认知心理学进阶第八讲：磁共振实验设计

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Courtesy of Drs. Xun Liu & Joe Yazhuo Kong @IPCAS

1

Outline

- Factors to Consider
- Block Designs
- Event-related Designs
- Mixed Designs
- Guidelines and Good Practices

2

2

FACTORS TO CONSIDER

3

3

fMRI Experimental Design: A Basic Plan

Define mental process to examine → Define tasks to manipulate that process → Measure fMRI data during tasks → Compare fMRI data between tasks

Replace “fMRI data” with “RT” and you have cognitive psychology!

4

4

Study Design

- “based on an intervention in a system (brain) and observation of the modulation of the system response (BOLD effect) resulting from this ‘provocation’ (cognitive task, or in this context, *paradigm*)” - *Amaro & Barker 2006 (Brain & Cognition)*
- *i.e.* We want to manipulate the participants’ experience and behaviour in some way that is likely to produce a functionally specific neurovascular response.
- Can you test your hypothesis like this?

5

Experimental Design: Terminology

- Variables
  - Independent vs. Dependent
  - Categorical vs. Continuous
- Contrasts
  - Experimental vs. Control
  - Parametric vs. subtractive
- Comparisons of subjects
  - Between- vs. Within-subjects
- Confounding factors
- Randomization, counterbalancing

6

6

Terminology

- **Trial**: replication of a condition, consist of one or more components
- **Inter-Trial Interval (ITI)**: time between the onset of successive trials
- Components may be brief bursts of neural activity, **events**, or periods of sustained neural activity, **epochs**
- **Stimulus Onset Asynchrony (SOA)**: time between onset of trial components (even if components are not stimuli *per se*)
- **Inter-Stimulus Interval (ISI)**: time between the offset of one component and the onset of the next

7

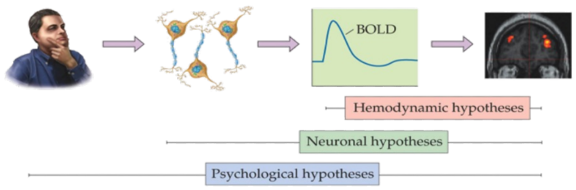
fMRI Experimental Design

- Controlling the timing and quality of cognitive operations (IVs) to influence brain activation (DVs)
- What can we control?
  - Stimulus properties (what is presented?)
  - Stimulus timing (when is it presented?)
  - Subject instructions (what do subjects do with it?)
- What are the goals of experimental design?
  - To test specific hypotheses (i.e., hypothesis-driven)
  - To generate new hypotheses (i.e., data-driven)

8

8

Hypotheses about fMRI Data



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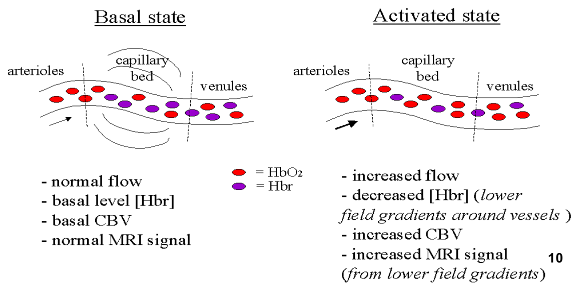
fMRI BOLD: Overview



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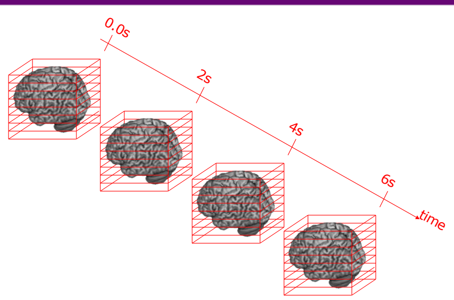
fMRI data are 4 Dimensional



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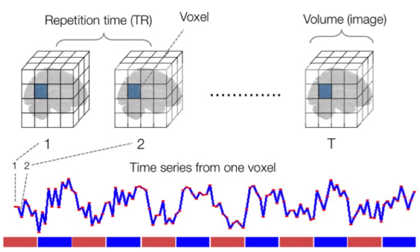
11

fMRI Data Time Series



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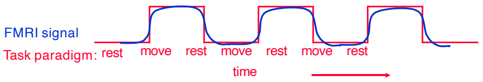
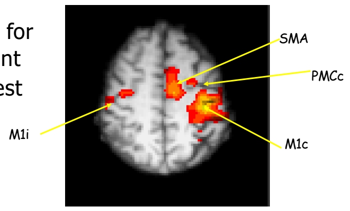
12

