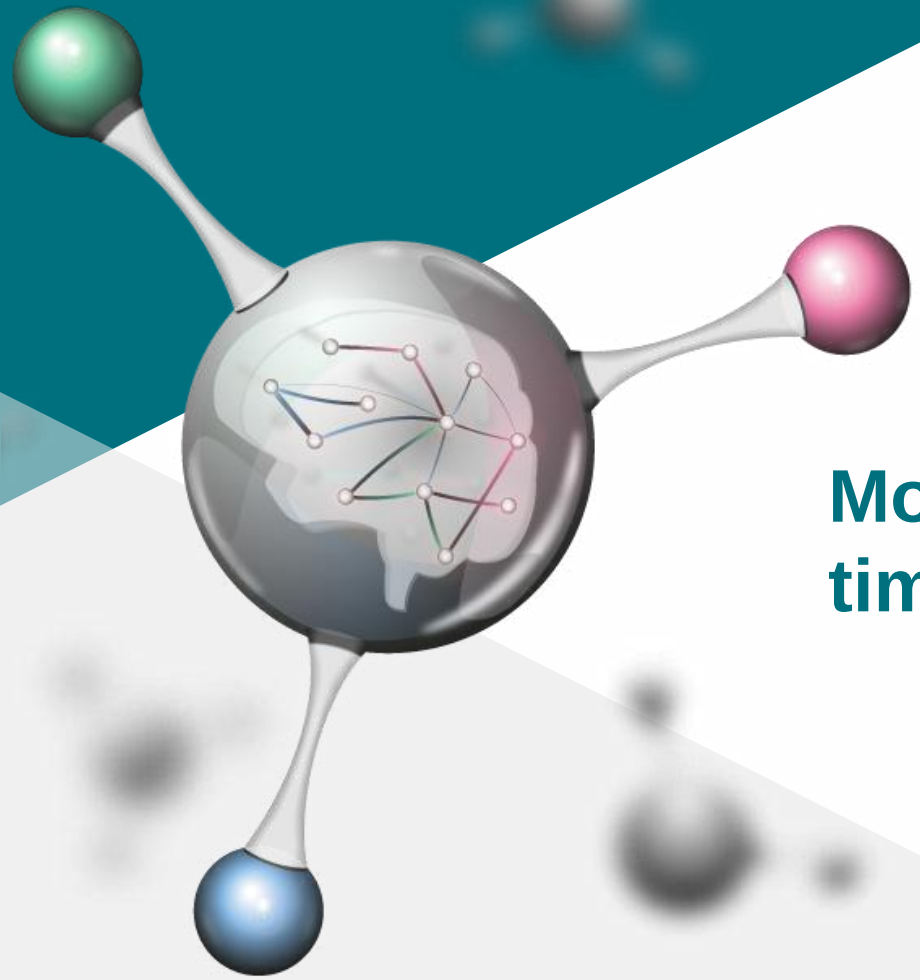


Molecular imaging and brain connectomics: time for a molecular imaging perspective?

Arianna Sala

Coma Science Group, GIGA Consciousness, University of Liège
Centre du Cerveau2, University Hospital of Liège

