Imaging Neurovascular Impairment After Stroke:
A Novel Diagnostic Method for Rehabilitation?

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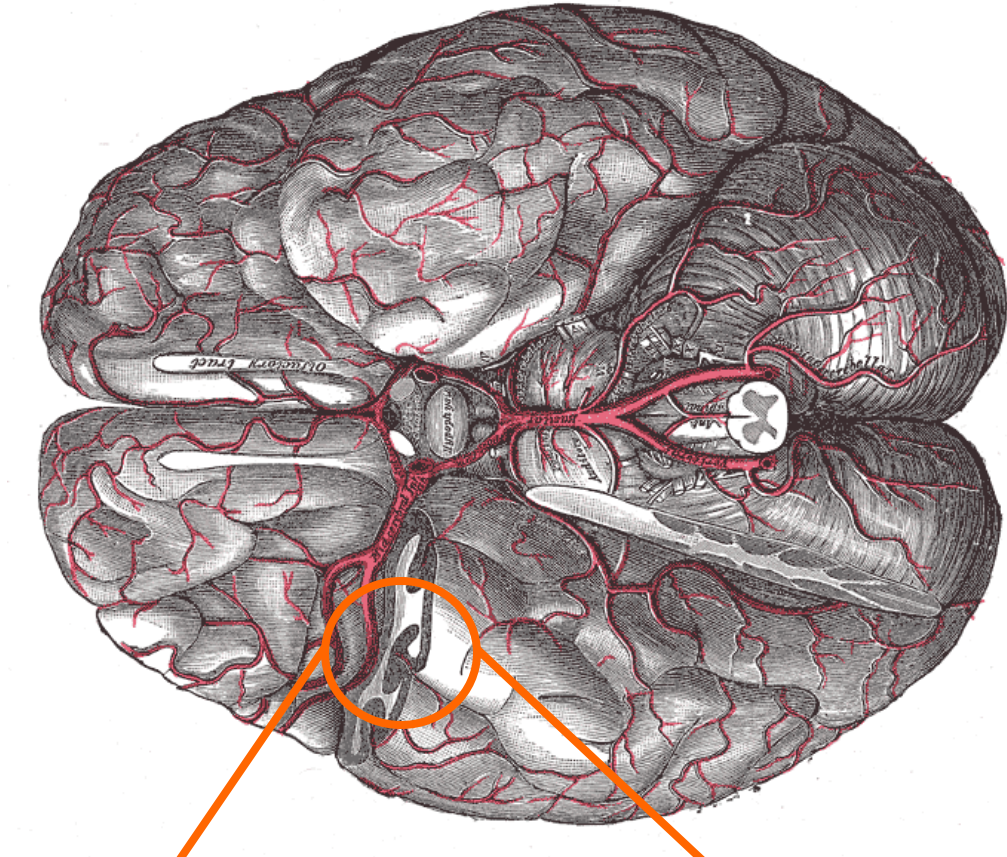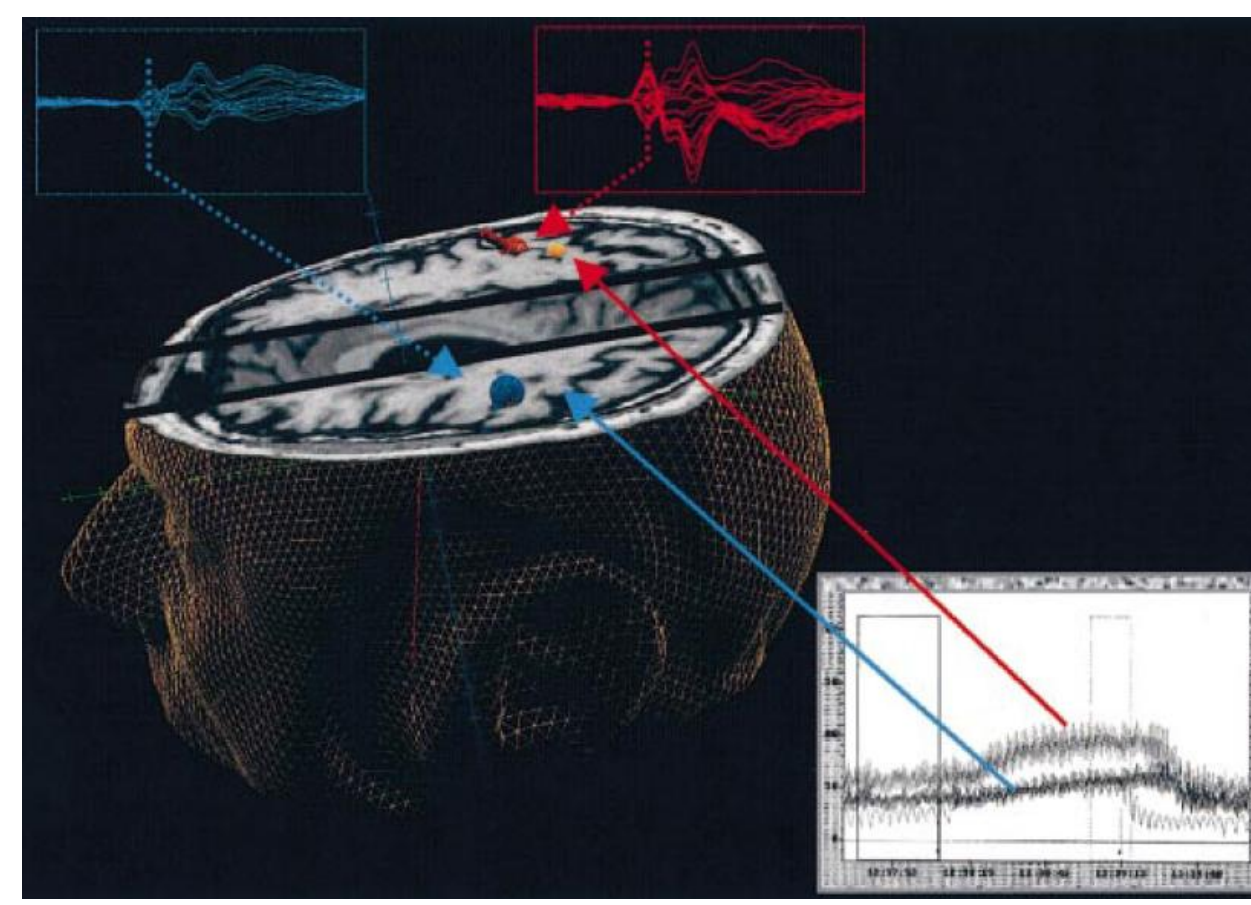
Introduction

Regional cerebral blood flow is regulated by the "neurovascular unit"

[Gray, Anatomy, Random House, 1977]