A very simple experiment

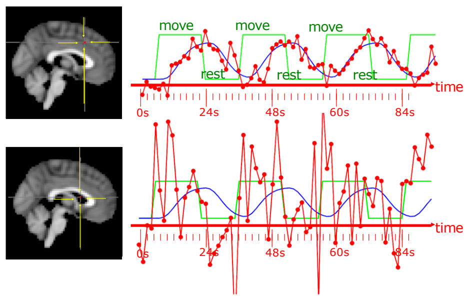


Activation for movement versus rest



13

Analysis: one voxel at a time



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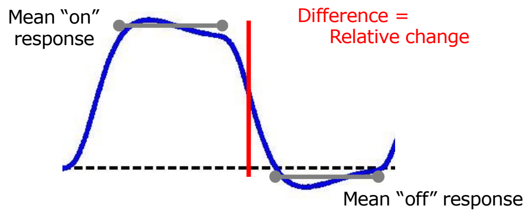
BOLD is a relative measure

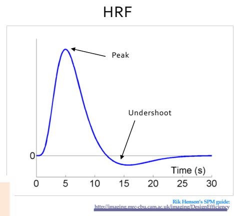


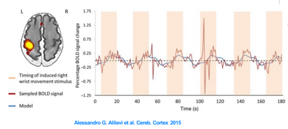
Sensitivity depends on maximizing relative change

15

BOLD impulse response

- Response to a brief burst of neural activity
- Predicted fMRI time series: Convolved stimulus function with the haemodynamic response function (HRF)

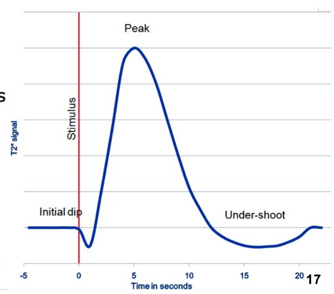




16

Haemodynamic Response

- HRF is slow to peak
- Peak response comes 4-6s after stimulus onset
- Can vary in time-to-peak across brain areas and across subjects
- Returns to baseline about 21s after stimulus ends



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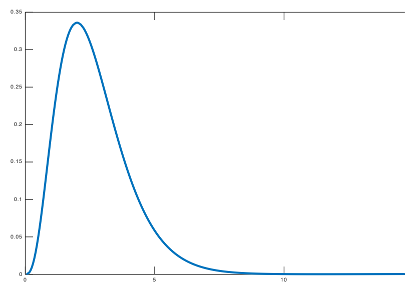

MATLAB

gampdf (Gamma probability density function)

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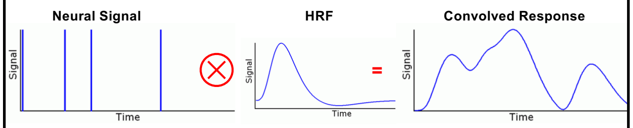
Temporal Properties of fMRI Signal

- We predict the HRF by convolving the neural signal by the HRF
- We want to maximize the amount of predictable variability



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20

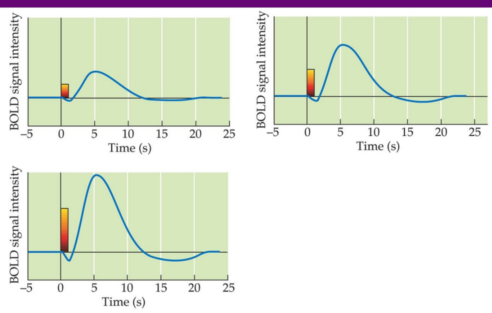
fMRI Signal

- There are two crucial aspects of the BOLD effect
  - The HRF is very sluggish
    - Delay between brain activity and changes in fMRI images (~5s)
  - The HRF is additive
    - Doing a task twice causes about twice as much change as doing it once

21

21

Assumption I: Scaling



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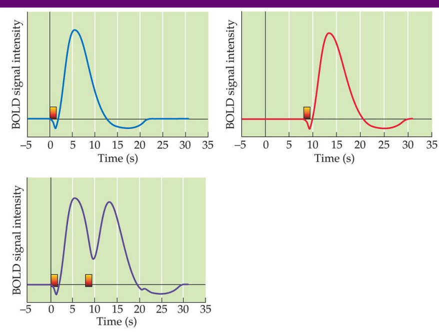
22

Assumption II: Superposition



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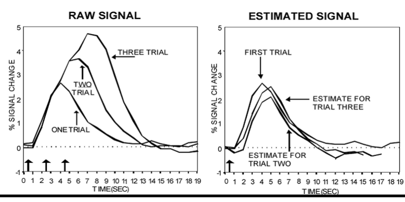
23

Additive BOLD Effects

- Three stimuli presented rapidly result in almost 3 times the signal of a single stimuli (e.g. Dale & Buckner, 1997)
- Crucial finding for experimental design
- Note there are limits to this additivity effect, but the basic point is that more stimuli generate more signal (see Birn et al. 2001)

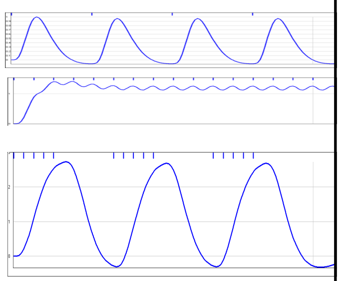


24

24

Comparing Predictable HRF

- Consider 3 paradigms:
  1. Fixed ISI: one stimuli every 16 seconds.
     – Inefficient
  2. Fixed ISI: one stimuli every 4 seconds.
     – Insanely inefficient: virtually no task-related variability
  3. Block design: cluster five stimuli in 8 seconds, pause 12 seconds, repeat.
     – Very efficient.
     – Cluster of events is additive. Note peak amplitude is x3 the 16s design.



