fNIRS研究設計流程

近紅外腦功能資料處理工作坊

http://www.ym.edu.tw/~cflu/CFLu_course_fnirsWorkshop.html

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講習內容安排

- 09:10~11:00 fNIRS原理簡介
- 10:10~11:00 fNIRS實驗設計
- 11:10~12:00 fNIRS探頭擺放設計與位置確認
- **12:00~13:30 用餐與休息**
- 13:30~14:20 fNIRS實驗操作技巧
- 14:30~15:20 fNIRS標準訊號處理流程
- 15:30~16:20 fNIRS數據結果呈現與相關性分析

神經活化生理機轉

Physiology of neural activity

Aspects of Neural Activity

Synaptic transmission
- Local field potential (LFP)
- Input to the neuron

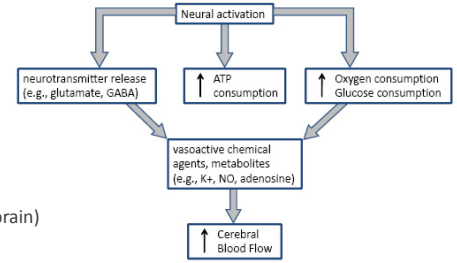
Action potentials (spikes)
- Output signals
- Permit communications between neurons

Neurovascular Coupling

ATP is essential for neural activity
- Restoration of ionic gradients
- neurotransmitter recycling

Glycolysis
- a small amount of ATP

Oxidative glucose metabolism (90% in brain)
- a large amount of ATP



Cerebral metabolism depends on a constant supply glucose and oxygen

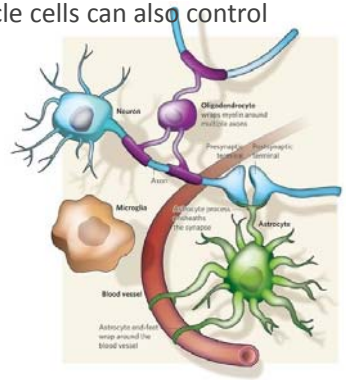
Neuroovascular coupling, scholarpedia.

Neurovascular Coupling

Multiple mechanisms…
- Astrocytes links neurotransmitter activity (glutamate cycling) to vascular responses.
- Direct neuronal innervation of smooth muscle cells can also control blood flow.

Requirement of metabolic nutrients

Elimination of waste products
- CO2 and excessive heat



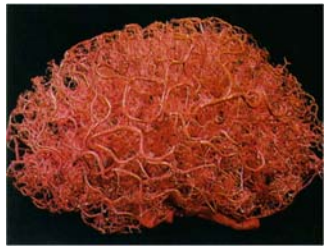
Neurovascular Coupling

A continuous supply of energy substrates is maintained by CBF

Neural activity
- Blood perfusion via capillaries ↑
- regional cerebral blood flow (rCBF) ↑
- regional cerebral blood oxygenation (rCBO) ↑

Changes in rCBF or rCBO can be used to map brain activity
- Functional neuroimaging

Brain vascular system: glucose and oxygen

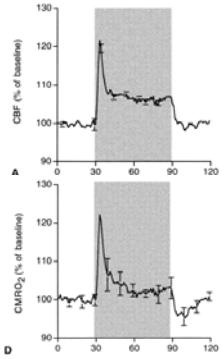


Zlokovic & Apuzzo, 1998.

CBF and O2 Consumption Mismatch

During neural activity…
- The fractional increases in CBF and glucose comsumption are similar in magnitude.
- Oxygen consumption increases much less than CBF.

➔ A net increase of oxygen in the blood and tissue.



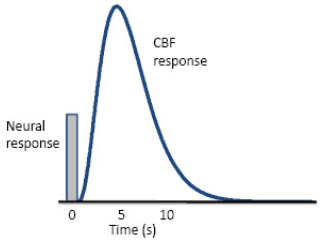
CMRO2: cerebral metabolic rate of oxygen

Ances et al., JCBFM 2001.

Coupling Properties

Use of vascular responses to infer neural activity

- **Time**: lack of temporal information in vascular response
- **Space**: focal activation of neurons ⇔ local vascular response?
- **Amplitude**: linear relationship?

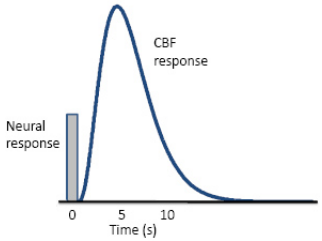


Coupling Properties: Time

CBF vs. neural activation

- Delayed by 1 ~ 2 s
- Peaks 4 ~ 6 s after the neural response

Fast modulation of neural activity is unlikely to be reflected in the vascular response.



