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2014 功能性磁振造影工作坊

fMRI 實驗設計概念

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參考資料來源：線上

- Duke BIAC
  - http://www.biac.duke.edu/education/courses/fall08/fmri/
- Dr. Jody Cuhlam's fMRI for newbies
  - http://culhamlab.ssc.uwo.ca/fmri4newbies/Tutorials.html
- U of Michigan fMRI training course
  - http://sitemaker.umich.edu/fmri.training.course/2012_lecture_notes

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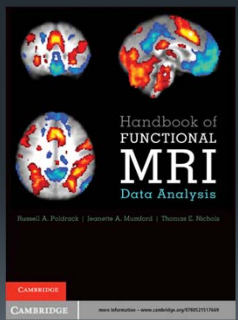
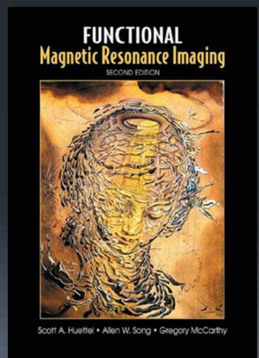
參考資料來源：教科書





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Experiment

- The controlled test of a hypothesis.
- Manipulate one or more independent variables
- Measure one or more dependent variables
- Evaluate those measurements using tests of statistical significance.

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Experimental Designs

- The organization of an experiment to allow effective testing of the research hypothesis.
- Well-designed experiments
  - Test specific hypothesis
  - Can rule out confounding factors
  - Minimize costs

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Elements of An Experiment

- Independent variable (IV)
  - Aspects of the experimental design that are intentionally *manipulated* and that are hypothesized to cause changes in DV
  - Conditions or levels
    - At least two conditions/levels for an IV
- Dependent variable (DV)
  - Quantities that are measured to evaluate the effect of IV
  - RT, accuracy, trajectory, … etc.
  - ERP, fMRI, MEG

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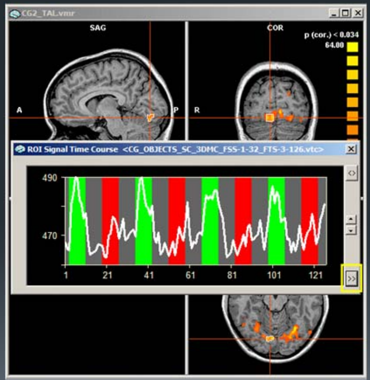
Goal of an fMRI Experiment



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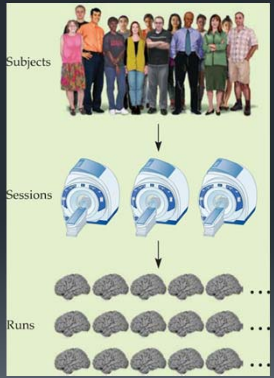
Terminology in an fMRI Experiment



- Conditions
- Trials
- Events
- Blocks

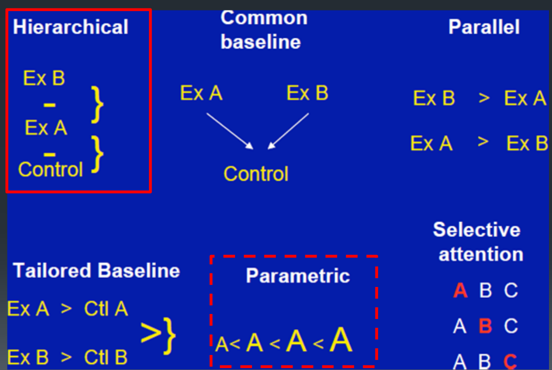
Conceptual & Methodological Aspects of Experimental Designs

- Conceptual design
  - How to design proper tasks to measure the mental process of interest?
- Methodological design
  - How to construct task paradigms to optimize the efficiency and power to measure the effects of interest, given multiple constraints in fMRI environment?

