Experimental Design

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SNSF Research Fellow, University College London

SPM course 2026



Experimental Design & Good Research



Research Question

what process do I want to measure

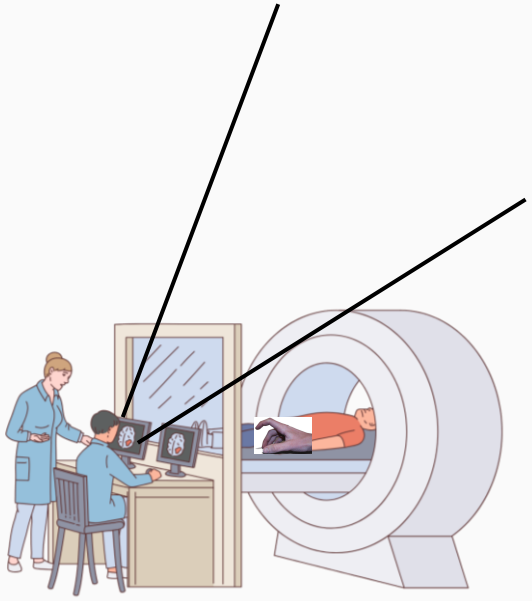


Experimental Design

how to measure that process?

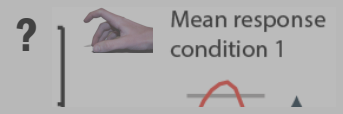
Why do we need a good design?

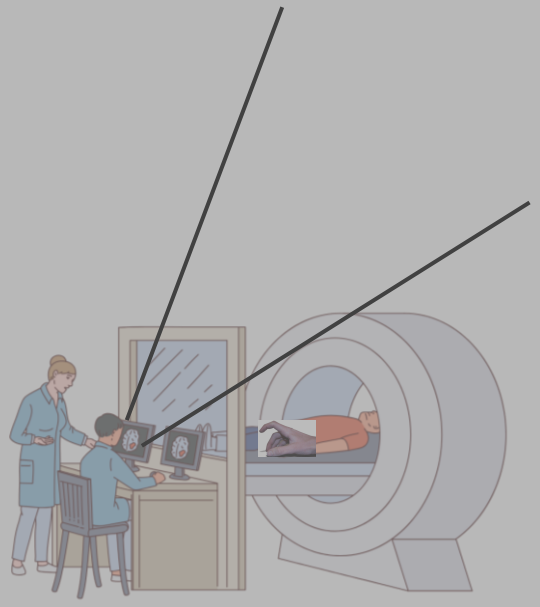




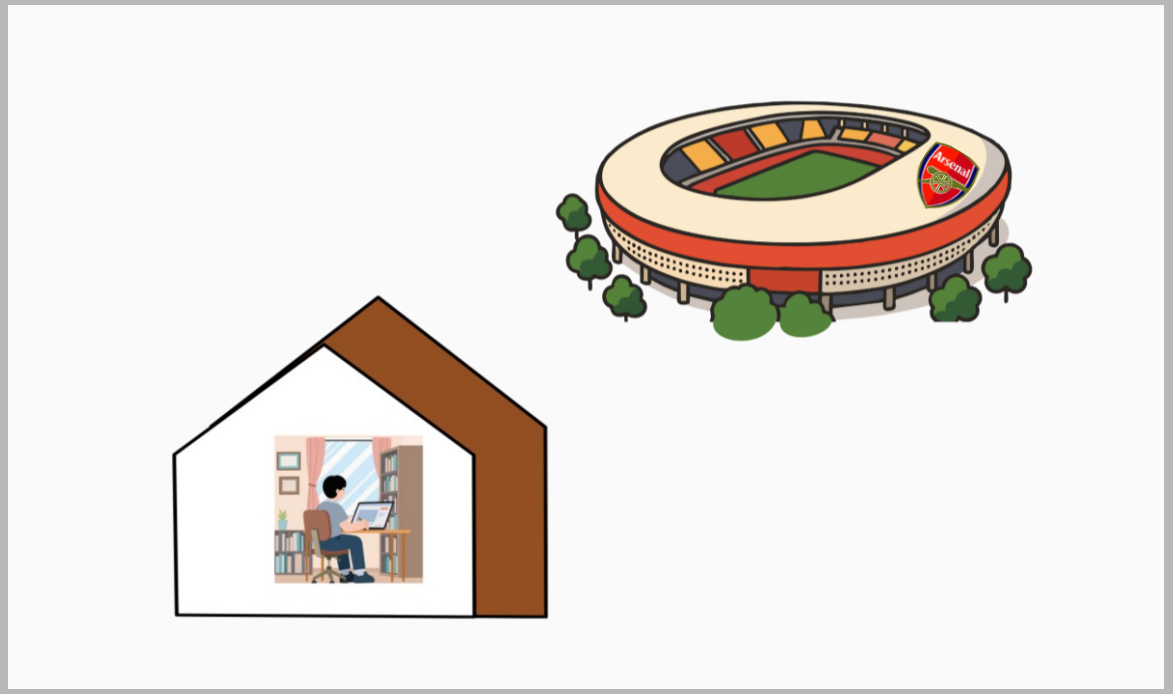
The BOLD signal is <u>not</u> an absolute measure of neural activity.

Why do we need a good design?

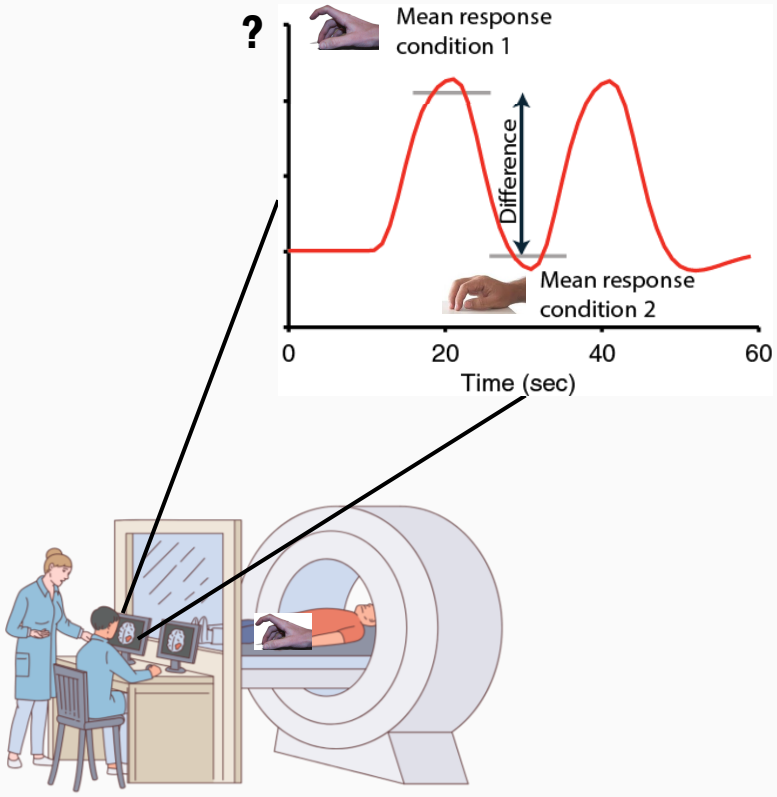




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Why do we need a good design?



The BOLD signal is not an absolute measure of neural activity.

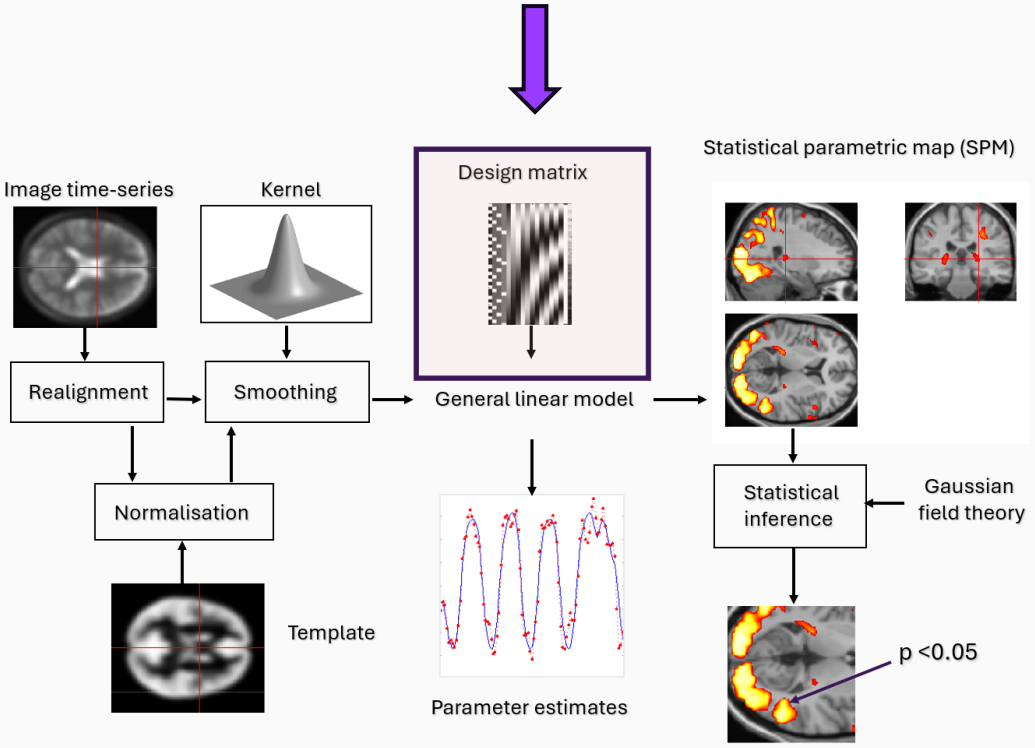
=> Hence, we must compare activity across conditions.

Capturing the process of interest depends on how much you can maximise the difference in activity between two conditions

(i.e. design sensitivity)

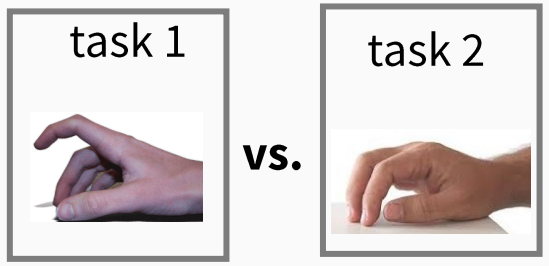
When to think about the experimental design?





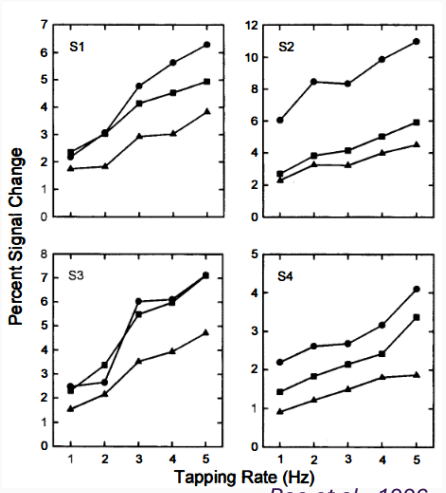
Nothing beats a good experimental design!!

Types of experimental design



Categorical

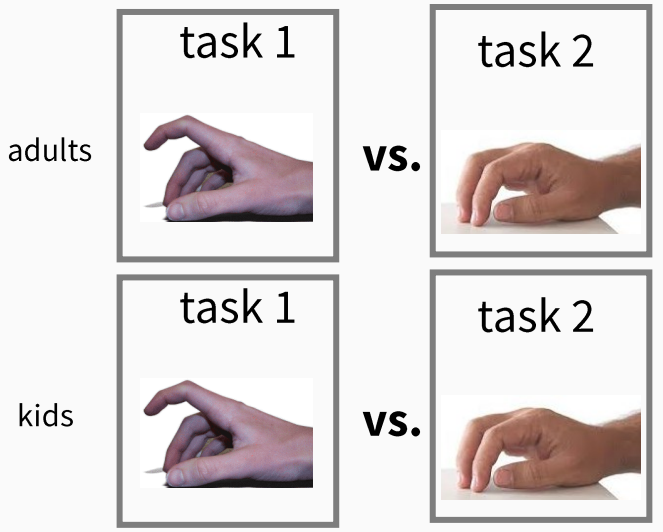
Which brain regions differentiate two conditions?



