Integration of cytoarchitecture and brain-wide connectivity reveals topographic organization of macaque insula networks

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1 A *lobe-cation* for integration

- The insula is the **hub** of interoception[1,2]
- Interoception is the **perception** and **integration** of signals that describe the physiological state of the body[3,4]
- Dysfunction of insula has wide ranging implications for **physical** and **mental** health[5,6]

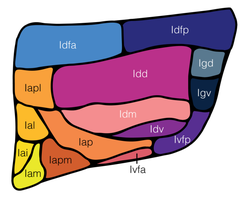
2 A cortical blueprint

- The flow of interoceptive information can be mapped onto organized and **distinct** cytoarchitectural subregions[7]
- Insula subregions as a collective represent a highly **integrated** whole brain network[8]

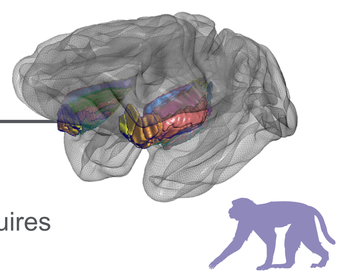
Granular: *primary sensory input*

Dysgranular: *integration*

Agranular: *visceromotor output, affective processing*



3 Multiscale analysis



- Technical challenges across **scale**

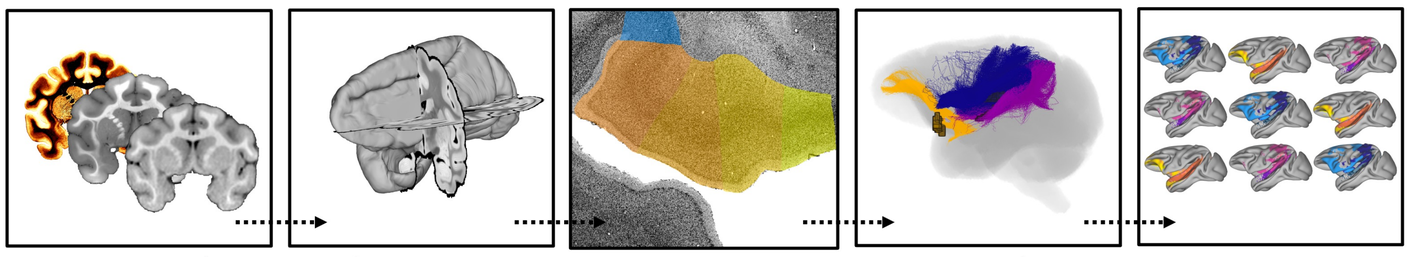
  > microscale – highly specific, but requires post mortem tissue, restricted to small areas or a few tracts

  > macroscale – whole brain networks but low resolution

- **Translatable animal models** can help to bridge these scales [9-12]

(*Mic*)ro to (*Mac*)ro Macaque: an extendable workflow to unify data across scales

4 Analysis across scales and subjects



Acquisition of multi-scale/modality data for whole brain

3D alignment across scale of single subject

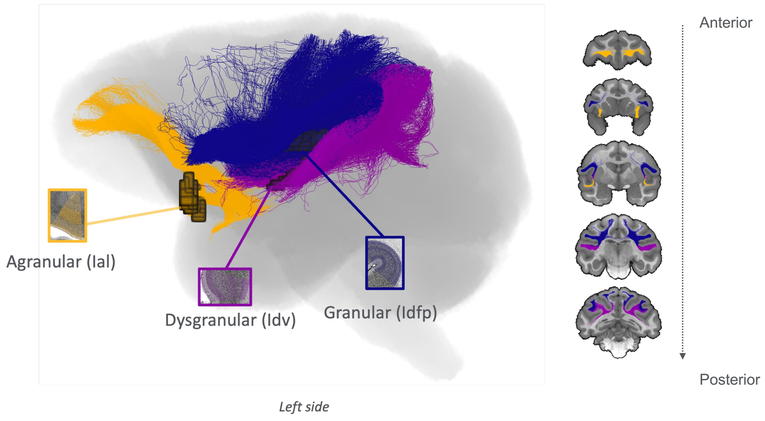
Cellular Segmentation

Convergent inferences in Central Space

Translation to population

MicMac: 10.3 year old healthy female rhesus macaque
Extensive histology, high resolution ex vivo MRI, and in vivo MRI have been aligned in a central space[13,14]
Alignment allows translation of expert parcellation across scale and modality, from volumes to cortical surfaces.

