

Dynamic causal modelling of brain-behaviour relationships

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Overview

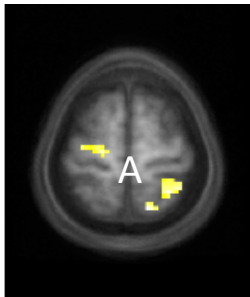
- ✓ DCM: introduction
- ✓ Augmenting DCM with behavioural outputs
- ✓ Proof of concept: inhibitory control

Overview

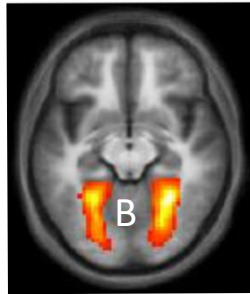
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Functional segregation / integration

localizing brain activity:
functional segregation

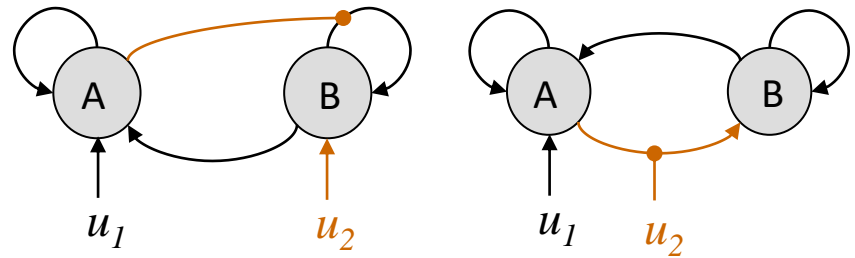


u_1



$u_1 \times u_2$

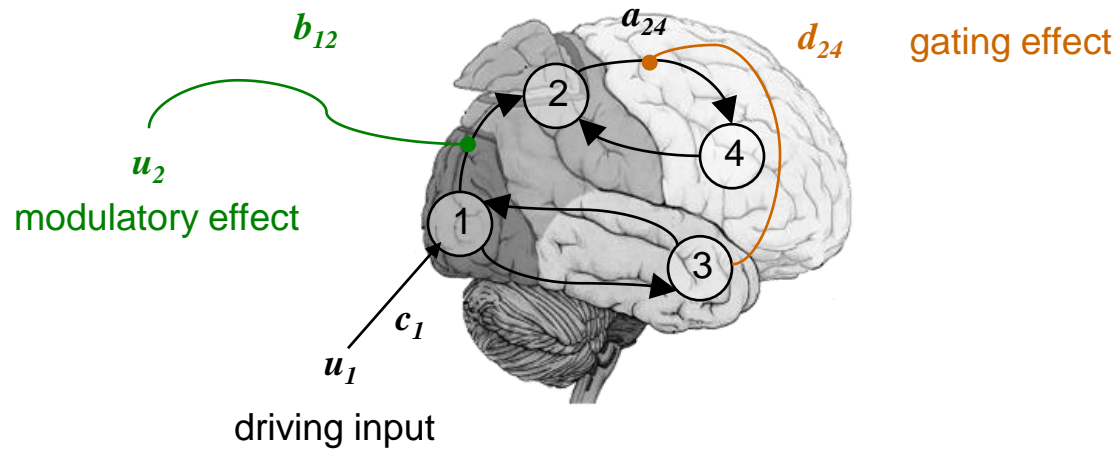
effective connectivity analysis:
functional integration



« Where, in the brain, did
my experimental manipulation
have an effect? »

« How did my experimental manipulation
propagate through the network? »

System identification: agnostic neural dynamics

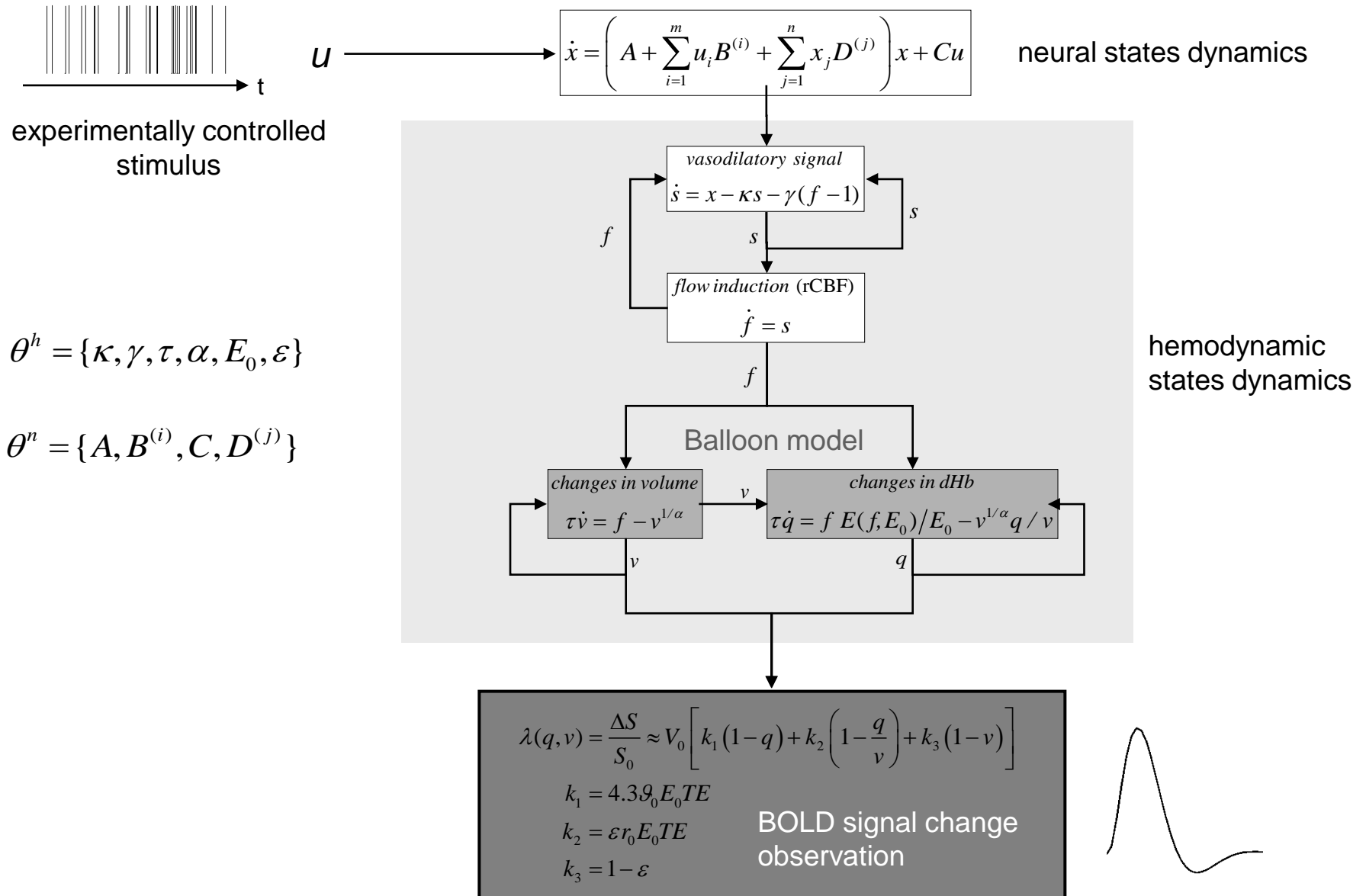


$$\dot{x} = f(x, u) \approx \underbrace{f(x_0, 0)}_0 + \frac{\partial f}{\partial x} x + \frac{\partial f}{\partial u} u + \boxed{\frac{\partial^2 f}{\partial x \partial u} u x} + \boxed{\frac{\partial^2 f}{\partial x^2} \frac{x^2}{2}} + \dots$$

nonlinear state equation:

$$\dot{x} = \left(A + \sum_{i=1}^m u_i B^{(i)} + \sum_{j=1}^n x_j D^{(j)} \right) x + Cu$$