Rao et al., 1996

Parametric

Which brain regions show systematic relationship with the "amount" of the process of interest?



effect of age on finger tapping-induced brain activation

Turetsky et al., 2018

Factorial

Does the effect of a condition on brain activation, as compared to another task, change between different contexts?

Types of experimental design

Subtraction: handles the baseline challenge assuming pure insertion

Conjunction: test multiple hypotheses and isolates effects

Linear and non-linear: adaptation, cognitive dimension, and more

Model-based: many applications, e.g. tracking underlying variables

Interactions, baselines, linear/non-linear interactions

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A vs B

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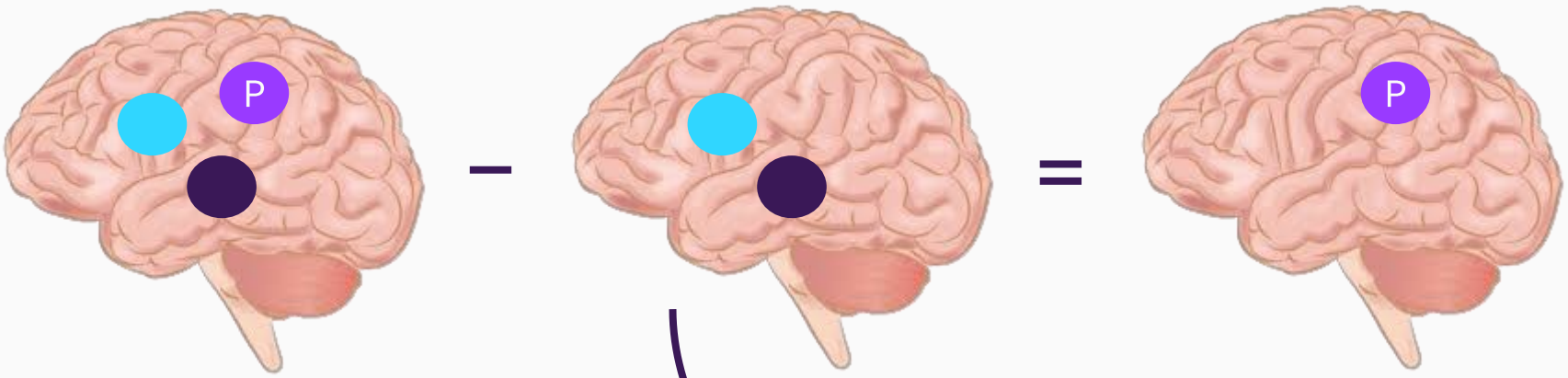
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Categorical Design

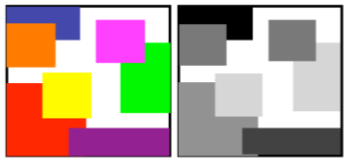
• SUBTRACTION

Research Question: Identify the neural structures related to a *single* process P

Procedure: Contrast a task *with* P, against a task *without* P

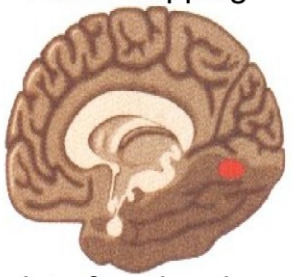


A nice example:



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

Brain mapping



Isolate functional area

Bishop, 2014

Categorical Design

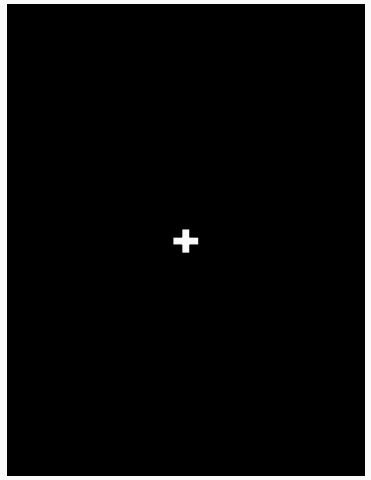
• SUBTRACTION

Control conditions



(Task: name?)

Different stimuli and task



(Control: none)

rest is never truly rest: mind-wandering, thinking about the task, not actually controlling for other processes, etc

Research Question: Which neural structures support face recognition?

Control: How to find a baseline that activates all processes aside from face recognition?

Categorical Design

- **SUBTRACTION**

Control conditions



(Task: name?)

Different stimuli but same task



(Control: name?)

object type is so different there is no control for face perception

Research Question: Which neural structures support face recognition?

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Categorical Design

• SUBTRACTION

Control conditions



(Task: famous?)

Same stimuli <u>and</u> same task



(Control: famous?)

Research Question: Which neural structures support face recognition?

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Categorical Design

- **SUBTRACTION**

Control conditions



(Task: famous?)

Same stimuli <u>and</u> same task

participants might start thinking hard about whether they know a the "non-famous" face



(Control: famous?)

Research Question: Which neural structures support face recognition?

Control: How to find a baseline that activates all processes <u>aside from</u> face recognition?

Categorical Design

- **SUBTRACTION**

Control conditions



(Task: name?)

(Exactly) same stimuli but different task



(Control: gender?)

likely to have implicit "face recognition", potential interactions

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Categorical Design

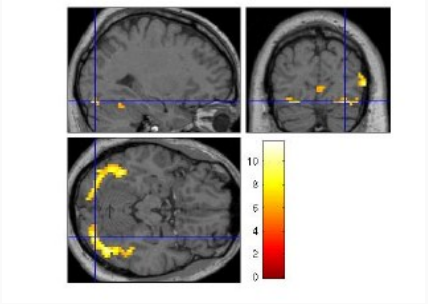
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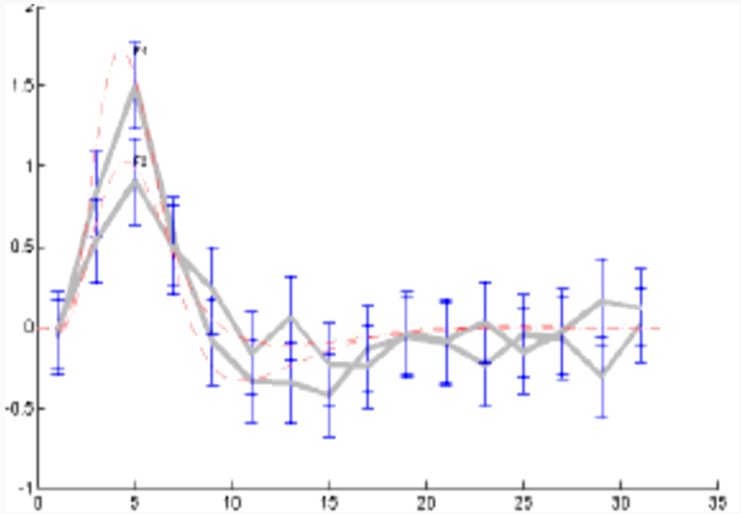
(Task: name?)



(Control: gender?)



Habituation over time: Repeated stimuli exposure over time decreases activation



stimulus time

/ to have implicit "face
on", potential interactions

Research Quest

Control: How to find a baseline that activates all processes aside from face recognition?

Categorical Design

- **SUBTRACTION**

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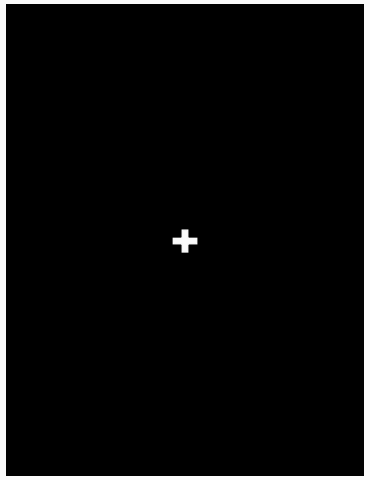
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Categorical Design

- **SUBTRACTION**

Control conditions


(Task: name?)


(Control: none)



(Control: name?)


(Control: famous?)


(Control: gender?)

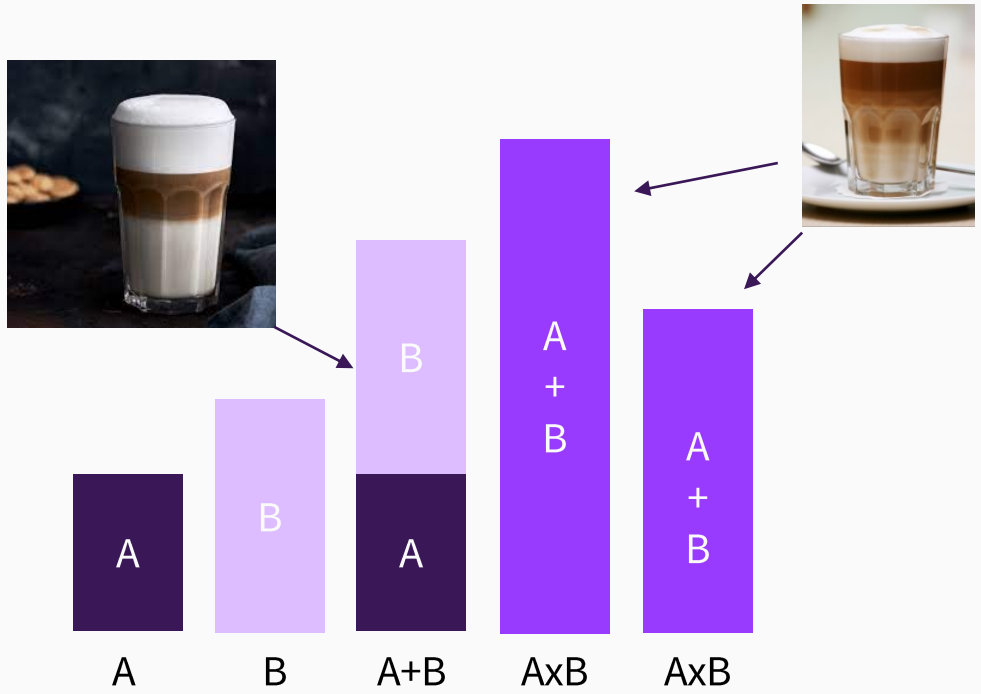
Research Question: Which neural structures support face recognition?

Depending on which control task you choose you experimental design will answer different research questions!