- slow reaction of smooth muscle cells
- slow diffusion and uptake of neurovascular mediators

Coupling Properties: Space

Spatial resolution of the vascular response

Vascular point spread function (PSF)

- 1~5 mm
- Depends on imaging conditions: monitoring tech., magnetic field, pulse sequence, species, and brain regions.

Gray matter,

- densest network of capillaries, intervessel distance of ~ 25 μm

Coupling Properties: Amplitude

In general, amplitude coupling appears to be largely linear.

- For stimulus durations larger than 4 s

Various nonlinearities have been noted

- neural responses below a certain amplitude may not evoke a CBF response
- neural responses may saturate, while vascular responses continue to increase

Alteration Factors

Disease
- the chemical mediators
- the dynamics of the vascular system
- hypertension, diabetes, and AD alter Ionic channels on vascular smooth muscle

Aging
- change the vascular system
- increasing tortuosity or reducing elasticity of the blood vessels

Pharmacology
- Diazoxide is used as a vasodilator →large vascular responses with little or no change in neural activity.
- Hypercapnia (the concentration of CO_2 in the blood ↑) → vasodilation.

實驗設計
Experimental Design

Reference: *Basics of Experimental Design for fMRI: Block Designs & ER designs* http://www.fmri4newbies.com

Concept of Exp. Design

If neuroimaging is the answer, what is the question?
- Stephen M. Kosslyn (1999). *Phil Trans R Soc Lond B*.

Is your study designed to answer questions about the functioning of the brain?

Does your study bear on specific questions about the roles of particular brain regions?

Considerations in fNIRS

The foreknowledge of the location

The expected characteristics of the activation signal

The specific hypothesis addressed by the study

➔ Block design or Event-related (ER) design ?

Location of activation

Limited source and detector optodes

Limited to the outer layers of the brain (approximately 5-8 mm)

The depth sensitivity may be adjusted based on the source-to-detector distance

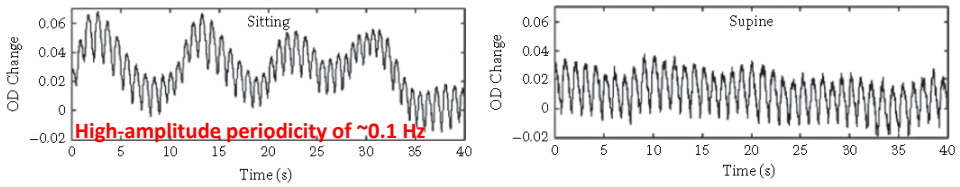
- Visual cortex vs. prefrontal cortex

Baseline Recording

without stimulation

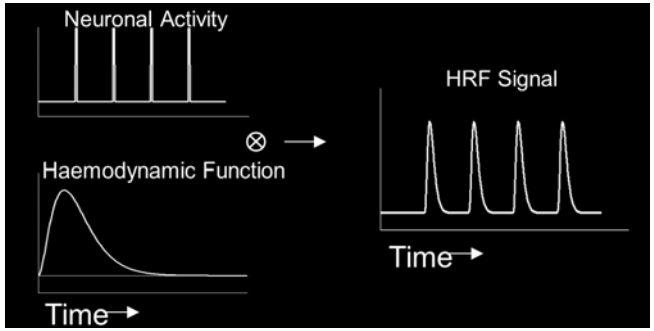
Eye-closed resting for a subject

- 830nm, at C3 location
- The Mayer wave (~0.1 Hz), a systemic blood pressure oscillation, is more prominent when stand ing or sitting
- Vascular physiology, vasomotion or autonomic regulation