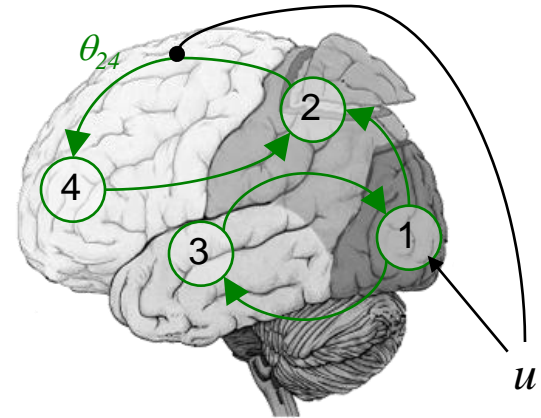
The neuro-vascular coupling



Parametric statistical approach

- DCM: model structure

$$\begin{cases} y = g(x, \varphi) + \varepsilon \\ \dot{x} = f(x, u, \theta) \end{cases} \quad \xRightarrow{\text{likelihood}} \quad p(y|\theta, \varphi, m)$$



- DCM: Bayesian inference

parameter estimates:

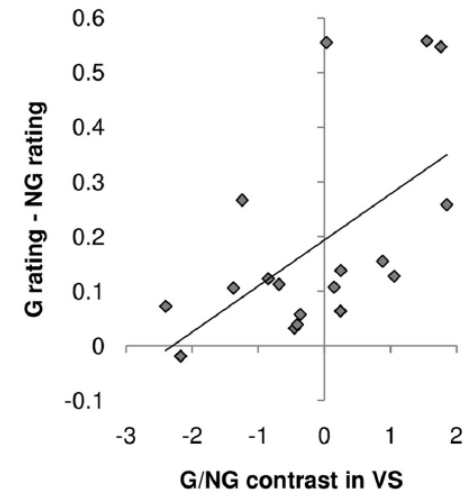
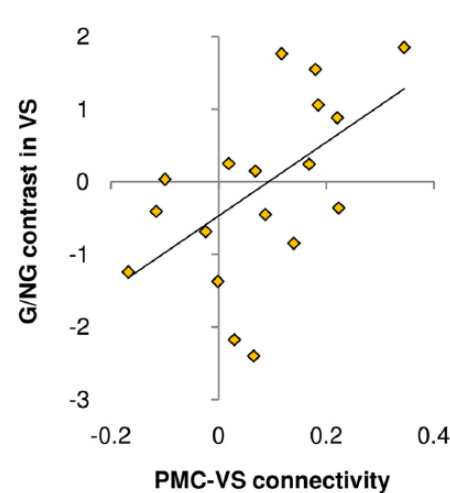
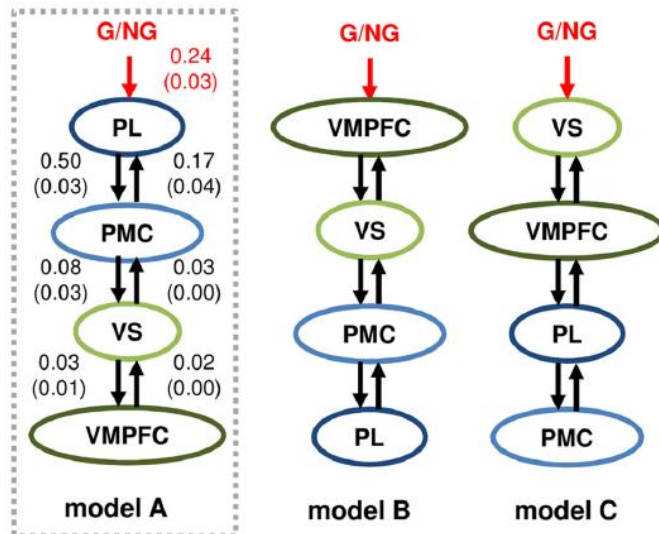
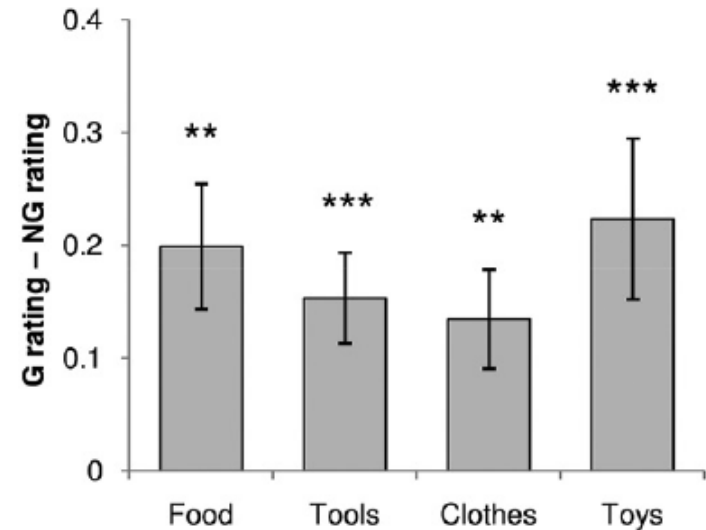
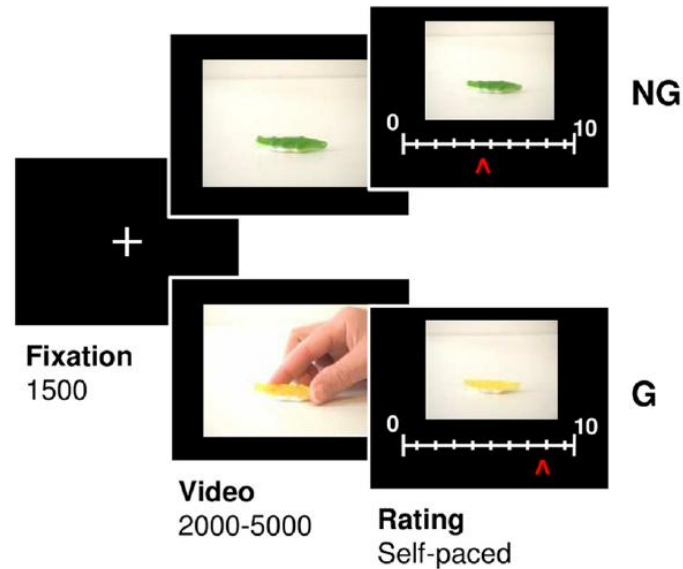
$$\hat{\theta} = \int \theta p(y|\theta, \varphi, m) p(\theta|m) p(\varphi|m) d\theta d\varphi$$

priors on parameters

model evidence:

$$p(y|m) = \int p(y|\theta, \varphi, m) p(\theta|m) p(\varphi|m) d\varphi d\theta$$