Categorical Design

• SUBTRACTION

Problem: Subtraction assumes that (1) cognitive components can simply be added and (2) there are no interactions between said components

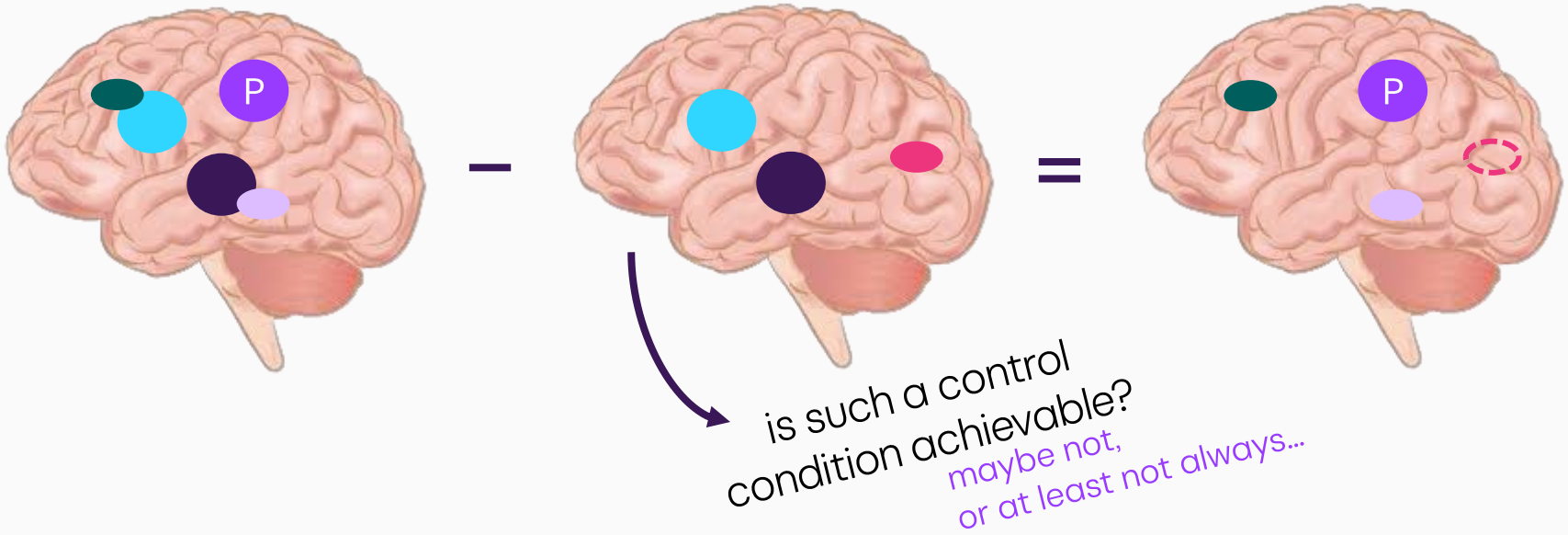


Example thanks to Dr. Carolin Moessnang (previous lecturer)

Categorical Design

• SUBTRACTION

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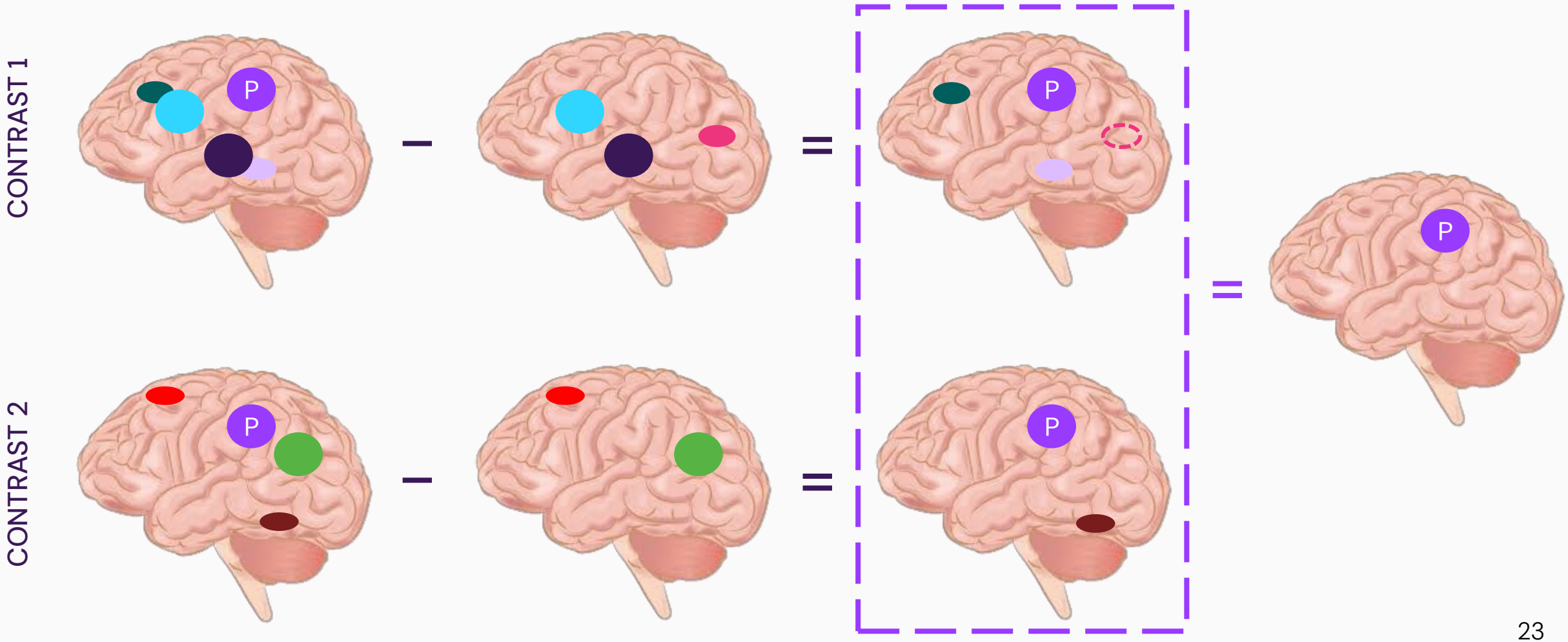
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Categorical Design

- CONJUNTCTION



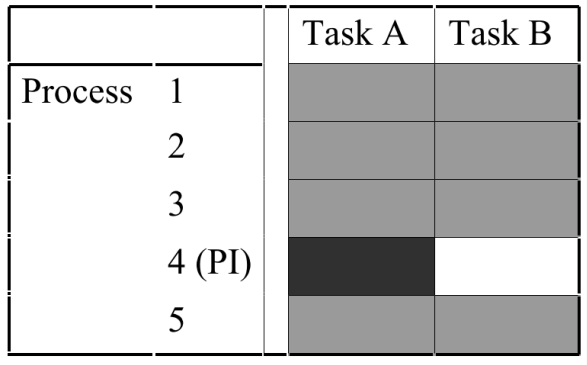
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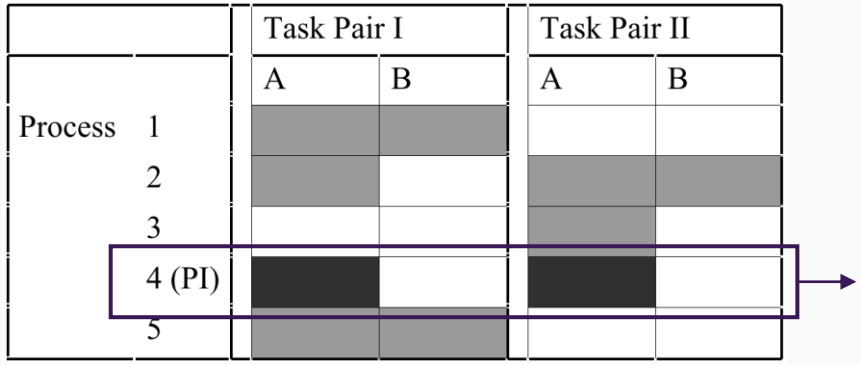
Procedure: Isolate the same cognitive process via two or more separate contrasts, hence identifying the context-invariant activation associated with process P

Subtraction



(very hard to find such a control)

Conjunction analysis



Only the process of interest (P4) is common to all task pairs!

Categorical Design

• CONJUNTCTION

Example

Research Question: Identify the neural processes that support phonological retrieval .



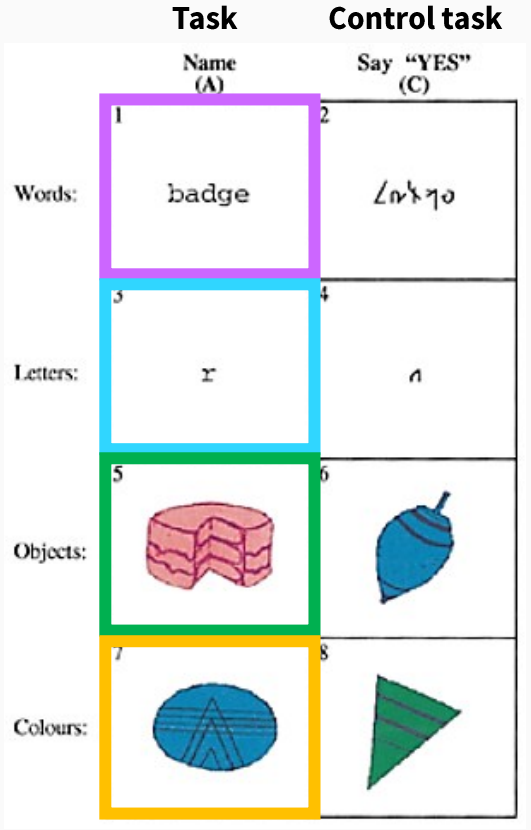
Visual analysis

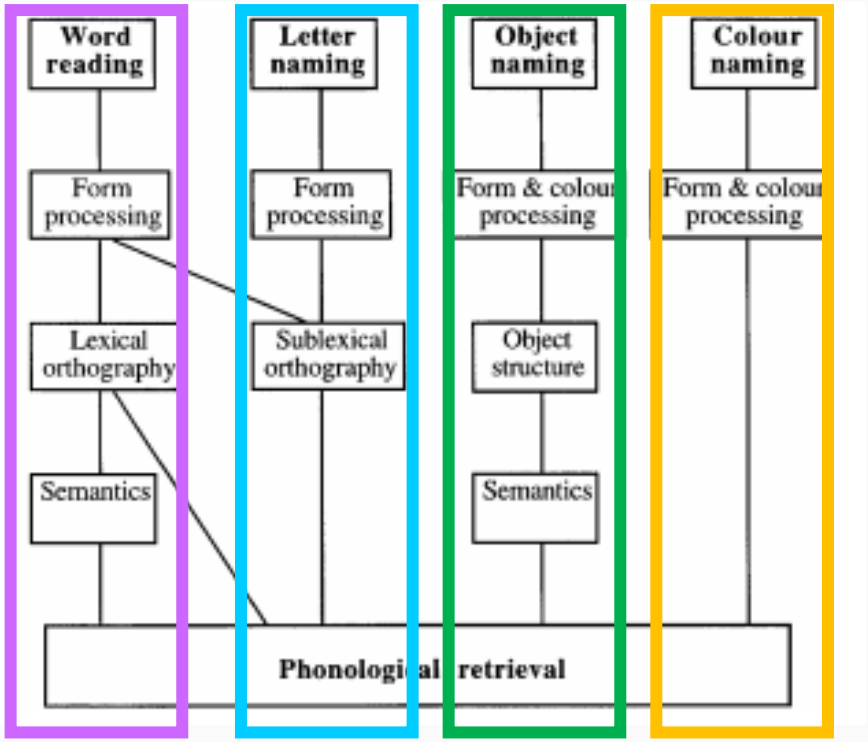
Categorical Design

- **CONJUNTCTION**

Example

Research Question: Identify the neural processes that support phonological retrieval.





Price & Friston (1996)

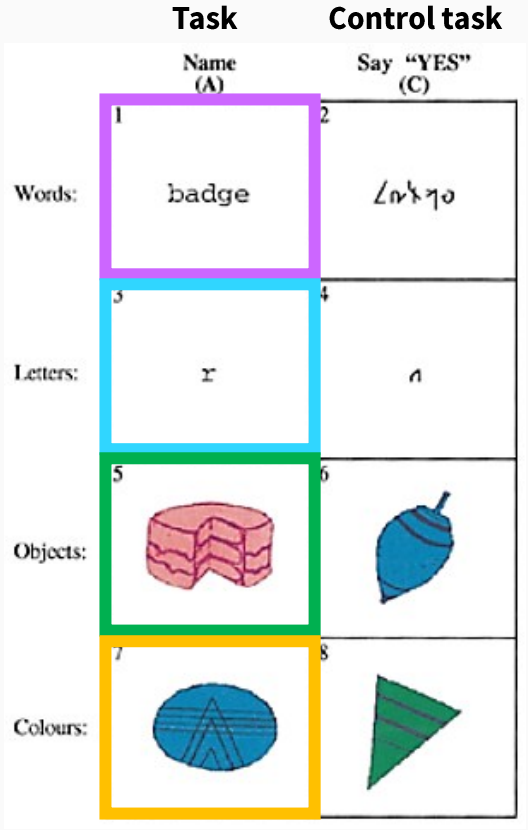
Phonological retrieval is the only cognitive component common to all task-pair differences.

