# The effect of motion on fMRI BOLD resting state low-frequency fluctuation

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## Introduction

In the neuroscience community, there is growing interest in the study of spontaneous brain function using fMRI BOLD contrast. Recent findings document spatially localised coherent spontaneous low-frequency (0.01 - 0.1 Hz) fluctuations (LFF) [1] in specific regions commonly referred to as resting state networks (RSN). While interesting phenomena per se, LFF and RSNs are also altered in brain diseases [2] and altered brain state (sleep [3], sedation [4] ), which hold promise for potential clinical applications. Although increase in power of LFF has been reported in both sleep and sedation in humans, the underlying mechanism is not understood. Of note, a prominent rise in LFF has also been observed in the white matter in humans suggesting non-neuronal causes [4]. The fact that LFF are sensitive to spurious correlations related to cardiac and respiratory motion is well known, but the potential influence of head motion has not been assessed. In this study, we aimed to assess the role of subvoxel subject motion as a potential biasing factor in LFF studies of sedation prone to potential between-condition motion bias.

## Material and Methods

Data from a previous in-house midazolam sedation fMRI study were used: 15 healthy male volunteers (mean age 26.6, age range 18-35) were scanned in resting state baseline and midazolam sedation condition (Ramsey scale 3). 430 volumes of standard functional single-shot echo-planar images (EPI; TR=2100ms, TE=60ms, flip angle 90º, 64x64x35 matrix, resolution 3.25*3.25*3mm) were acquired for each scan. The following FSL pre-processing steps were applied: motion correction, high-pass 0.01 Hz frequency filter and non-brain voxel extraction. Spatial smoothing and low-pass filtering was deliberately avoided in order not to introduce uncontrolled effects. For each session, registration matrices to MNI space were computed and their inverse used to register MNI based ROIs to individual acquisitions. Anatomical ROIs were created by thresholding anatomical probability maps from the Harvard-Oxford and Juelich Atlas included in FSL 4.0. The following ROIs were chosen: Auditory Cortex (AC), Motor cortex (MC), visual cortex (VC), callosal white matter (WM). For each ROI of each subject, power spectra were computed (FFT was applied on the average time-course and its absolute value squared). For each ROI, the spectral power in the bandwidth of 0.01-0.06 Hz pre- and post-sedation was compared at the group level using a Wilcoxon Signed Ranks Test. The effects of specific data-processing steps (orthogonalization with respect to motion parameters and global mean) were investigated.

## Results

A significant increase of LFF power in sedation was observed for the VC (p=0.02) and WM (p=0.01). The changes in MC (p=0.36) and AC (p=0.12) (Fig.1) were not significant. An example situation is shown on Fig. 2. In most subjects sedation was accompanied by an apparent increase of head motion. Pearson cross-session correlation of LFF power with mean relative translations or rotations were all positive, but depended on ROI and chosen motion parameter, with highest correlation (r=0.65,p=0.0001) for mean relative y-translations with VC LFF power. One method of controlling for the effect of sedation-related motion is to orthogonalize ROI time-courses with respect to motion parameters and global mean. This lead to a pronounced decrease of the observed LFF power in all ROIs in both baseline (69%, 70%, 58%, 15% for AC,MC,VC,WM) and sedation (53%, 75%, 59%, 15%) (Fig.3). The resulting sedation effect proved significant for AC, VS, WM (p=0.01) and non-significant for MC (p=0.46). To avoid uncorrected motion, we then tested whether differences in LFF would persist after discarding periods of time affected by motion by choosing the best 2'44'' minutes. The shorter time-frame also improves comparability with previously published midazolam study [4]. The selection-process was semi-automated and based on the minimisation of the maximal difference in any of the six rigid body motion parameters. Even after this correction, increasing trends in LFF power persisted for two of the ROIs (VC: p=0.06, WM: p=0.05), as well as the difference between the amounts of motion. As a final step, we have accounted for motion by regressing the mean of relative (i.e. between consecutive volumes) translations and rotations out of the LFF power. Regression was performed across subjects for each ROI separately. After this, no significant change or trend in LFF was found in any of the ROIs (i.e. all p-values>0.5).

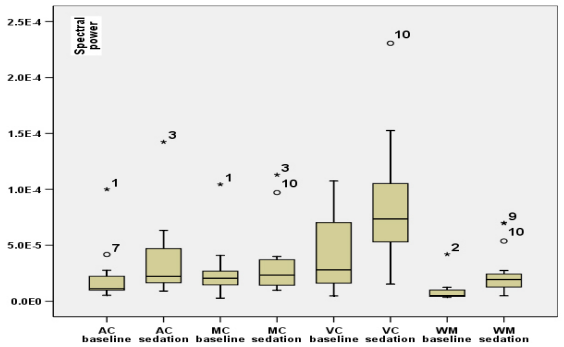


Figure 1: Spectral power distributions

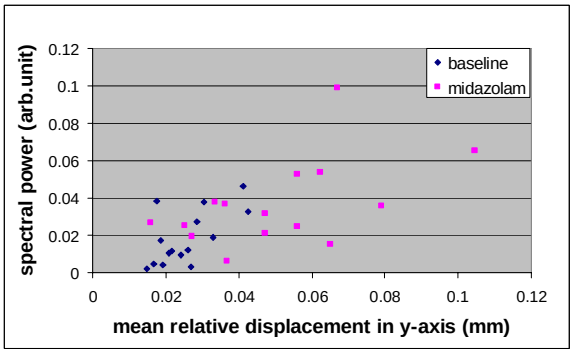


Figure 2: Effect of sedation on motion and LFF power in the VC

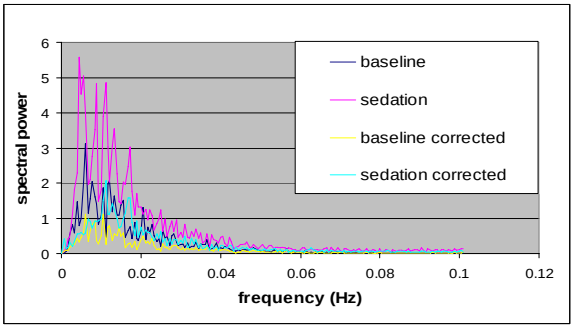


Figure 3: LFF spectra for visual cortex (power in arbitrary units)

## Conclusion

A strong effect of motion was observed on the LFF power.
Even after standard motion correction, substantial part of LFF power was attributable to motion parameters. Furthermore, the observed apparent increase in LFF after midazolam sedation (similar to previously reported increases in early sleep and sedation) could be explained by the observed increases in motion. Our results show that extreme caution is needed when interpreting LFF changes and all confounds potentially related to manipulated variable such as motion should be taken into account. Thorough control and potential correction of residual motion effects beyond standard motion correction is required to analyze changes in LFF between conditions/disease groups where a motion bias cannot be excluded.

## References

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