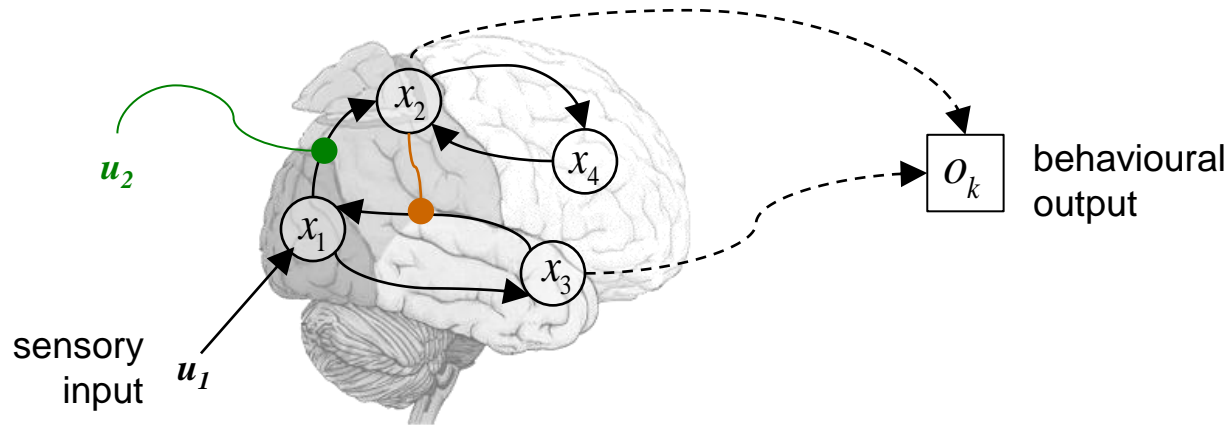
Assessing “mimetic desire” in the brain



Overview

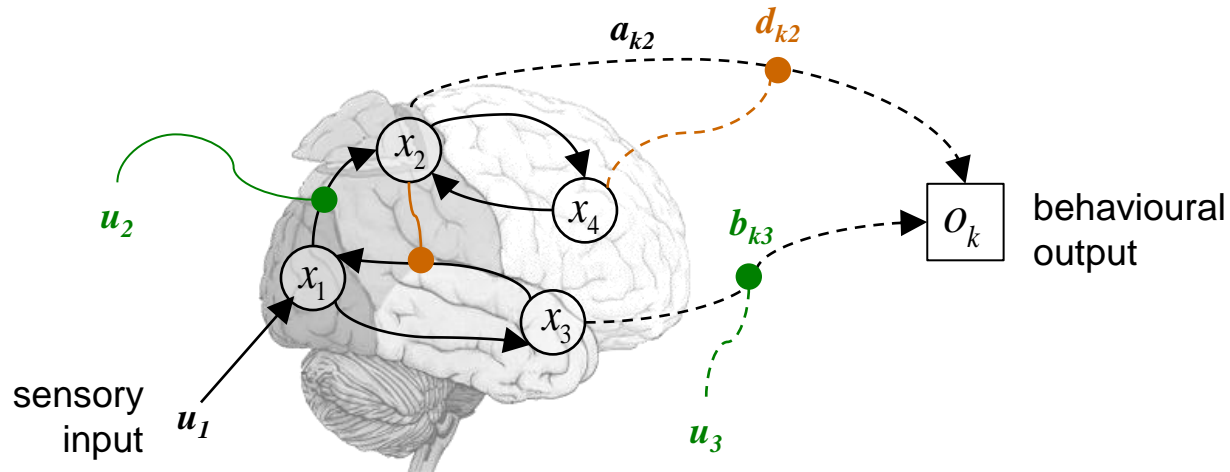
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Identifying the brain-behaviour mapping



- ✓ modelling the brain input-output transform (through the network)
- ✓ decomposing the relative contribution of brain regions and their interactions to the behavioural response

Identifying the brain-behaviour mapping



$$p(o|x) = s(r)^o (1 - s(r))^{1-o}$$

$$r(t) = h(x(t), u(t)) \otimes K(t)$$

$$K(t) = e^{-\alpha t} \Rightarrow \dot{r} = h(x, u) - \alpha r$$

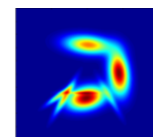
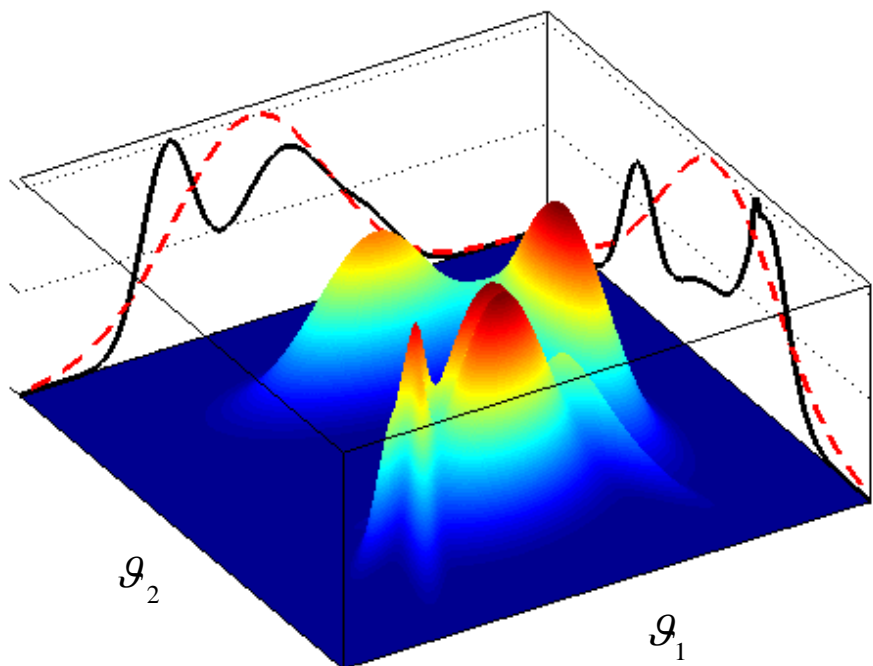
$$h(x, u) \approx h(0, 0) + \boxed{\frac{\partial h}{\partial x} x} + \frac{\partial h}{\partial u} u + \boxed{\frac{\partial^2 h}{\partial x \partial u} ux} + \boxed{\frac{\partial^2 h}{\partial x^2} \frac{x^2}{2}} + \dots$$

variational Bayesian inference

$$\ln p(y|m) = \underbrace{\left\langle \ln p(\mathcal{G}, y|m) \right\rangle_q}_{\text{free energy : functional of } q} + S(q) + D_{KL}(q(\mathcal{G}); p(\mathcal{G}|y, m))$$

free energy : functional of q

mean-field: approximate marginal posterior distributions: $\{q(\mathcal{G}_1), q(\mathcal{G}_2)\}$



$p(\mathcal{G}_1, \mathcal{G}_2 | y, m)$

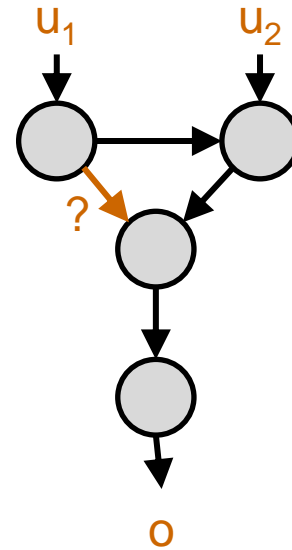
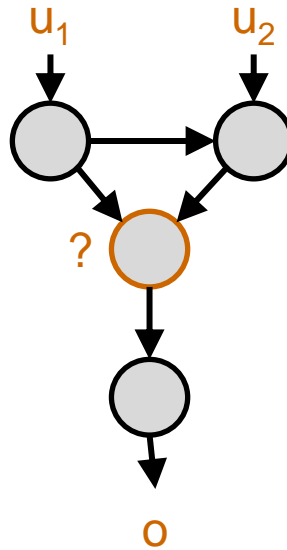
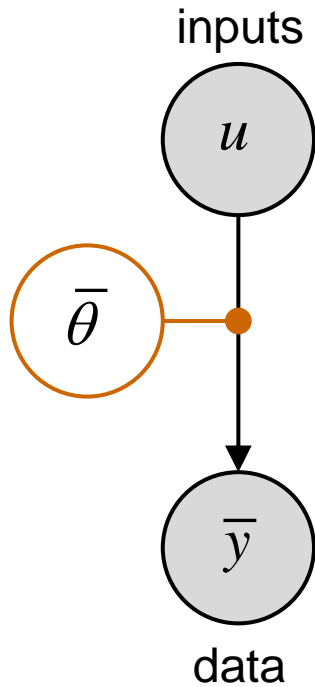