25

25

Optimal Experimental Design

- Maximizing both Detection and Estimation
  - Maximal variance in signal (incr. detect.)
  - Maximal variance in stimulus timing (incr. est.)
- Limitations on Optimal Design
  - Signal saturation
  - Subject's predictability

26

26

Optimal Experimental Design

- Experimental designs for functional magnetic resonance imaging (fMRI) experiments can be characterized by
  - their detection power, which is a measure of the variance in the estimate of the amplitude of functional activity
  - their estimation efficiency, which is a measure of the variance in the estimate of the hemodynamic response function (HRF)

Efficiency, power, and entropy in event-related fMRI with multiple trial types Part I: theory
Thomas T. Liu and Lawrence R. Frank

27

27

Conceptual & Methodological Aspects

- There are two aspects of fMRI design that are important to distinguish
- Conceptual design
  - How do we design tasks to properly measure the processes of interest?
- Methodological design
  - How can we construct a task paradigm to optimize our ability to measure the effects of interest, within the specific constraints of the fMRI scanning environment?

28

28

Finding Significant Effects

- Statistics are based on the ratio of explained predictable versus unexplained variability

$$t = \frac{\text{Signal}}{\text{Noise}} \qquad F = \frac{\text{Signal+Noise}}{\text{Noise}}$$

- We can improve statistical efficiency by
  - Increasing the task related variance (signal)
    - Designing Experiments
  - Decreasing unrelated variance (noise)
    - Spatial and temporal processing
  - Good signal in our fMRI data
    - Physics

29

29

Designing an Experiment

- Designing fMRI studies
  - fMRI signal is sluggish and additive
  - Efficient designs maximize predictable changes in HRF
  - Efficient designs are often very predictable (e.g., block designs)
    - Participant may anticipate events in a block design
    - Techniques for balancing efficiency and psychological validity

30

30

Comparison Strategies

Subtraction
Factorial
Parametric

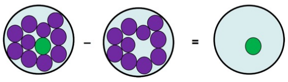
31

31

Subtraction

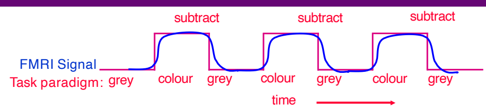
- 'Subtracting' an image taken during a control condition from an active condition
- Any BOLD signal difference between images (above set statistical limits) is assumed to represent all brain regions involved in that task
- Implies no interactions among cognitive components of a task so they can be cognitively added (Pure Insertion)
- This assumption is false most of the time (if not always!)

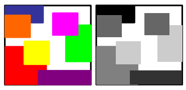
Example: **[Task with *P*] – [task without *P*] =** ***P***



32

Simple experiment: subtraction





Colour > No colour
Luminance = Luminance
Contrast = Contrast
Shape = Shape

Brain mapping

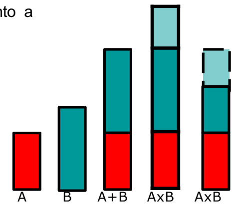
Isolate functional area

33

33

Problems with subtractive designs

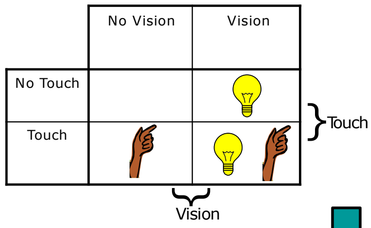
- Depends on the assumption of 'Pure Insertion'
  - i.e. the idea that you can insert a single component process into a task without affecting other processes
  - Can get interactive effects



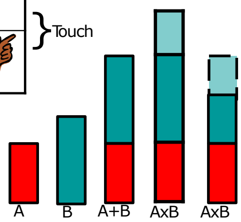
Friston et al., (1996) *Neuroimage* 34

34

Alternative 1: Factorial designs



Allows you to characterise interactions between component processes – i.e., effect that one component has on another (does not make assumption of pure insertion)



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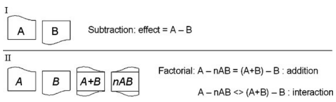
35

Factorial

- Allows testing for interaction between cognitive components
- Requires evidence when defining task components
- Subjects perform tasks which are cognitively intermingled one moment, then separated in another instance
- Simpler if one assumes linearity between BOLD responses from the different conditions



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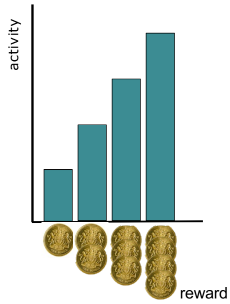
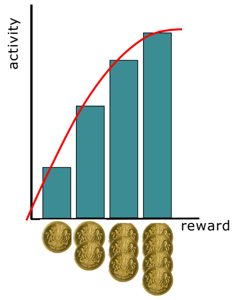
Alternative 2: Parametric design



