Scan order effects in PET activation studies are caused by motion artefact

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Introduction

- Linear changes in PET signal across session
- Scan order (SO) or Time effect
- Very common (perhaps universal)
- Striking similarity across studies
- Large effect (eigenimage analysis)

Plan

- Three typical studies
- Analysis over scan order
- Investigation of movement effects
- Reproduction of effect in simulated data

Studies

- Study 1
  - MRC Cyclotron Unit, Hammersmith Hospital, London, UK
  - ECAT 953B scanner
  - Rest vs gestures of the right hand
  - 7 subjects
- Study 2
  - Wolfson Brain Imaging Centre, Cambridge, UK
  - GE Advance scanner
  - Memory encoding and retrieval
  - 6 subjects
- Study 3
  - Functional Imaging Laboratory, London, UK
  - Exact HR+ scanner
  - Rest vs word listening vs word repetition
  - 8 subjects
- All studies
  - Bolus injection of H_20^{15}
  - Initial transmission scan for attenuation correction
  - 12 emission scans per subject (session)
  - Scans reconstructed using filtered back projection
  - Task order randomized within subject

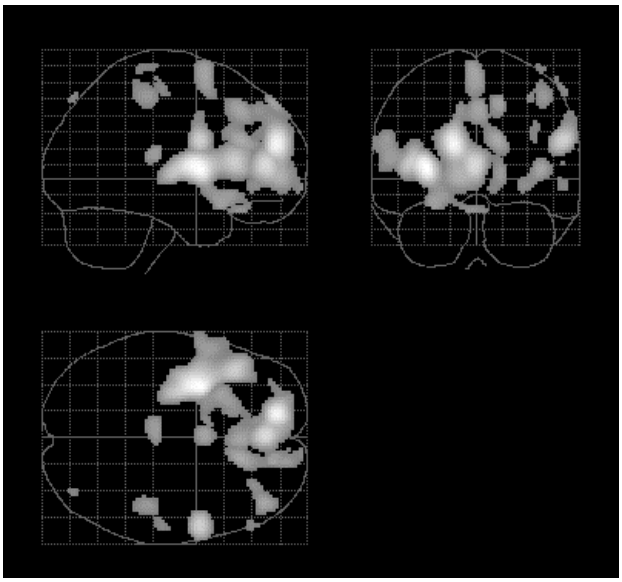
Methods

- Processing using spm 99b software
- Realignment parameters
  - Image origins set to the midline of the anterior commisure (AC)
  - Scans realigned within subject in the usual way
  - Realignment parameters can be extracted from saved realignment matrices (.mat files) output from spm realignment.
    Thus we derived 6 rigid body realignment parameters (translations, in X, Y and Z, in mm, and rotations in X, Y and Z, in radians, both relative to the AC), for each scan, for each subject, relative to the first scan for that subject.
- Statistical analysis and display
  - 16 mm smoothing prior to analysis
  - Proportional scaling
  - Standard statistical model for each study
    - Factors for subjects and conditions
    - 2 task related covariates for study 2
  - Other covariates added to the model for each study as appropriate, i.e. either or both of:
    - Scan order (1 for first scan for each subject, 2 for second, etc...)
    - 6 movement parameters as above.
  - All SPMs thresholded at $p<0.001$ uncorrected for display

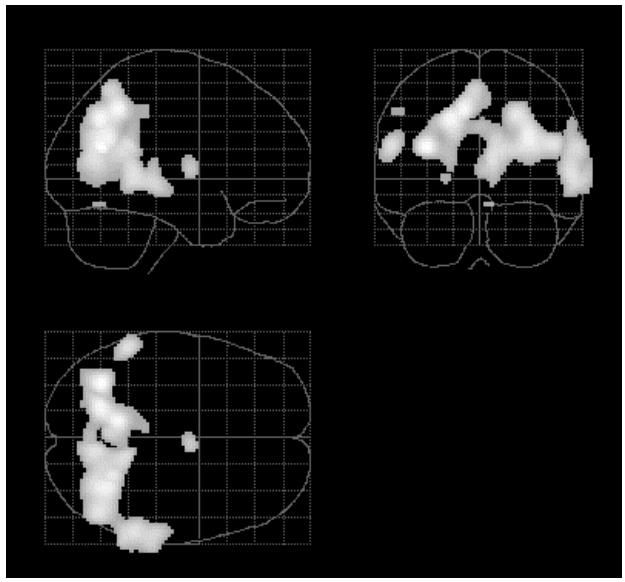
Analysis 1 - scan order effects across studies