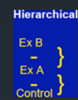
Good Practices in fMRI Experimental Designs

- Evoke the cognitive processes of interest
- Maximize data collection from each subject
- Maximize sample size
- Choose conditions and timings that maximize evoked changes in the process of interests
- Minimize correlation between BOLDs of successive events
- Correlation between behavioral performance and activation

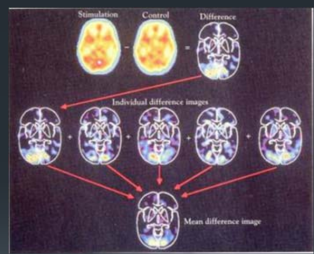
Conceptual Designs



Hierarchical Design



- The subtraction method
  - Acquire data under two conditions
  - These conditions putatively differ only in the cognitive process of interest
- Compare brain images acquired during those conditions
- Regions of difference reflect activation due to the "subtracted" process of interest



Petersen et al., 1988

Hierarchical subtraction

example from Petersen, 1991

- Rest Control
- Auditory words vs. rest: A1, word recognition centers

  \- } Sensory

- Visual words vs rest: visual areas, word form areas
- Reading or repeating words vs passive words: motor areas

  \- } Motor

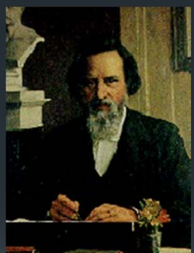
- Generating words vs. repeating: semantic (language) areas

  \- } Semantic

The Pure Insertion Assumption

- Subtraction requires a strong assumption of "pure insertion"
  - Insertion of a single cognitive process does not affect any of the other processes (no *interactions*)
- Failure of PI means that the results cannot be interpreted with regard to the specific cognitive process of interest
- PI must hold at both neural and cognitive levels
- Also make assumptions about equivalence of task effort and difficulty level

Mental Chronometry



F. C. Donders
Dutch physiologist
1818-1889

- use reaction times to infer cognitive processes
- fundamental tool for behavioral experiments in cognitive science

Classic Example

T1: Simple Reaction Time

- Hit button when you see a light

Detect Stimulus → Press Button

T2: Discrimination Reaction Time

- Hit button when light is green but not red

Detect Stimulus → Discriminate Color → Press Button

T3: Choice Reaction Time

- Hit left button when light is green and right button when light is red

Detect Stimulus → Discriminate Color → Choose Button → Press Button

Time →

Subtraction Logic
(A + B) - A = B

T2: Detect Stimulus | Discriminate Color | Press Button

\-

T1: Detect Stimulus | Press Button

=

Discriminate Color

Subtraction Logic
(A + B) - A = B

T3: Detect Stimulus | Discriminate Color | Choose Button | Press Button

\-

T2: Detect Stimulus | Discriminate Color | Press Button

=

Choose Button

Limitations of Subtraction Logic

Assumption of pure insertion
- You can insert a component process into a task without disrupting the other components
- Widely criticized

Subtraction Logic: Brain Imaging Example

Hypothesis (circa early 1990s): Some areas of the brain are specialized for perceiving objects

Simplest design: Compare pictures of objects vs. a control stimulus that is not an object

seeing pictures like

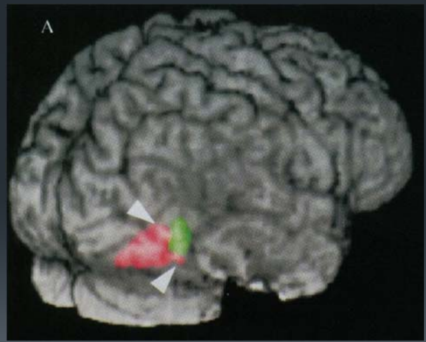
minus

seeing pictures like

= object perception

Malach et al., 1995, PNAS

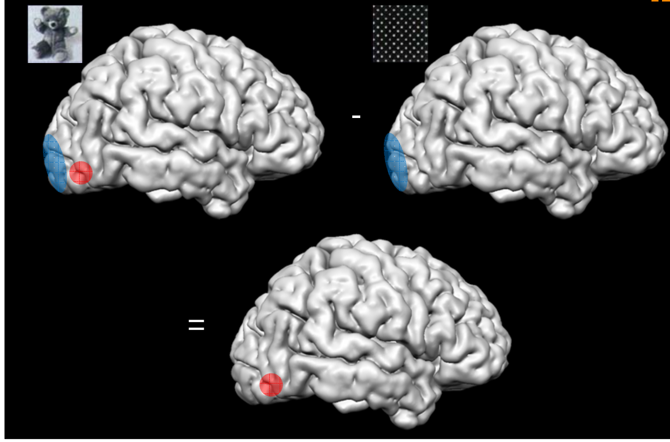
Objects > Textures



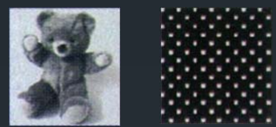
Lateral Occipital Complex (LOC)

Malach et al., 1995, PNAS

fMRI Subtraction



Other Differences



- Is subtraction logic valid here?
- What else could differ between objects and textures?

