

Supplementary Information

“Insula cortex gates the interplay of action observation and preparation for controlled imitation”

S1 Methods - Further detail on DCM specification

A DCM is a collection of nodes (regions) and the directed connections between them. For task fMRI, VOIs are selected as network nodes based on the task effects in the data (see Methods). DCMs are then specified by 4 matrices which are the terms in the neural state-equation (Friston et al, 2003; Marreiros, Stephan, & Friston, 2010; Stephan et al. 2010) If n is the number of nodes and i the number of inputs then these matrices are,

- A-matrix: an $[n \times n]$ matrix of intrinsic connections (edges between nodes) for inter- and intra-node communication, can be framed as bidirectional/unidirectional or feed-back/-forward and lateral connections.
- B-matrix: an $[n \times n \times i]$ matrix of task-related modulator effects, induced context-dependent changes in connectivity; bilinear term state equation. For example: a second-order interaction between the driving inputs (task conditions) and activity in a source node related to a response in a target node. See Results Section 3.1.
- C-matrix: an $[n \times i]$ matrix for the driving inputs based on the known perturbations of the experimental paradigm, e.g. stimulus properties/ task conditions.
- D-matrix: an $[n \times n \times n]$ matrix for nonlinear modulations from one node onto the connection between 2 other nodes. Note these D-matrices are only specified for nonlinear DCMs and not included in bilinear DCMs. See Results Section 3.1.

For the present study, the matrices across all 48 DCM designs were specified using custom MATLAB batchscripts to call the DCM functions from the SPM12 toolbox.

S1.1 Node selection from GLM and intrinsic connections

Four regions of interest were selected as the nodes included in all DCM hypotheses: The node for V5/MT was defined by the peak signal-change ($p < 0.05$ FWE corrected) across all task conditions over baseline within the AAL defined left middle temporal gyrus (MNI coordinates: [-44 -66, 12];

note the same peak was also identified when WFU Pickatlas (Maldjian et al., 2003) toolbox was used to define the ROI with left MT mask). This region was chosen as it is an area within early visual cortex sensitive to visual motion and it responded strongly to all four task conditions (see Results Section 3 Fig. 3.B for beta-estimate plots). It was hence modelled as receiving driving inputs related to visual movement stimuli across all conditions. The MOG peak [-28, -66, 26] was highlighted by an interaction effect driven by the factorial combination intentional imitation. SMA is known to be critical for motor planning, and a peak [-4, 14, 48] identified for the main effect of action-preparation was used for the third VOI. Finally, the VOI within the left anterior insula cortex [-30, 20, 2] was based on the main effect of SRC and interpreted to reflect conflict-detection, response-inhibition and goal maintenance processing within the cingulo-opercula network for cognitive control (Dosenbach et al., 2008; Nelson et al., 2010).

S1.2 Specification of intrinsic network edges (A-matrix)

Across all models, two areas were positioned as ‘fully’ connected with all other network nodes: the MOG and the insula. For example, in our base design for connections (DCM A-matrix), the MOG was bi-directionally linked to the insula node and to both the SMA and V5MT, while these latter two regions were themselves not directly connected.

This design was informed by literature on the functional and structural connectivity of these particular areas. The peak coordinate centred on for the **MOG node** of our models was located near the intraparietal sulcus and angular gyrus of the IPL. This region is a confluence of temporo-parieto-occipital cortices, where subcortical white matter tracts form a crucial hub of intra- and inter-cortical structural connectivity providing high-level multimodal integration (De Benedictis et al., 2014). Relevant to action observation processes, functional connectivity between the insula, parietal, and occipital cortices are integrated with a general posterior to anterior organisation. This organisation has been argued to allow the transformation of stimuli from IPL-occipital connections through to anterior IPL connections with the prefrontal cortex and insula cortex (Uddin et al., 2010). Given this prior information, our DCM hypotheses framed the MOG node as being “fully” connected within our models.

Regarding the **anterior insula cortex**, this area is involved in a very wide range of tasks (Craig, 2010). The insula cortex has been firmly posited as an integral hub in the salience network, via

strong coupling with the anterior cingulate cortex to facilitate rapid links to the motor system and assist appropriate responses to salient stimuli (Menon and Uddin, 2010). This fits well with the insula cortex being included within the cingulo-opercula control network (Dosenbach et al., 2008). This cingulo-opercula network is comprised of the anterior insula cortex, the anterior prefrontal cortex, frontal operculum, dorsal anterior cingulate cortex and thalamus; and is argued to function in counter-part to a fronto-parietal network, together framed as dual-networks for cognitive control (Cai et al., 2014a; Dosenbach et al., 2008). Structurally, the anterior insula connects with posterior insula as well as frontal, parietal, and temporal lobes (Faillenot et al., 2017), and bilaterally with the SMA (Cauda et al. 2011). These details informed our A-matrix design for the insula node being modelled as connected with all the other regions in our model network.

The SMA has been reliably related to higher order motor planning and preparation for voluntary, intentional movements (Cunnington et al., 2005). Coupled with our task effects on BOLD signal changes highlighting involvement of the SMA for intentional compared with incidental action contexts, we viewed this as representing higher order planning for task-relevant SR pairs. Thus, we hypothesised this node as effectively connected with higher order regions of our network, the insula and MOG, but not with V5/MT (low-level perception of visual motion).