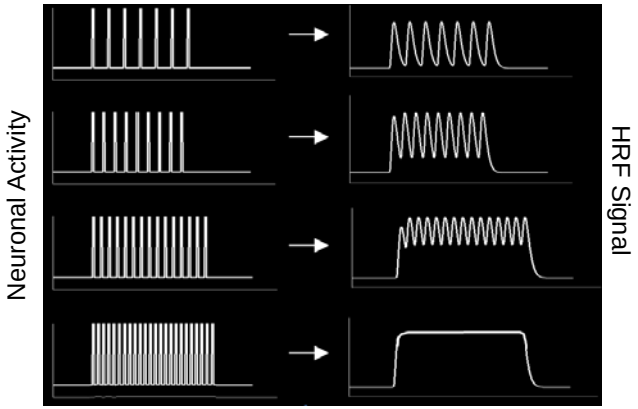


Convolution of Single Trials

Anticipated temporal profile of HRF



Convolution of Single Trials

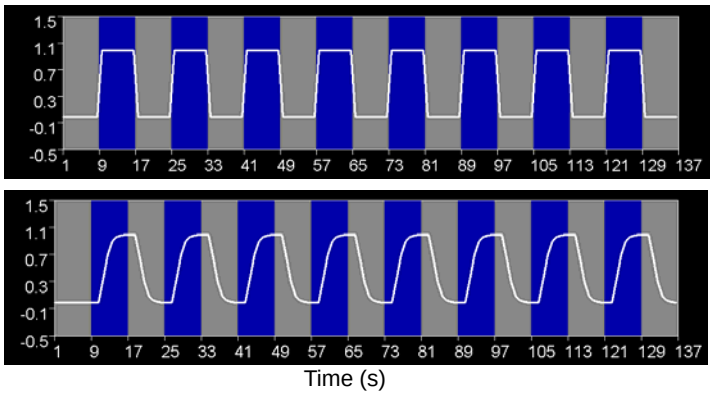


Temporal dynamics of signal

Block design

raw time course

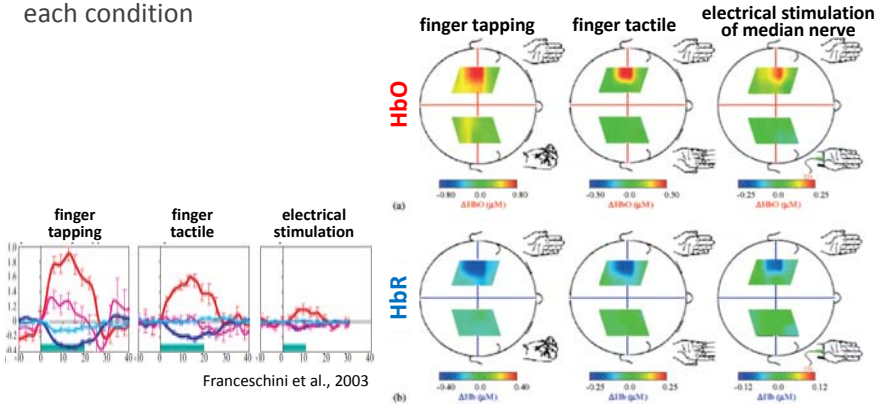
HRF-convolved time course



fNIRS evoked response

Blocked design

alternated stimulation periods (20s) and rest periods (20s), 10 blocks for each condition



Franceschini et al., 2003

Statistical Power

The probability of rejecting the null hypothesis when it is actually false

- if there's an effect, how likely are you to find it?

Effect size
- More trials/blocks

Sample size
- More subjects, more runs

Signal to noise ratio
- Careful setup, fewer artifacts

➔ increase power

Put conditions in a run

As far as possible, put the two/all conditions you want to compare within the same run.

Why?
- subjects get drowsy and bored
- Instrumentation may have different amounts of noise from one run to another (e.g., baseline shift)
- May cause stats differently between runs

Experiment Duration

Short enough that the subject can remain comfortable without unnecessary moving or distraction

Long enough that studied condition can be included in run

- Simplify the task condition, usually 2~6 conditions
- At least 3 repetition for each condition
  -

Ideal duration is between 10 to 30 minutes

Block Design

Repeating Sequence

We could just order the epochs in a repeating sequence…

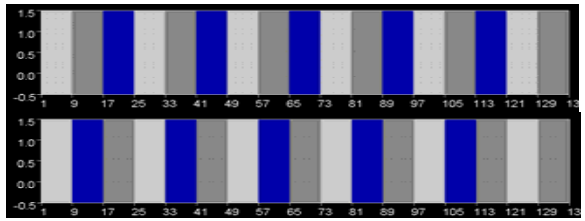
Problem: There might be order effects (especially for cognitive study)

Solution: Counterbalance with another order

Caution: remember the order !

repeating sequence

counterbalance

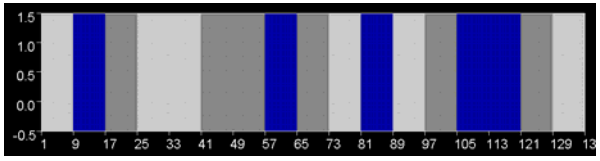


Block Design

Random Sequence

We could make multiple runs with the order of conditions randomized…

Problem: To avoid flukiness, you'd want to have different randomization for different runs and different subjects, but then you're going to spend ages defining protocols for analysis