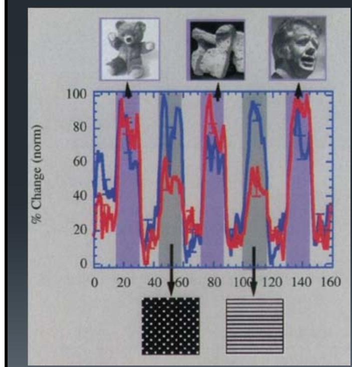
Objects > Textures
- object shapes
- irregular shapes
- familiarity
  - namability
- visual features (e.g., brightness, contrast, etc.)
- actability
- attention-grabbing

Source: Dr. Jody Culham's fMRI for newbies

Other Subtractions

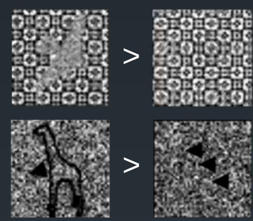
Lateral Occipital Complex

Visual Cortex (V1)

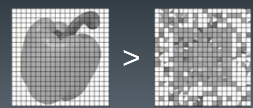


Malach et al., 1995, PNAS

Grill-Spector et al., 1998, Neuron



Kourtzi & Kanwisher, 2000, J Neurosci



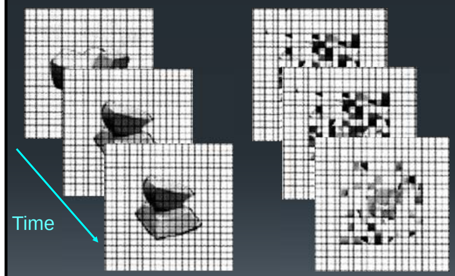
Source: Dr. Jody Culham's fMRI for newbies

Dealing with Attentional Confounds

fMRI data seem highly susceptible to the amount of attention drawn to the stimulus or devoted to the task.

How can you ensure that activation is not simply due to an attentional confound?

Add an attentional requirement to all stimuli or tasks.



Example: Add a "one back" task

- subject must hit a button whenever a stimulus repeats
- the repetition detection is much harder for the scrambled shapes
- any activation for the intact shapes cannot be due only to attention

Other common confounds that reviewers love to hate:
- eye movements
- motor movements

Source: Dr. Jody Culham's fMRI for newbies

Change only one thing between conditions!

As in Donders' method, in functional imaging studies, two paired conditions should differ by the inclusion/exclusion of a single mental process

How do we control the mental operations that subjects carry out in the scanner?

i) Manipulate the stimulus
   - works best for automatic mental processes

ii) Manipulate the task
   - works best for controlled mental processes

DON'T DO BOTH AT ONCE!!!

Source: Nancy Kanwisher

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Parametric Design

A<A<A<A

- Employs continuous variation in a stimulus/task parameter
  - working memory load, stimulus contrast
- Inference:
  - Modulation of activity reflects sensitivity to the modulated parameter
- Can demonstrate more than "where is the activation": instead, how does this region compute variable X
- May make control task unnecessary

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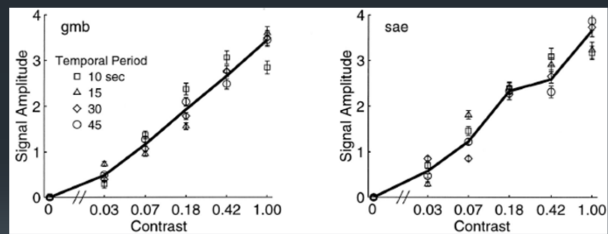
Boynton et al. (1996)



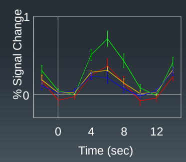
You will see more examples in Prof. Shiwei Wu's lectures.