- Scan order entered as covariate into standard model for each study

Results - study 1

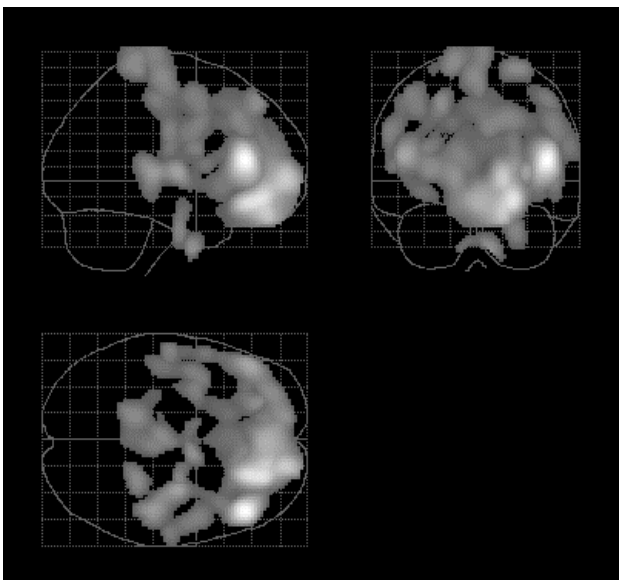


Signal increases linearly with SO

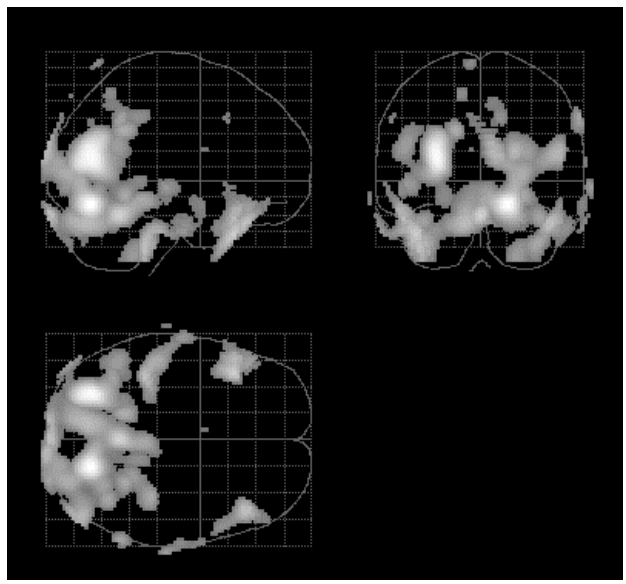


Signal decreases linearly with SO

Results - study 2



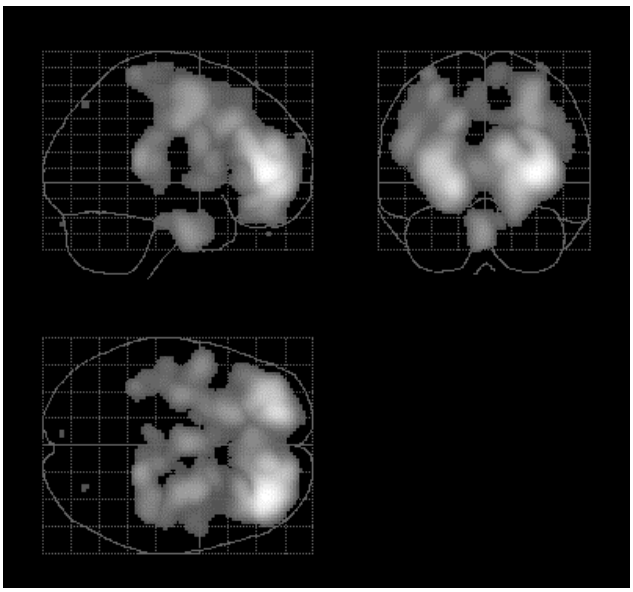
Signal increases linearly with SO



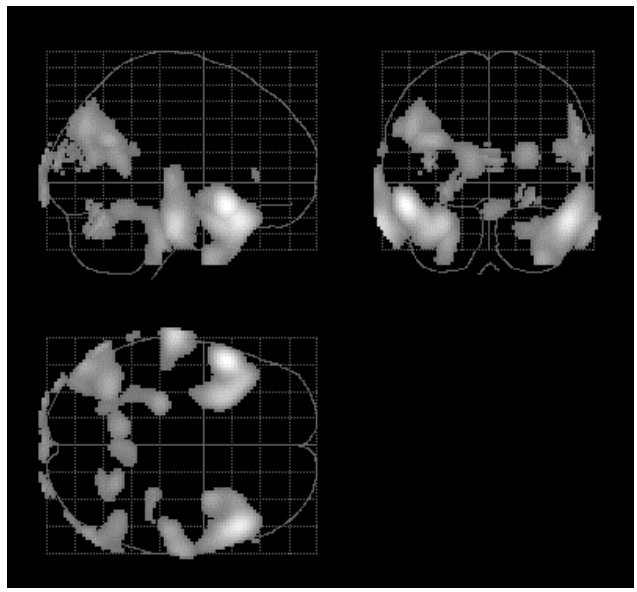
Signal decreases linearly with SO

Analysis 1 - continued

Results - study 3