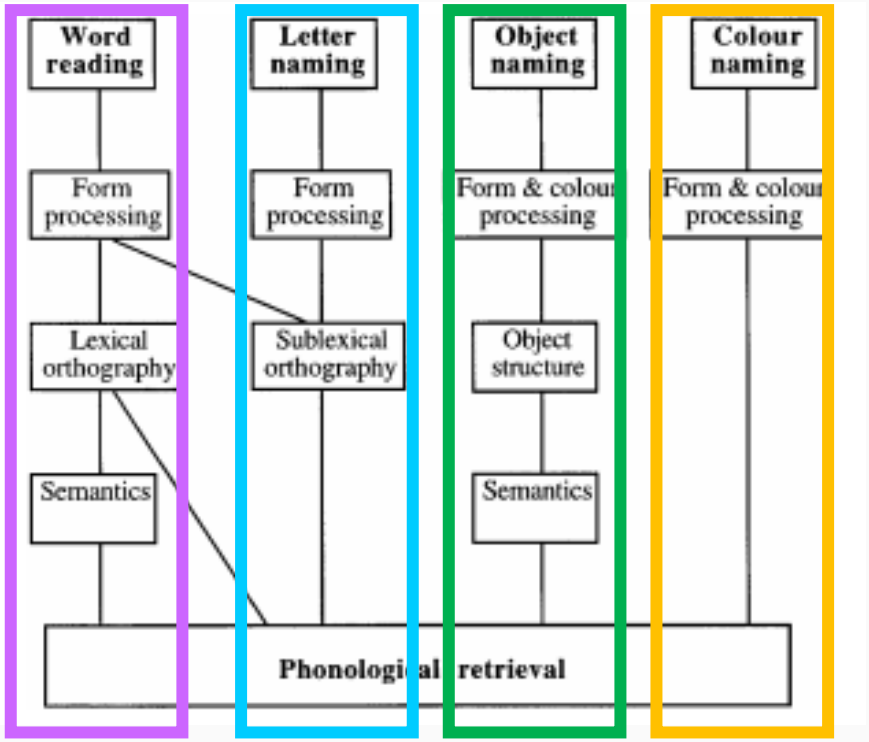
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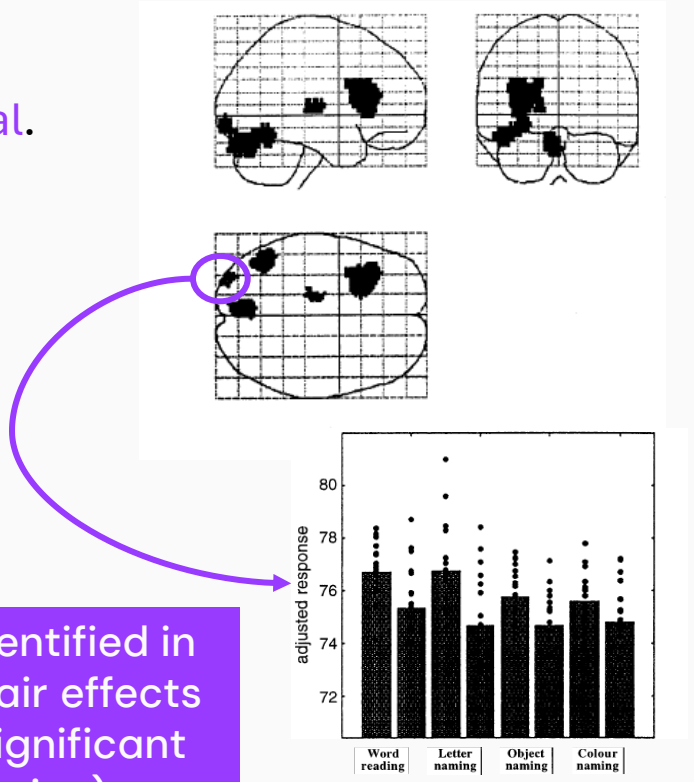
- **CONJUNTCTION**

Example

Research Question : Identify the neural processes that support phonological retrieval.







Areas are identified in each task-pair effects are jointly significant (conjunction)

→ Associated with process of interest (phonological retrieval)

Price & Friston (1996)

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Parametric Design

- (NON-)LINEAR RELATION

Research Question: Does activity in a region vary systematically with a continuous change in a condition?

Procedure: Varying a stimulus parameters in a continuum (e.g. steps of 2) and relating that to BOLD



(linear)



(polynomial)



(behavioural readouts)

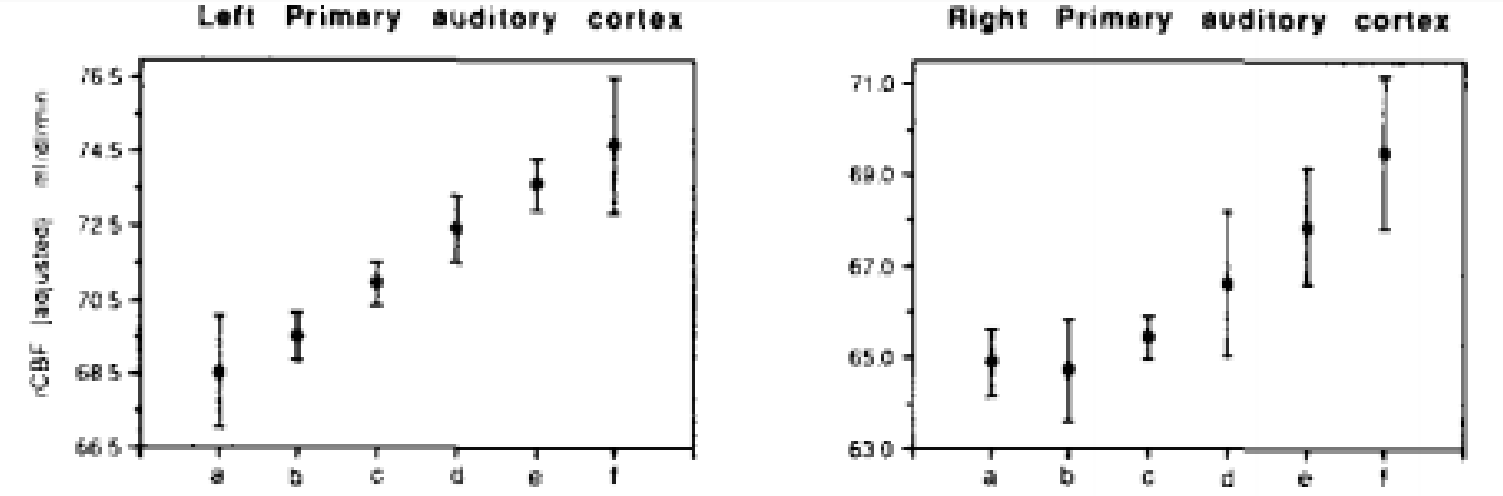
Advantage: Avoids pure insertion by not inserting new processes. The baseline is the lowest level.

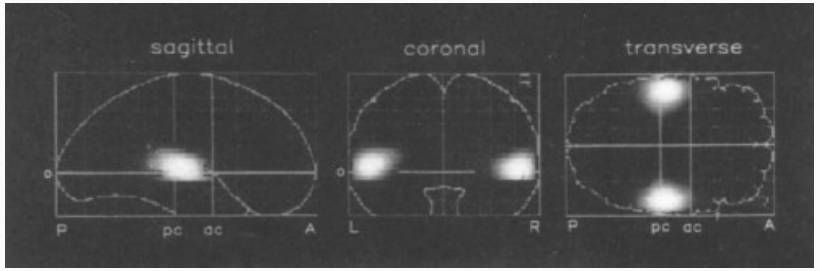
Parametric Design

- **LINEAR RELATION**

Auditory words presented at different rates (rest, 5 rates between 10wpm and 90 wpm)

Activity in primary auditory cortex is linearly related to word frequency





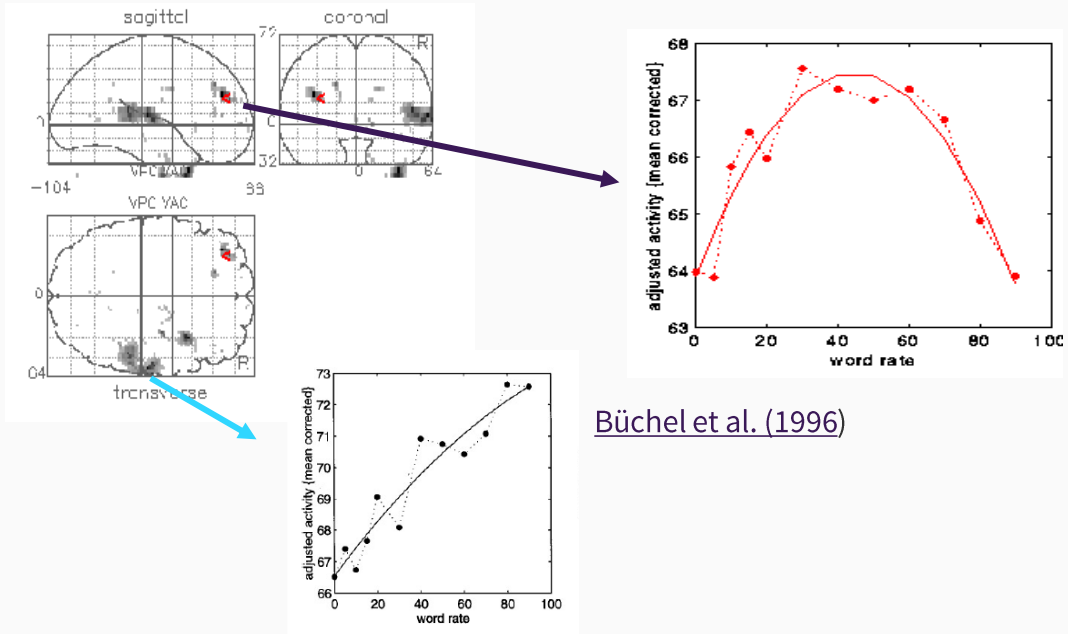
Price et al. (1992)

Parametric Design

- **NON-LINEAR RELATION**

Words presented at different rates but now to people who had a stroke and people who had not.

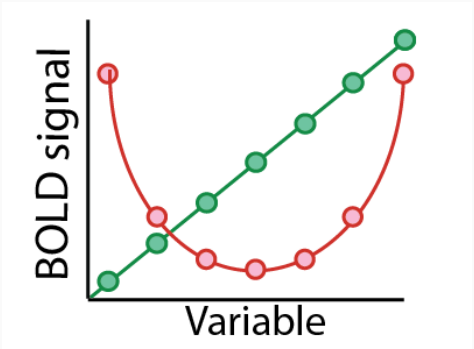
While activity increased linearly in healthy people, those who had a stroke showed a quadratic relation between words per minute and activation in the left prefrontal cortex



Büchel et al. (1996)

Polynomial expansion:
$f(x) = b_1 x + b_2 x^2 +$
...up to $(N-1)^{th}$ order for N levels

SPM offers polynomial expansion as option during creation of parametric modulation regressors.