arianna.sala@uliege.be

Premise

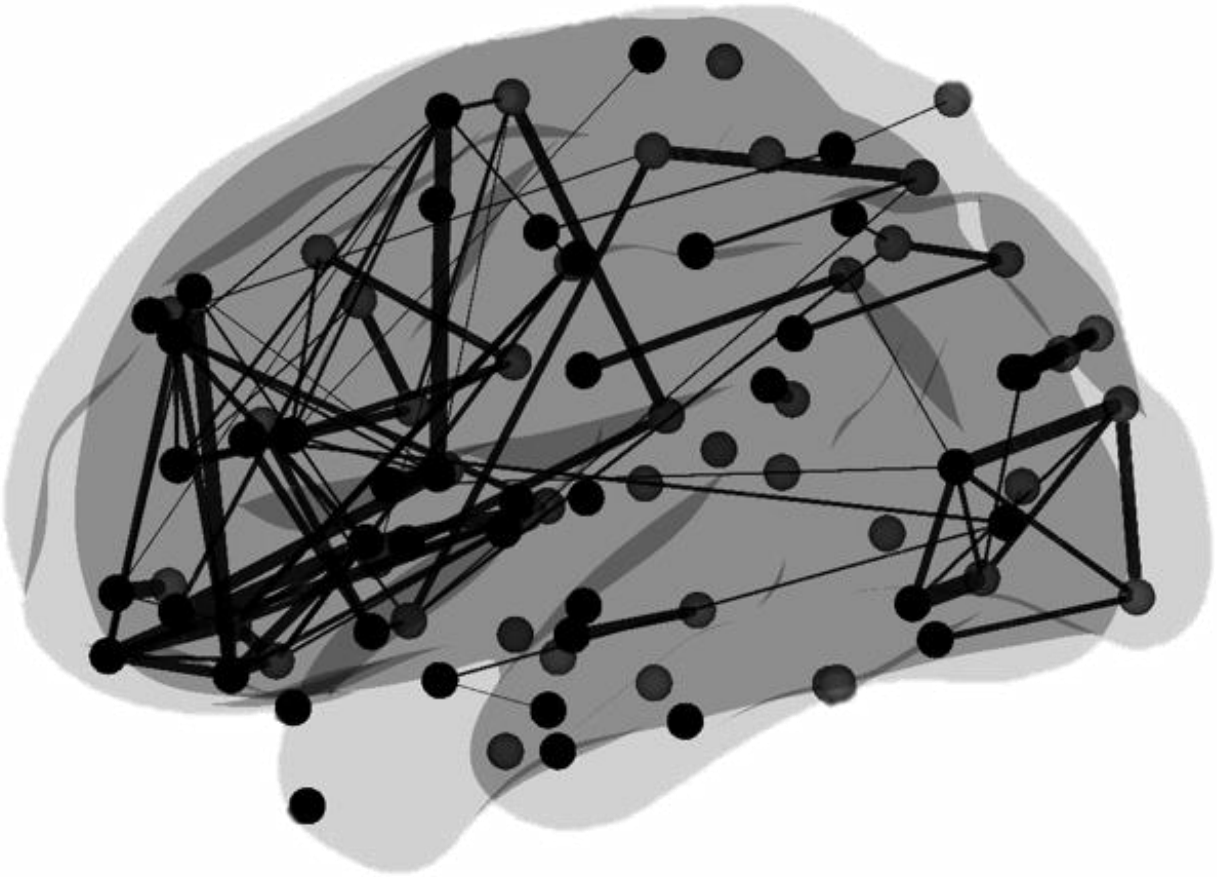
OPINION | VOLUME 27, ISSUE 4, P353-366, APRIL 2023 Download Full Issue

Brain connectomics: time for a molecular imaging perspective?