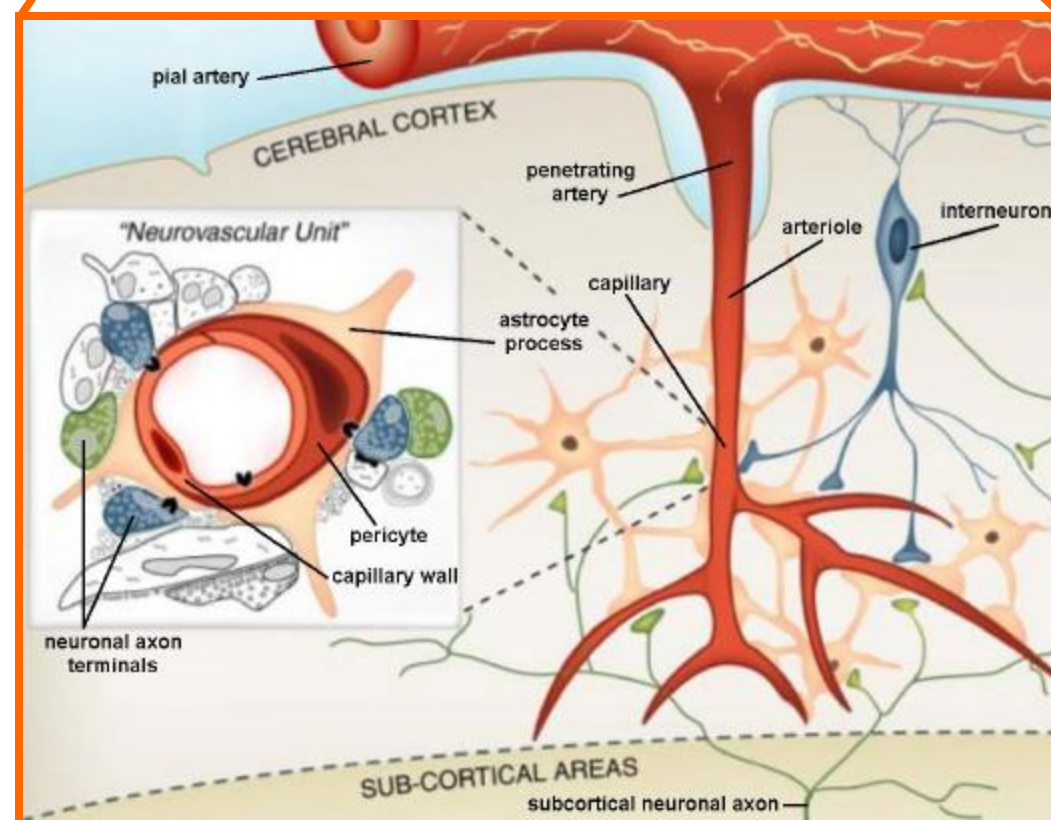[Hamel, J. Appl. Physiol., 2006]

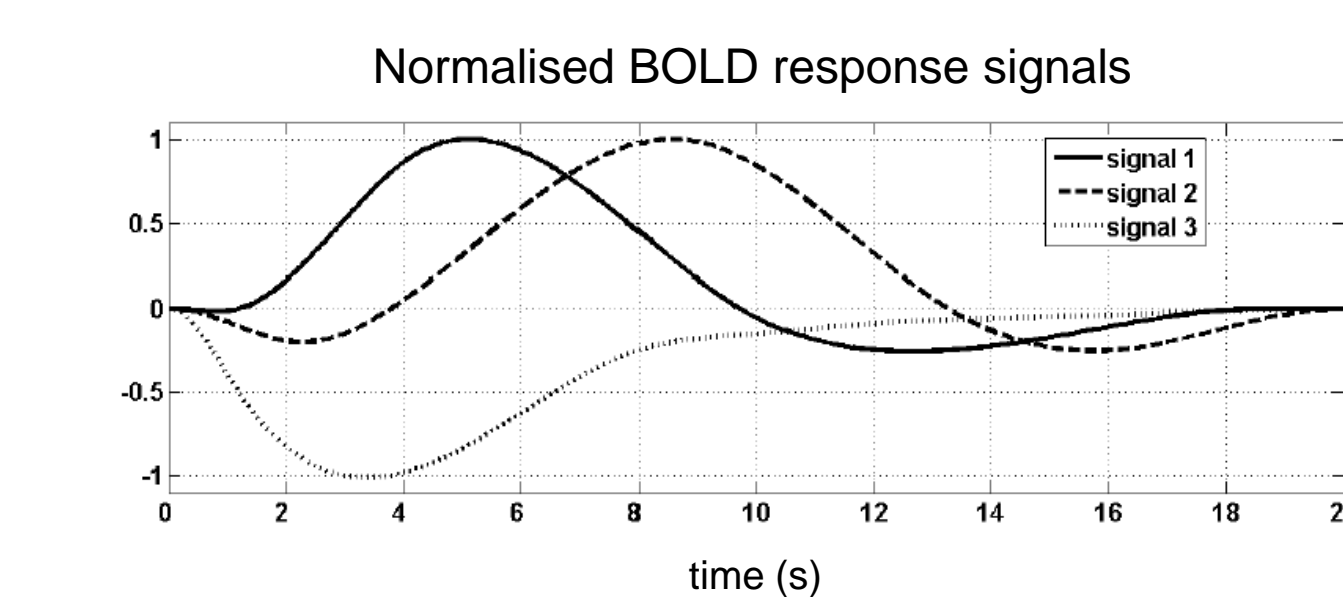**Stroke can impair functional hyperemia despite persistent neuronal activity**

[Rossini et al., Brain, 2003]

**Alteration of the blood oxygen level dependent (BOLD) signal has been observed post stroke**

Normalised BOLD response signals

- Functional hyperemia causes an increase in regional cerebral blood flow (rCBF) in relation to neural activity
- This process is altered in cerebrovascular disease
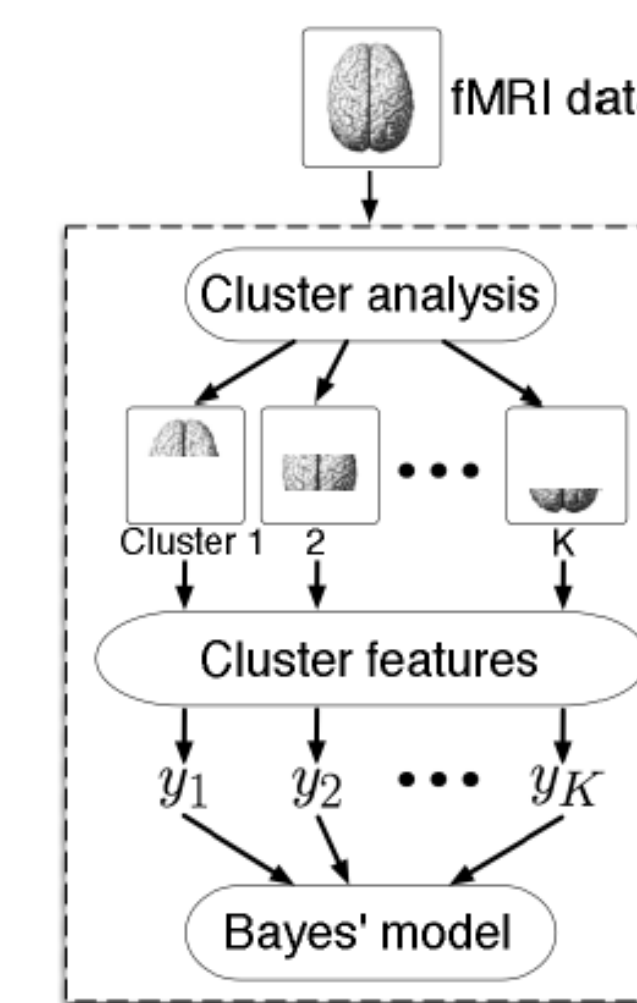- Imaging functional hyperemia may help to localise and evaluate neurovascular impairment