$p(\mathcal{G}_{1 \text{ or } 2} | y, m)$



$q(\mathcal{G}_{1 \text{ or } 2})$

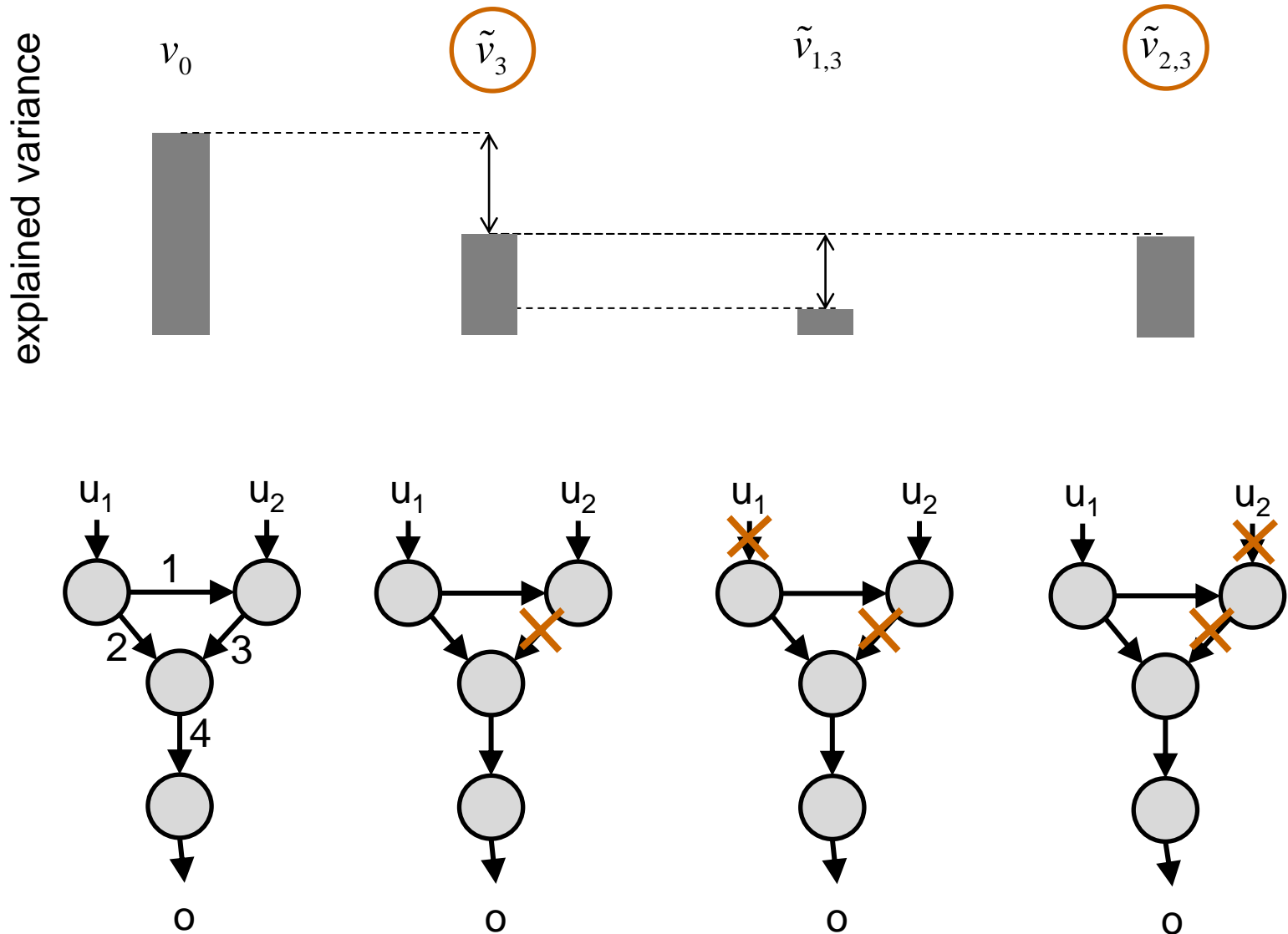
bDCM: artificial lesions' analysis



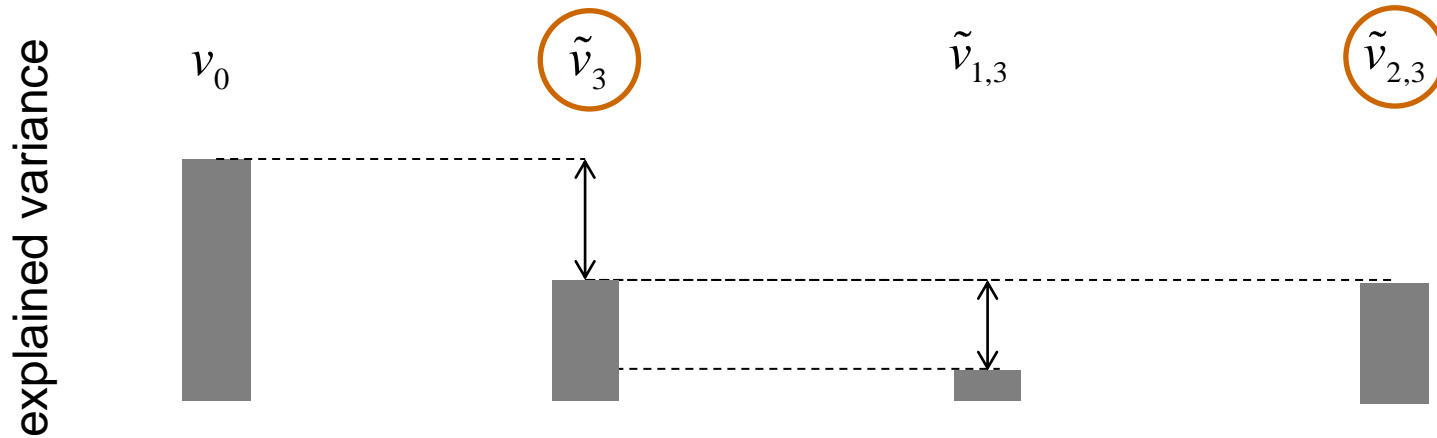
→ *interventional* predictive density:

$$p(\tilde{o} | \bar{y}, \text{do}[x_i = 0]) = \int_{\text{do}[x_i = 0]} p(\tilde{o} | \bar{\theta}) p(\bar{\theta} | \bar{y}) d\bar{\theta}$$

bDCM: behavioural susceptibility analysis



bDCM: behavioural susceptibility analysis



→ for each pair of network feature and input:

$$\chi_{k,j} = 1 + \frac{\Delta \tilde{v}_k - \Delta \tilde{v}_{j,k}}{\Delta \tilde{v}_j}$$

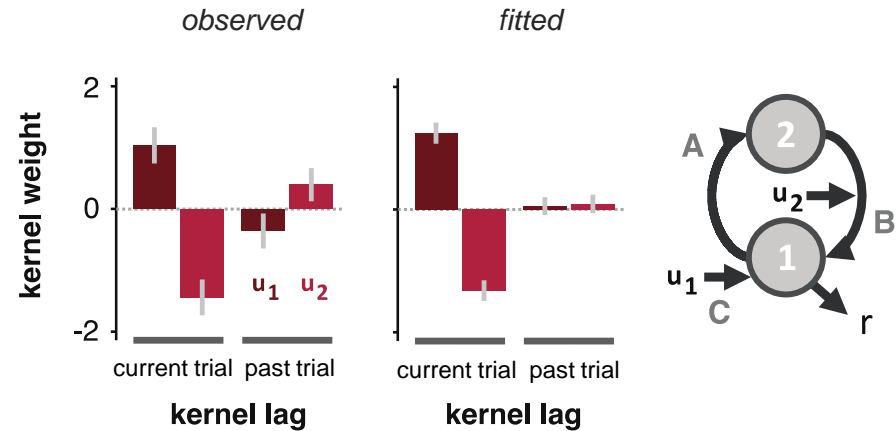
$$\Delta \tilde{v}_{j,k} = v_0 - \tilde{v}_{j,k}$$

$$v_0 = 1 - \frac{\sum_t (o_t - E[o_t | \bar{y}])^2}{\sum_t (o_t - \langle o \rangle)^2}$$