Methodological Designs

- Blocked designs
- Event-related designs
- Mixed designs

Detection vs. Estimation

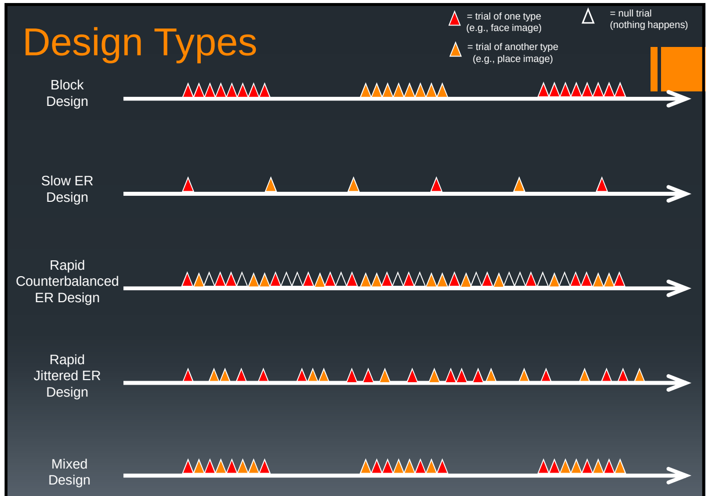
- Detection: determination of whether activity of a given voxel (or region) changes in response to the experimental manipulation
- "which voxel?"



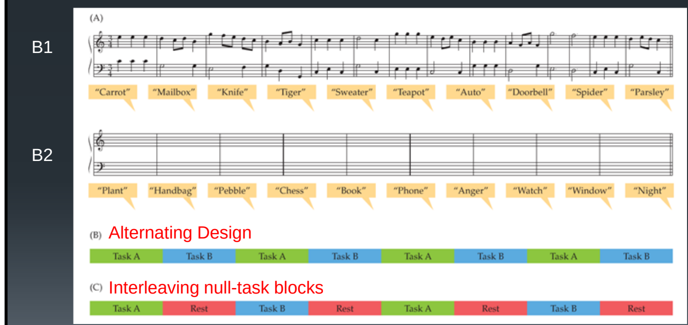
- Estimation: measurement of the time course within an active voxel in response to the experimental manipulation
- "How does signal change in a voxel?"

Definitions modified from: Huettel, Song & McCarthy, 2004, Functional Magnetic Resonance Imaging

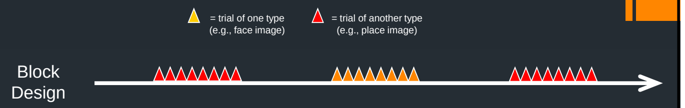
Design Types



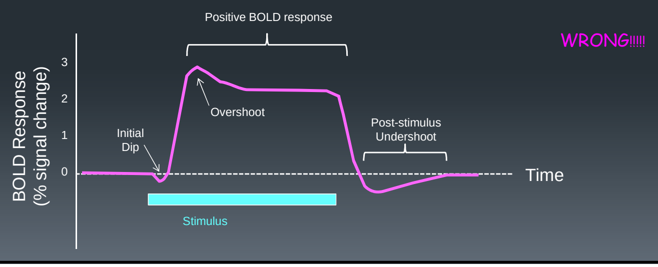
Blocked Designs



Block Designs



Early Assumption: Because the hemodynamic response delays and blurs the response to activation, the temporal resolution of fMRI is limited.



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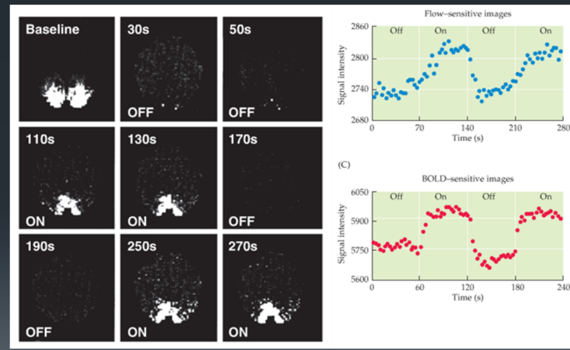
First fMRI Results with a Block Design



Kwong et al. (1992) PNAS

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Recommendations for Using Blocked Design

- Length of a block
  - 10s ~ 1 minute
    - Task property
    - Fatigue and practice
  - Equivalent for conditions or combination of conditions to be compared
- Evoking the same mental process throughout a block

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Advantages and Disadvantages of Blocked Design

- High detection power
- Trade-off of block length
  - Long block
    - Larger differences between conditions
  - Short block
    - Avoid confounding with low frequency scanner drift
    - Increase SNR at the task frequency
- Rule of thumb
  - Block length at HR duration (10~15 s)

