In Action Execution and Observation the Cerebellum Exerts a Differential Control over the Excitatory/Inhibitory Dynamics of Inter-Regional Effective Connectivity

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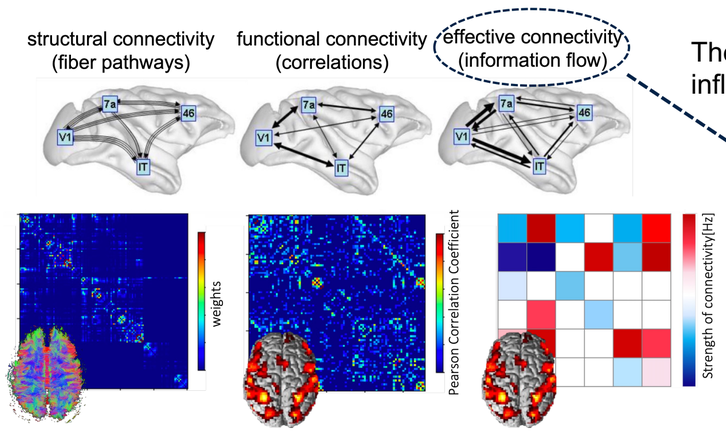
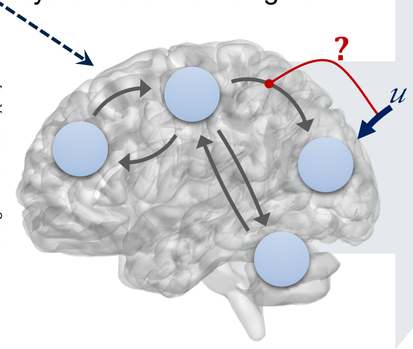
Introduction

A step further to explain brain connectivity



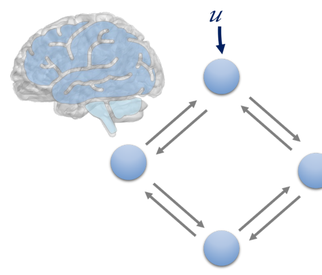
Adapted from Honey et al.,2007; Casiraghi et al., 2019; Palesi et al., 2020; Lorenzi et al., 2024

The direction and inter-regional influence of the complex neural system is still an enigma

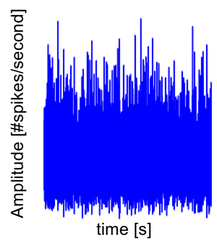


Dynamic Causal Modelling (DCM)

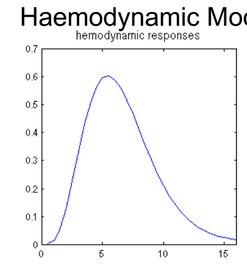
DCM goal is to uncover **the underlying neural mechanisms** of causal interactions by quantifying the **effective connectivity** between regions



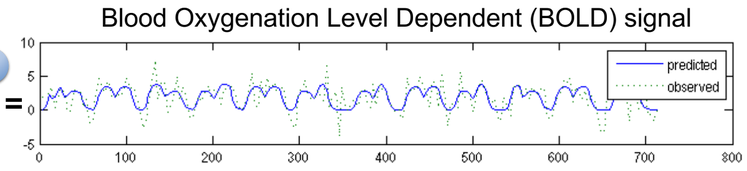
Neuronal Model



Haemodynamic Model



Blood Oxygenation Level Dependent (BOLD) signal



The neuronal model represents the neural activity that drives dynamic interactions between brain regions and that is linked to the BOLD signal through an hemodynamic model.

Goal

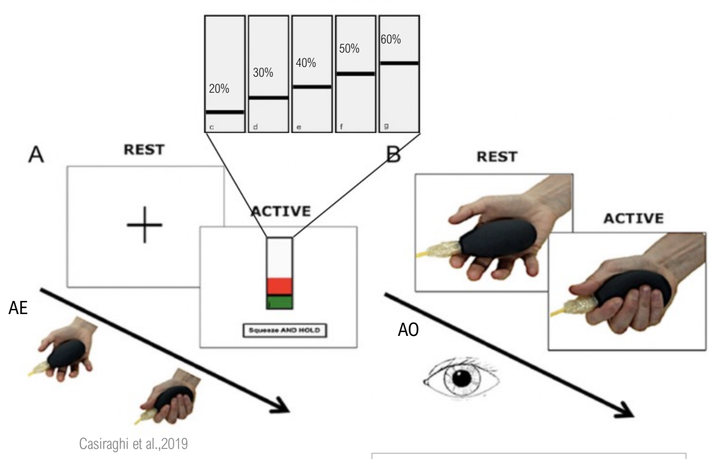
AIM: Unveiling the differences in Cerebro-Cerebellar causal relations during Action Execution (AE) and Action Observation (AO)