- Test for a non-binary relationship between brain activity and task
  - e.g. more money
  - ●= more activity in reward area
- Avoids concept of subtraction/ "pure insertion"
- Can test quite specific hypotheses e.g. computational regressors

37

Parametric design



- Can be less powerful than simpler designs
- Quantitative assumptions about relationship between stimuli and brain activity

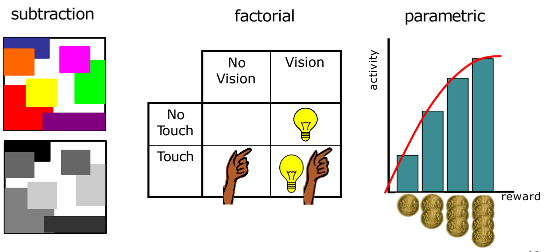
38

Parametric

- Increasing cognitive demand of a task without changing its nature
- Any increase in BOLD between trials would imply a heavy association between active regions and parameter being manipulated
- Can separate functionally relevant areas from others involved in the maintenance of the cognitive process
- Simple in principle…
- Can pose a challenge to systematically 'step-up' cognitive demand
- Might involve recruiting other cognitive processes not present at lower levels

39

Design types summary



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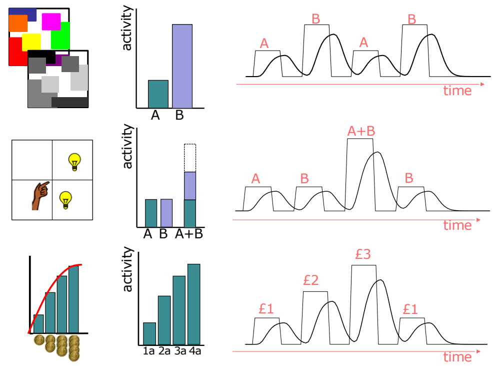


41

41

fMRI Design Types

- Blocked Designs
- Event-Related Designs
  - Periodic Single Trial
  - Jittered Single Trial
- Mixed Designs
  - Combination Blocked / Event-Related

42

42

BLOCK DESIGNS

43

43

What are Blocked Designs?

- Blocked designs segregate different cognitive processes into distinct time periods

Task A	Task B	Task A	Task B	Task A	Task B	Task A	Task B

Task A	REST	Task B	REST	Task A	REST	Task B	REST

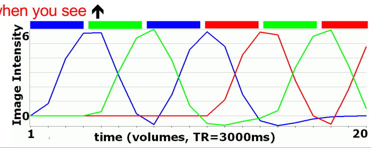
44

44

Block Designs

- aka ‘Box Car’, or ‘Epoch’ designs
- Different cognitive processes occur in distinct time periods
  – Three conditions, each repeated 14 times (once every 900ms)
    1. Press left index finger when you see ←
    2. Press right index finger when you see →
    3. Do nothing when you see ↑

Note huge predictable variability in signal



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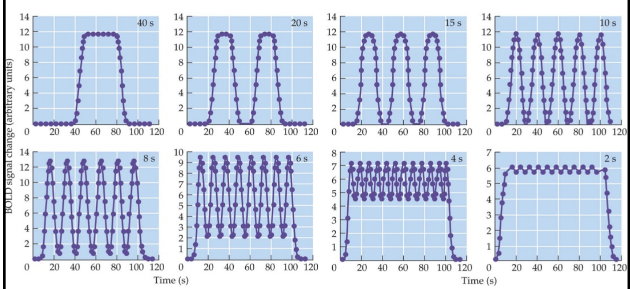
Balance Power and Efficiency



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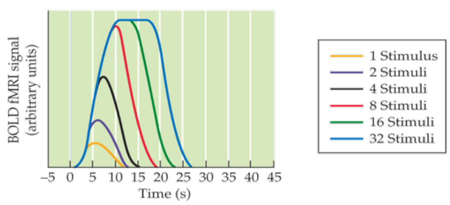
Power in Blocked Designs

Summation of responses results in large variance



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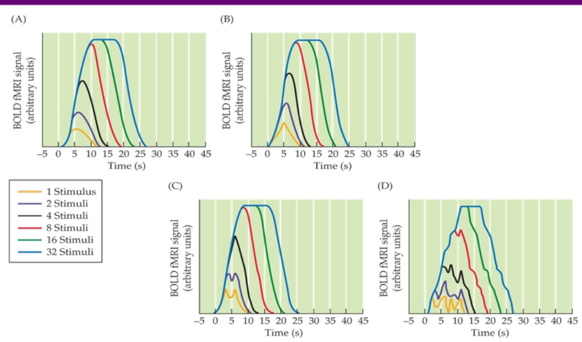
HDR Estimation in Blocked Designs