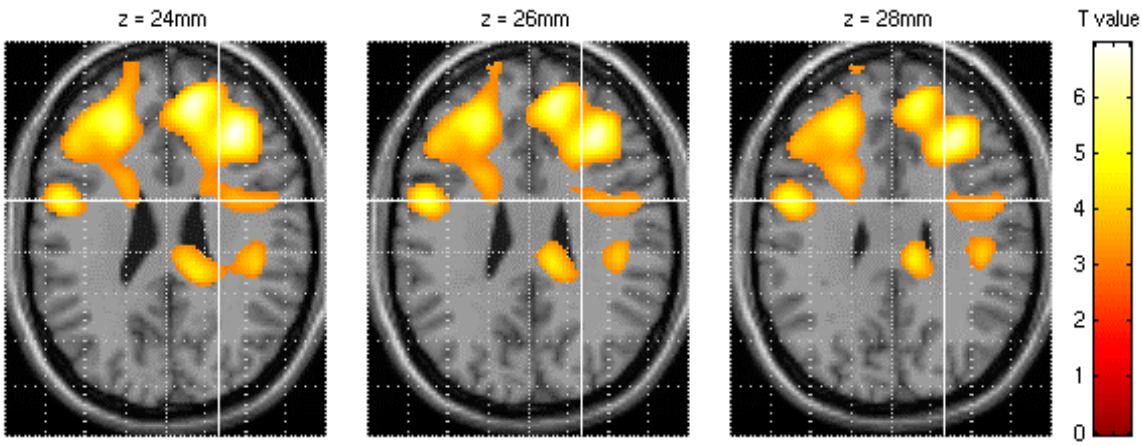


Signal increases linearly with SO



Signal decreases linearly with SO

Results - study 3 - overlays



Representative slices of signal increase SPM overlaid on template brain, showing distribution in gray and white matter frontally

Analysis 2 - movement parameters and scan order

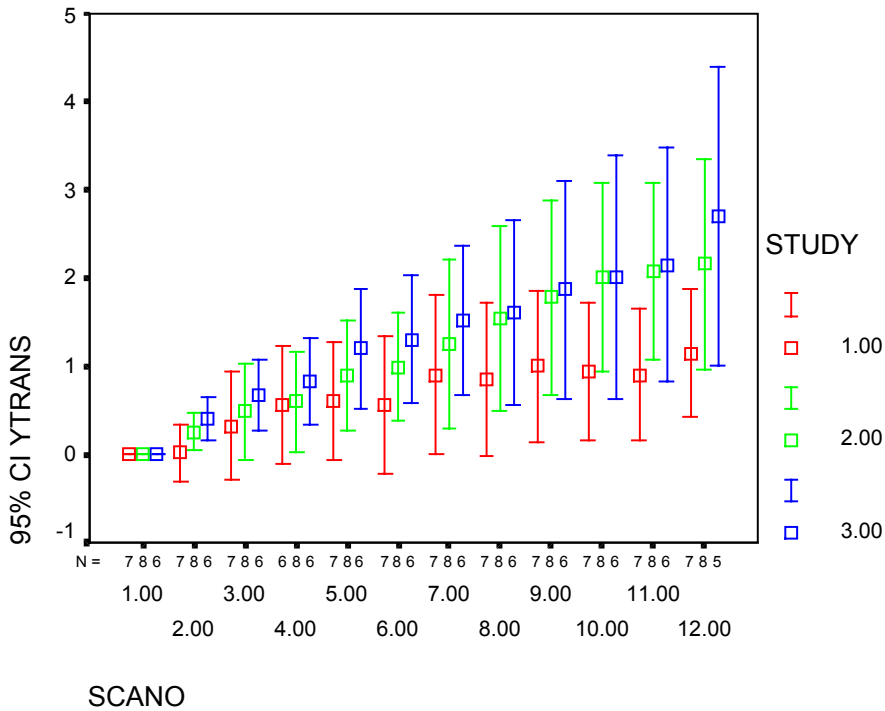
- Scan order correlated strongly with some of the movement parameters (MPs):