Methods

We evoke responses in the sensorimotor system and monitor motor responses during BOLD fMRI
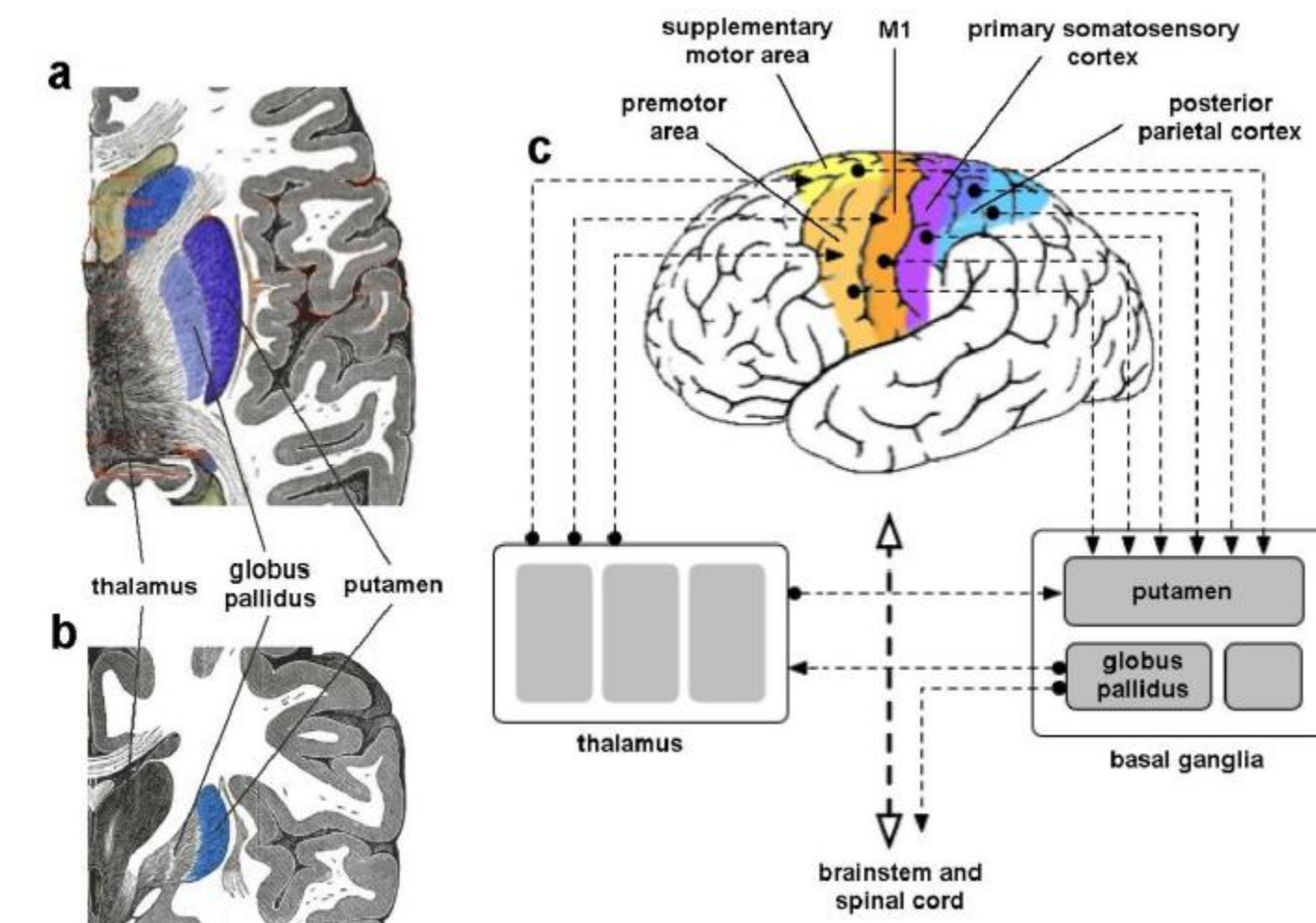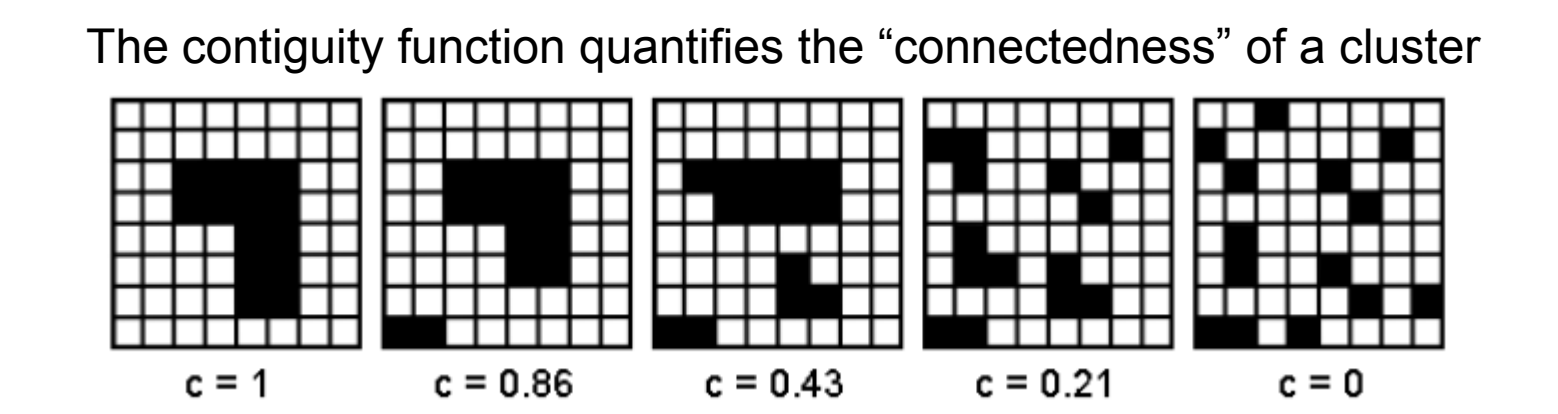