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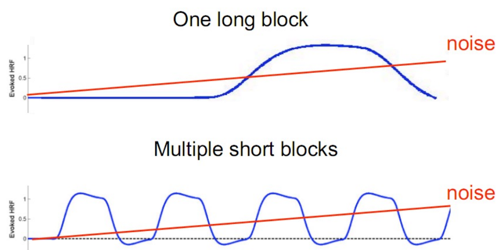
48

Noise Interferes with Long Blocks



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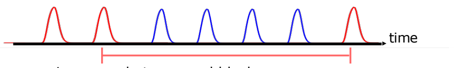
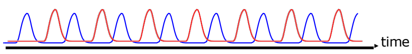
Block design: (even) more considerations

Cycle time:



- Long gap between red blocks
- Power will be lost when data are low pass filtered

Block order:



- On average, red blocks come later in scan (bad)
- Counterbalance order to avoid this (ABBABAAB etc)

50

Choosing Length of Blocks

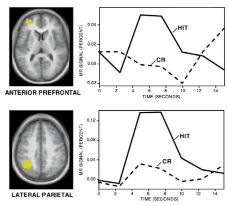
- Longer block lengths allow for stability of extended responses
  - Hemodynamic response saturates following extended stimulation
    - After about 10s, activation reaches max
  - Many tasks require extended intervals
    - Processing may differ throughout the task period
- Shorter block lengths move your signal to higher frequencies
  - Away from low-frequency noise: scanner drift, etc.
- Periodic blocks may result in aliasing of other variance in the data
  - Example: if the person breathes at a regular rate of 1 breath/5sec, and the blocks occur every 10s

51

51

Limitations of Blocked Designs

- While block designs offer statistical power, they are very predictable
  - e.g. participants know they will press the same finger 14 times in a row.
- Many tasks not suitable for block design
  - e.g. novelty detection, memory, etc.
  - Cannot post-hoc sort data from block designs (e.g. Konishi, et al., 2000 examine correct rejection vs hits on episodic memory task)



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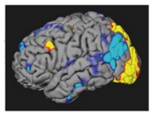
Limitations of Blocked Designs

- Block designs good for detecting activation, but poor for estimating HDR

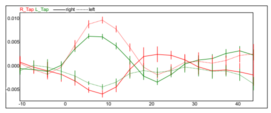
Detection

which areas are active?



Estimation

what is the time course of activity?



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Blocked Design

- Advantages
  - Simple (for you and for subject)
  - Minimize task switching
  - Maximum power
  - Does not depend on accurate HRF model
  - Robust to uncertainty in timing
  - Straightforward analysis
- Disadvantages
  - Not all tasks can be blocked
  - Subjects can anticipate conditions - order and duration
  - Does not allow separation of response to individual trials
  - No timing information

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EVEN-RELATED DESIGNS

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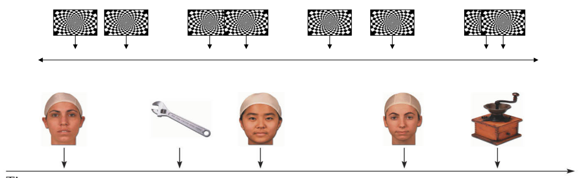
What are Event-Related Designs?

- Event-related designs associate brain processes with discrete events, which may occur at any point in the scanning session



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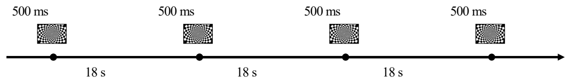
Periodic Single Trial Designs

- Stimulus events presented infrequently with long inter-stimulus intervals (ISI)



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58

Why Event-Related Designs?

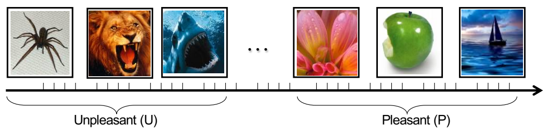
- Randomize condition/stimuli order
  cf. Confounds of blocked designs (Johnson et al., 1997)
- Post-hoc classification of trials
  e.g. According to subsequent assessment (Kim et al., 2007)
- Some events can only be indicated by the subject (during the experiment)
  e.g. Event is determined by subject's decision (Liu et al., 2007)
- Some trials cannot be blocked
  e.g. Odd-ball designs (Clark et al., 2000)
- Better model for blocked stimuli too?
  e.g. State-item interactions (Chawla et al., 1999)

59

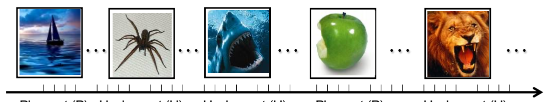
59

Why Event-Related Designs?

Blocked designs may trigger expectations and cognitive sets



Event related designs can minimize expectation/strategy



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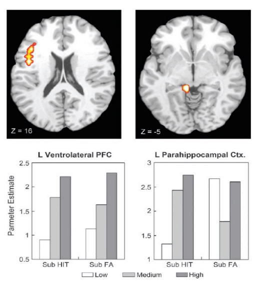
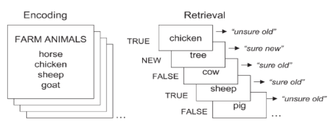
61

61

Post-Hoc Sorting of Trials





Using information about fMRI activation at memory *encoding* to predict behavioral performance at memory *retrieval*.