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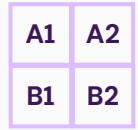
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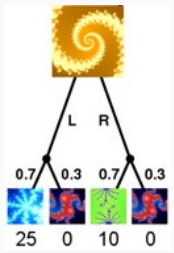


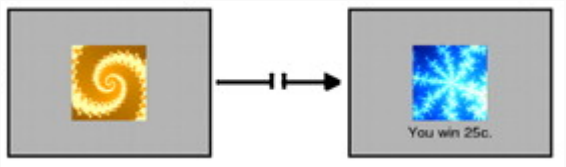
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Parametric Design

- **MODEL BASED**

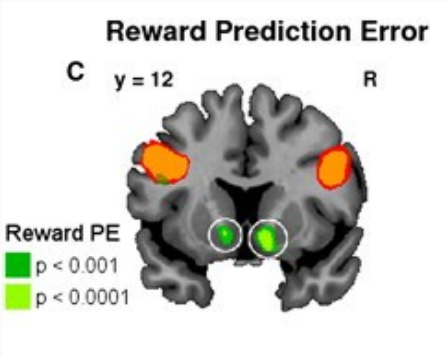
Signals derived from a computational model are correlated against BOLD, to determine brain regions showing a response profile consistent with the model, e.g. Rescorla-Wagner prediction error





Time-series of a model-derived reward prediction error





Gläscher & O'Doherty (2010) Gläscher et al. (2010)

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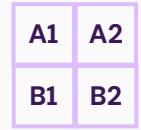
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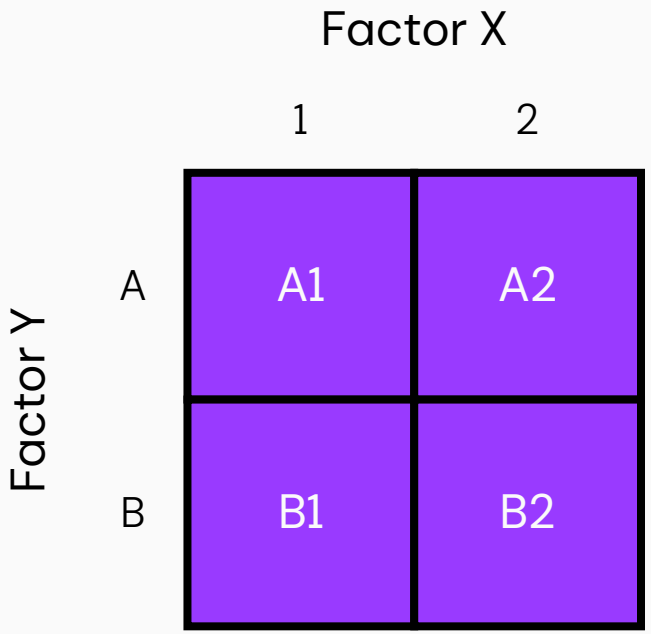
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Factorial



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Factorial Design



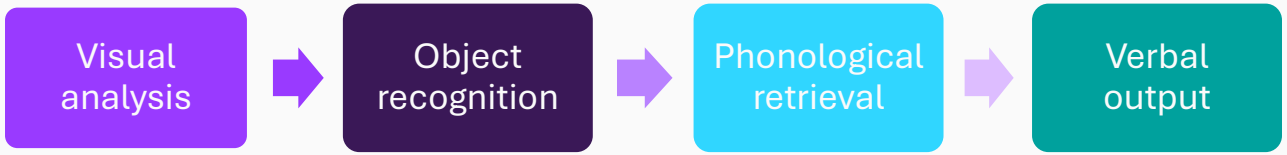
The most efficient type of design:

Can test main effects and interactions directly resolving the problem of pure insertion.

Factorial Design

Research Question: Is the inferiotemporal cortex sensitive to both object recognition and phonological retrieval of object names?





Factorial Design

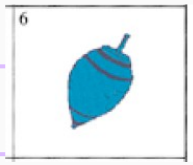
Research Question: Is the inferiotemporal cortex sensitive to both object recognition and phonological retrieval of object names?

A Say 'yes' when you see an **abstract image**



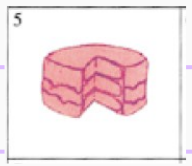
Visual analysis → Verbal output

B Say 'yes' when you see an **object**



Visual analysis → Object recognition → Verbal output

C **Name** the object



Visual analysis → Object recognition → Phonological retrieval → Verbal output

Price & Friston (1996)

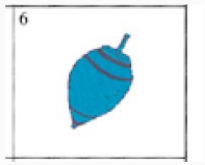
Factorial Design

Research Question: Is the inferiotemporal cortex sensitive to both object recognition and phonological retrieval of object names?

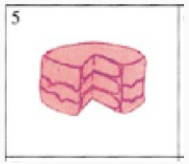
A — Say 'yes' when you see an **abstract image**



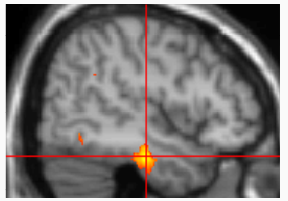
B — Say 'yes' when you see an **object**

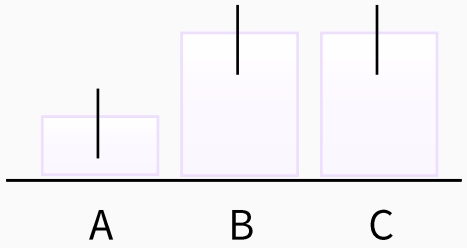


C — **Name** the object



Results in inferotemporal cortex: Friston et al., (1997)





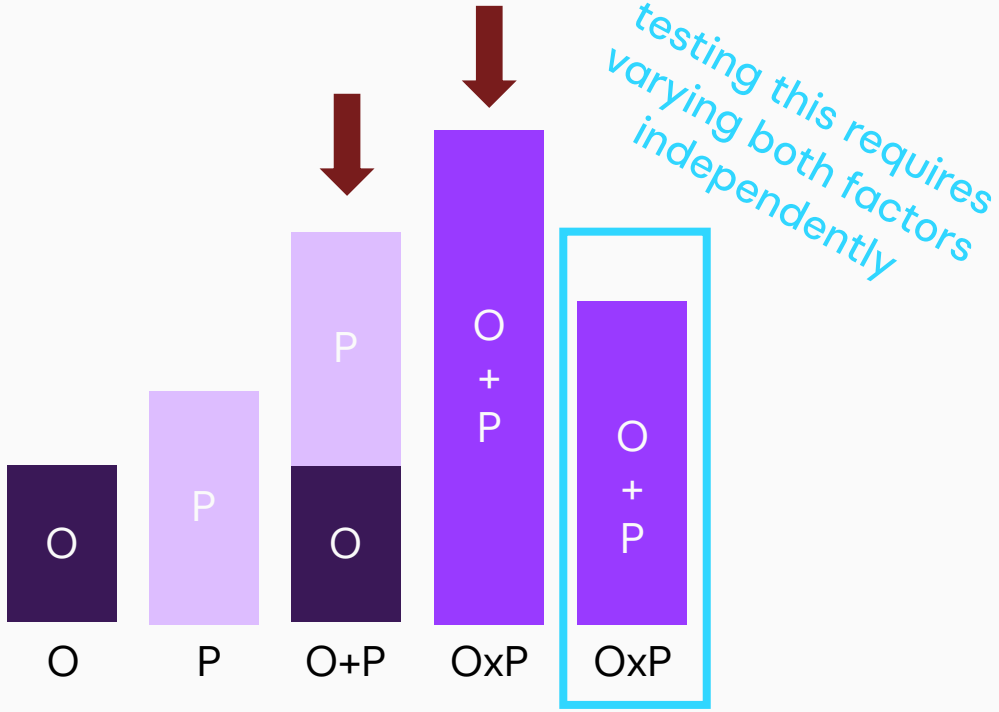
B	>	A	Object recognition
C	>	A	Object recognition in phon. retrv. context
C	=	B	IT not involved in phonological retrieval?!

Price & Friston (1996)

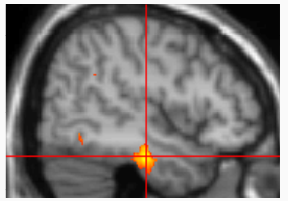
Factorial Design

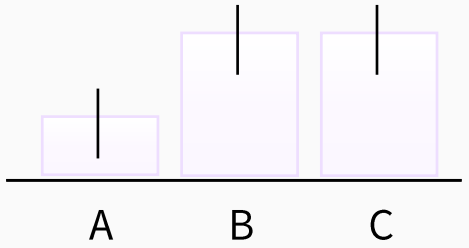
Research Question: Is the inferiotemporal cortex sensitive to both object recognition and phonological retrieval of object names?

Is the task a sum of its components or does O modulate P beyond what P is in isolation? *(or vice-versa)*



Results in inferotemporal cortex: Friston et al., (1997)





B	>	A	Object recognition
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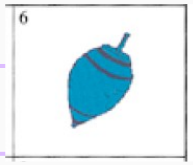
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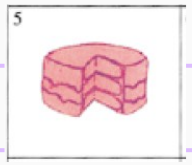
Visual analysis → Verbal output

B — Say 'yes' when you see an **object**



Visual analysis → Object recognition → Verbal output

C — **Name** the object



Visual analysis → Object recognition → Phonological retrieval → Verbal output

D — **Name** the colour



Visual analysis → Phonological retrieval → Verbal output

Phonological retrieval in the **absence** of object recognition

Price & Friston (1996)

Factorial Design

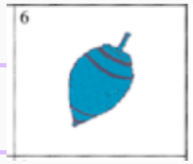
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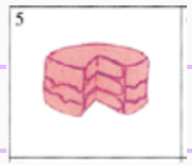
Visual analysis → Verbal output

B — Say 'yes' when you see an **object**



Visual analysis → Object recognition → Verbal output

C — **Name** the object



Visual analysis → Object recognition → Phonological retrieval → Verbal output

D — **Name** the colour

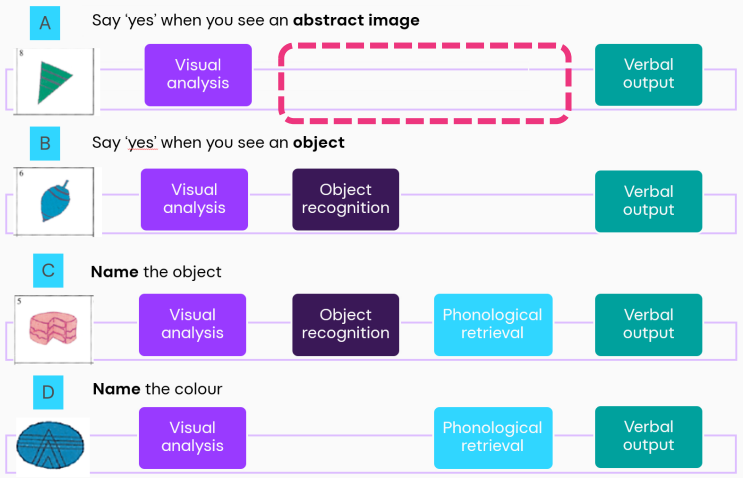


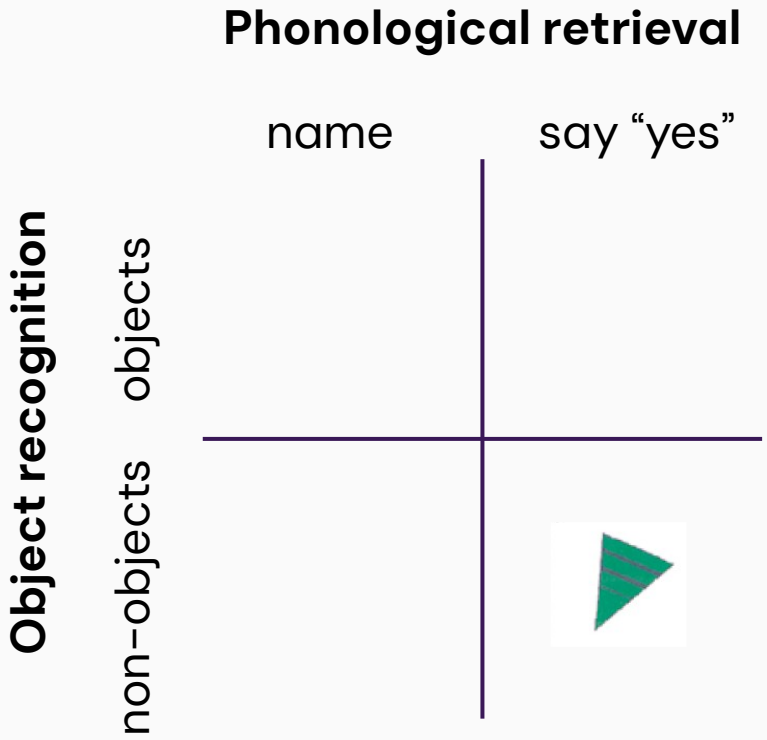
Visual analysis → Phonological retrieval → Verbal output

