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Probabilistic Logic for Coordinate-Based Meta-Analysis of Functional Segregation in the Brain

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Authors:

Majd Abdallah¹, Valentin Iovene², Demian Wassermann²

Institutions:

¹INRIA, Palaiseau, France, ²INRIA, Palaiseau, Ile-de-France

First Author:

Majd Abdallah

INRIA

Palaiseau, France

Co-Author(s):

Valentin Iovene

INRIA

Palaiseau, Ile-de-France

Demian Wassermann

INRIA

Palaiseau, Ile-de-France

Introduction:

Accurately mapping cognitive processes to distinct brain regions [1-3] requires meta-analytic synthesis of neuroimaging databases [4-6], which have become crucial to human brain mapping. However, current meta-analytic query systems are limited to expressions of already known facts, which precludes the generation of new knowledge about functional segregation in the brain. A novel framework using a probabilistic logic programming tool called NeuroLang overcomes this shortcoming, enabling an expressively-rich formalism of functional segregation queries in a natural language syntax, while endowing results with probabilities of them being true.

Here, we leverage the expressive power of NeuroLang to study the functional segregation in the posterior cingulate cortex (PCC). A central node in the default mode network [8], the PCC is widely known to subserve internally-directed cognitive processes [9]. However, recent evidence suggests that this region is associated with disparate cognitive processes [5,9], with the dorsal PCC involved in cognitive control and ventral PCC supporting internally-directed cognition. The approach showcased in this study provides a tool that can validate

findings and enable future investigations into uncharted brain regions.

Methods:

We use NeuroLang, a domain-specific probabilistic logic programming language [7], able to express complex reverse inference queries on CBMA databases. Reverse inference asks which terms, generally associated with cognitive processes, are most probably associated with a given activation pattern. We use the DiFuMo functional parcellation [10] to define two subregions of the PCC. For the CBMA database, we use NeuroQuery [3]. NeuroQuery calculates term-to-study associations from the full text of studies and is well-suited for reverse inference.

Peak activation coordinates and term-to-study associations reported by studies in the database are encoded in NeuroLang, alongside DiFuMo regions. Predicate logic allows us to represent this knowledge, using predicates such as `TermAssociation(visual, 18183754)`, that encodes that study 18183754 is associated with the term 'visual'. Queries on this program can be expressed and used to infer new knowledge.

Solving a reverse inference query is done by estimating conditional probabilities $P[\text{TermAssociation}(t, s) \mid Q]$ of term t being associated with study s , given a query Q over CBMA data. To differentiate function across PCC subregions, we define Q as a segregation query that selects studies reporting activations in a PCC subregions but not in the other one (i.e. segregating the other component). More formally, this is written as

$P[\text{TermAssociation}(t, s) \mid \text{RegionReported}(vPCC, s) \wedge \neg \text{RegionReported}(dPCC, s)]$

where \neg is the logic negation operator. This is done for the vPCC, segregating the dPCC, and vice-versa. We run this query and analyse the resulting probabilities to identify cognitive functions most probably associated with each subregion, while performing subsampling of all NeuroQuery studies to derive empirical probability distributions (Fig. 2).

Results:

Consistent with recent evidence [9], our results suggest differential involvements of d-/v PCC in cognition (Fig. 2). Particularly, terms generally associated with "Cognitive Control" are more likely to appear in studies that report only dPCC and not vPCC activations. In contrast, terms associated with internally-directed cognitive processes, such as "Self Reference", are more likely to appear in studies reporting only vPCC and not dPCC activations. A code to replicate the findings can be found in [11].

Conclusions:

In this study, we used probabilistic first-order logic to assess the functional segregation in the PCC, with findings supporting recent evidence of differential roles for d-/v PCC. Through this methodological approach, we hope to empower the cognitive neuroscience community with an expressive and powerful language that can aid in exploring and developing new hypotheses of brain-behavior relationships.