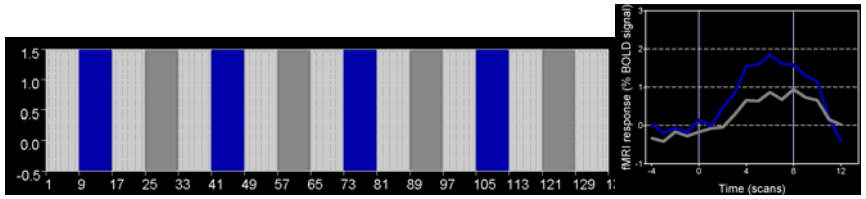
Block Design

Regular Baseline

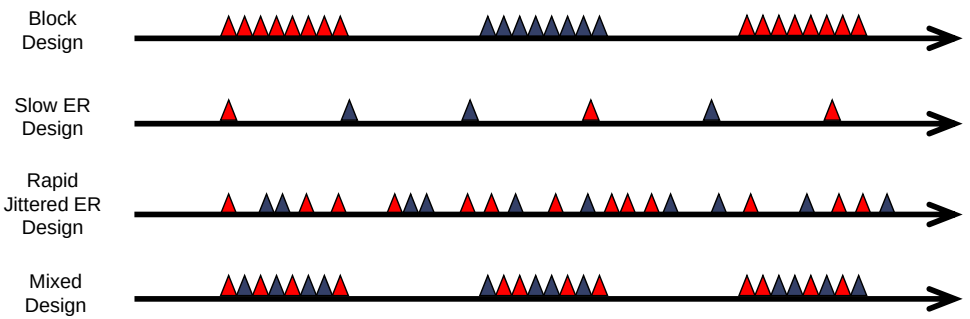
A fixation baseline between all stimulus conditions (either with regular or random order)

Benefit: With event-related averaging, this regular baseline design provides nice clear time courses, even for a block design

Problem: Spending half of scan time collecting the condition you care the least about



Design Types



Block Designs

Pros & Cons

Pros

- high detection power (identify channels of activation)
- has been the most widely used approach
- accurate estimation of hemodynamic response function is not as critical as with event-related designs

Cons

- poor estimation power (measure the time course of Hb)
- subjects get into a mental set for a block
- very predictable for subject
- can't look at effects of single events (e.g., correct vs. incorrect trials, remembered vs. forgotten items)
- long experiment duration with too many conditions (e.g., more than 4 conditions + baseline)

Slow Event-Related Designs

Pros & Cons

Pros

- excellent estimation
- useful for studies with delay periods
- very useful for designs with motion artifacts (grasping, swallowing, speech) because you can tease out artifacts
- analysis is straightforward

Cons

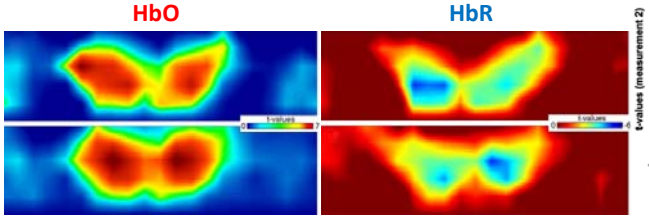
- poor detection power because you get very few trials per condition by spending most of your sampling power on estimating the baseline
- subjects can get VERY bored and sleepy with long inter-trial intervals

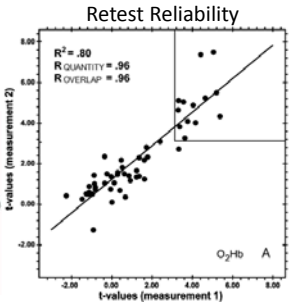
Reliability of ER fNIRS

a simple checkerboard for 1200 ms reversing in contrast at 6 Hz followed by 13.8 s of a black screen presentation

number of trials was set to n = 60

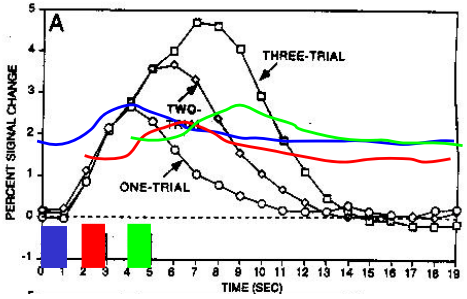
retest interval = 3 weeks





Plichta et al., 2006

Linearity of BOLD signal



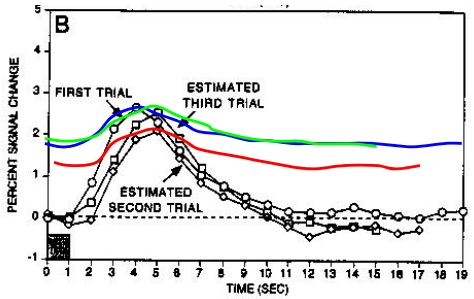
Linearity:
"Do things add up?"

red = 2 - 1

green = 3 - 2

Dale & Buckner, 1997

Linearity of BOLD signal



Sync each trial response
to start of trial

Not quite linear but good enough!
(with interval of 2~4 s)

Dale & Buckner, 1997

Similar Concepts can be applied to fNIRS signals.