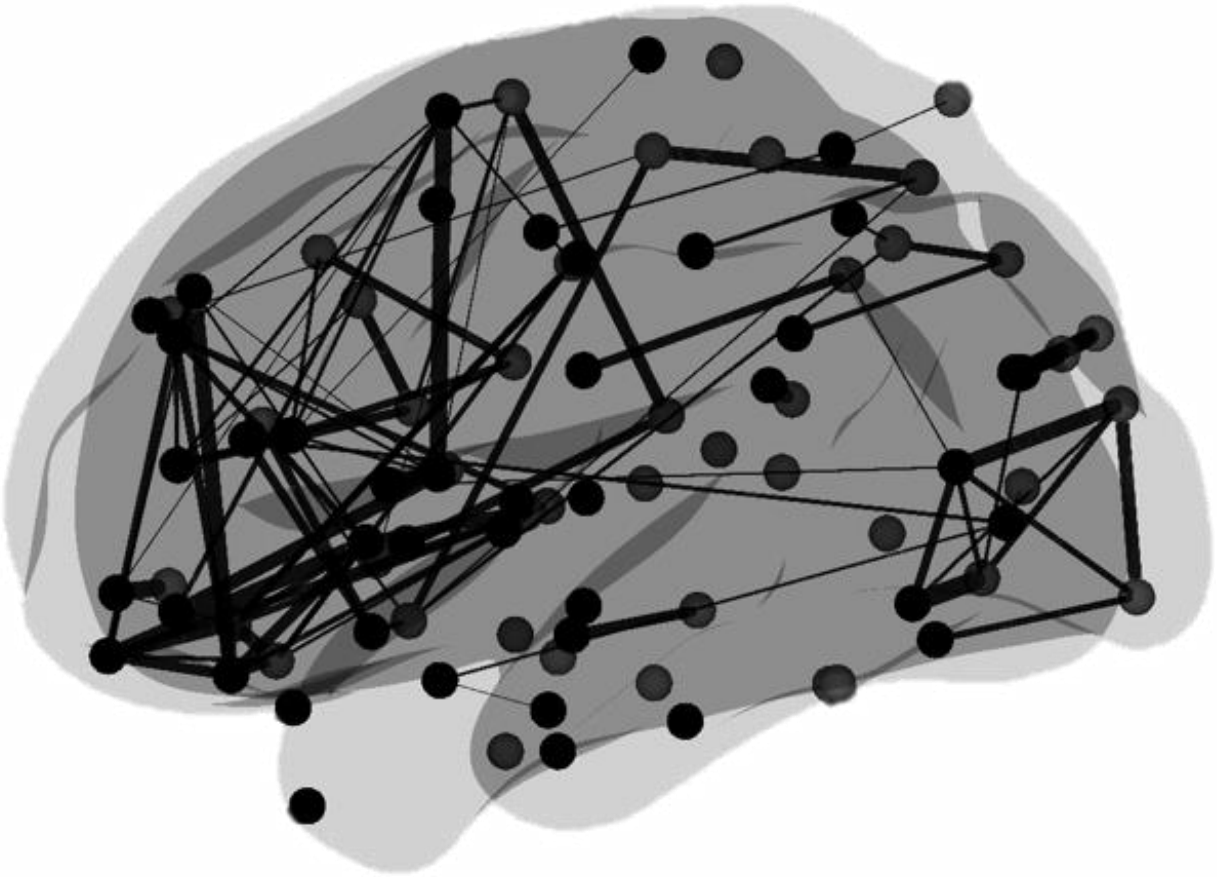
Arianna Sala • Aldana Lizarraga • Silvia Paola Caminiti • Vince D. Calhoun • Simon B. Eickhoff • Christian Habeck • Sharna D. Jamadar • Daniela Perani • Joana B. Pereira • Mattia Veronese • Igor Yakushev • Show less • Show footnotes

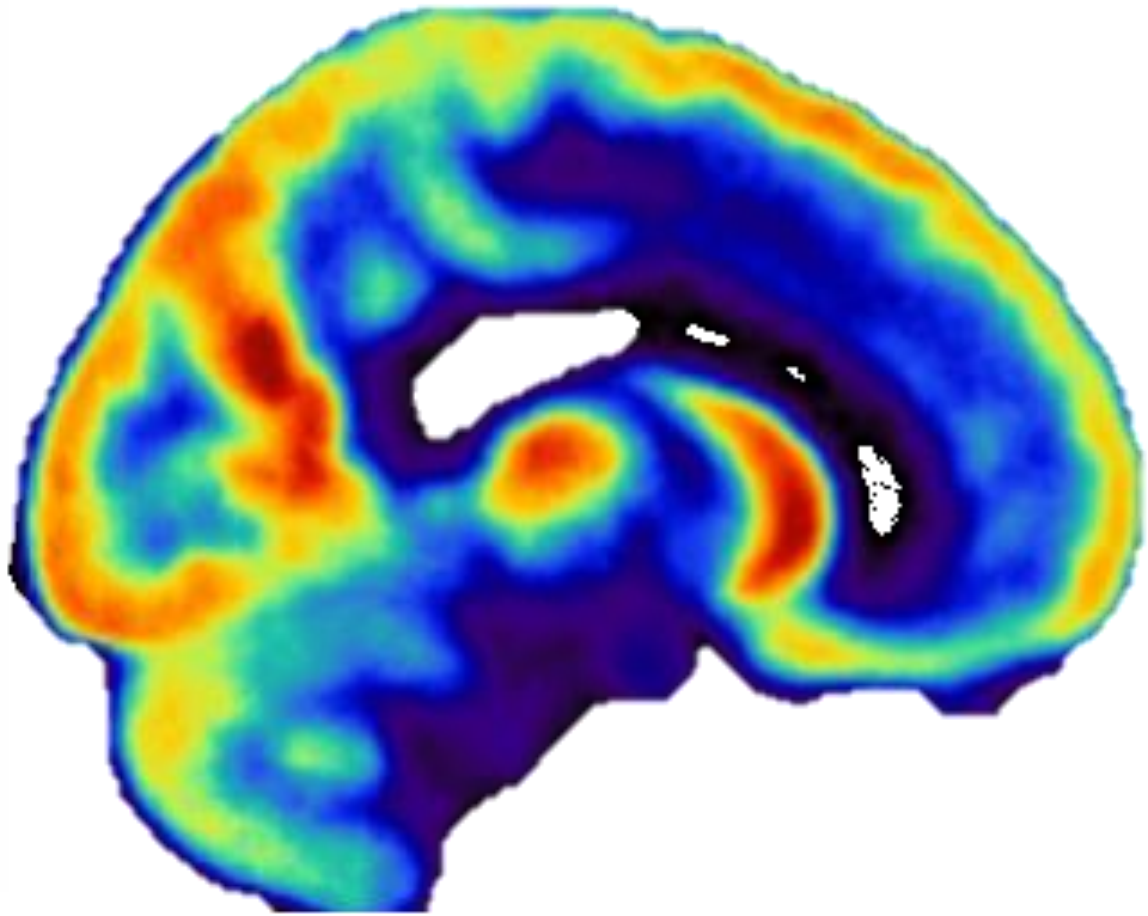
Published: January 06, 2023 • DOI: https://doi.org/10.1016/j.tics.2022.11.015 • Check for updates