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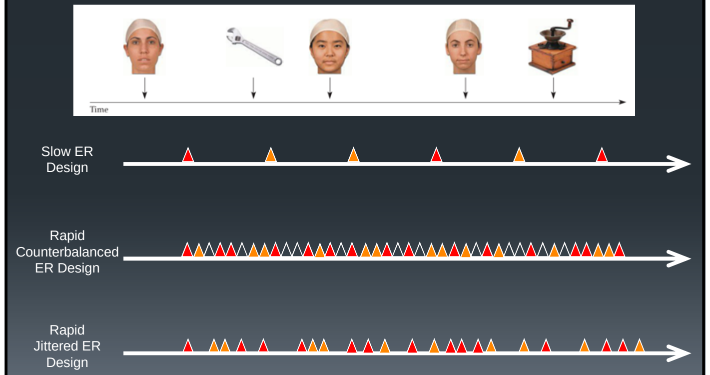
Event-related Designs



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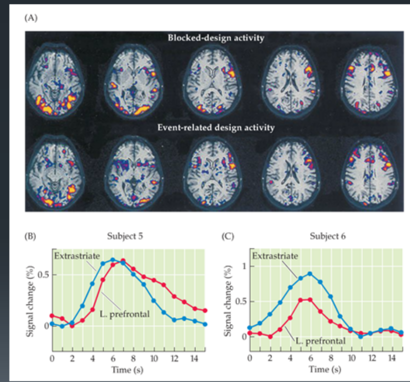
ER-fMRI Showing Timing Differences



Buckner et al. (1996)

Slow Event-Related Designs

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Periodic (Slow) ER Design

- Fixed and long ISI
  - Usually > 15s
  - Each event evokes a complete HR, and corresponding BOLD are selectively averaged.
  - Inefficient
  - How about making it fast?

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Efficiency

- Relative measure of desirability of an estimator or experiment design
- Proportional to power: higher efficient design more likely detects activations
- Involves comparisons of potentially infinite possibilities/procedures
- **"Given a particular sort of hypothesis to be tested, and with all the constraints for fMRI, how should I present my stimuli to maximize my effect size?"**

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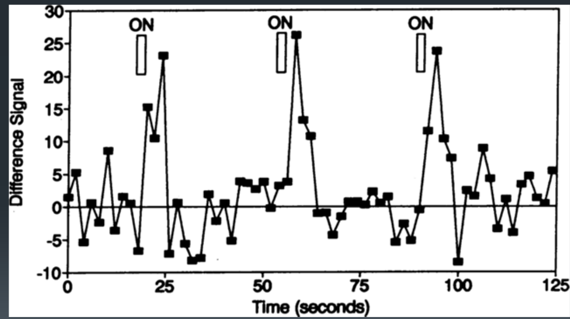
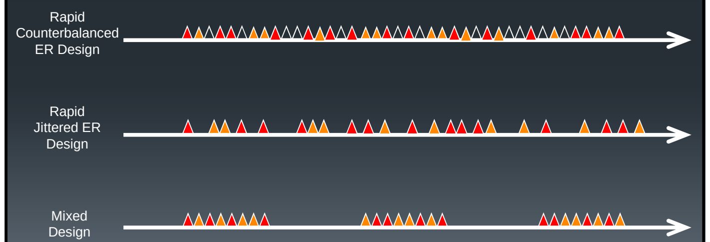
First fMRI Results with an Event-Related Design



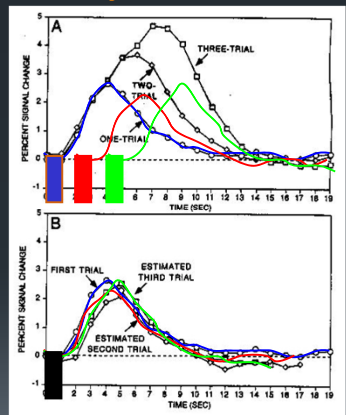
Blamire et al. (1992) PNAS

"Do You Wanna Go Faster?"