From Kim and Cabeza, 2007

62

62

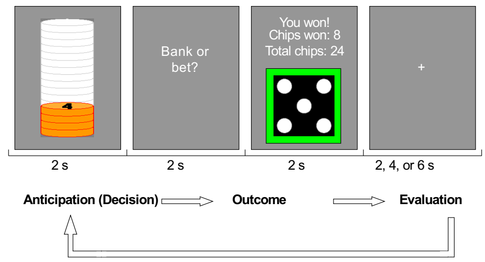
Why Event-Related Designs?

- Randomize condition/stimuli order
  cf. Confounds of blocked designs (Johnson et al., 1997)
- Post-hoc classification of trials
  e.g. According to subsequent assessment (Kim et al., 2007)
- Some events can only be indicated by the subject (during the experiment)
  e.g. Event is determined by subject's decision (Liu et al., 2007)
- Some trials cannot be blocked
  e.g. Odd-ball designs (Clark et al., 2000)
- Better model for blocked stimuli too?
  e.g. State-item interactions (Chawla et al., 1999)

63

63

Reward Processing



Liu et al. (2007)

64

64

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65

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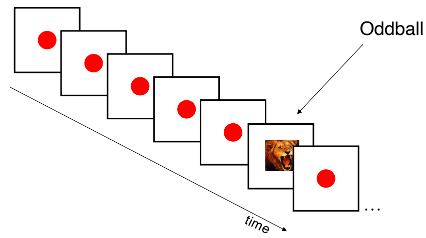
Stimulus Context



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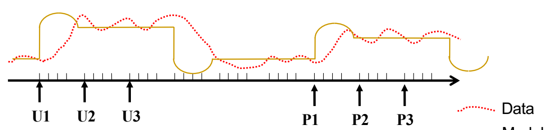
67

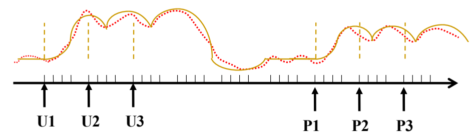
67

"Event" Model of Block Design

"Epoch" model assumes constant neural processes throughout block



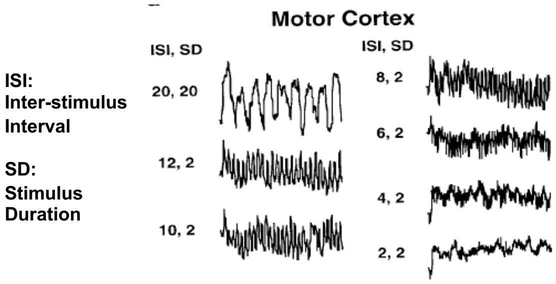
"Event" model may capture state-item interactions (with longer SOAs)



68

68

Why Not Short, Periodic Designs?



From Bandettini and Cox, 2000

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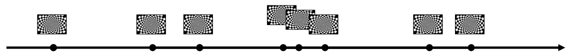
Jittered Single Trial Designs

- Varying the timing of trials within a run
- Varying the timing of events within a trial



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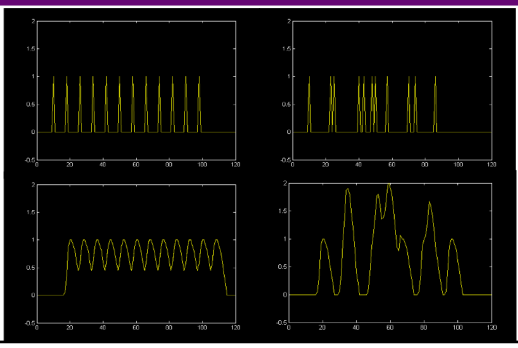
Jittering on Stimulus Variance

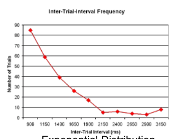


72

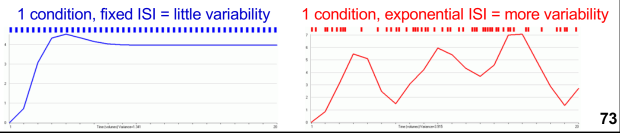
72

Jittered Inter-Stimulus-Interval (ISI)

- Dale et al. suggest using exponential distribution for inter-trial-intervals (ITI)
- Exponential Distribution:
  - Many trials have short duration
  - A few trials have long duration
  - Efficient because jittering makes events block-like



Exponential Distribution

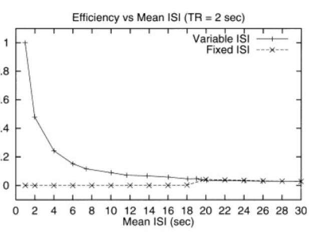


73

73

ISI, Power and Efficiency

- Fixed ISI: low statistical power
  - Fixed ISI have most power if >12 sec between stimuli
  - At that rate, only a few dozen trials in a 10 minute scan
- In theory, variable ISI can offer much more efficiency than fixed ISI