[Adapted from Gray, Anatomy, 1977, and Kandel et al., Principles of Neural Science, 2000]
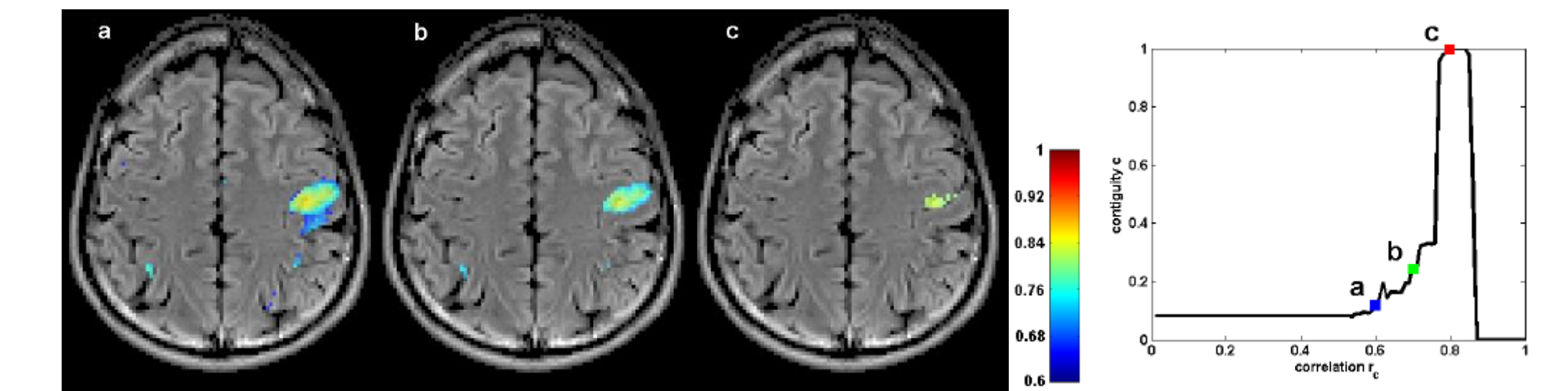
An event-related visual feedback-controlled motor task is designed to include a wide range stroke patients

Hand grip device

a — Rest   b — Event   c — Response

Automatic region-of-interest generation by time series cluster analysis

fMRI data → Cluster analysis → Cluster 1, 2, ... K → Cluster features → $y_1, y_2, \cdots y_K$ → Bayes' model

BOLD response signal identification using a Bayesian hierarchical correlation model

$$\alpha$$
$$\beta_1 \quad \beta_2 \quad \cdots \quad \beta_K$$
$$y_1 \quad y_2 \quad \cdots \quad y_K$$
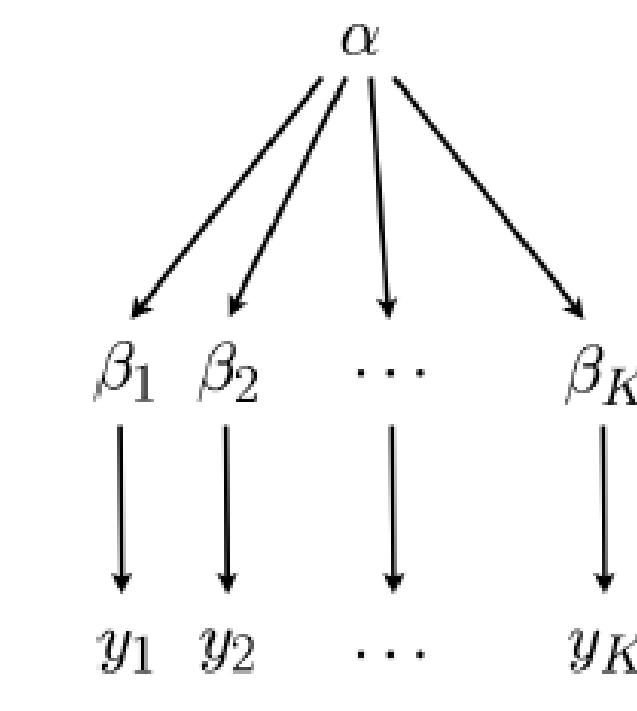
[Adapted from Gelman et al., Bayesian Data Analysis, 2004]
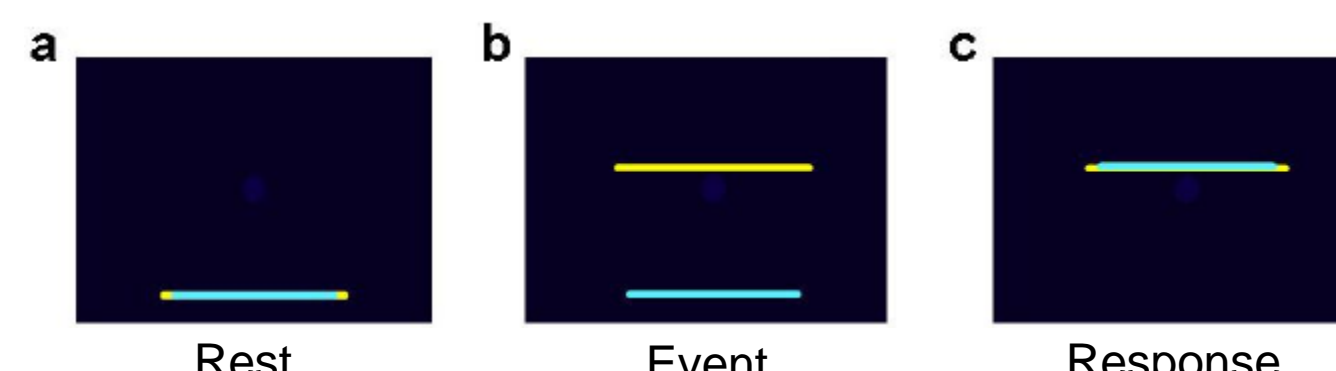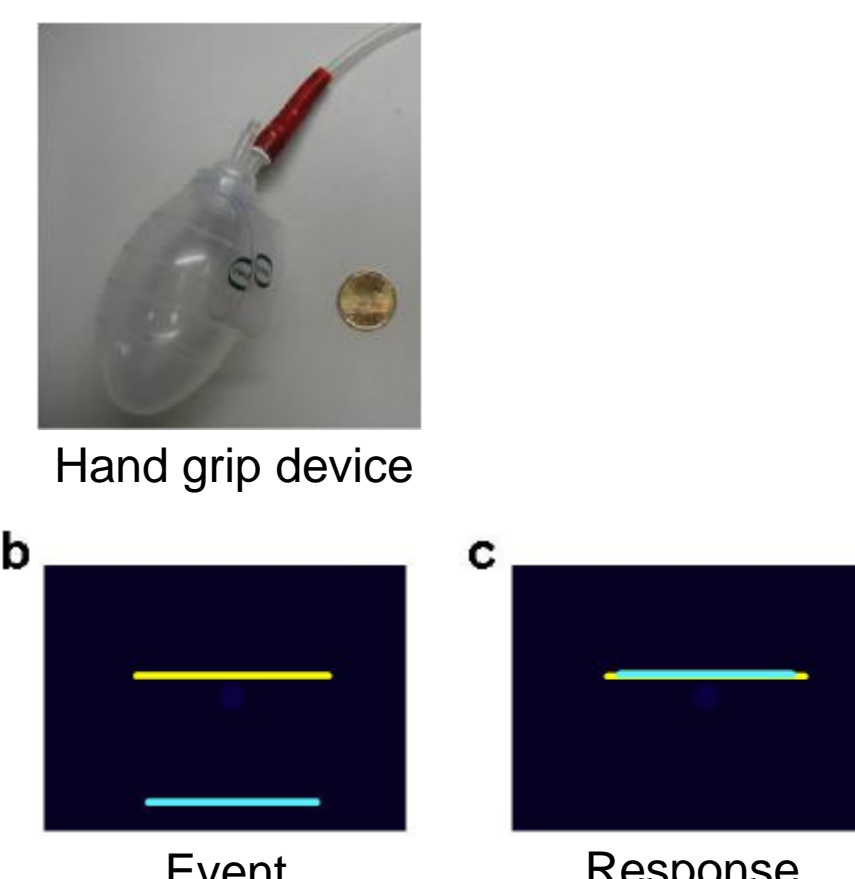
Spatial structure of voxel clusters are characterised by the contiguity function