Phonological retrieval in the **absence** of object recognition

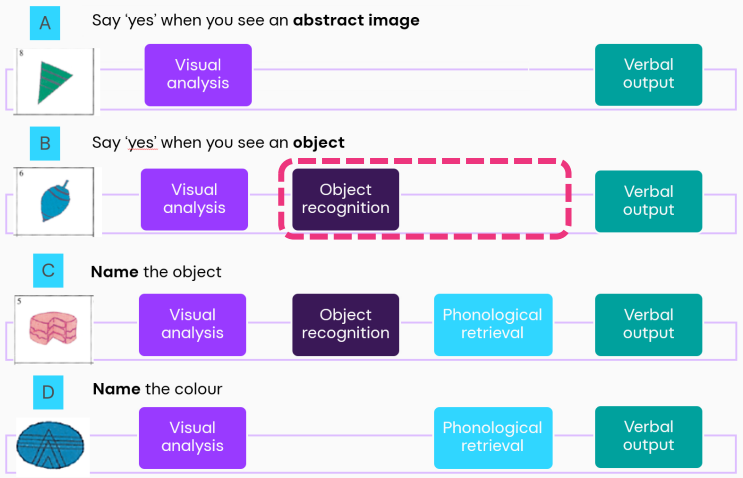
Price & Friston (1996)

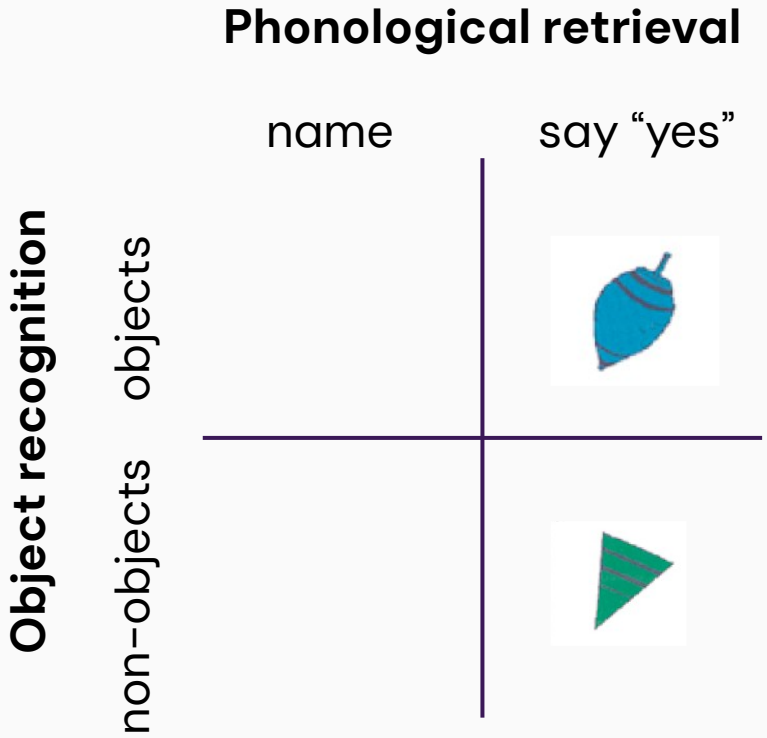
Factorial Design



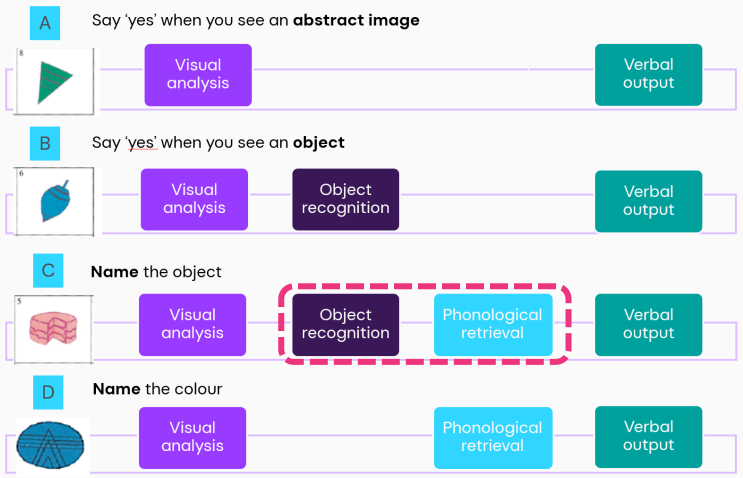


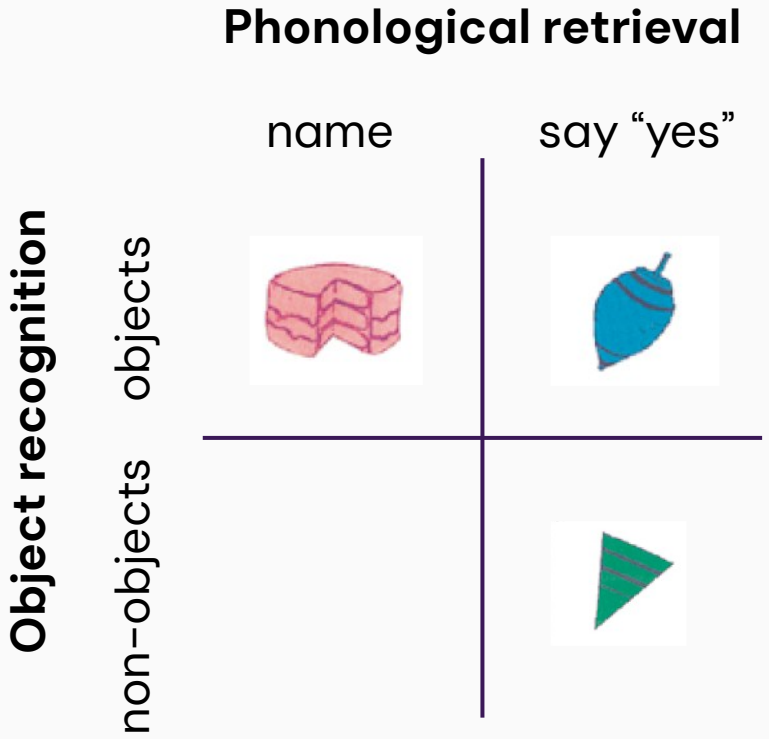
Factorial Design



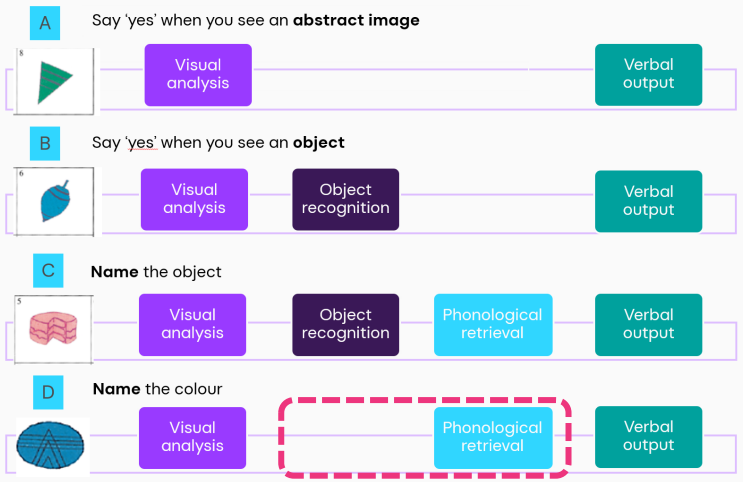


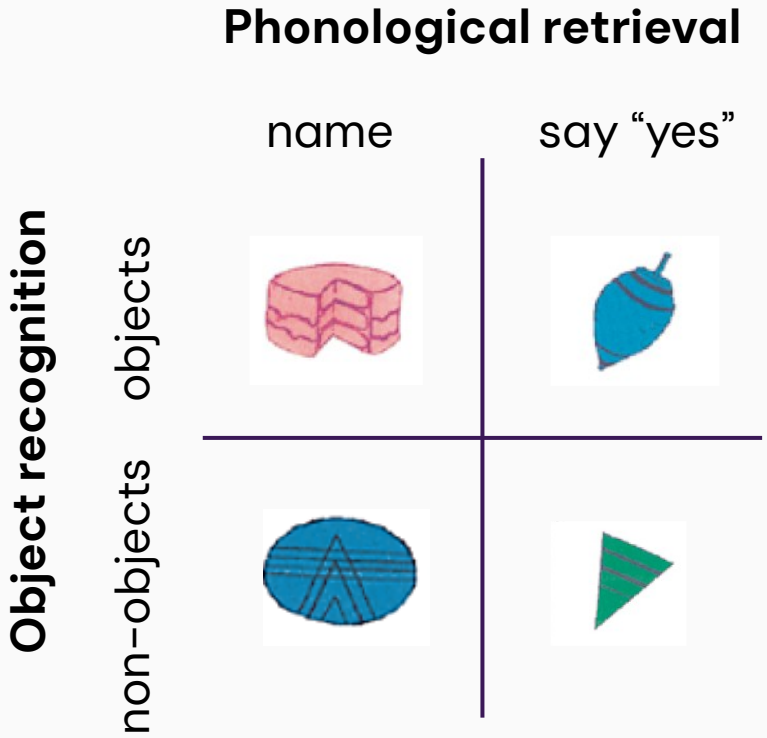
Factorial Design



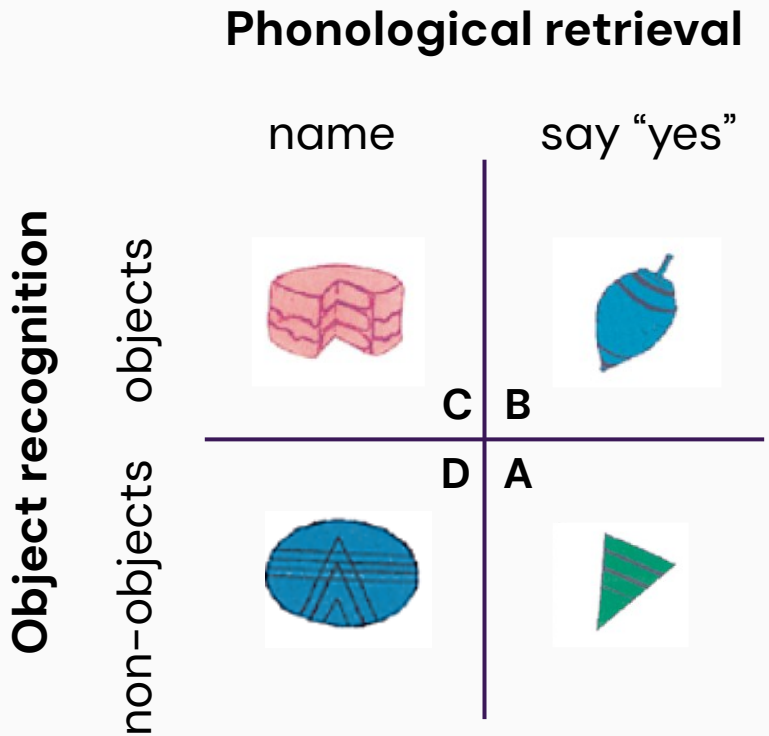


Factorial Design

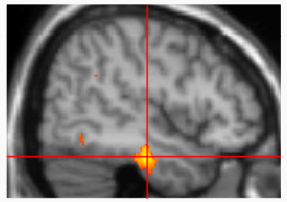


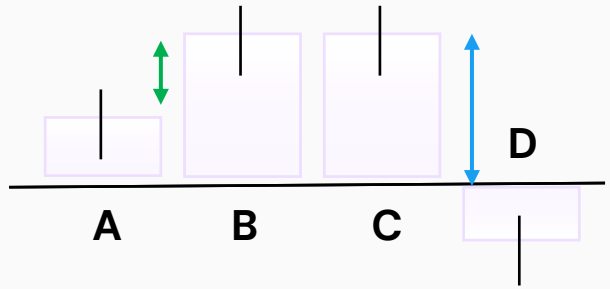


Factorial Design



Results





B > A Object recognition in the *absence* of phonological retrieval

C > D Object recognition in the *context* of phonological retrieval

Pure insertion: The activation for object recognition should be identical!