74

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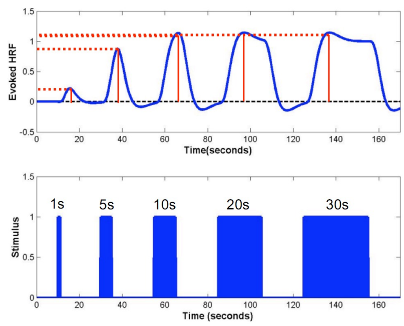
Blocked Designs



No further efficiency benefit to increasing block length once reach10-20s

Other considerations: shorter the block, more task switching, harder to establish 'attentional' or 'task' set

75

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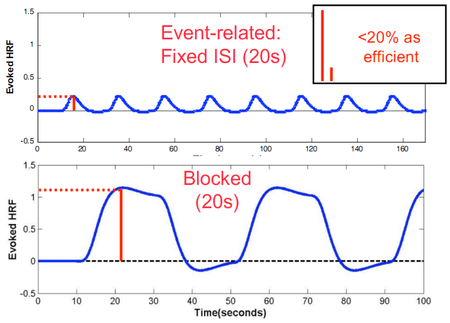
Event-Related Designs



76

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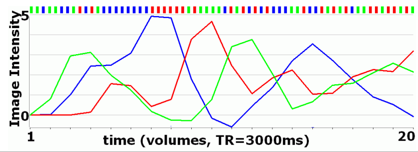
Why Not Event-Related Designs?

- Much less power than block designs
  - Simply randomizing trial order of the block design, the typical event related design has <25% power
  - Here, we ran 50 iterations and selected the event related design with the most power
    - Still has half of the power than the block design
    - Note this design is not very random: runs of same condition make it block-like and increase the power



77

77

Event-Related Designs

- Advantages
  - Flexible – removes anticipation, allows for surprises
  - Good estimate of time course of HRF
  - Post hoc sorting of trial types, e.g. correct vs. incorrect; remembered vs. forgotten stimuli
  - Can separate our response to task components – e.g., cue, target, response
  - High temporal resolution
- Disadvantages
  - More things can go wrong
  - Reduced power
  - Typically results in longer experiments
  - More dependent on accurate HRF modeling
  - Increased task switching

78

78

MIXED DESIGNS

79

79

Combining Blocked/Event-Related

- Both blocked and event-related design aspects are used (for different purposes)
  - Blocked design: *state-dependent* effects
  - Event-related design: *item-related* effects
- Analyses can model these as separate phenomena, if cognitive processes are independent
  - “Memory load effects” vs. “Item retrieval effects”
- Or, interactions can be modeled
  - Effects of memory load on item retrieval activation

80

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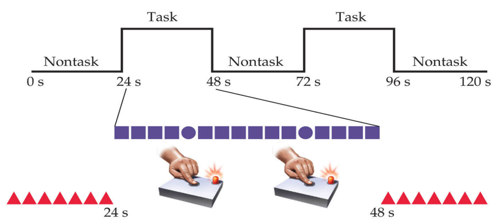
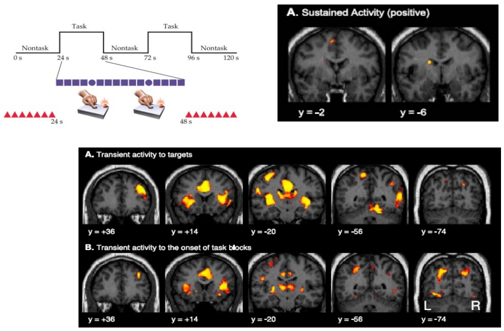
Mixing Events within a Block



81

81

Sustained and Transient Effects



82

82

Issues in Design Efficiency

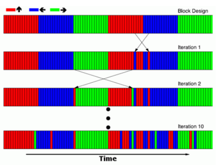
- Not all random designs are equally efficient!
- Design efficiency is defined in relation to some contrast
- Efficiency may interact with predictability and expectation

83

83

Permuted Blocks

Permuted block designs offer possible some unpredictability



Permuted Design:

1. Start with a block design
2. Randomly swap stimuli
3. Repeat step 2 for *n* iterations

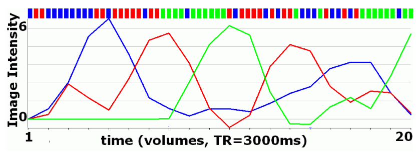
More iterations = less predictable, less power

84

84

Permuted Blocks

- Below you can see the study design after 10 permutations
- Permuted block designs can offer a balance of power and predictability



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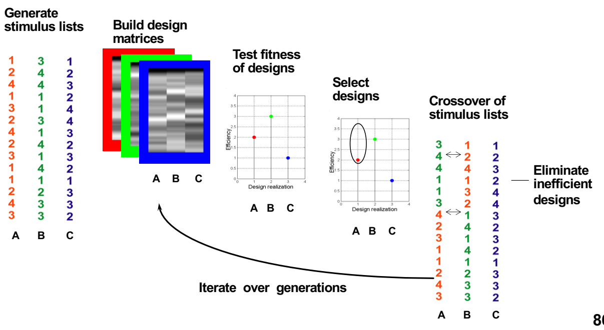
Iterative Genetic Algorithms