5 Cortical *cyto*-graphy

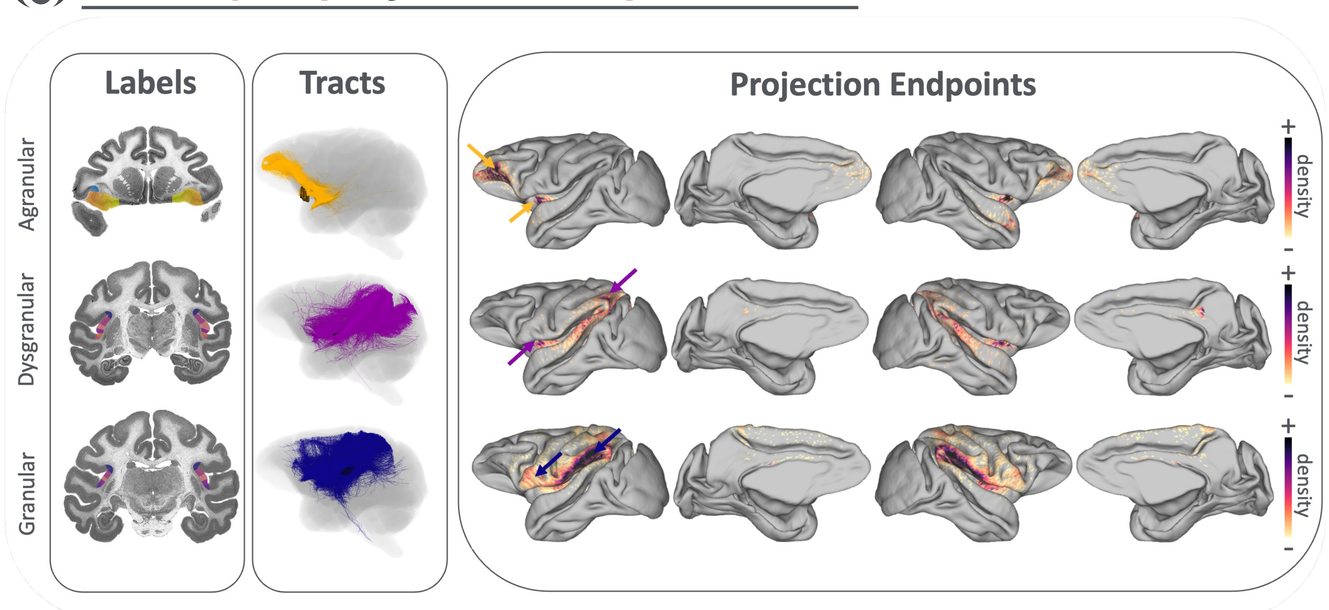


Left side

15 subregions per side were defined using 2x2 micron histology (3 shown)[15]
Tractography performed in subject space (b=4000s/mm^2)[16,17]

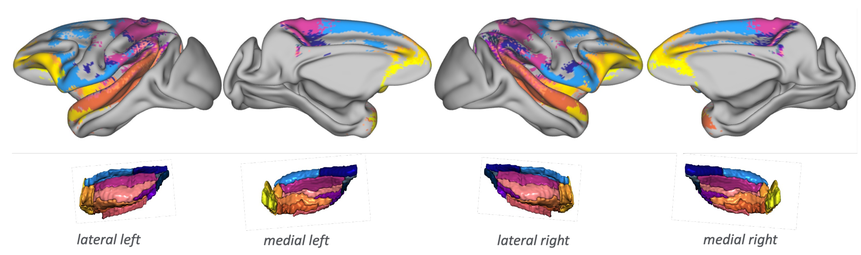
Translation of cortical targets from MicMac to *in vivo* subjects

6 Density of projection endpoints



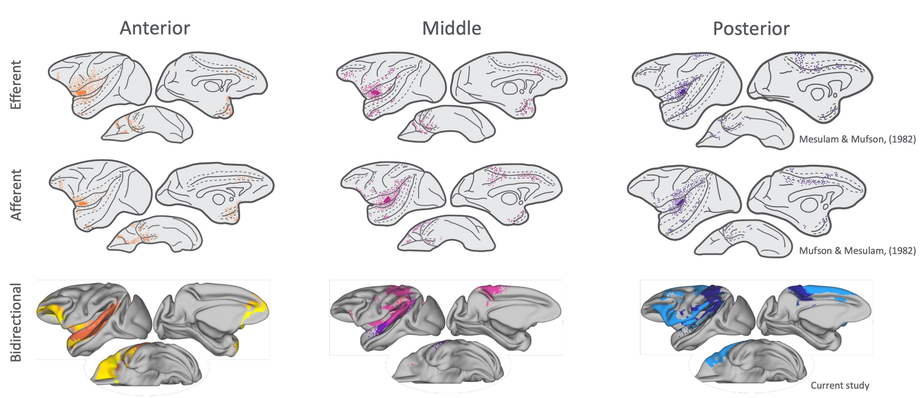
- Tractography was used to reconstruct the connections between the histologically defined subregions and cortical targets
- The density of projection endpoints is displayed on the cortical surface
- Analysis was repeated at the group level using identical protocols and analyses to in vivo MicMac data
- Results from 16 middle to older age subjects (3M/13F; 7-20 years) are shown in 89/8
- Tract tracing data has been restyled from two foundational studies of the insula [18,19] and reviewed in [20]

7 Mapping suggests topography of insula



**group level results

8 Comparison to tract tracing



*Distinct projection targets suggest a structured **topography** similar to primary sensory regions.*
*These results were **repeatable** for an in vivo cohort of middle to older aged animals and show generally **high correspondence** with tract tracing techniques.*

Frequently Asked Questions

- **Why such high b-values (/ what is that)?**
  B-values indicate the amount of diffusion weighting on an image. More = Increased sensitivity to tissue features like axons. Most clinical protocols use ~ 1000s/mm^2, but we find high b-values improve recovery of long-range projections when doing whole brain analysis.

- **Why not just look at human brain?**
  Projects such as BigBrain have reconstructed massive whole brain histology datasets in individual human brains, but it is nearly impossible to time lock post mortem histology and in vivo MRI in humans. Here the macaque monkey provides a critical tool to investigate the relationship of cytoarchitecture alongside MRI (a translational tool we can use for humans!), while also having similar wiring principles and organization compared to humans.

References

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Opportunities

& there is so much more to discover ~ *Come join us!*

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