This is not true!

→ The inferotempral cortex shows a *stronger differentiation* between object and non-object *in the context of phonological retrieval*!

Factorial Designs & Parametric Interactions

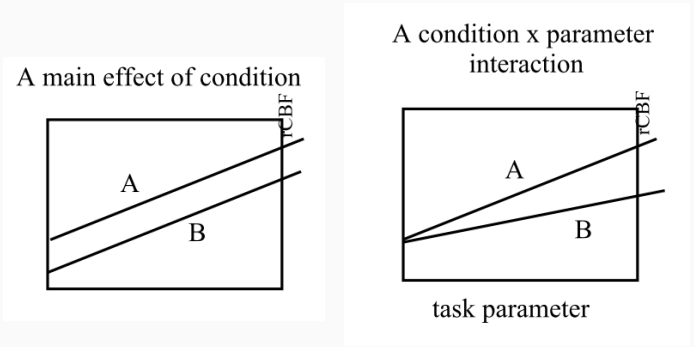
Research Question: How does neural activity change with word production rate for repeated vs new words?

A Producing new words

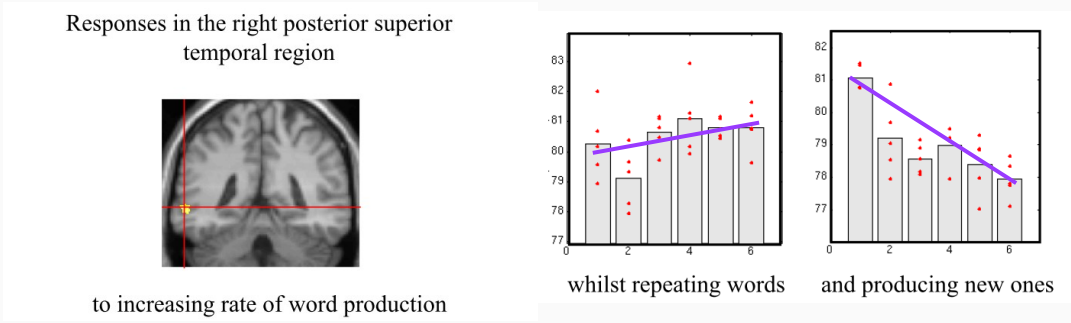
B Repeating the same word



Rate: words per min



(hypothesised effects)



(actual results)

Subtraction: handles the baseline challenge assuming pure insertion

Conjunction: test multiple hypotheses and isolates effects

Linear and non-linear: adaptation, cognitive dimension, and more

Model-based: many applications, e.g. tracking underlying variables

Interactions, baselines, linear/non-linear interactions

Categorical

A vs B

Which brain regions differentiate two conditions?

Parametric

AAAA

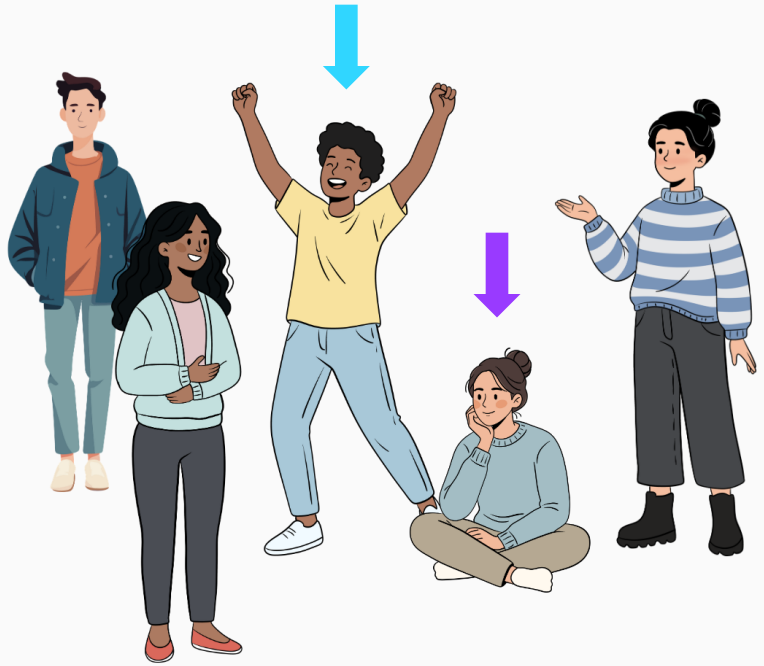
Which brain regions show systematic relationship with the "amount" of the process of interest?

Factorial

A1	A2
B1	B2

Does the effect of a condition on brain activation, as compared to another task, change between different contexts?

Extrinsic



Intrinsic

Intrinsic factors

Research Question: Which neural processes underpin distinguishing self from other voices?

Procedure: Participants hear a continuum of voice recording where their voice is mixed with a stranger and must identify if it's predominantly them or someone else.



assuming you already have the perfect design in everything we discussed prior, what may be a fatal flaw in this experiment?



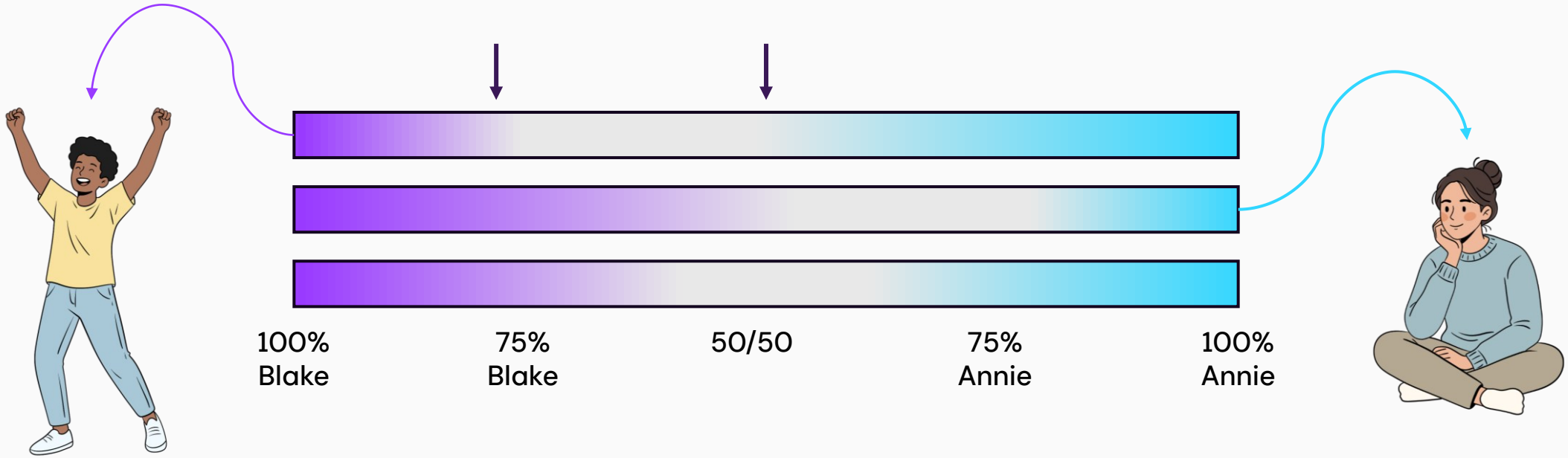
100% Blake | 75% Blake | 50/50 | 75% Annie | 100% Annie



Intrinsic factors

Research Question: Which neural processes underpin distinguishing self from other voices?

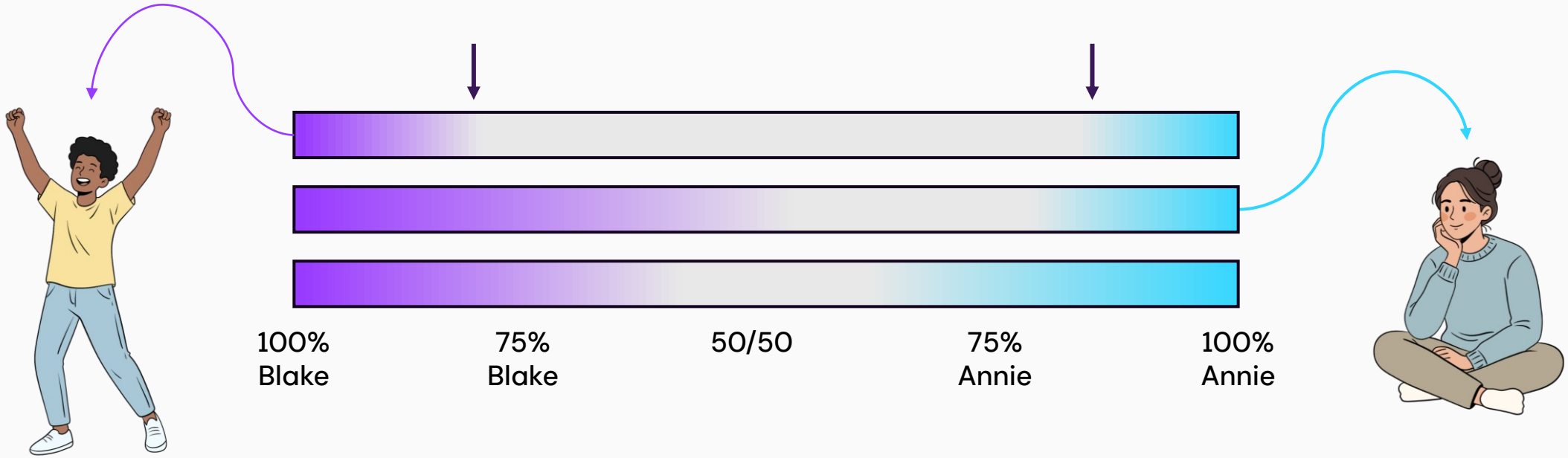
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Intrinsic factors

Research Question: Which neural processes underpin distinguishing self from other voices?

Procedure: Participants hear a continuum of voice recording where their voice is mixed with a stranger and must identify if it's predominantly them or someone else.