The contiguity function quantifies the "connectedness" of a cluster

$c = 1$ $c = 0.86$ $c = 0.43$ $c = 0.21$ $c = 0$

Layout of a cluster's voxels at three different points (a,b,c) along its contiguity function

Temporal structure of response signals are characterised by the causal cross-correlation function
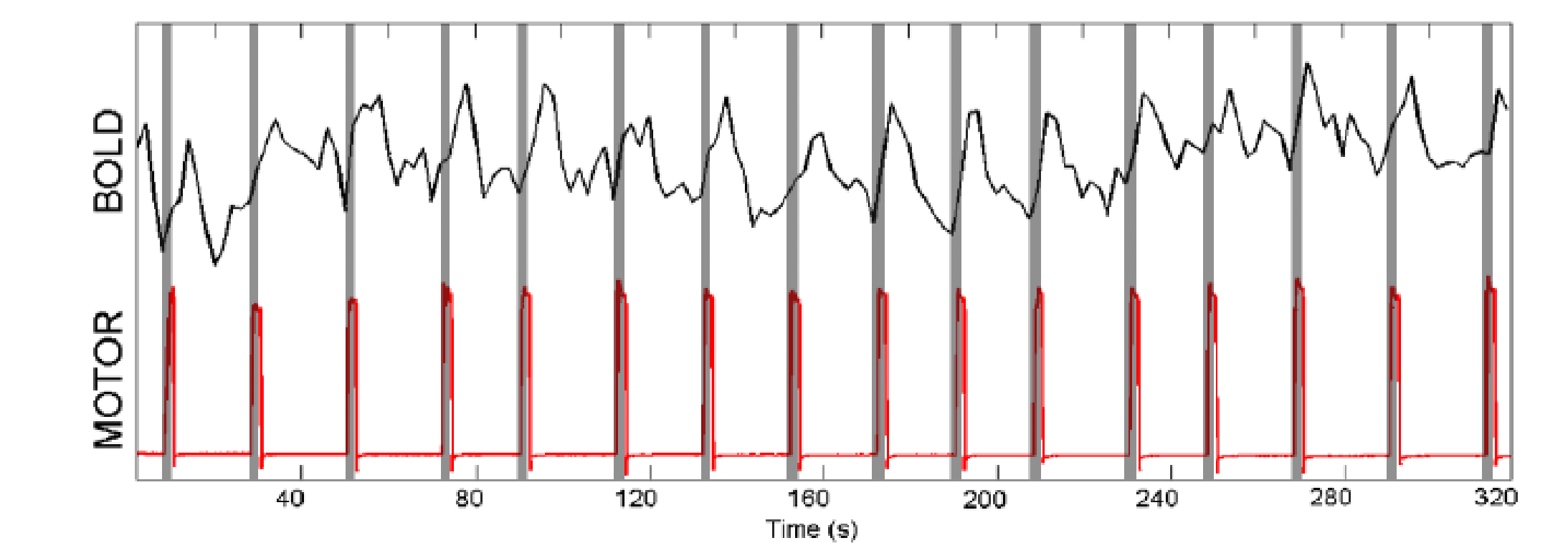

- Sensorimotor system is evoked by hand gripping while motor and BOLD fMRI signals are measured
- Single-handed grip force target is calibrated to ~25% of maximum, while both hands are monitored
- Scanning process is noninvasive and takes ~15 mins

- Novel analytical method was developed to 1) find distinct BOLD responses, 2) characterise BOLD signal space-time structure, and 3) infer salience of signals using hierarchical Bayesian analysis
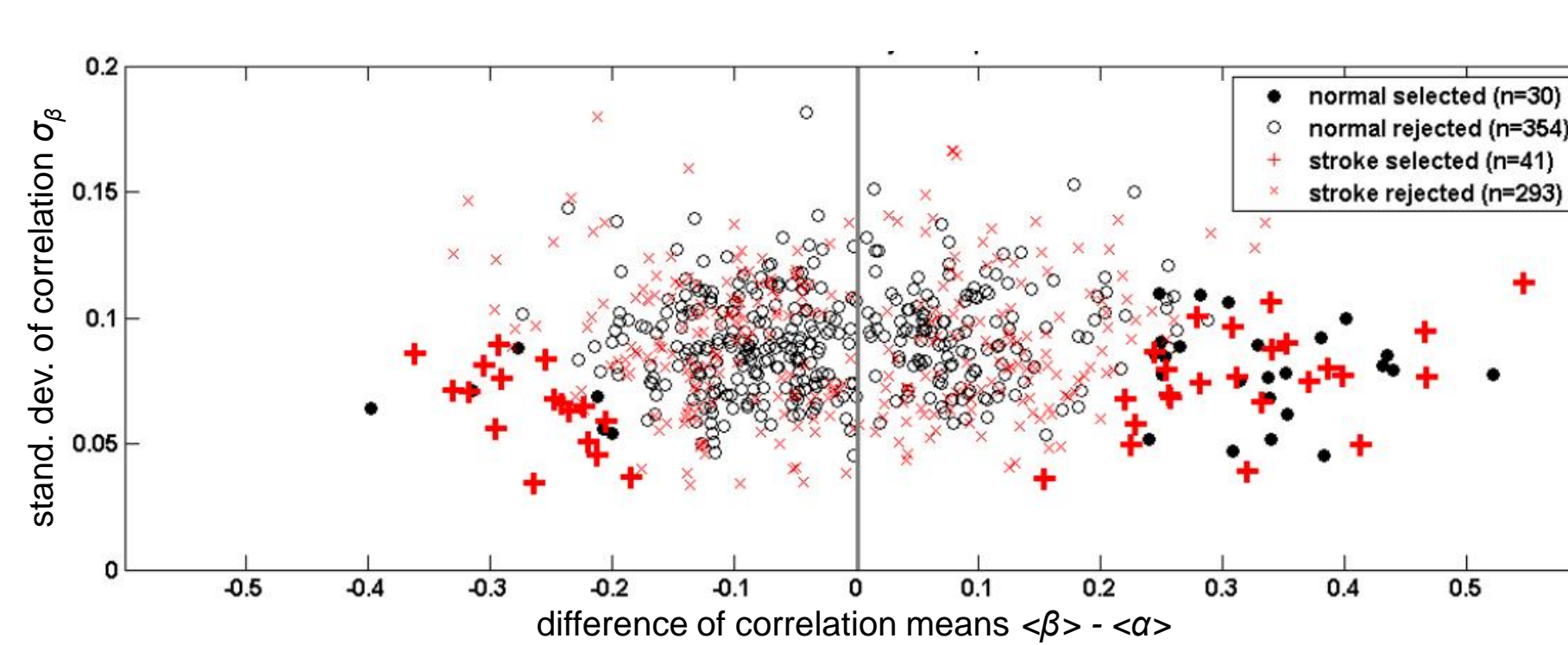- β and α model regional and global dependencies