Modeling and Analysis Methods:

Methods Development ¹

Neuroanatomy, Physiology, Metabolism and Neurotransmission:

Anatomy and Functional Systems

Cortical Anatomy and Brain Mapping ²

Neuroinformatics and Data Sharing:

Databasing and Data Sharing

Workflows

Keywords:

FUNCTIONAL MRI

Informatics

Meta- Analysis

Open-Source Code

Open-Source Software

Workflows

Other - Coordinate-based meta-analysis

¹¹²Indicates the priority used for review

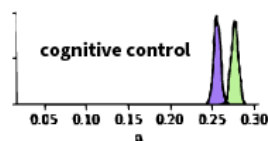
Graphical Abstract: Application Example

Using **NeuroLang** to differentiate functions of the vPCC and dPCC through meta-analytical reverse inference

Segregation reverse inference querying in NeuroLang

Segregation query: what is the probability of study **association with a given cognitive process** for studies that **report activations within one subcomponent (e.g. dPCC) but not the other (e.g. vPCC)?**

Expressed with probabilistic logic programming

$$P[\text{FunctionAssociation}(\text{Working_Memory}, S) | \text{RegionReported}(\text{vPCC}, S) \wedge \neg \text{RegionReported}(\text{dPCC}, S)]$$


Comparing resulting probabilities across many bootstrapped samples of NeuroQuery

Cognitive Control

inhibitory control / stroop / attention shift / control processes / control network / attention shifting / cognitive control / response selection / conflict resolution / response inhibition / Proactive control / response conflict / goal maintenance / behavioral inhibition / decision making / attentional control / multi-tasking / flexibility / goal directed / set shifting / task switching / stroop task

Terms grouped by their associated cognitive function

Self Reference

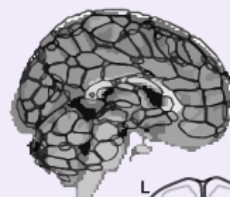
introspection / self knowledge / self evaluations / self / self referential / self evaluation / self concept

Theory of Mind

tom / emotional intelligence / mentalizing / theory mind

DiFuMo functional parcellation

Dictionary-learned functional modes



Defining the vPCC and dPCC from DiFuMo components

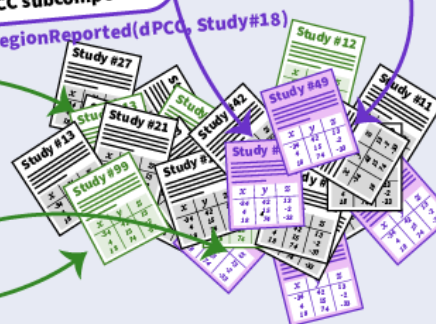


Selecting studies reporting activations in PCC subcomponents

RegionReported(dPCC, Study#18)

TermInStudy(self reference, Study#12)