Connectivity



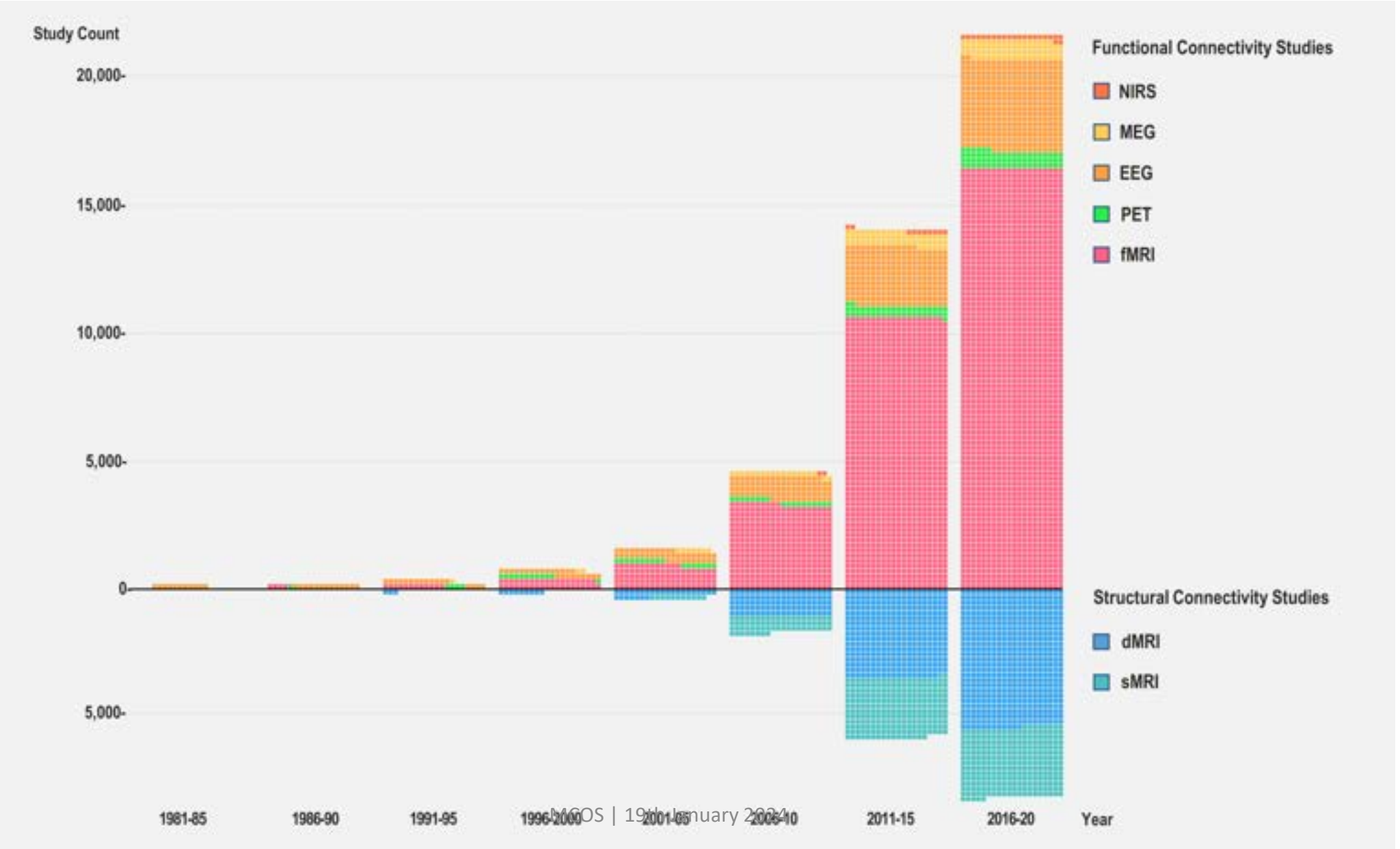
Molecular Connectivity



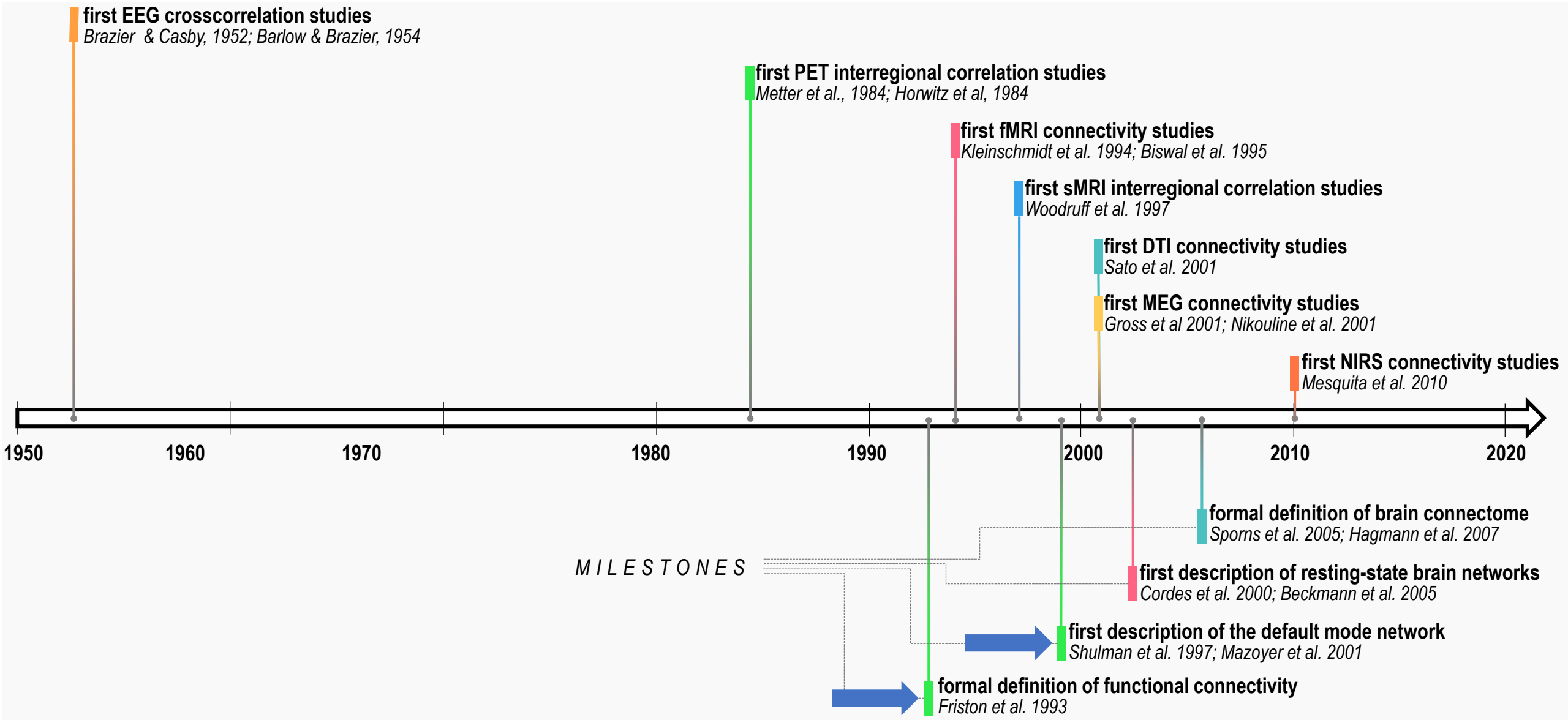


Courtesy of Tommaso Volpi, PhD