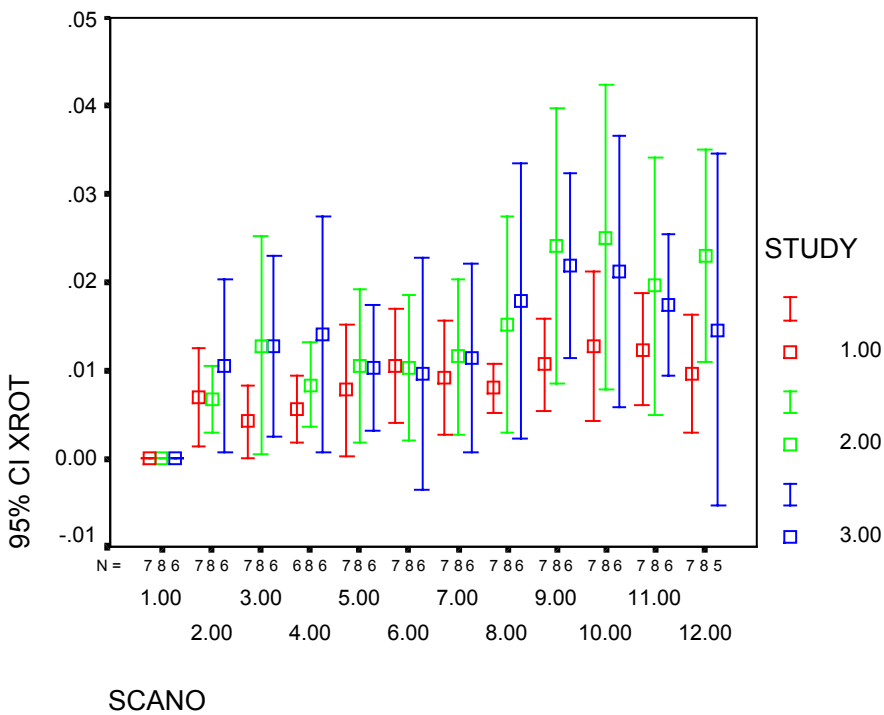
	Translations			Rotations		
	X	Y	Z	X	Y	Z
Study 1	0.11	0.43	-0.26	0.43	-0.22	0.07
Study 2	0.12	0.68	-0.17	0.3	0.11	0.44
Study 3	0.05	0.61	0.05	0.46	-0.09	0.34

Table: correlation coefficients of movement parameters with scan order for each of the three studies.

- The correlations reflect a consistent direction of subject movement during the scanning session.
- In terms of the AC, subjects tend to translate backwards and rotate upwards, suggesting a drift of the back of the head down the scanner, with compensatory rotation to maintain forehead position.