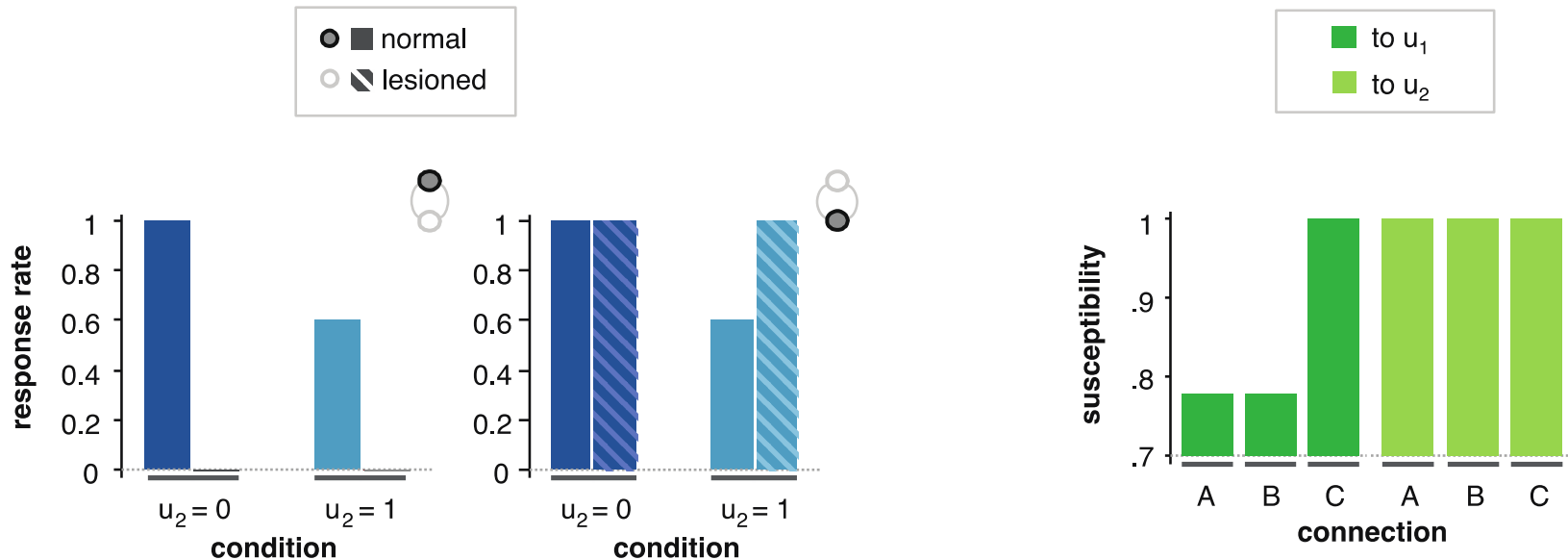
$$\tilde{v}_{j,k} = 1 - \frac{\sum_t (o_t - E[\tilde{o}_t | \bar{y}, \text{do}[u_j = 0, \theta_k = 0]])^2}{\sum_t (o_t - \langle o \rangle)^2}$$

bDCM: post-hoc analysis example

→ Volterra decompositions:



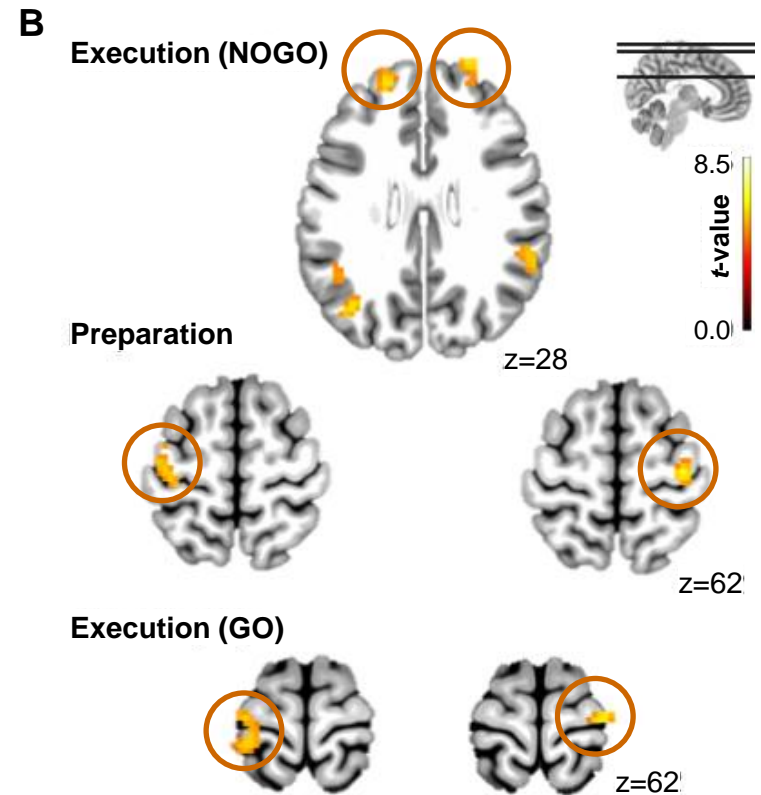
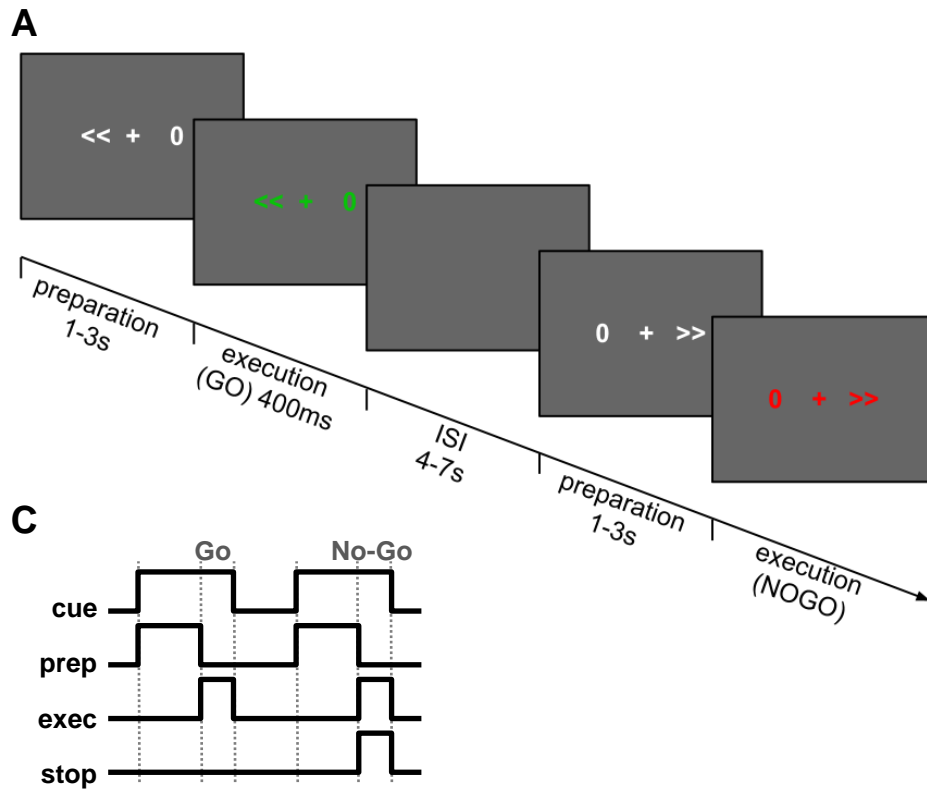
→ *bDCM*'s susceptibility analyses:



Overview

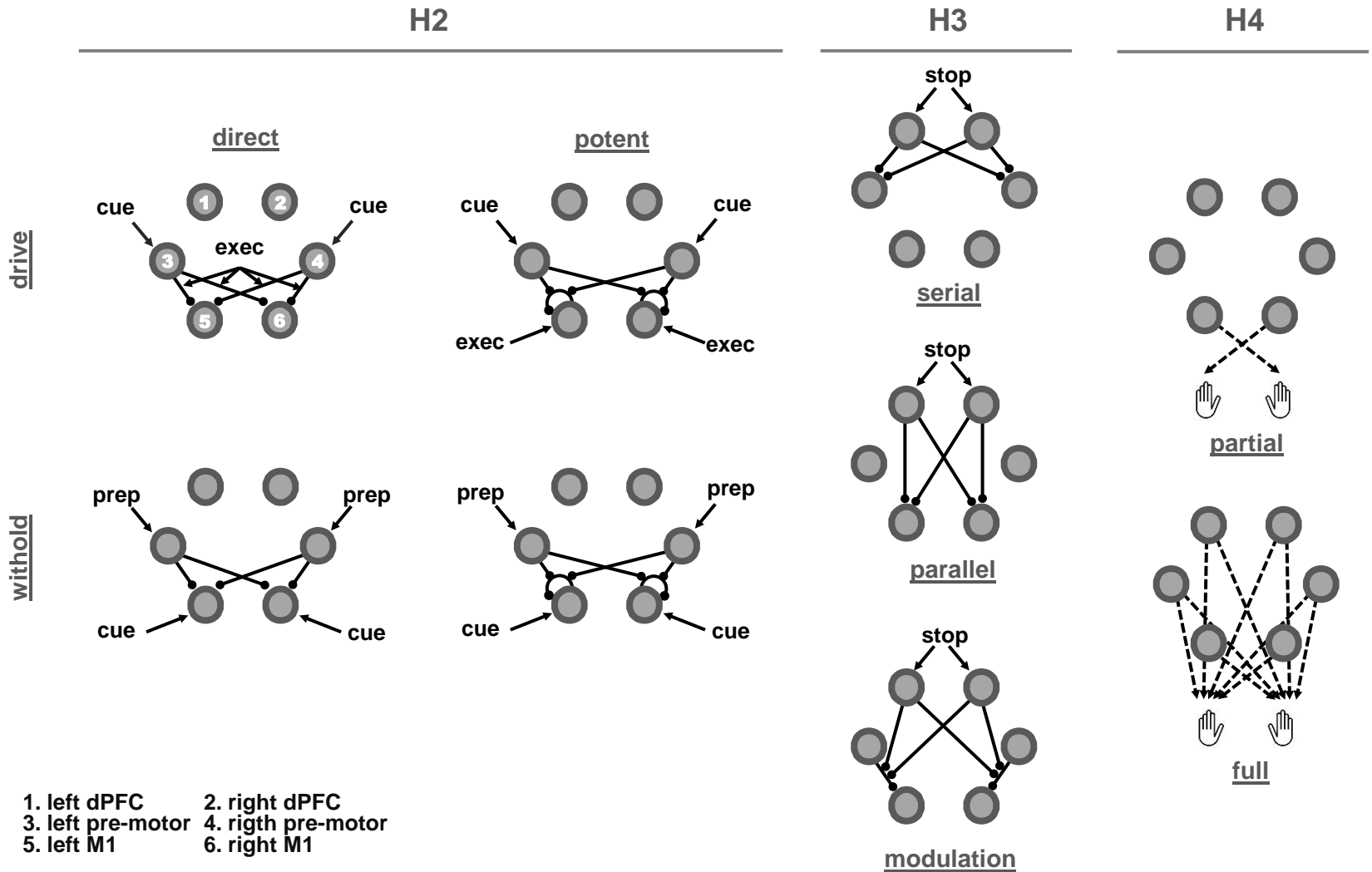
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Go/noGo: paradigm and fMRI results

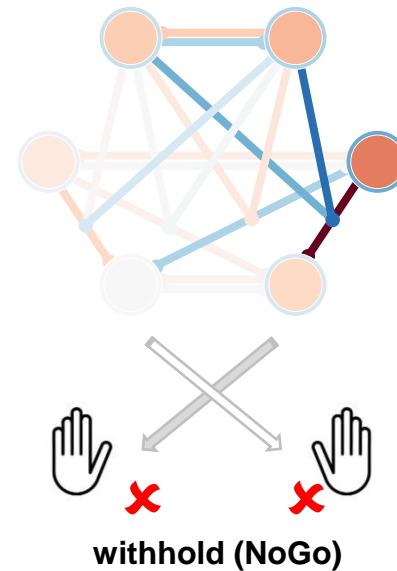
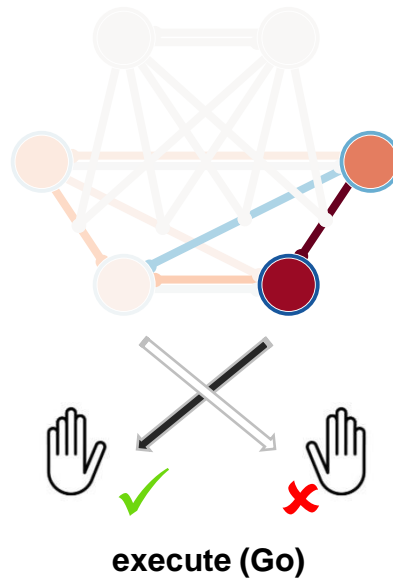
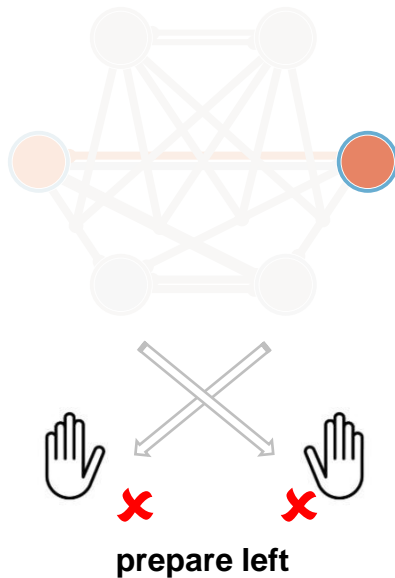
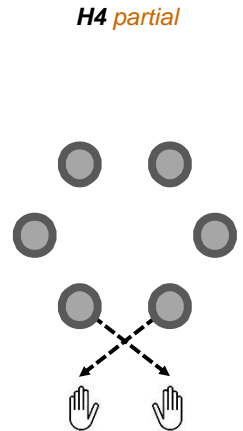
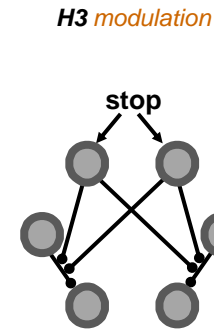
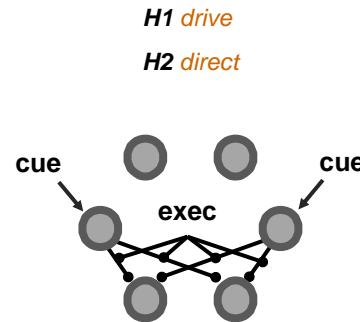
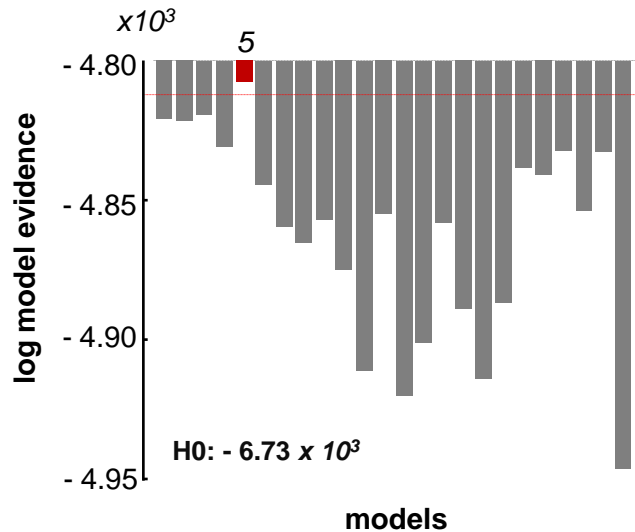


