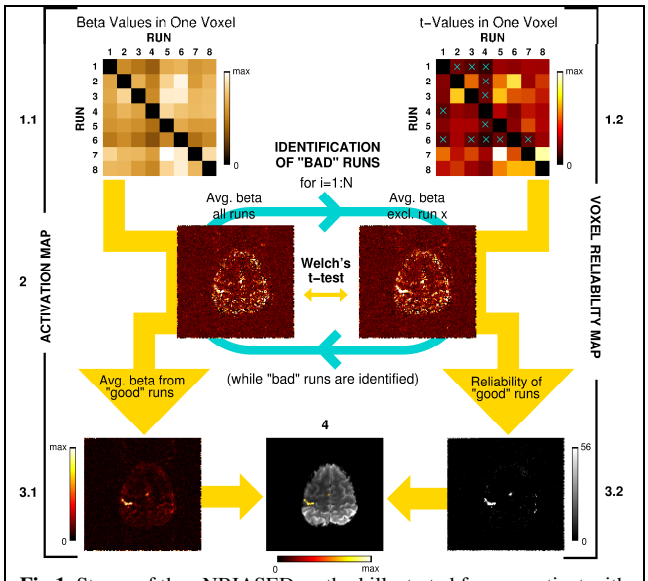

Fig.1. Stages of the uNBIASED method illustrated for one patient with 8 runs.

Analysis: EPI runs were slice time and motion corrected, and coregistered [4-6] to the first run. A second-order polynomial fit to the time course signal in each voxel was subtracted to correct baseline fluctuations. In the first step of the uNBIASED method, the beta value for each voxel and each pair of runs was calculated as the fit of the time series for that voxel in run x to that in run y and repeated for all combinations of non-identical pairs of runs. Average beta values were calculated voxel-wise from all these combinations (Fig.1, step 1.1 and 3.1). For each voxel, the number of first level t values above the threshold defined by p<0.001 (uncorr.) were counted (Fig.1, step 1.2 and 3.2). To identify "bad" runs, pair-wise parametric testing between average beta maps from all pairs of runs and those that exclude a particular run was performed with a Welch's t-test calculated over an expanded ROI around the activation area and assessed at a Bonferroni corrected significance. This process was repeated until no more runs were excluded (Fig. 1, step 2). Updated voxel reliability maps were used to isolate consistently activated voxels from "good" runs (Fig.1, step 4). GLM analysis was performed with SPM8 to assess activation for each run in each patient for validation of the identification of "bad" runs.

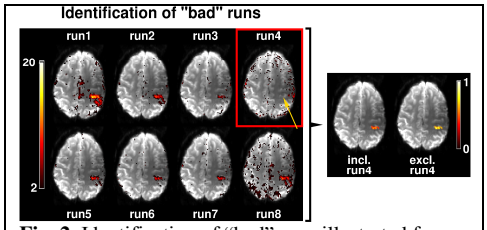

Fig. 2. Identification of "bad" runs illustrated for one patient (8 runs) with run 4 identified as "bad" in uNBIASED. *(left)* GLM analysis for each run. A red frame marks a run identified as "bad" in step 2. A yellow arrow marks absent activation. *(right)* UNBIASED results including and excluding run 4, demonstrating an increase in activation values after the exclusion of run 4.

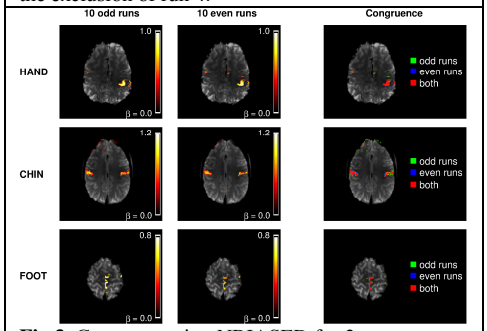

Fig.3. Congruence in uNBIASED for 3 motor paradigms (hand, chin and foot task).

To test the reproducibility of uNBIASED results, odd and even runs acquired from healthy volunteers were analyzed separately and activation maps were compared. Congruence maps of activation originating from the analysis of both or separate groups of runs was calculated.

Results: UNBIASED identified no "bad" runs in 6 patients and one "bad" run in 4 patients. Average beta values in the activated region increased after exclusion of that run. Results for one patient are illustrated in Fig. 2. Run 4 was identified as "bad" in uNBIASED. GLM activation maps for that run (red frame) confirm that motor activation was weak (not visible at this threshold). The reproducibility of the method is apparent by the high extent of overlap between results from distinct groups of runs for 3 distinct motor tasks (Fig. 3) and from the high Dice coefficients calculated for each task (Hand: 0.81, Chin: 0.68, Foot: 0.42).

Discussion: In addition to identifying neuronal activation without reference to task timing [7], the method is capable of automatically identifying unreliable runs. Being model-free, uNBIASED is expected to be sensitive to neuronal activity when the response does not agree with the GLM prediction due to compromised performance or modified hemodynamic coupling.

Conclusion: Identification and exclusion of "bad" runs led to an increase in the average beta values on the activated region, indicating the importance of "bad" run exclusion from the analysis. The reproducibility of the method is illustrated by the agreement between activation results from repeated executions of the same task.

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References: [1] Stippich, C., et al., Radiology, 2007. 243(3): p. 828. [2] Fujiwara, N., et al., NeuroImage, 2004. 21(4): p. 1464. [3] Levin, D.N., et al., NeuroImage, 2001. 13(1): p. 153. [4] Beisteiner, R., et al., Hum Brain Mapp, 2010. 31(12): p. 1951. [5] Beisteiner, R., et al., NeuroImage, 2011. 57(3): p. 1015. [6] Foki, T., et al., NeuroImage, 2007. 37(1): p. 26. [7] Cardoso, P., et al. (2013), Proc. of the HBM, Poster #3495