- Yes, but we have to test assumptions regarding linearity of BOLD signal first



Linearity of BOLD response



Source: Dale & Buckner, 1997

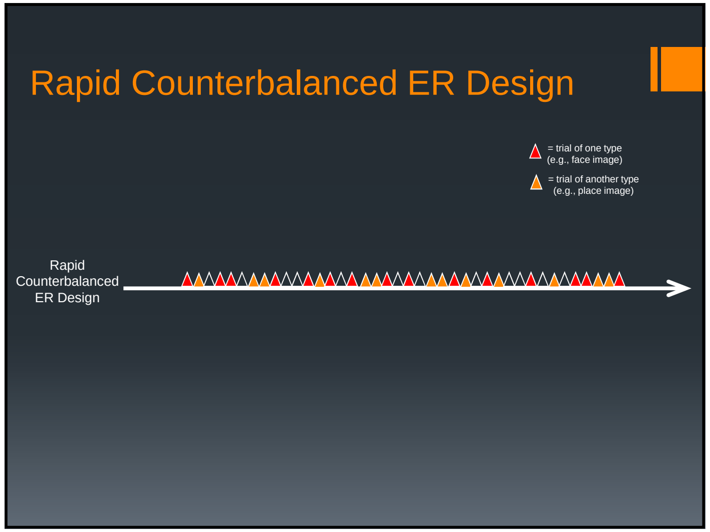
Linearity:
"Do things add up?"