Methods

Grip Force and BOLD Response

We aimed to identify and quantify regional BOLD responses to Grip Force variations when performing and observing a squeeze ball task

fMRI Protocol

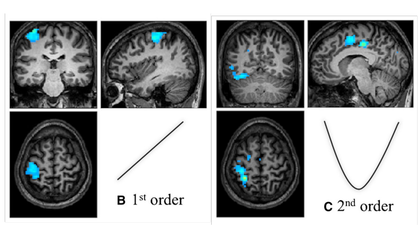


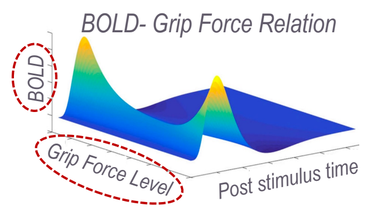
Casiraghi et al.,2019

3T Philips Achieva MRI scanner, high-resolution 3DT1 anatomical scan and three event-related fMRI scans

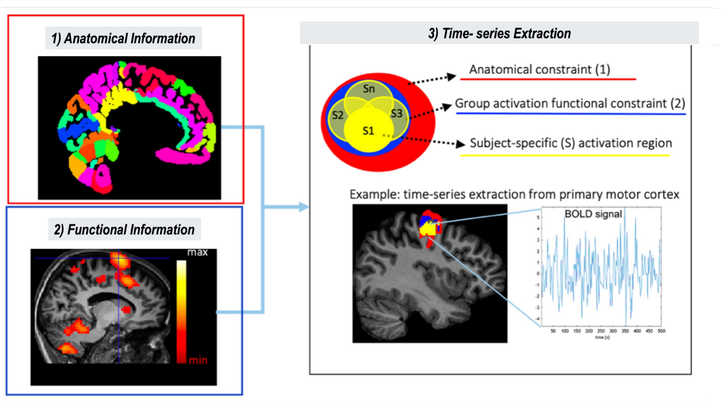
Action Execution (AE): 21;
Action Observation (AO): 9 healthy volunteers; all right-handed

Investigating Linear and Non-linear Responses





Alahmadi et al.,2016

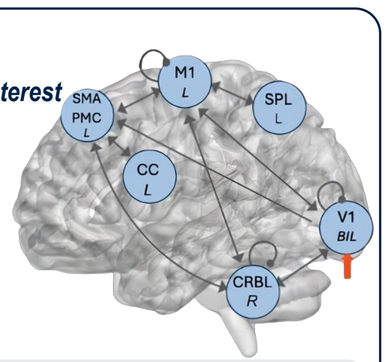


Time-series were extracted by doing a conjunction analysis

Model Construction

Visuomotor Network - Regions of Interest

V1_BIL: *Bilateral primary visual cortex*
M1_L: *Left primary motor cortex*
CC_L: *Left cingulate cortex*
SPL_L: *Left superior parietal lobule*
SMAPMC_L: *Left supplementary motor area & premotor cortex*
CRBL_R: *Right cerebellum*



Step 1 (S1)

Direct influences:
How do the regions embedded in the visuomotor network influence each other in AE and AO?

Step 2 (S2)

Nonlinear modulations:
Who drives the non-linearities in the visuo-to-plan functional pathway?

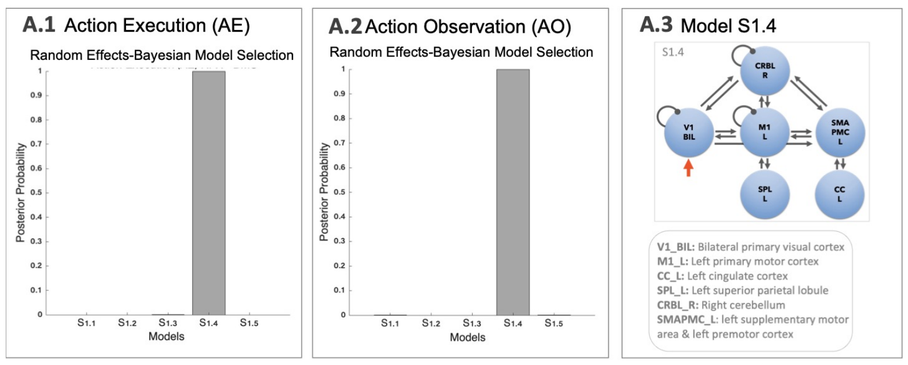
*By comparing different causal models, **Bayesian Model Selection (BMS)** determined the most likely causal architecture that best explains the observed data*