Results

Motor task performance in right & left hands
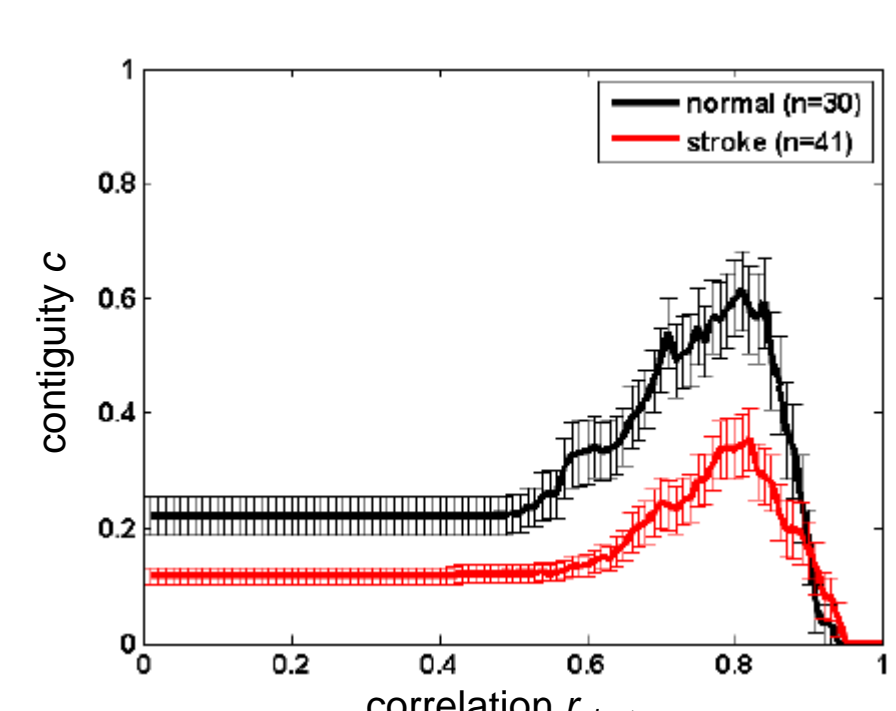
Normal   Patient 1   Patient 2   Patient 3   Patient 4
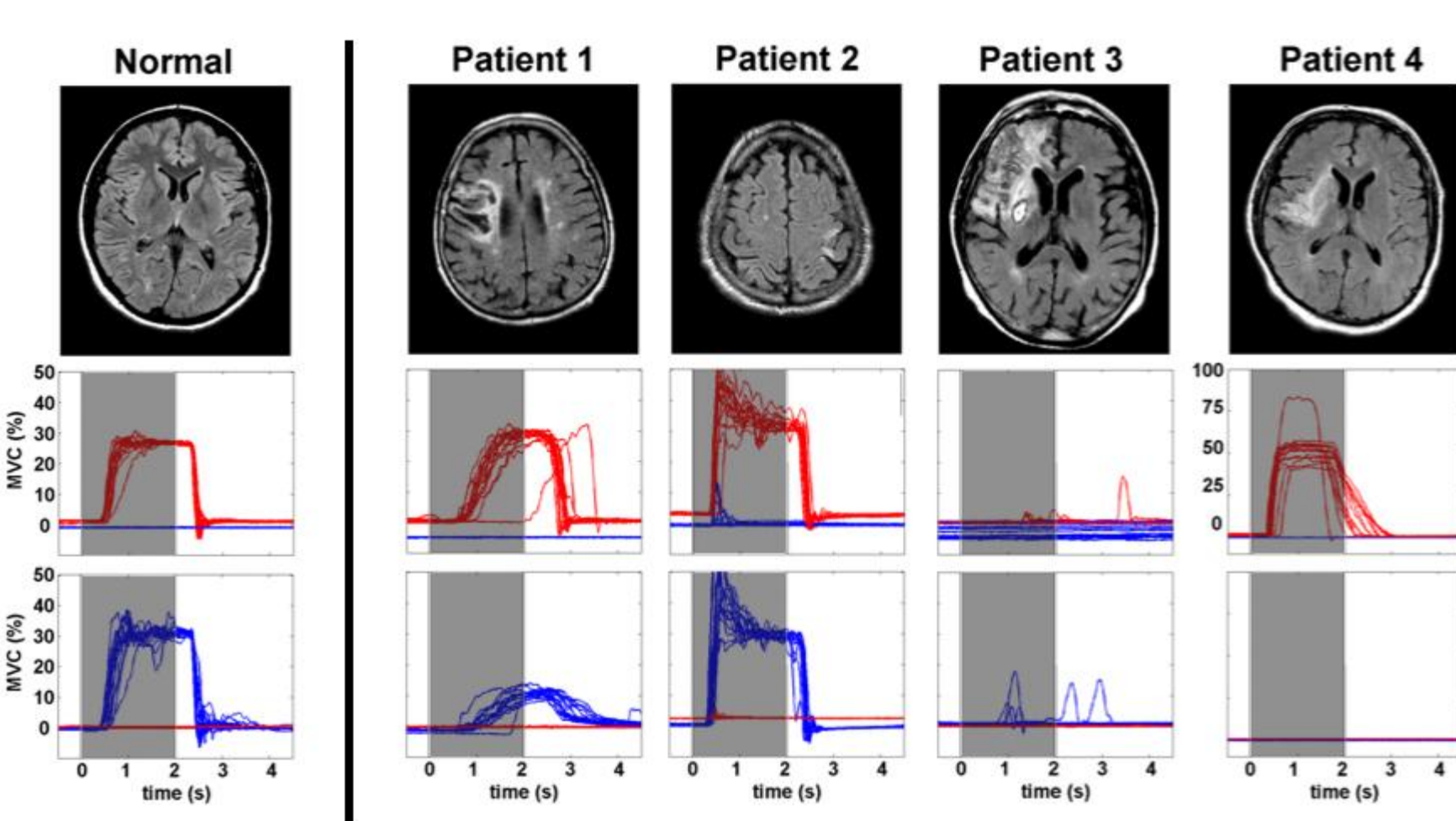
Grey regions indicate the event's onset and duration