Movement by time

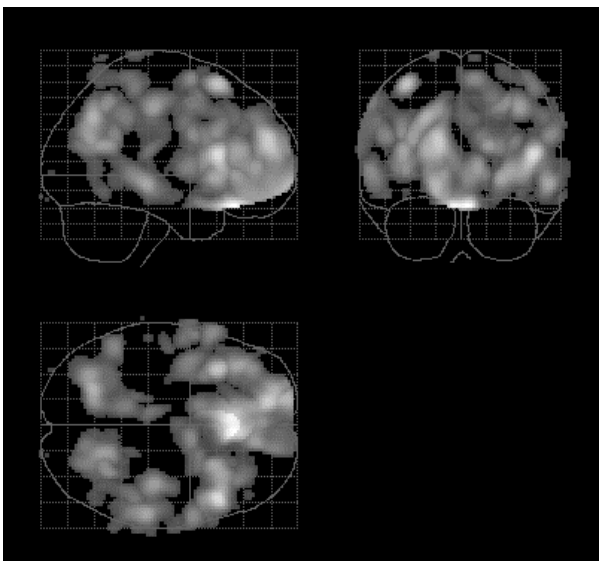




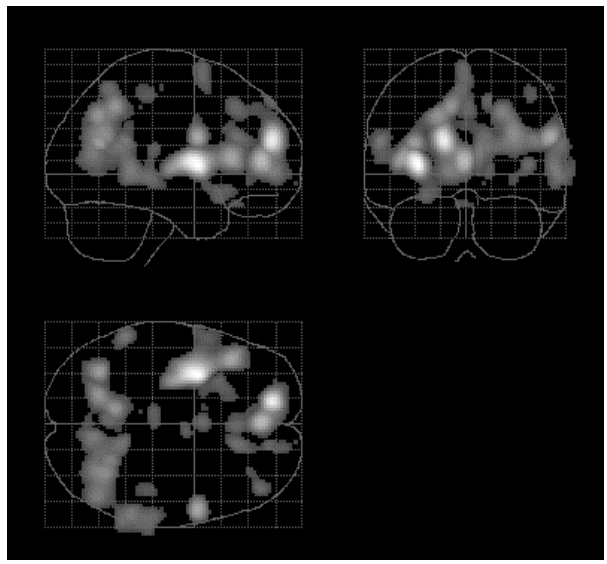
Analysis 3 - movement parameters and PET signal

- Movement parameters (MPS) added to the statistical model for each study *instead of* scan order.
- Effect of MPs assessed using F map to show areas with significant variance explained by addition of MPs to the model. We compared this MP F map to the equivalent F map for adding SO to the basic statistical model.

Results - study 1 - comparison of MPs and SO F maps



F map for addition of movement parameters to basic model



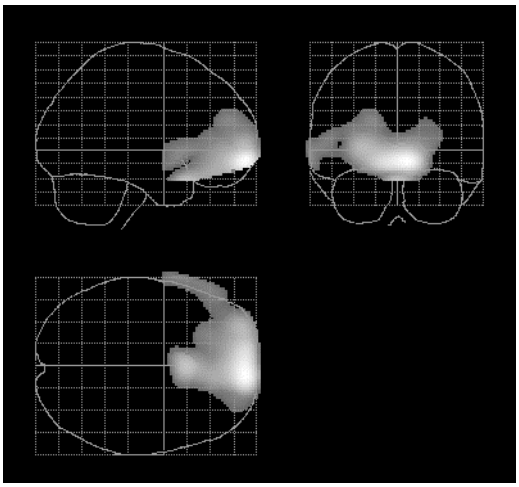
F map for addition of scan order to basic model

- Results were if anything more striking for studies 2 and 3, with the same trend to wider significant voxel extent for the MPs F map. For all 3 studies the p value for the maximum F was more significant with F maps for the MPs than for equivalent SO F maps.

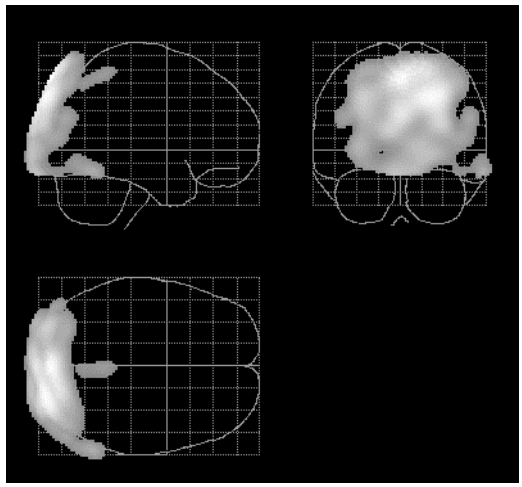
Analysis 4 - reproducing the SO effect in simulated data

- The results of our analyses suggested that movement might be the primary source of the variance apparently explained by scan order. We hypothesized this might be due to the mismatch of the initial transmission scan with the subsequent emission scans when the subject moves. To test this we attempted to reproduce the effect of transmission / emission mismatch to see whether it reproduced the scan order effect. For this simulation we used the data of study 1. The algorithm was as follows:
  - Reconstruction of the first scan for each subject without applying attenuation correction
  - Simulation of this scan after movement, by reslicing the first scan after applying the movements estimated in our original realignments for scans 2, 3 etc, for each subject
  - Forward projection of these images with simulated movement to sinograms
  - Rereconstruction of these simulated sinograms after applying the original attenuation correction from the transmission scan
  - SPM realignment and normalization for the simulated scans for each subject
  - A standard SPM analysis, with subject as factor, proportional scaling, and SO as a covariate

Analysis 4 - results



Simulated signal increases linearly with SO



Simulated Signal decreases linearly with SO

Conclusions

- Add movement parameters to statistical model
- Probably add scan order also
- Always randomize conditions across time
- Analyze movement by condition to make sure there is no stimulus correlated movement
- Bear the SO/MP effect in mind when interpreting previous studies