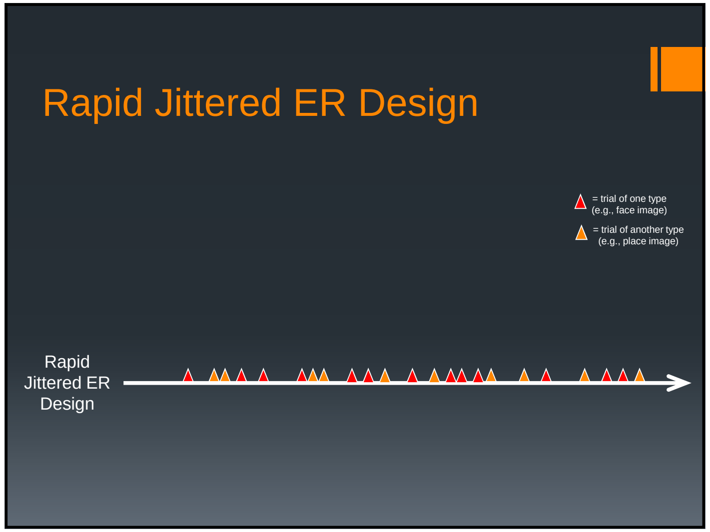
red = 2 - 1

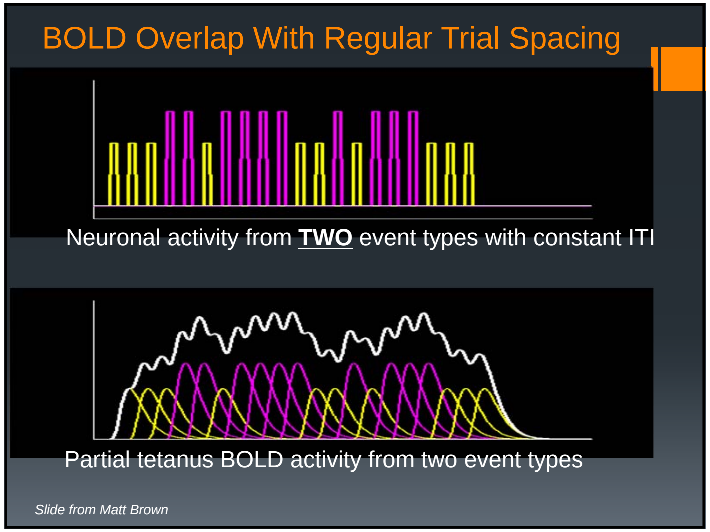
green = 3 - 2

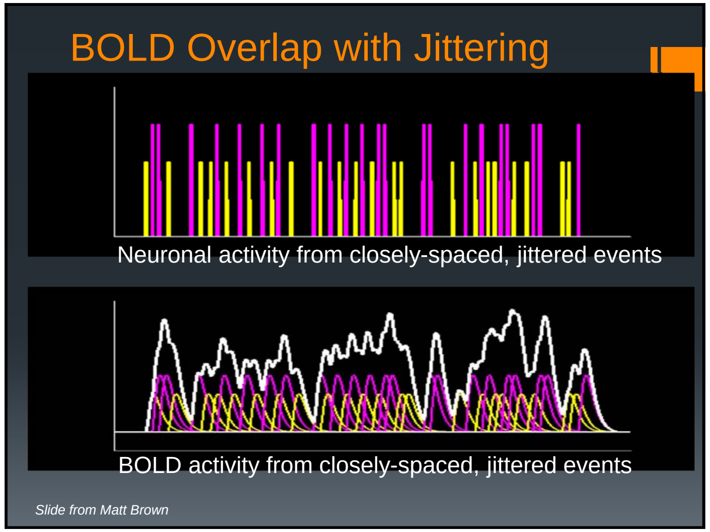
Sync each trial response to start of trial

Not quite linear but good enough!

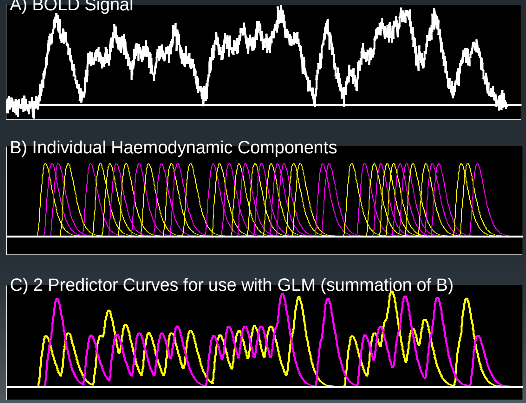

Rapid Counterbalanced ER Design
= trial of one type (e.g., face image)
= trial of another type (e.g., place image)
Rapid Counterbalanced ER Design


Rapid Jittered ER Design
= trial of one type (e.g., face image)
= trial of another type (e.g., place image)
Rapid Jittered ER Design


BOLD Overlap With Regular Trial Spacing
Neuronal activity from TWO event types with constant ITI
Partial tetanus BOLD activity from two event types
Slide from Matt Brown

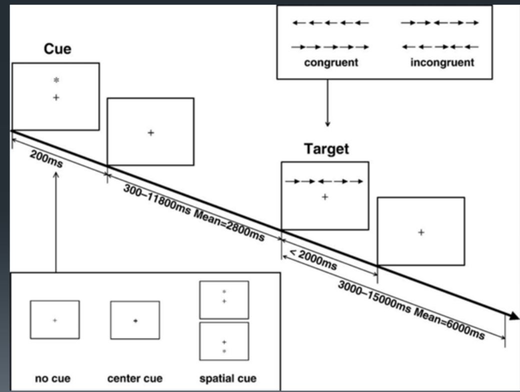

BOLD Overlap with Jittering
Neuronal activity from closely-spaced, jittered events
BOLD activity from closely-spaced, jittered events
Slide from Matt Brown