Distribution of selected and rejected cluster parameters

- normal selected (n=30)
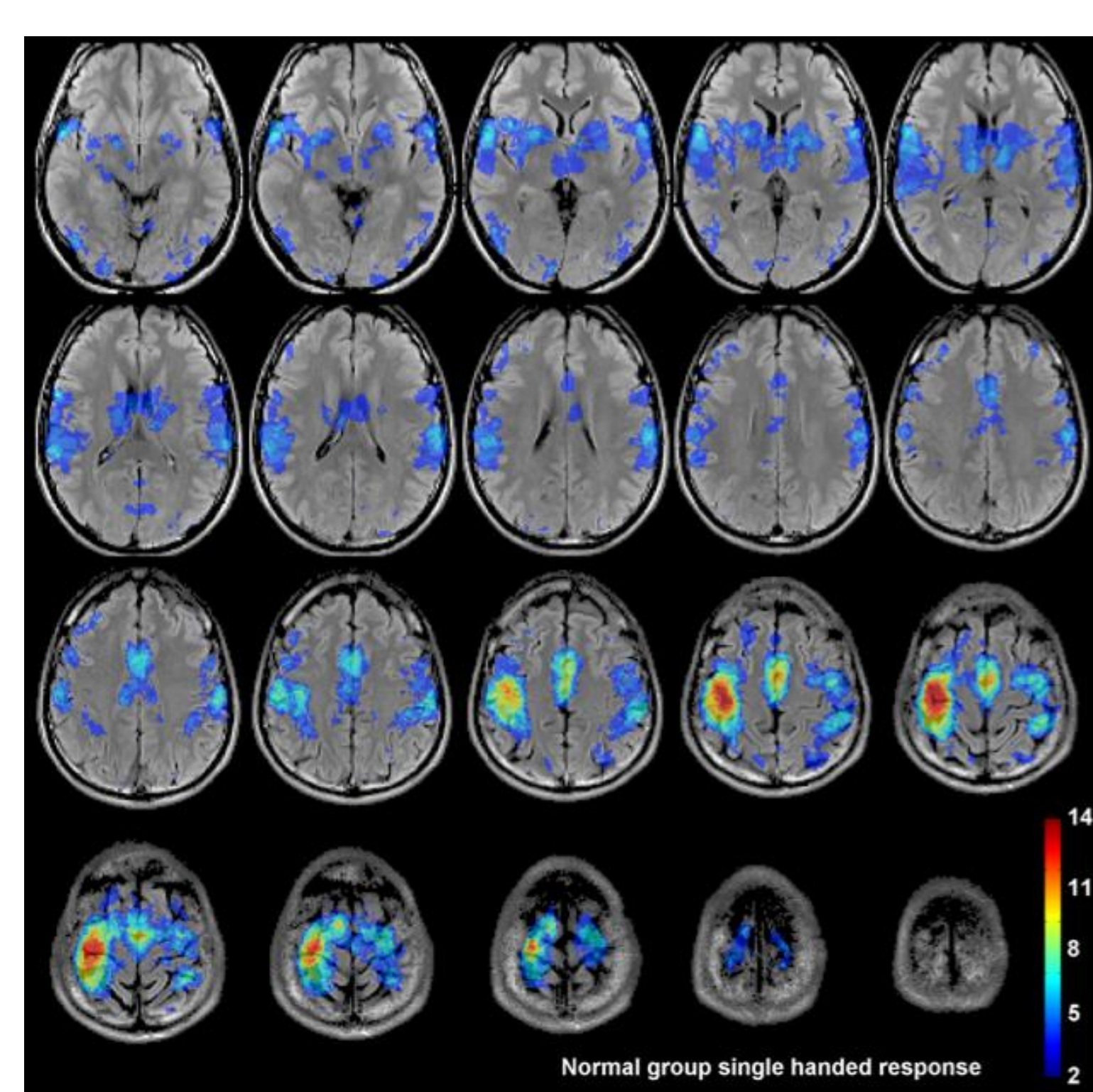- normal rejected (n=354)
- stroke selected (n=41)
- stroke rejected (n=293)

Mean contiguity function of selected clusters

normal (n=30)   stroke (n=41)

Cross-correlation maxima of selected clusters

normal (n=30)   stroke (n=41)
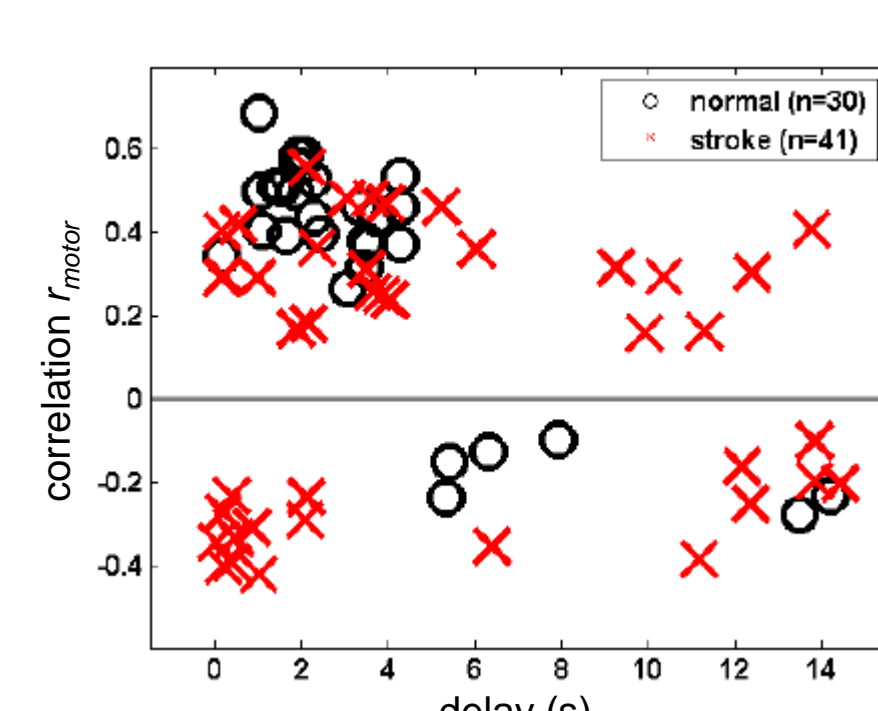
Aggregate BOLD response in normal group

Normal group single handed response

Comparison of BOLD responses in aggregate between normal subjects and stroke patients

NORMAL GROUP — left hand

STROKE GROUP — non-paretic hand / paretic hand
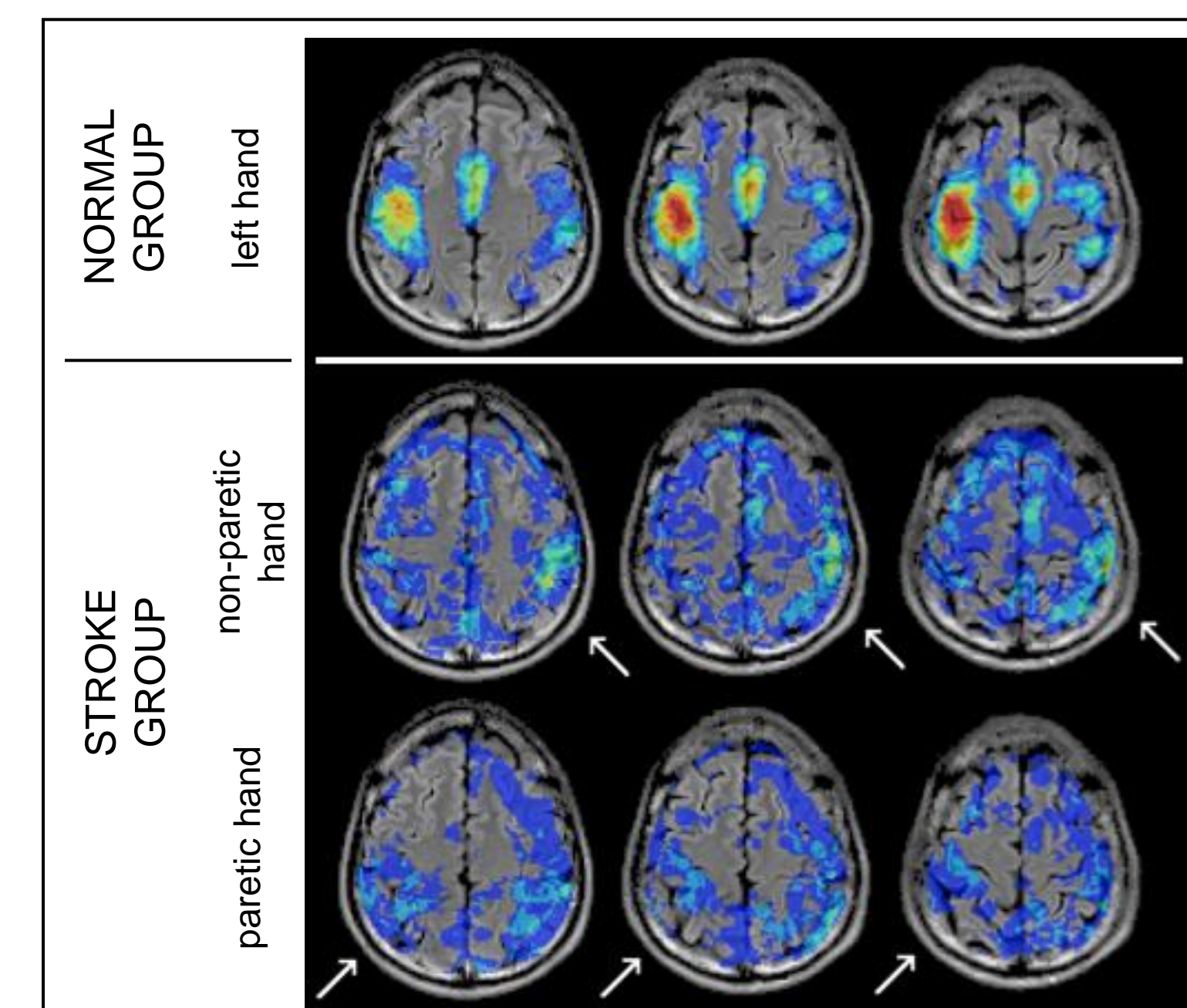
Arrows indicate where the sensorimotor response was expected