Go/noGo: model comparison set

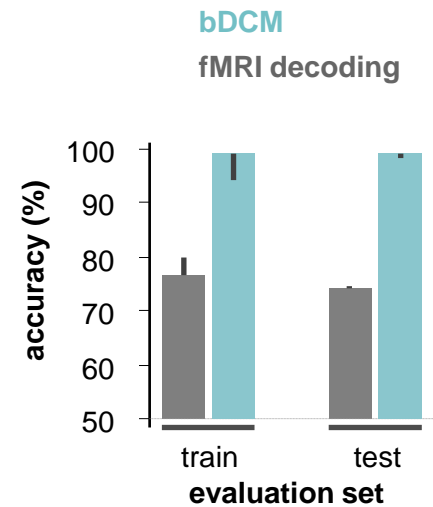
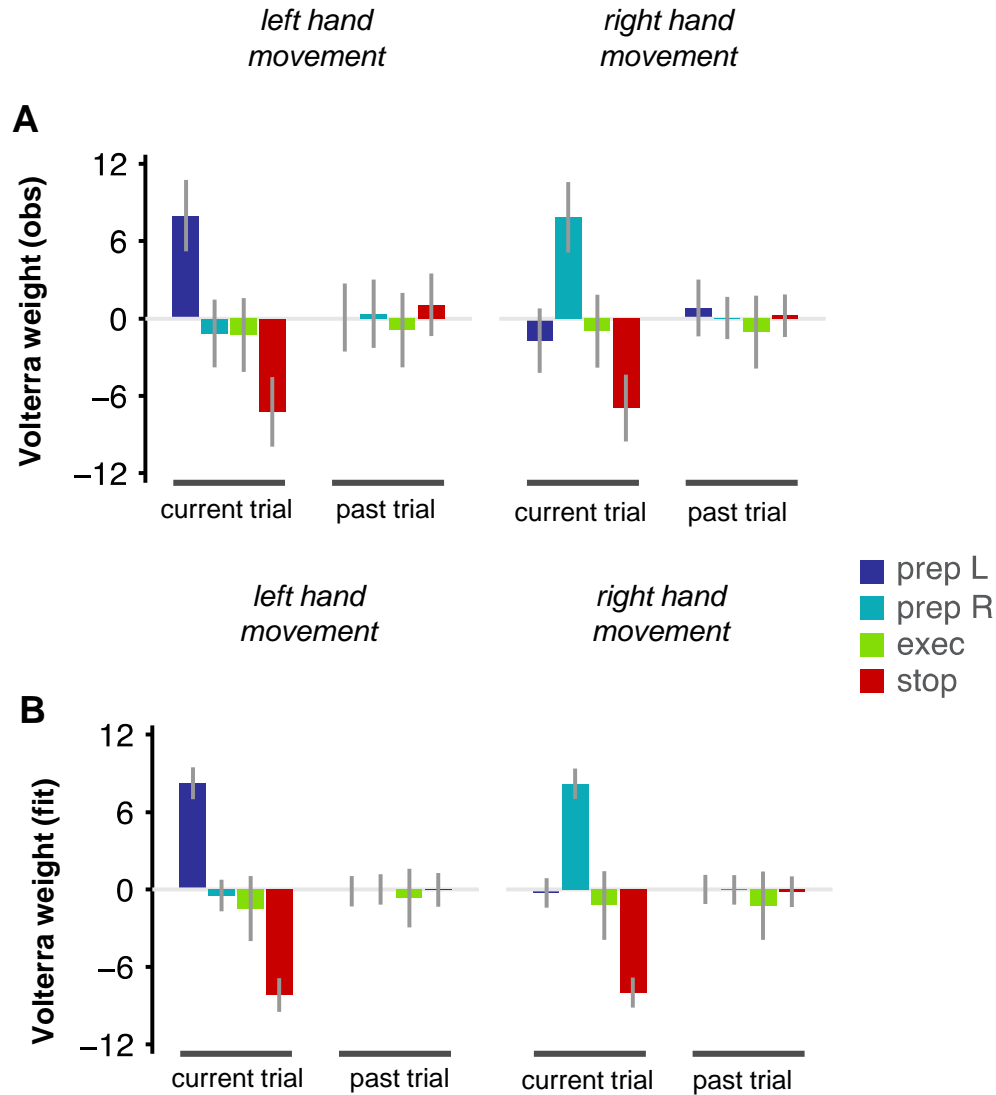
H1



Go/noGo: Bayesian model selection

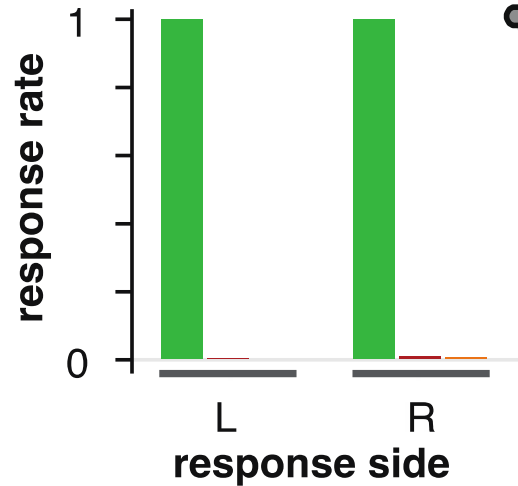


bDCM: construct validity

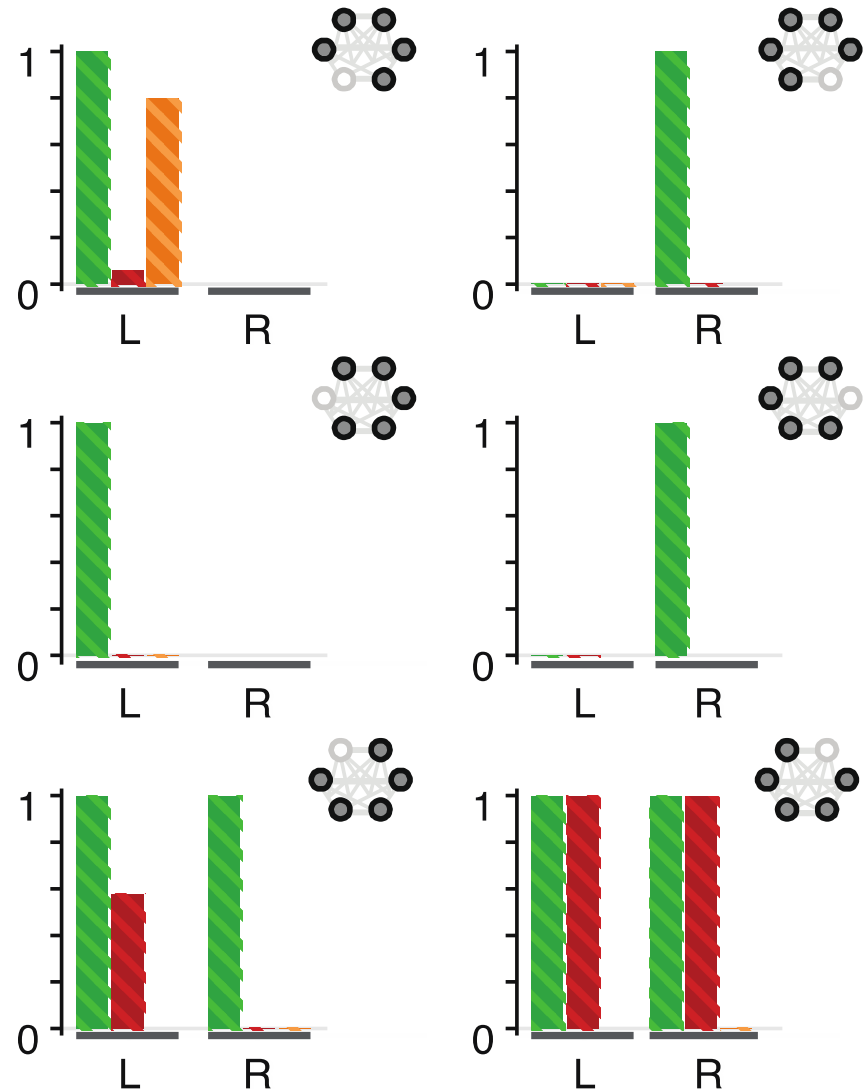


Go/noGo: lesion-induced behavioural deficits

A



B



response type:

- Correct Go
- Error NoGo
- Wrong hand

node state:

- normal
- lesioned

Go/noGo: lesion-induced behavioural deficits

A

response rate



L response

response type

- Correct G
- Error NoG
- Wrong hand

node state:

- normal
- lesioned



Inhibition and the right inferior frontal cortex: one decade on

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²Department of Psychology and Behavioural and Clinical Neuroscience Institute, University of Cambridge, Cambridge, UK

³Departments of Psychology and Neuroscience, University of Texas, Austin, TX, USA

In our TICS Review in 2004, we proposed that a sector of the right inferior frontal cortex (rIFC) in humans is critical for inhibiting response tendencies. Here we survey new evidence, discuss ongoing controversies, and provide an updated theory. We propose that the rIFC (along with one or more fronto-basal-ganglia networks) is best characterized as a brake. This brake can be turned on in different modes (totally, to outright suppress a response; or partially, to pause), and in different contexts (externally, by stop or salient signals; or internally, by goals). We affirm inhibition as a central component of executive control that relies upon the rIFC and associated networks, and explain why rIFC disruption could generally underpin response control disorders.

Introduction

Since Ferrier in the 19th century [1], it has been posited that one of the functions of the prefrontal cortex (PFC) is to inhibit behavior. In our previous review [2], we defined inhibition psychologically as 'the suppression of inappropriate responses, stimulus-response mappings or task-sets when the context changes, and suppression of interfering memories during retrieval.' We claimed that such inhibition depends on the rIFC (uniquely among PFC regions) and that, neurally, one-way rIFC could implement its function is via a subcortical projection to the subthalamic nucleus (STN). Here we reappraise these claims based on 10 years of evidence and in light of several challenges (e.g., [3–7]). We focus on a narrower psychological definition of inhibition, that is, of response tendencies. This is an exemplary case in which there is (i) the largest amount of evidence, (ii) a clear operationalization at the behavioural level via stopping or slowing, and (iii) a relation to one or more prefrontal-basal-ganglia circuits with the requisite features for suppression of motor responses.