Results

Fixed Effective Connectivity winning model (S1 outcomes)

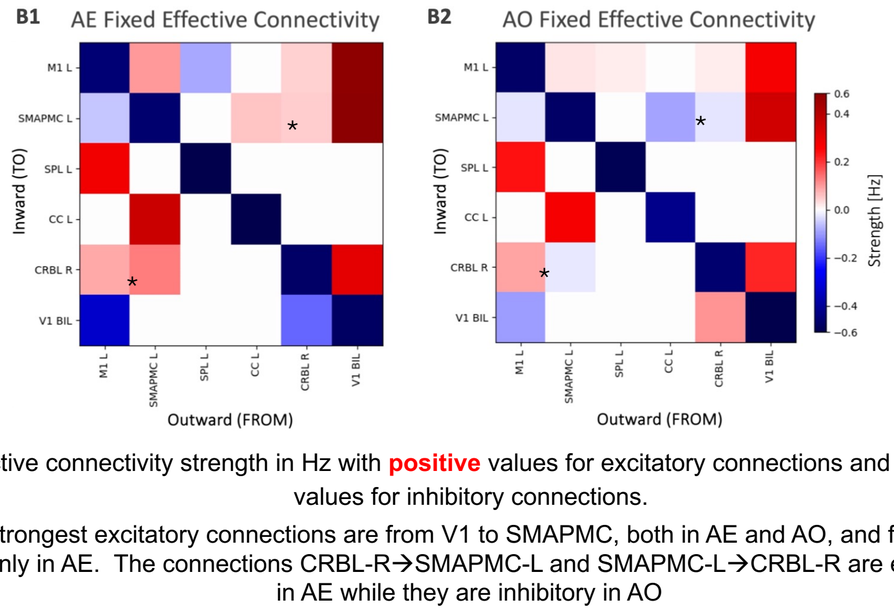
A) Bayesian Model Selection

Winning model structure



BMS with random effects (RFX-BMS) identified Model S1.4 as the "winning model" with posterior probability > 90% in both action execution (AE, panel A.1) and action observation (AO, panel A.2).

B) Fixed Effective Connectivity

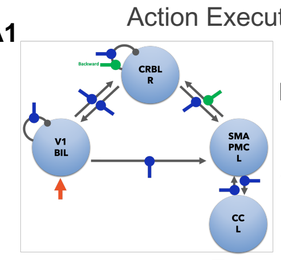


Effective connectivity strength in Hz with **positive** values for excitatory connections and **negative** values for inhibitory connections.

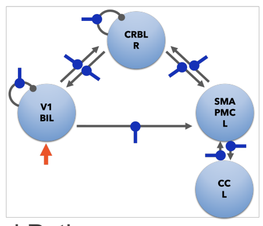
The strongest excitatory connections are from V1 to SMAPMC, both in AE and AO, and from V1 to M1 only in AE. The connections CRBL-R→SMAPMC-L and SMAPMC-L→CRBL-R are excitatory in AE while they are inhibitory in AO

Modulation of the Fixed Effective Connectivity (S2 outcomes)

