Mapping the dominant direction of the structural network of the macaque prefrontal cortex reveals its hierarchical structure

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Introduction

Various models have been put forth to explain the modus operandi of the prefrontal cortex (PFC). One such model postulates an hierarchical anterior-posterior gradient within the PFC[1]. The structural architecture of the macaque PFC seems to support such a model. The hierarchical model is characterized by the principles of asymmetry, i.e. more anterior regions (region 10) have more efferents towards posterior ones (region 8) than vice versa, and contiguity, reciprocal connections are “valid” among spatially adjacent regions. However, a formal quantification of the principles and the predictions of such an “asymmetry based hierarchical” (ABH) model is lacking. We thus aimed to perform such a quantification and also relate the ABH with another concept of hierarchy based on the laminar patterns of the PFC connections (LBH) [2].

Materials and Methods

• PFC represented as a directed graph by using a published dataset on macaque PFC connectivity based on Walker’s parcellation scheme [3].

• The principles of asymmetry and contiguity are mathematically represented with eq. 1 & 2 respectively. Maximally and minimally hierarchical reference networks were created by minimizing eq. 3.

• For the LBH optimization estimated laminar patterns of PFC connections were based on predictions from the structural model [2]. Eq.4 was used for the LBH optimization.

(1) $$En = \sum_{i \to j} [H(m_j - m_i)]$$

(2) $$En = \sum_{i \to j} [H(m_j - m_i) \cdot \delta_{i,j}]$$
$$\delta_{i,j} = \begin{cases} 1, C(i,j) = 0 \\ 0, C(i,j) = 1 \end{cases}$$

(3) $$En = (Cost_{Desired} - Cost_{Actual})^2$$

(4) $$En = \sum_{i \to j} [g((m_i - m_j) \cdot LB_{i \to j}) \cdot abs(LB_{i \to j})]$$
$$g(x) = \begin{cases} 0, & x > 0 \\ 1, & x \leq 0 \end{cases}$$

Results

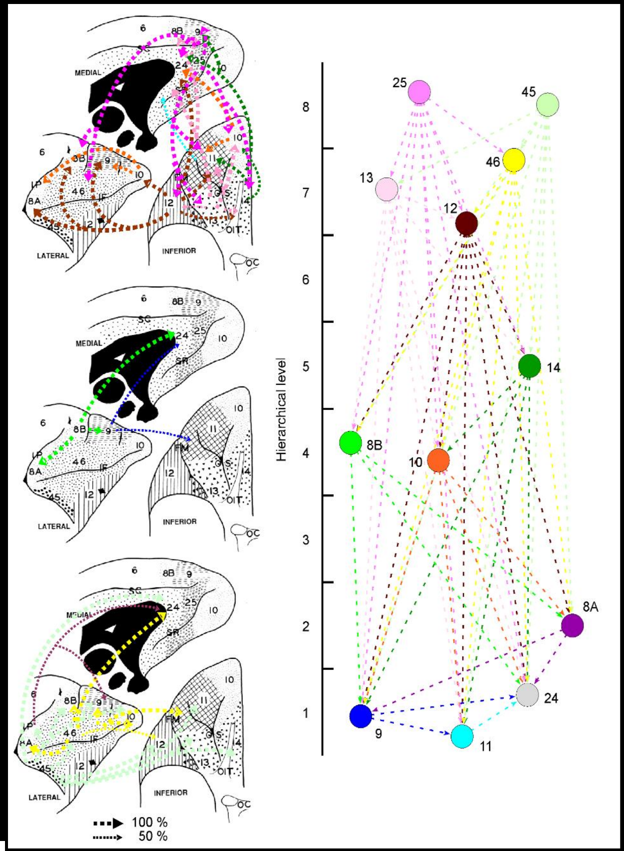

Fig 1. Hierarchical diagram depicting the most frequent (>50%) efferents termed as hierarchical in the ABH optimization. The hierarchical diagram is overlaid on Walker’s parcellation scheme offering an anatomical view of the layout. A graph layout is also depicted with the PFC regions assigned to the hierarchical level for which a peak was observed across the solutions (see Fig. 2).

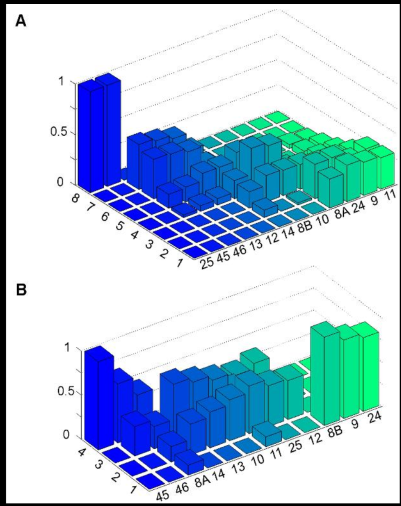

Fig 2. Distribution of the hierarchical levels over 1000 solutions for **A.** Cost function 1 (eq 1) and **B.** Cost function 2 (eq. 2).

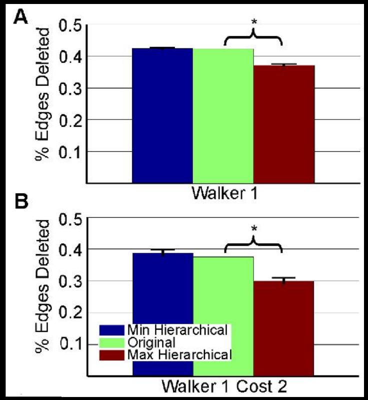

Fig 3. Relation of the original PFC network with max and min hierarchical reference networks for **A.** Cost function 1 (eq. 1) and **B.** Cost function 2 (eq. 2).

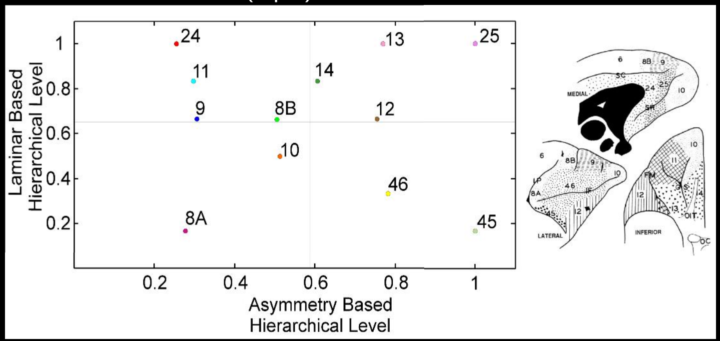

Fig 4. Scatter plot depicting the results for the ABH and LBH. The results are uncorrelated and offer diverge information on PFC regions. For instance “broadcasters” as revealed by ABH (regions 45 and 25) are differentiated through their position in the LBH (45 is low in the LBH thus its hierarchical efferents constitute “feedforward” connections whereas region 25 exhibits “feedback” ones).

Conclusions -The ABH optimization does not reveal an anterior-posterior gradient with region 10 on top (Fig. 1 & 2).

-The macaque PFC is wired in a “non-optimal” hierarchical way (Fig. 3).

-The ABH and LBH optimization do not correlate and offer a richer picture on PFC architecture (Fig. 4).

-The LBH seems a more plausible working hypothesis for an anterior-posterior hierarchy within the PFC.

Refs: [1] Badre D & D’Esposito M (2009) Nat Rev Neuroscie 10:659-69 [2] Barbas H & Rempel-Clower N (1997) Cereb Cortex 7:635-646 [3] Kötter R, Hilgetag CC, Stephan KE (2001) Neurocomputing 38-40:741-746