We start by reviewing the evidence that the rIFC is critical for stopping action outright. We then address two major branches of criticism: whether the rIFC is the critical

PFC node for inhibition and whether the rIFC implements a function other than inhibition. We then show that the rIFC is also important for pausing and braking responses, in addition to outright stopping. This broader role for the rIFC could explain why rIFC dysfunction occurs in neuropsychiatric disorders – a weakness in this system will affect many types of inhibitory response control. Finally, we discuss the reverse inference problem – under what circumstances can researchers interpret rIFC activation as indicating inhibition in their task?

The role of the rIFC within a network for outright action stopping

To properly engage a neurocognitive response inhibition process, a task must require the stopping of a response that is already initiated. The stop signal task [8] does this, as do some versions of the Go/NoGo task, and some other response-overriding tasks [9–12]. Much research now shows that the rIFC is activated by, and is critical for, outright stopping (reviewed in [1,13–17]). Other studies, using high spatio-temporal resolution electrocortigraphy (ECoG), show that rIFC activity occurs before the stopping process ends [e.g., before stop signal reaction time (SSRT)] [18–20]. The subregion of the rIFC most commonly implicated is the pars opercularis (Box 1); however, there is also often activation of right (and left) insula, pars orbitalis and triangularis, and the inferior frontal junction (see meta-analysis [15,17]).

In 2004 we proposed that the rIFC implements inhibition via the STN. Much evidence now supports the role of the STN, in humans [3,21–24], monkeys [25], and rodents [26]. The rodent study [26] showed that STN was active on both successful and failed stop trials (always receiving a stop signal), but that its target, the basal ganglia output nucleus (the substantia nigra (SNr), which inhibits the thalamus), increased firing only if stopping was successful. This confirms our earlier conjectures [2,22] that the Go command is implemented by the direct pathway, and that stopping counteracts this via the STN (with some data suggesting the STN is activated via the hyperdirect pathway [25]).

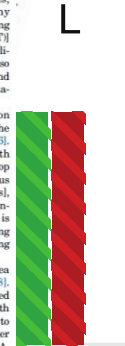
Outside the PFC, the presupplementary motor area (preSMA) is also implicated in stopping [11,19,27,28]. The preSMA is functionally and structurally connected with the rIFC (Box 1), and white matter variability in both the preSMA and the rIFC, and their connections, relates to the speed of stopping [29–31]. It is not yet clear whether the rIFC triggers the STN directly, or via the preSMA.

Effects of Focal Frontal Lesions on Response Inhibition

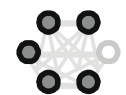
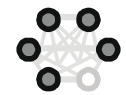
Terence W. Pickett^{1,2}, Donald T. Stuss^{1,2}, Michael P. Alexander^{3,4}, Tim Shallice^{3,5}, Malcolm A. Binns⁶ and Susan Gillingham¹

¹Rotman Research Institute at Baycrest, Toronto, Ontario M6A 2B1, Canada; ²Departments of Medicine and Psychology; ³Medical Center, Toronto, Canada; ⁴Beck Institute for Cognitive and Behavioral Sciences; ⁵Department of Neurology; ⁶Harvard Medical School, Boston, MA, USA

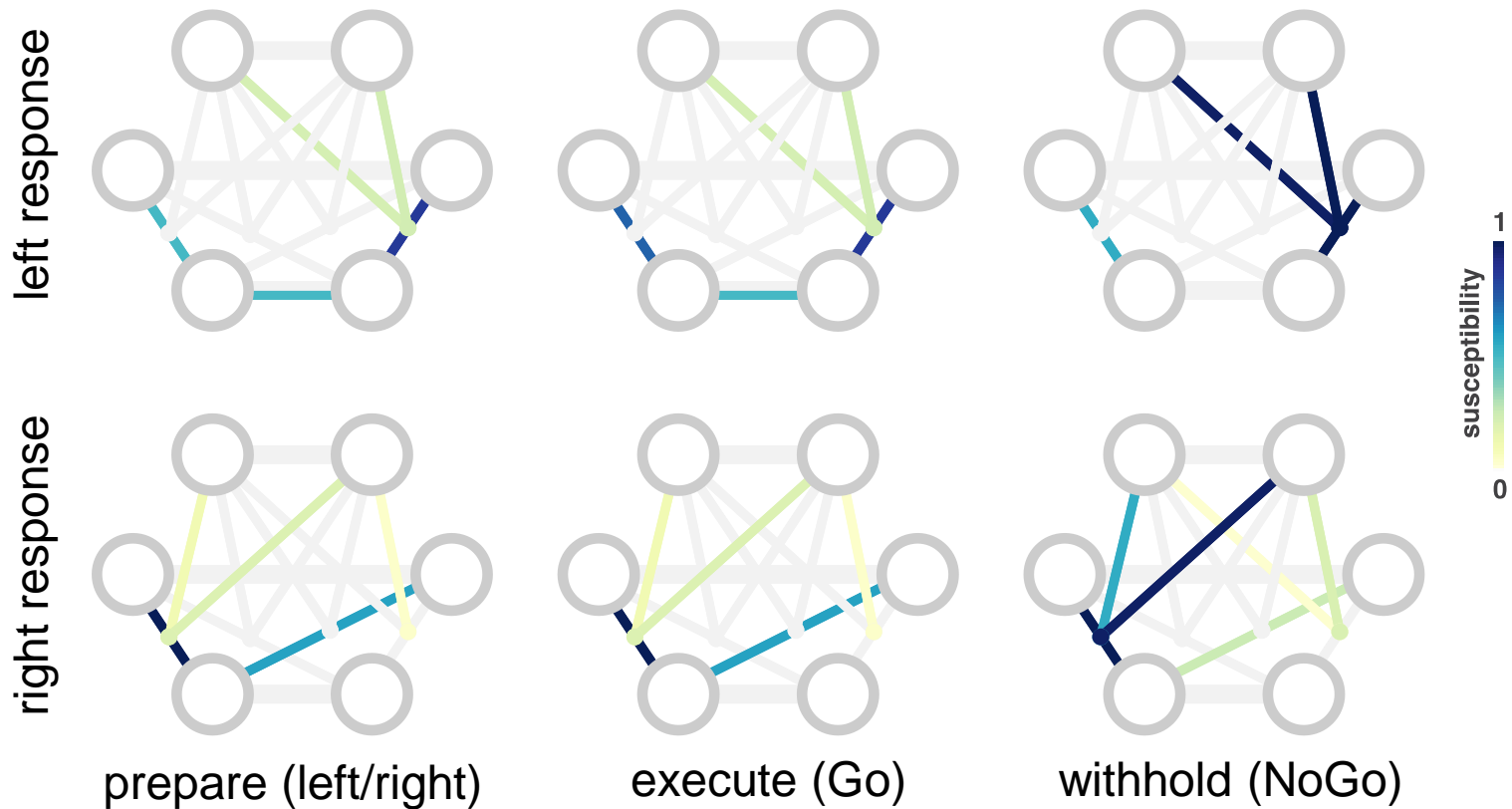
The go-no-go task has been used since the 1950s to study response inhibition. It shows a high rate of correct responses (approx. 90%) and a low rate of errors (approx. 10%). The task is used to study response inhibition in healthy individuals and in patients with various neurological disorders.



L R L R



Go/noGo: behavioural susceptibility analysis



Overview

- ✓ DCM: introduction
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This is hard work by Lionel Rigoux!

Discussion

- ✓ Cognitive function = input-output transform
 - *bDCM*: outputs = $f(\text{inputs})$ u.c. realistic intermediary states
- ✓ *Funnelling*, modulating and mediating
- ✓ “Model-based fMRI”?
- ✓ Limitations (dimensionality, data balance, pre-stimulus activity, behavioural mapping, susceptibility index)
- ✓ Bridging the gap between neuroimaging studies on healthy subjects and neuropsychological studies on brain-damaged patients
- ✓ Functional degeneracy and functional recovery