Intrinsic factors

- **STAIRCASE**





Use a staircase procedure **before** the main experiment to establish the point of subjective-equality
(i.e. individual-specific 50%)

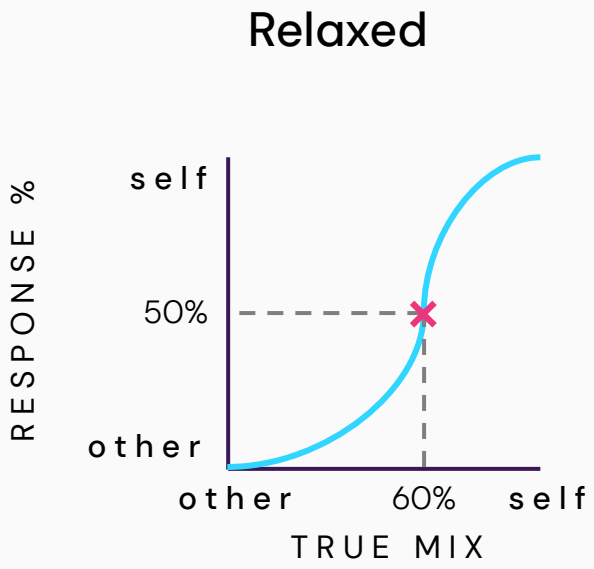
The staircase may require stimuli equivalents to those used in the experiment rather than the exact same ones, to avoid learning effects

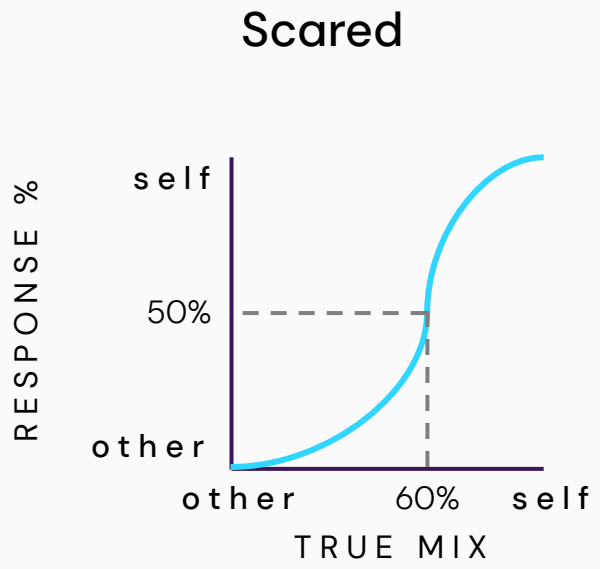
Intrinsic factors

Research Question: Do neural processes underpinning the distinction between self and other voices change between based on context?

Procedure: Repeat the previous experiment in relaxing and scary contexts.







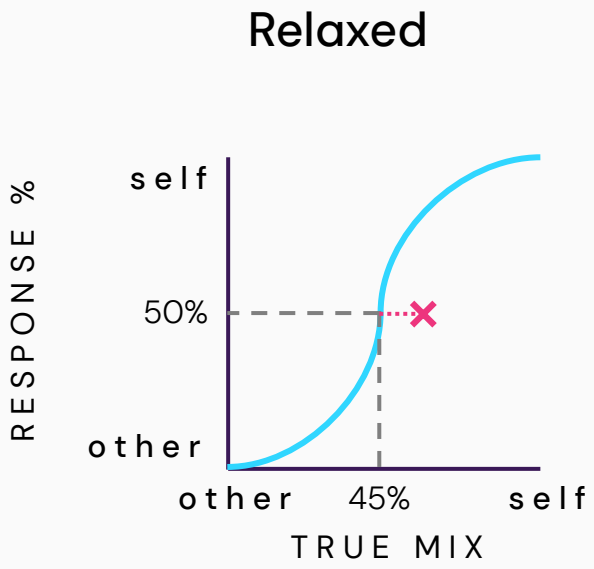


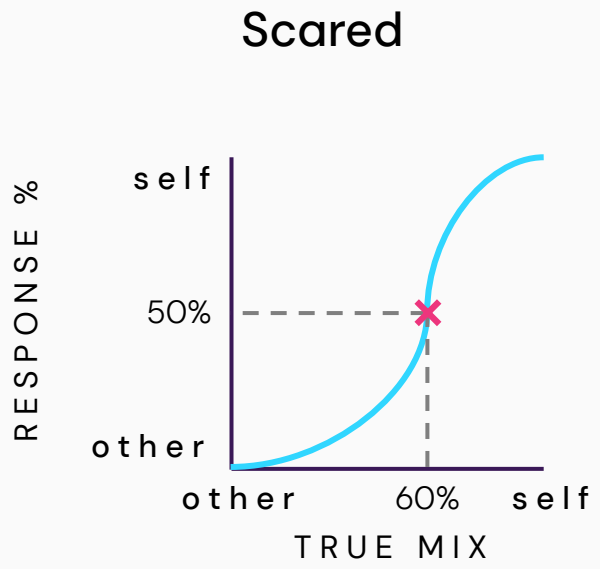
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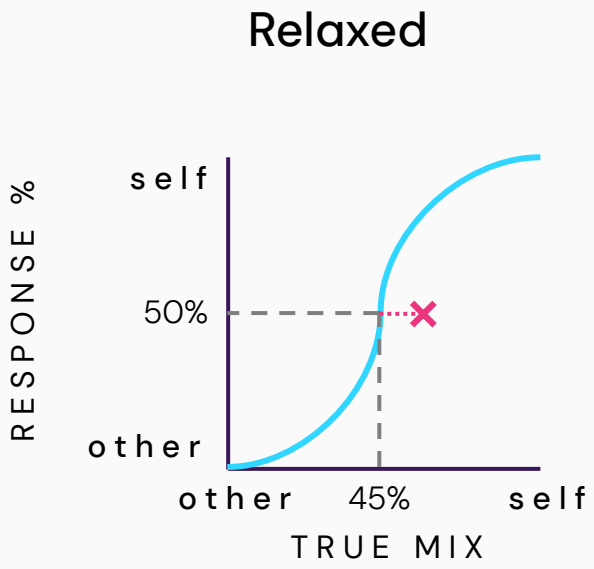


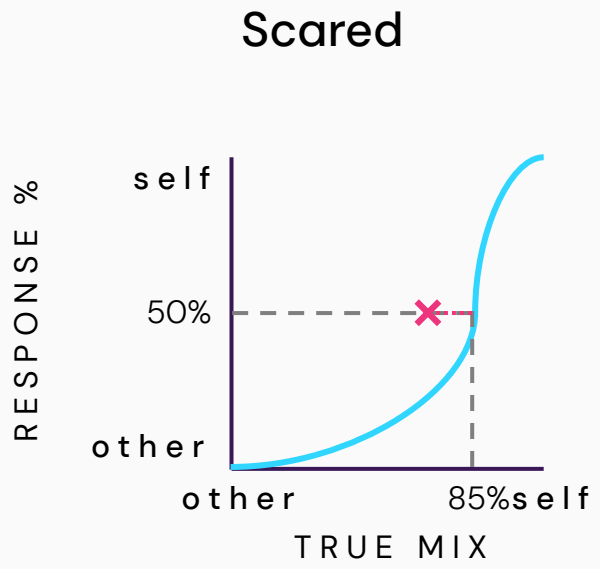
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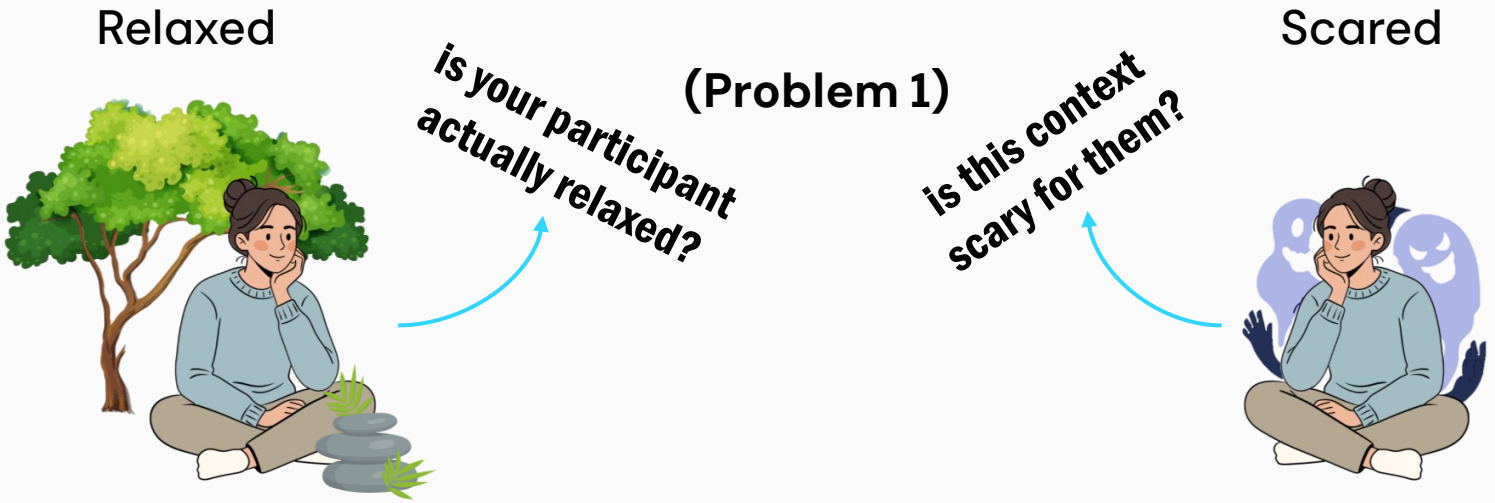






Intrinsic factors

- INDIVIDUAL COVARIATES



Problem 2: Are these contexts eliciting equivalent responses across participants?

Problem 3: In this scenario staircase may lead to habituation.



Intrinsic factors

- INDIVIDUAL COVARIATES

Relaxed





Scared



Potential solution: Participants rate relaxed/scared for respective context, and these ratings are added as regressors that indicate the levels of the feeling-of-interest for your analyses

EXTRINSIC

Subtraction: handles the baseline challenge assuming pure insertion

Conjunction: test multiple hypotheses and isolates effects

Linear and non-linear: adaptation, cognitive dimension, and more

Model-based: many applications, e.g. tracking underlying variables

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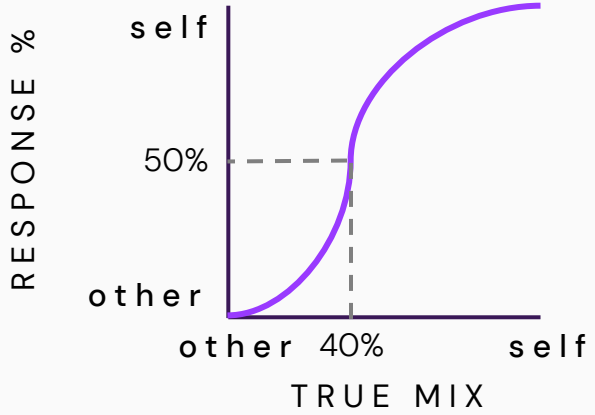
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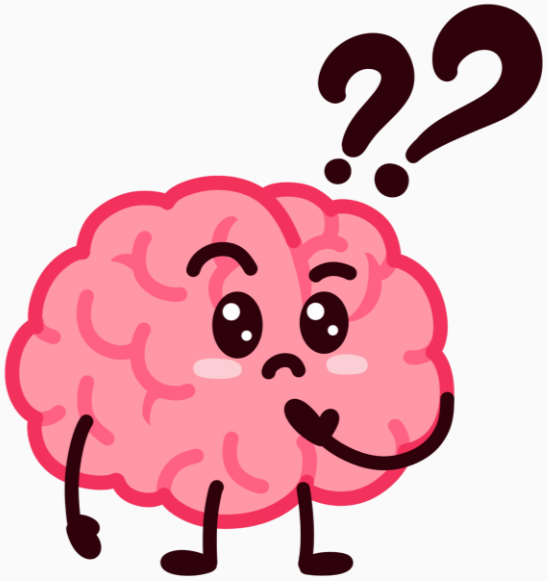
INTRINSIC







Questions



Special thanks to **Professor Carolin Moessnang** (previous lecturer) for various examples and to **Dr. Olivia Kowalcyzk**