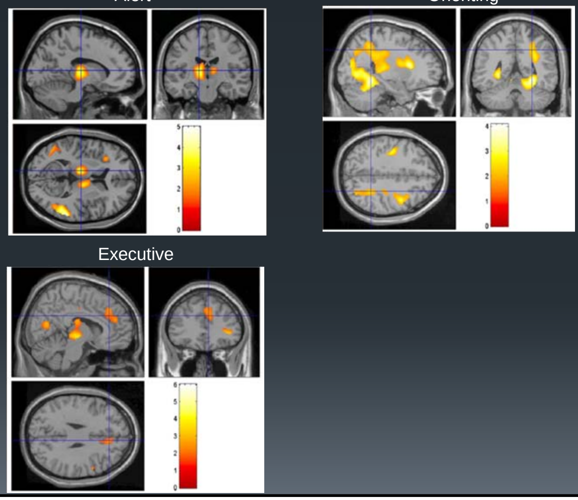
Fast fMRI Detection



Slide from Matt Brown

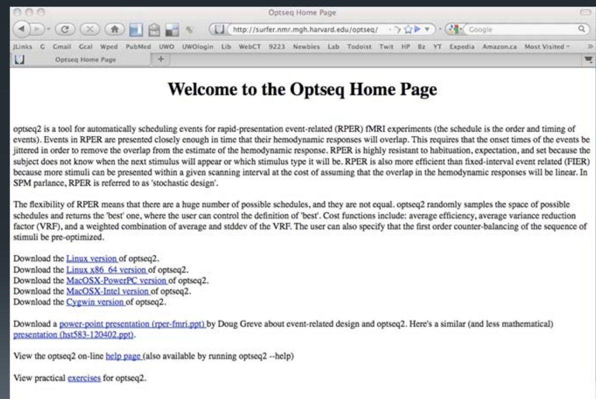
Fan et al. (2005) NeuroImage





Algorithms for Picking Efficient Designs

Optseq2



Optseq Home Page

http://surfer.nmr.mgh.harvard.edu/optseq/

Welcome to the Optseq Home Page

optseq2 is a tool for automatically scheduling events for rapid-presentation event-related (RPER) fMRI experiments (the schedule is the order and timing of events). Events in RPER are presented closely enough in time that their hemodynamic responses will overlap. This requires that the onset times of the events be jittered in order to remove the overlap from the estimate of the hemodynamic response. RPER is highly resistant to habituation, expectation, and set because the subject does not know when the next stimulus will appear or which stimulus type it will be. RPER is also more efficient than fixed-interval event related (FIER) because more stimuli can be presented within a given scanning interval at the cost of assuming that the overlap in the hemodynamic responses will be linear. In SPM parlance, RPER is referred to as 'stochastic design'.

The flexibility of RPER means that there are a huge number of possible schedules, and they are not equal. optseq2 randomly samples the space of possible schedules and returns the 'best' one, where the user can control the definition of 'best'. Cost functions include: average efficiency, average variance reduction factor (VRF), and a weighted combination of average and stddev of the VRF. The user can also specify that the first order counter-balancing of the sequence of stimuli be pre-optimized.

Download the Linux version of optseq2.
Download the Linux x86_64 version of optseq2.
Download the MacOSX-PowerPC version of optseq2.
Download the MacOSX-Intel version of optseq2.
Download the Cygwin version of optseq2.

Download a power-point presentation (rper-fmri.ppt) by Doug Greve about event-related design and optseq2. Here's a similar (and less mathematical) presentation (hst583-120402.ppt).

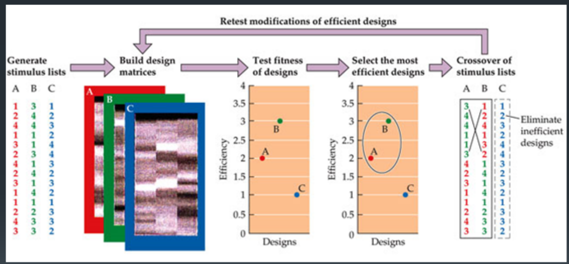
View the optseq2 on-line help page (also available by running optseq2 --help)

View practical exercises for optseq2.

http://surfer.nmr.mgh.harvard.edu/optseq/

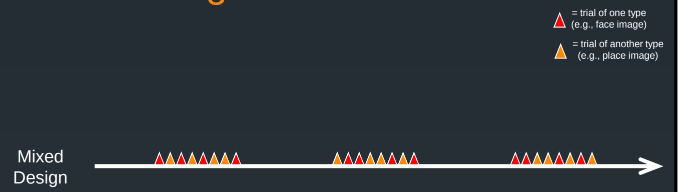
Algorithms for Picking Efficient Designs

Genetic Algorithms



http://wagerlab.colorado.edu/tools

Mixed Design



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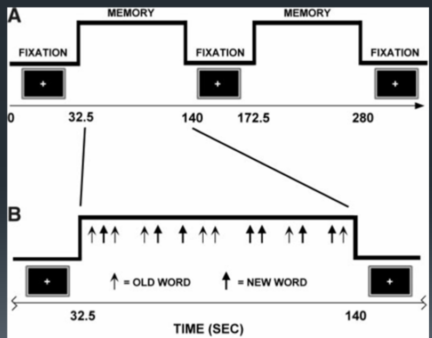
Mixed Design



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How NOT to Do An fMRI Experiment?

- ask a stupid question
  - e.g., “I wonder what lights up for daydreaming vs. rest”
- compare poorly-defined conditions that differ in many respects
- use a paradigm from another technique (e.g., cognitive psychology) without optimizing any of the timing for fMRI, e.g., 1 minute epochs
- never look at raw data, time courses or individual data, just plunk it all into one big stat model and look at what comes out
- publish a long list of activated foci in every possible comparison
- don’t use any statistical corrections
- write a long discussion on why your task activates the subcortico-occipito-parieto-temporo-frontal network