Individual case study separately identifies responding motor areas

Analysis result:
Normal 5
Session 2

Bayesian hierarchical model
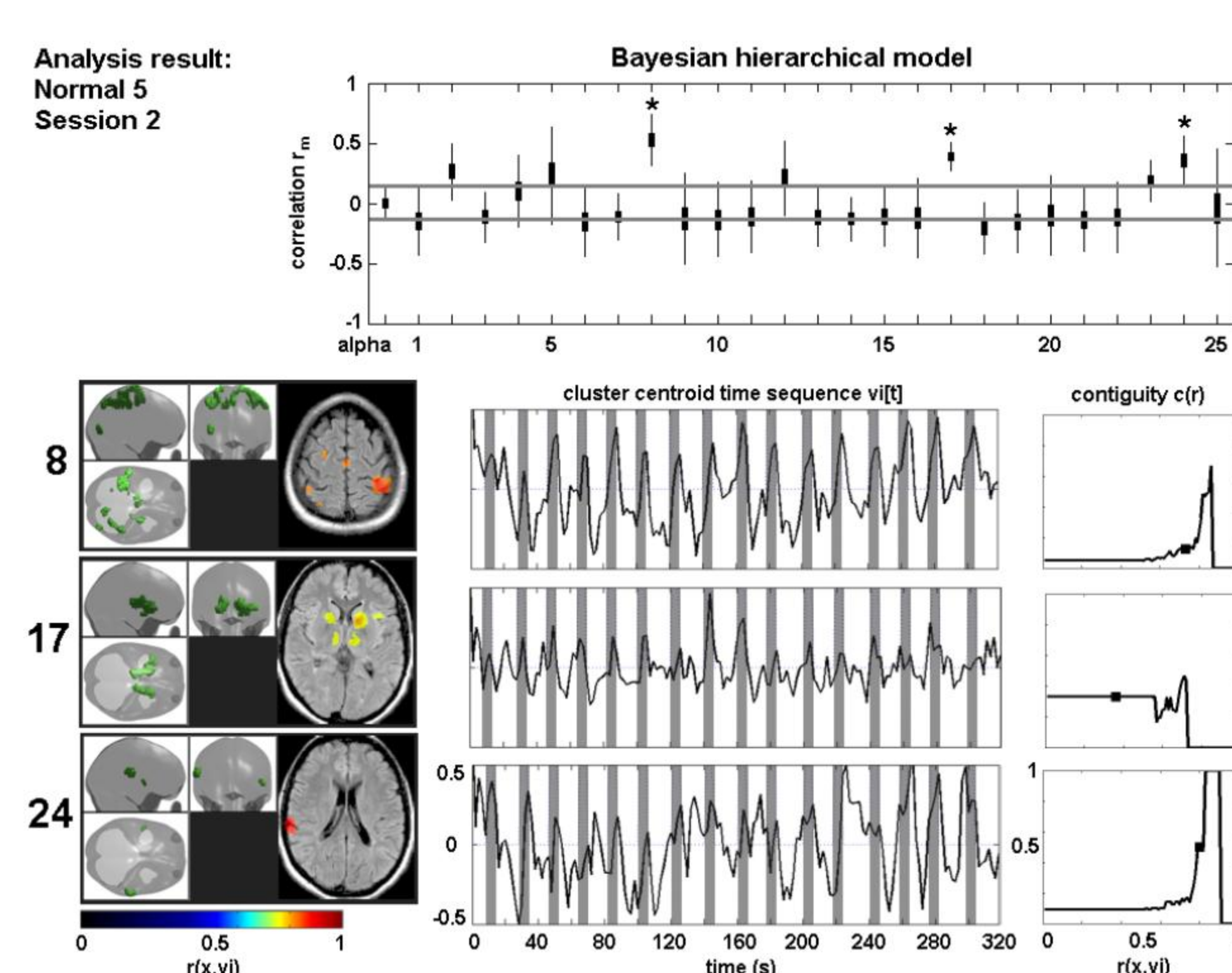
- Motor task performance varied, yet we obtained a 92% response rate
- Stroke group had 58% more signals than normal—many anticorrelated
- Stroke voxel clusters are less contiguous and less synchronised to motor signals than normal clusters
- Normal group shows clear, focused sensorimotor responses, while the stroke group shows a less consistent dispersion of responses

Conclusion

- Method produces consistent neurovascular responses in sensorimotor areas in normal group
- Motor task was applicable to stroke patients with a wide range of motor deficits
- Space-time characterisation indentifies neurovascular impairment as a decrease in BOLD signal contiguity and correlation to the motor task
- Future work will involve a longitudinal study to observe changes in the BOLD signal's space-time structure in recovering stroke patients
- Monitoring regional neurovascular impairment may provide new insights for rehab. programmes

References:
1. H. Grey, *Anatomy, Descriptive and Surgical*, Random House, 1977
2. E. Hamel, *J Appl Physiol*, 100, 1059-64, 2006
3. P. M. Rossini *et al*, *Brain*, 127, 99-110, 2003
4. E. R. Kandel *et al*, *Principles of Neural Science*, McGraw Hill, 2000
5. A. Gelman *et al*, *Bayesian Data Analysis*, Chapman & Hall, 2004
6. C. Gómez-Laberge *et al*, *IEEE T Biomed Eng*, 55, 2372-80, 2008
7. C. Gómez-Laberge *et al*, *Proc 31st Can Conf Med Bio Eng*, 2008
8. C. Gómez-Laberge *et al*, *IEEE T Biomed Eng*, submitted, 2010