A1 Action Execution (AE) Network



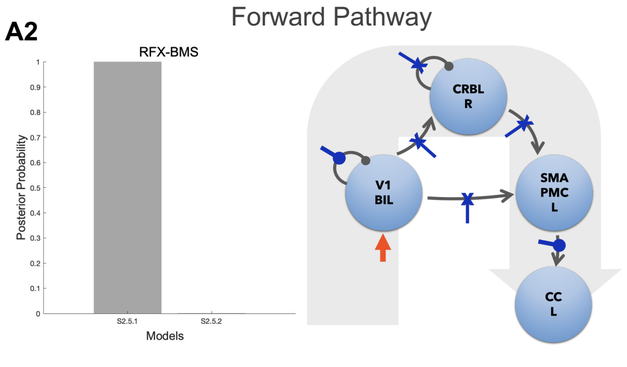
B1 Action Observation (AO) Network



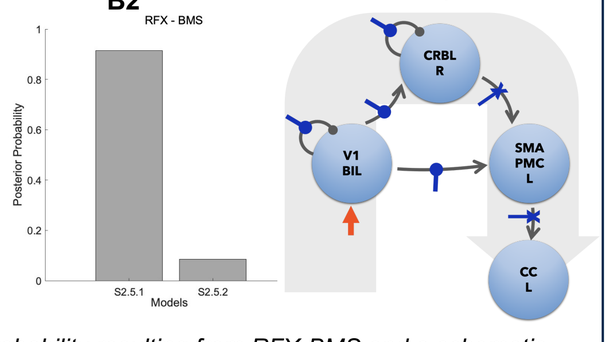
Forward and backward winning models are shown both for the AE and the AO conditions (Panel **A** and **B**, respectively).

A1 and B1 show *the S2-winning models with the modulations on connections between regions of the visuo-to-plan loop.*

A2 Forward Pathway

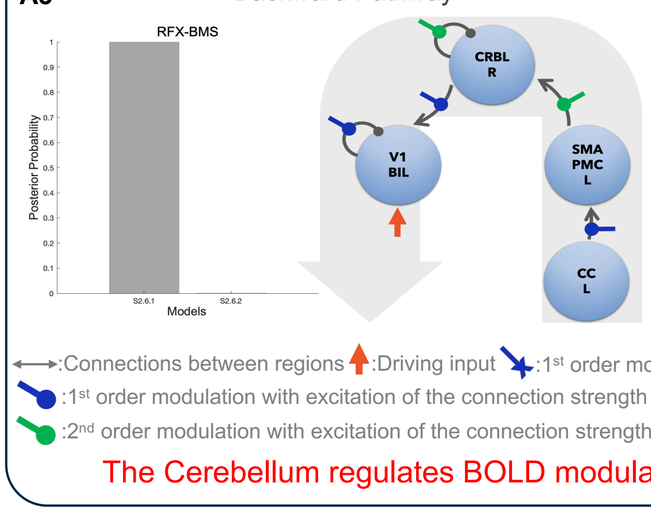


B2 Forward Pathway

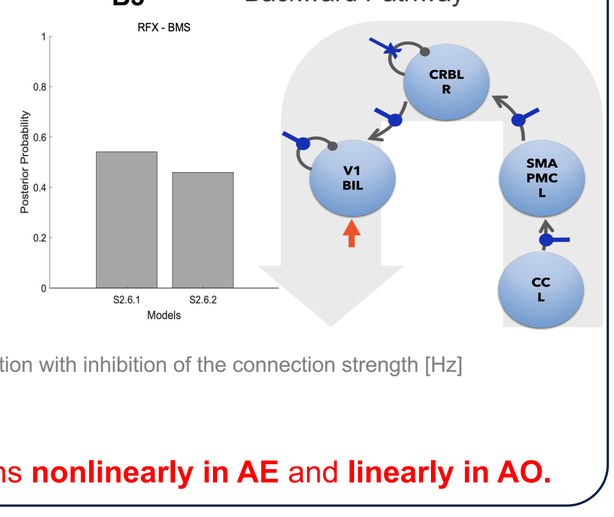


A2 - B2 & A3 – B3) *Each histogram shows the posterior probability resulting from RFX-BMS and a schematic representation of the S2-winning model for AE and AO forward loops (A2 & B2) and backward loops (A3 & B3).*

A3 Backward Pathway



B3 Backward Pathway



:Connections between regions :Driving input :1st order modulation with inhibition of the connection strength [Hz]
:1st order modulation with excitation of the connection strength [Hz]
:2nd order modulation with excitation of the connection strength [Hz]

The Cerebellum regulates BOLD modulations **nonlinearly in AE** and **linearly in AO.**

Conclusion

The presence of sensorimotor feedback in AE determines the way the cerebellum operates as a forward controller on motor planning areas.

Our next step will be investigating how sensorimotor control impacts on cerebro-cerebellar function and dysfunction in neuroinflammatory diseases such as Multiple Sclerosis (MS)

Acknowledgements

References
1.Friston et al., 2003. Neuroimage. 2. Penny et al., 2010. PLoS Computational Biology. 3. Alahmadi et al., 2016. Brain Structure and Function. 4.Casiraghi et al., 2019. Cerebral Cortex.

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