Flexible modelling permits robust detection of clinical fMRI activation for partial compliance to experimental task.

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Introduction Performance of a cognitive task in an fMRI experiment produces a haemodynamic response, which is detectable using a blood oxygen level dependent (BOLD) contrast. This response has been seen to vary spatially (1), and also as a function of cognitive state (2). It is also the case that many fMRI experiments, especially those involving patient groups, fail to detect any significant activation. One possible reason for this may be the non- or partial compliance of the subject to the fMRI protocol, such as non-performance of a task during one epoch of a block design study. This would lead to a BOLD response which would correlate less strongly with the assumed task response, leading to reduced significance.

Conventional fMRI analysis assumes that every repeated occurrence of a task epoch or event leads to the same level of response. Non-compliance can be controlled for using an in-scanner performance indicator. Despite this, response may still not be constant over time, due to habituation, variations in attention or perceived difficulty of the task. The present study wished to explore the utility of employing a more flexible model allowing each epoch in the block design paradigm to vary in amplitude, in order to judge the extent to which this phenomenon could influence fMRI results.

Methods Data was acquired during a continuous run of 200 EPI volumes in 10 minutes. The first five minutes consisted of five blocks of motor task (finger opposition) and rest, followed by 5 minutes of resting state data. This data set allowed construction of 5 datasets each of 5 minutes length, with different levels of task compliance, from full compliance (volumes 1-100, to low compliance (1 task block performed, volumes 81-180), as indicated in fig.1. For each dataset, the standard model, where each block amplitude is fixed, was compared to a flexible model 5 basis functions, modelling the amplitude of each block separately.

Simulated datasets were also constructed from the resting state section of the data, with regions of activation added, in order to directly assess the effect of lost degrees of freedom (going from the standard to flexible model) on the results, as well as to have strict control over true positives and their timecourse. Performance of the models in detecting simulated activation was assessed using response operator characteristic (ROC) curves.

Results Figure 2 shows how activation varied as a function of model (left – right) and level of compliance (top – bottom). We see that in cases where the compliance deviates from full, the standard model rapidly fails in detecting the site of activation. The flexible model is more robust to non-compliance, giving consistent activation even when the subject only complies 40% of the time. Already at 80% compliance (4 of 5 blocks), the flexible model outperforms the standard approach (as judged by extent of activation, and maximum t-statistic).These results are supported by the simulated data, where at full compliance the standard model was optimal (as determined by the area under the ROC curve), but for 80% compliance, the flexible model was better able to detect true positives without false positive contamination.

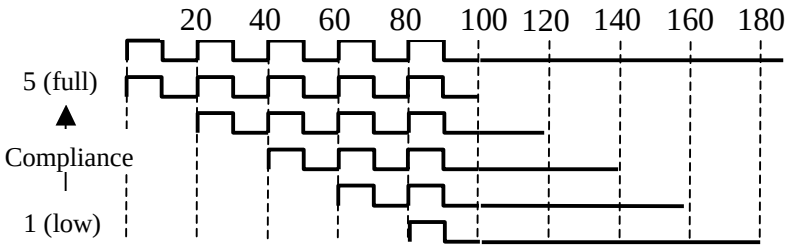

Figure 1. Experimental design. Top row represents actual dataset acquired. Other rows show subsets analysed to represent varying compliance, from high (5 blocks) to low (1 block)

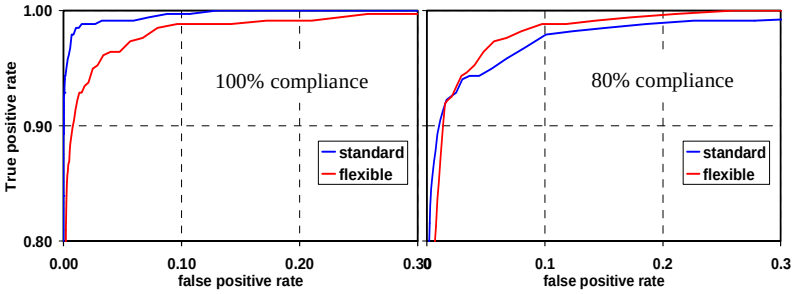

Figure 3. ROC curves for full (5 blocks, left) and high (4 blocks, right) compliance, for standard and flexible models.In the ideal situation, where the subject complies fully, the standard model outperforms the flexible model, but this situation is reversed when even one block is not performed.

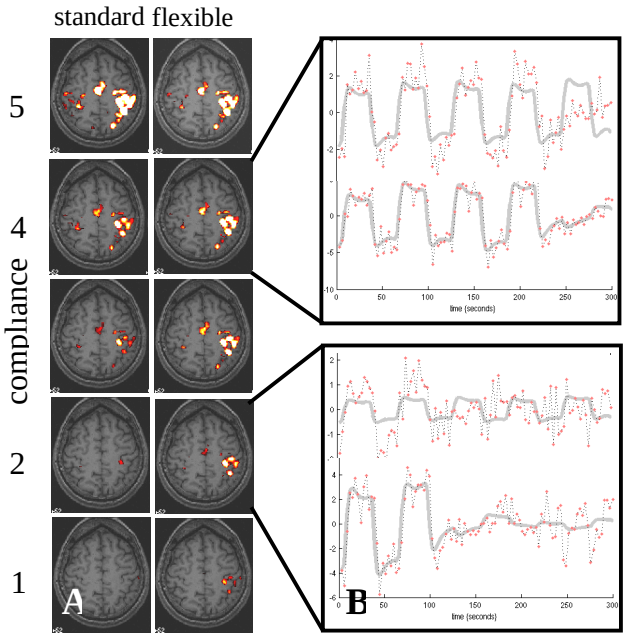

Figure 2. Results for low to full compliance with the standard model (2A, left) and flexible model (2A right), together with the fitted timecourse for a low (2, Fig 2B lower panel) and high (4, upper panel) compliance

Discussion This study has demonstrated that detection efficiency varies as a function of subject compliance, and that even at 80% compliance, a flexible model is better able to detect activation than the standard model. In subjects who fully comply with the experimental design, the standard model is better able to detect activation than the flexible model. This difference is expected, since when the standard model matches task-related variance in the data perfectly, the flexible model can only equal the standard model, but with decreased degrees of freedom, and hence lower significance. This difference is of limited importance since compliance with the model ensures high significance, so that activation is likely to be detected independent of model. In subjects who show non-optimal compliance, a flexible model is more readily able to detect activated voxels. This suggests that such a model would be beneficial when non- or partial compliance is suspected, or when the standard approach yields low significance. Further work is underway to assess how more generalized variability in compliance over time affects the results, as well as to retrospectively assess the frequency of such results in clinical fMRI datasets.

References

1. Buckner, 1998, Human Brain Mapping, 6, 373-377
2. McKeown, Makeig, Brown et al. 1998, Human Brain Mapping, 6(3), 160-188