86

86

Summary of Experimental Design

- Main Issues to Consider
  - What design constraints are induced by my task?
  - What am I trying to measure?
  - What sorts of non-task-related variability do I want to avoid?
- Rules of thumb
  - Blocked Designs:
    - Powerful for detecting activation
    - Useful for examining state changes
  - Event-Related Designs:
    - Powerful for estimating time course of activity
    - Allows determination of baseline activity
    - Best for post hoc trial sorting
  - Mixed Designs
    - Best combination of detection and estimation
    - Much more complicated analyses

87

87

GUIDELINES AND GOOD PRACTICES

88

88

General Guidelines

1. If possible, use block design
   – Keep blocks <40 sec
2. Limit number of conditions
   – Contrast of conditions far apart may be confounded by low frequency noise
3. Randomize order of events that are close to each other in time
4. Randomize SOA between events that need to be distinguished
5. Run as many people for as long as possible

89

89

Good Practices

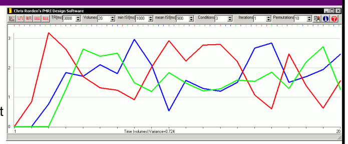
- Balance statistical power and compliance of participants
  – For how long do you think you can get good data out of a volunteer? Avoid head motion, poor task compliance
- Always counterbalance / (pseudo-)randomize events!
- Ask yourself questions:
  – What's the best design for your cognitive process of interest?
  – What's the best design for your task(s)?
  – What psychological factors might be at play?
  – What comparison(s) are you interested in?
- Maximize efficiency for your contrast(s) of interest, compare multiple designs, simulate!

90

90

Generate Your Own Experiments

- Set the TR (time per volume)
- Set the number of volumes
- Set minimum ISI – this will be time between trials for block designs
- Set the mean ISI – this will be the average time between trials for event related designs
- Set the number of conditions
- Iterations – you can compute hundreds of event related designs and choose the most efficient
  High iterations will lead to efficient but predictable designs
- Permutations – select the number of permutations for the permuted block design
  Fewer permutations lead to efficient but predictable designs



- Press the type of study you want to generate
1. Block
2. Permuted Block
3. Fixed ISI Event
4. Exponential ISI Event

91

91

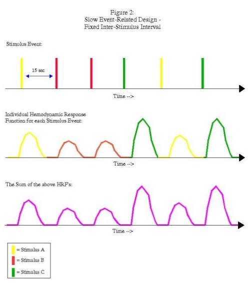
Generate Your Own Experiments

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.

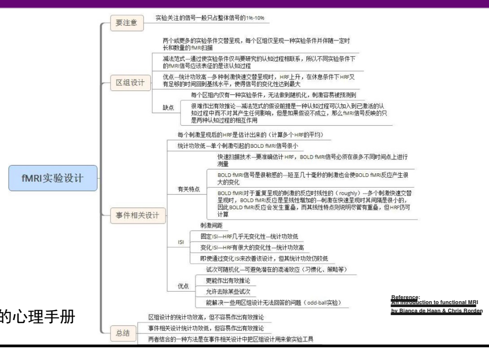


https://surfer.nmr.mgh.harvard.edu/optseq/
http://andysbrainblog.blogspot.com/2012/09/optseq-and-event-related-designs.html

92

92

其他参考资料



克里斯的心理手册

93

Types of Design

Hierarchical

Ex B
-
Ex A
-
Ctl

Tailored Baseline

Ex A > Ctl A
Ex B > Ctl B
>

Factorial Design

Ex A   Ex B

A x B

Common Baseline

Ex A   Ex B

Control

Parametric

A < A < A < A

Conjunction Design

A	B		D	
A		C	D	
	B	C		E

Parallel Comparisons

Ex B > Ex A

Ex A > Ex B

Selective Attention

A B C
A B C
A B C

Priming/Adaptation

A A
A B

94

94

Summary

- fMRI is not a 'magic bullet'
  - Researchers often think "I've got this task, let's run it with fMRI and see what happens."
  - Usually leads to uninterpretable results
    - reverse inference – i.e. long list of activated regions and an attempt to explain them by referring to previous studies
    - Simplistic claims based on localisation – We have discovered the neural basis of X
  - Need to design fMRI experiments with a clear hypothesis and ask what information we can get from fMRI that we can't get from a less expensive and less time-taking approach.
  - Designing an fMRI experiment involves a series of decisions about trade-offs and compromises,
    - e.g. collect as much data as possible but not at the expense of tiring out subjects and collecting low quality data
    - Design an interesting study but not try to ask too many questions – keep as simple as possible
  - Always remember, the scanner is a noisy, unfamiliar, uncomfortable environment. There is a limit to what the subject will put up with, and this will be (much) lower than what they will tolerate outside of the scanner

95

HAPPY DESIGNING AND SCANNING

96

96