Selecting studies associated with cognitive function terms



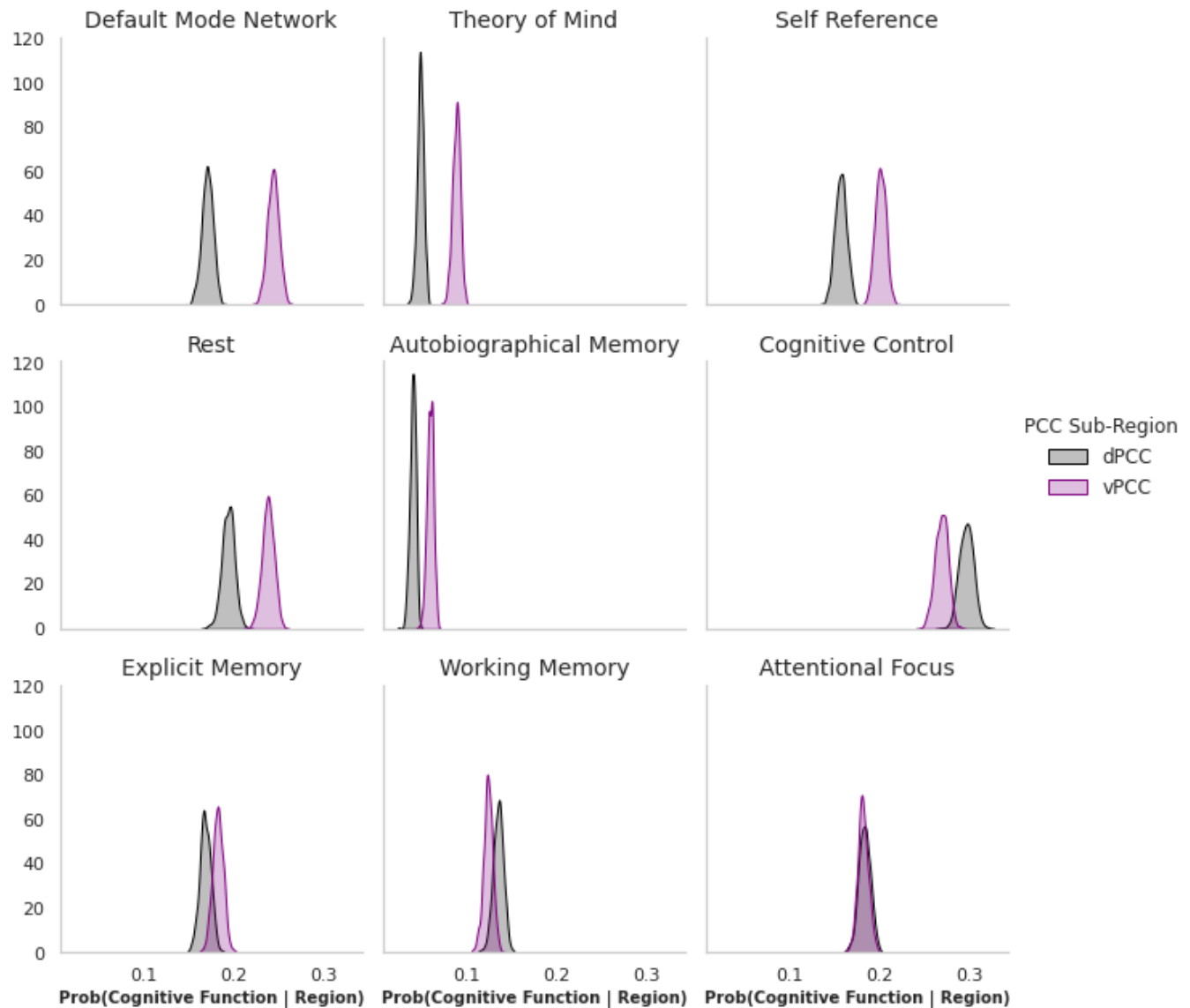
NeuroQuery CBMA database

Database of peak activation coordinates and TFIDF text features extracted from studies

(https://files.aievolution.com/prd/hbm2101/abstracts/abs_2410/2021-01-ohbm-graphical-abstract-01.png)

·A graphical abstract of the study describing its methodology

Functional Segregation of dPCC and vPCC Sorted by Approximate Evidence Amount of Segregation
(Histograms across 1,000 Random Splits (split size 80%) of 13,881 Articles from NeuroQuery)



(https://files.aievolution.com/prd/hbm2101/abstracts/abs_2410/facet_plot_histograms.png)

·Results of the reverse inference segregation query showing approximate evidence amount of functional segregation between dorsal and ventral PCC across disparate cognitive domains

My abstract is being submitted as a Software Demonstration.

No

Please indicate below if your study was a "resting state" or "task-activation" study.

Other

Healthy subjects only or patients (note that patient studies may also involve healthy subjects):

Healthy subjects

Was any human subjects research approved by the relevant Institutional Review Board or ethics panel? NOTE: Any human subjects studies without IRB approval will be automatically rejected.

Not applicable

Was any animal research approved by the relevant IACUC or other animal research panel?
NOTE: Any animal studies without IACUC approval will be automatically rejected.

Not applicable

Please indicate which methods were used in your research:

Other, Please specify - Coordinate-based meta-analysis and probabilistic first-order logic programming

For human MRI, what field strength scanner do you use?

If Other, please list - Not applicable

Which processing packages did you use for your study?

Other, Please list - Not applicable

Provide references using author date format

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[11] https://github.com/NeuroLang/meta-functional-connectivity/PCC_functional_specialization_example_Difumo_ROI.py