S1.3 Specification of driving inputs (C-matrix)

Our inclusion of area V5 was motivated as a low-level visual representation of movements, (ffytche et al., 1995; Zeki, 2016), as a bottom-up sensory signal for the observed action common to all task conditions. Thus, driving inputs to this node were ubiquitous to all hypothesised networks. Another potential driving input considered was early motor preparation which was modelled as a driving input to the SMA in a family of dual-input designs (Results Fig.3A).

S2 Results – Peak statistics for whole-brain GLM analysis

Table S1. Summary of peak statistics interaction effects (task-relevance x congruence) on task-related BOLD responses. Cluster-level FWE-correction $p < 0.05$.

Cluster-level FWE-corrected $p < 0.05$			Peak Statistics					
Cluster labelling	% labelled	size	Peak labelling	Peak co-ordinates x,y,z (mm)	p(uncor.)	p(FWE)	F	Z
Mid Occipital	67.5	120	*Mid Occipital	-28 -66 26	<0.0001	0.014	33.53	5.08
Mid Occipital	14.2		Mid Occipital	-24 -54 28	<0.0001	0.021	32.29	5.00
Angular Gyrus	18.3		Sup/Mid Occipital	-22 -74 30	<0.0001	NS	26.16	4.55

Notes: This cluster was formed by peak-level $p < 0.0001$ uncorrected and cluster-level $p(\text{FWE-corrected}) < 0.05$, corresponds to the purple overlay in Fig 3. Labelled by Automatic Anatomic Labelling (AAL) toolbox * indicates coordinate for DCM VOI

Table S2. Summary of peak statistics for main effects from whole-brain analysis of task-related BOLD responses. Peak-level FWE-correction $p < 0.05$.

Region by cluster labelling			Peak Statistics						
Cluster labelling	% labelled	Size	Peak labelling	Peak co-ordinates x,y,z (mm)			p(FWE)	F	Z
Main effect of Task-relevance (intentional versus incidental)									
<i>Extent Threshold: $k=25$ voxels; Peak-level FWE-corrected $p < 0.05$.</i>									
Sup Medial Frontal, SMA, Sup Frontal, MCC	89.08	174	*SMA	-4	14	48	<0.001	84.19	7.3
Mid / Sup Occipital <i>Unlabelled</i>	9.14	175	Mid Occipital	-20	-94	4	<0.001	52.55	6.12
Postcentral Precentral	64.58	48	Postcentral, Precentral	-42	-26	64	<0.001	47.29	5.87
Mid Frontal	25.81	31	Precentral, Mid Frontal	-30	-2	48	0.004	38.31	5.38
Precentral	3.23		Mid Frontal, Sup Frontal	-24	2	54	0.035	30.61	4.88
Mid Occipital <i>Unlabelled</i>	3.7	27	Mid Occipital	-32	-90	4	0.009	35.18	5.19
	96.3								
Main effect of Congruence (imitation versus counter-imitation)									
<i>Extent Threshold: $k=25$ voxels; Peak-level FWE-corrected $p < 0.05$.</i>									

Putamen	52.79	771	Insula	36	16	0	<0.001	68.7	6.78
IFG (Triangulars)	20.75		Insula, IFG (Triangulars)	38	26	4	<0.001	61.69	6.51
IFG (Orbitalis, Operculars, Rolandic) Insula	25.81 0.39		IFG (Opercularus)	44	12	6	<0.001	59.86	6.44
Inf Occipital	83.15	273	Mid Occipital, Inf Occipital	-42	-	-2	<0.001	64.76	6.63
Mid Occipital	1.83		Mid Occipital	-38	-	0	<0.001	46.58	5.83
			Mid Occipital	-36	-	8	0.001	42.35	5.61
IFG (Operculus) Insula	7.61 4.84	289	*Insula Insula	-30 -30	20 20	2 -8	<0.001 0.001	54.31 44.75	6.2 5.74
IFG (Orbitalis, Triangulars)	7.6		Insula	-44	14	0	0.001	43.11	5.65
Supramarginal	1.2	83	SupraMarginal	64	-	36	<0.001	53.02	6.14
<i>Unlabelled</i>	<i>98.8</i>				40				
SMA	50.77	130	SMA	12	10	68	<0.001	50.64	6.03
Sup Frontal	0.77		Sup Frontal	20	0	62	0.002	39.94	5.47
<i>Unlabelled</i>	<i>48.46</i>		Sup Frontal, SMA	14	0	72	0.006	36.29	5.26
Medial Sup Frontal	54.21	107	MCC	10	18	38	<0.001	48.1	5.91
MCC	0.93		SMA	4	10	54	0.004	37.86	5.35
SMA	0.93		SMA	10	18	56	0.006	36.57	5.27
<i>Unlabelled</i>	<i>43.93</i>								

Notes: Corresponds to Fig. 2 yellow overlay (Intentional/Incidental) and green overlay (Imitation/Counter-Imitation). Labelling by Automatic Anatomic Labelling (AAL) toolbox. SMA: Supplementary Motor Area; MCC: Mid-Cingulate Cortex; IFG: Inferior Frontal Gyrus; Sup: Superior; Inf: Inferior. *indicates coordinates used for DCM VOI.

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