Design Steps

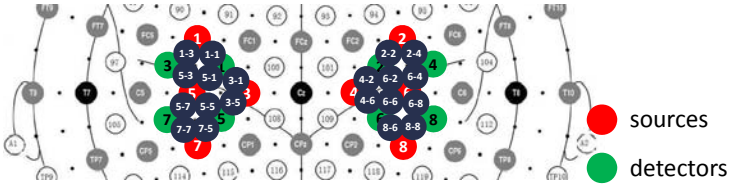
Participants' tolerance
- Age, disease …

Study aims
- Target Locations
- Number of conditions
- Anticipated signals

Experiment paradigm
- S-D arrangement, number of channel
- Block design or event-related design
- Task instruction & stimulation delivery

Log sheet
- Name, gender, age, history number/ID, habitual hand, study group
- Experiment paradigm and notation

Bilateral Arm lifting



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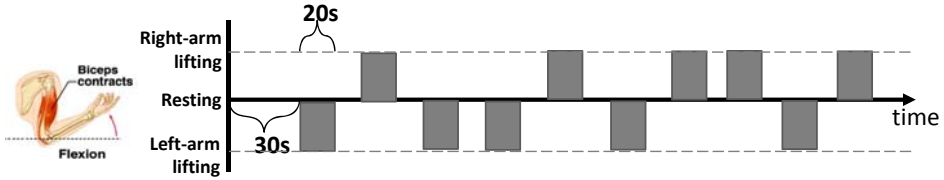
5-3	5-1	3-1	4-2	6-2	6-4
5-7	5-5	3-5	4-6	6-6	6-8
7-7	7-5			8-6	8-8

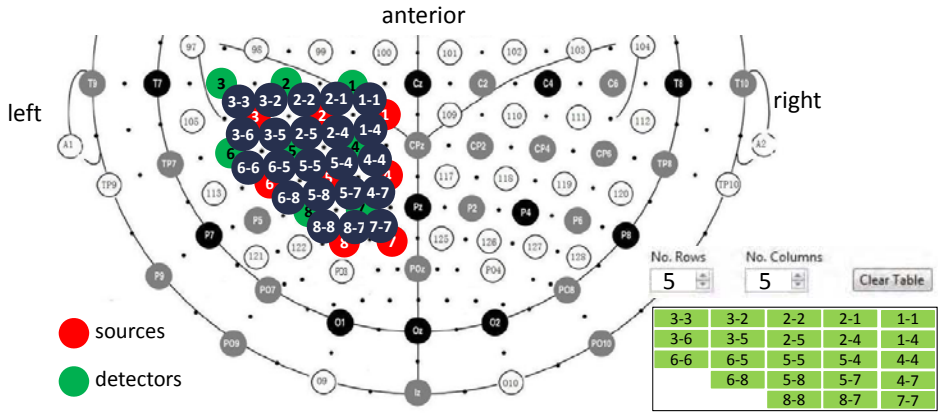
Block design diagram

Baseline	Relax and sit on an armchair (30s)	
Experiment I	Right-arm lifting (20 s)	**(Overall ~7.2 mins)**
Rest interval	Relax and sit on an armchair 20 s)	
Experiment II	Left-arm lifting (20 s)	

※Experiment States were marked by "**F1**" and Rest intervals were marked by "**F3**"



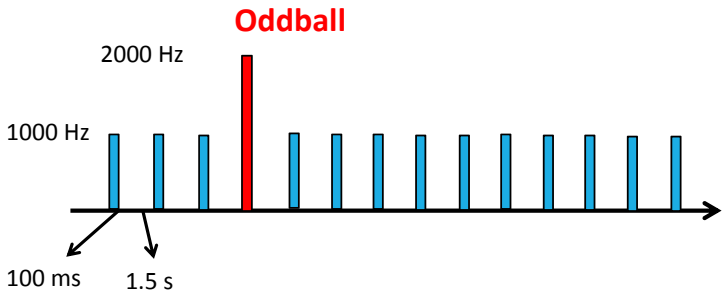
Oddball task



Event-Related design

12 oddball events (8% of total number)

3~6 regular tones before, and 10 after oddball



盧家鋒 **Chia-Feng Lu, PhD**

Q & A

Thanks for your attention :)