PET in current brain connectivity



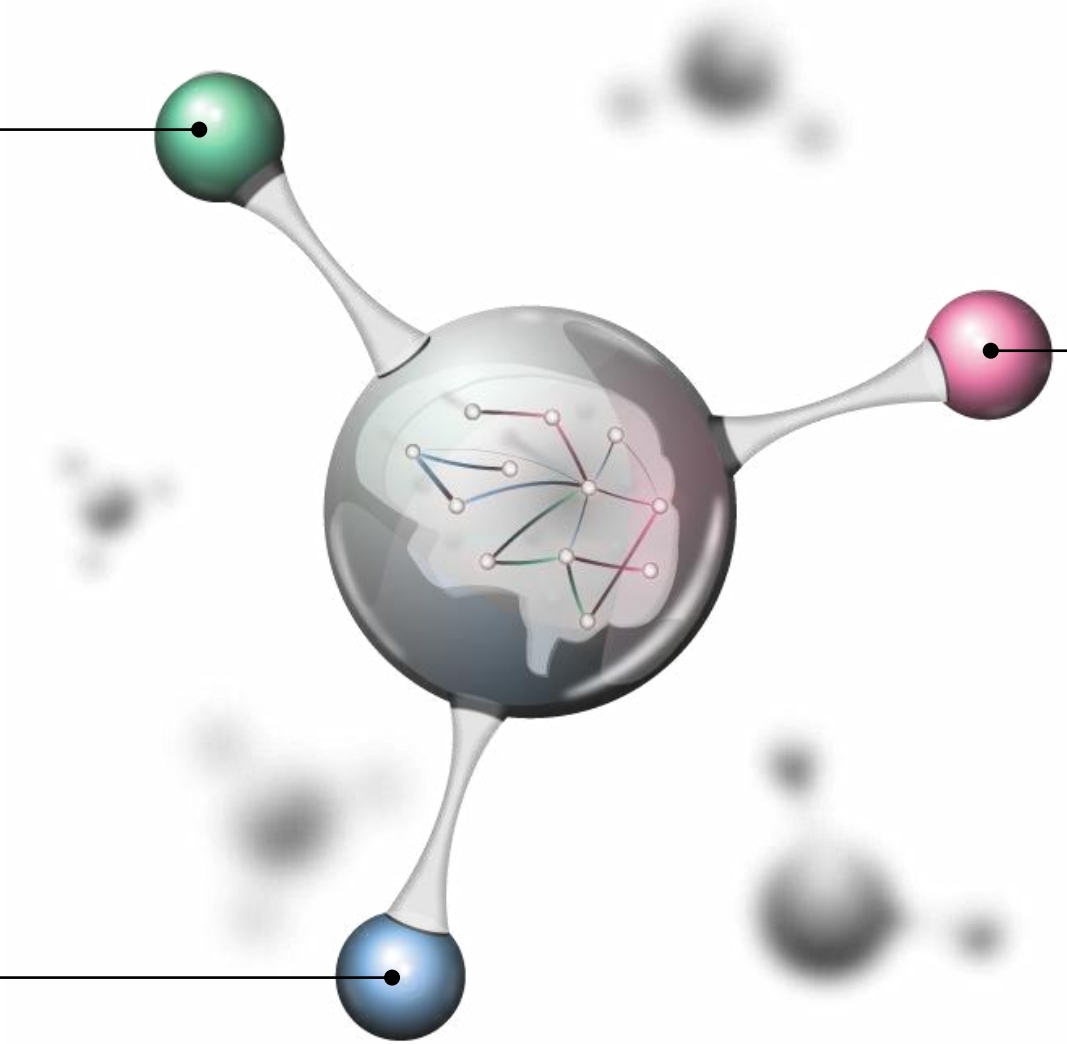
PET in the history of brain connectivity



Sala et al., 2023 TICS

Outline

Why

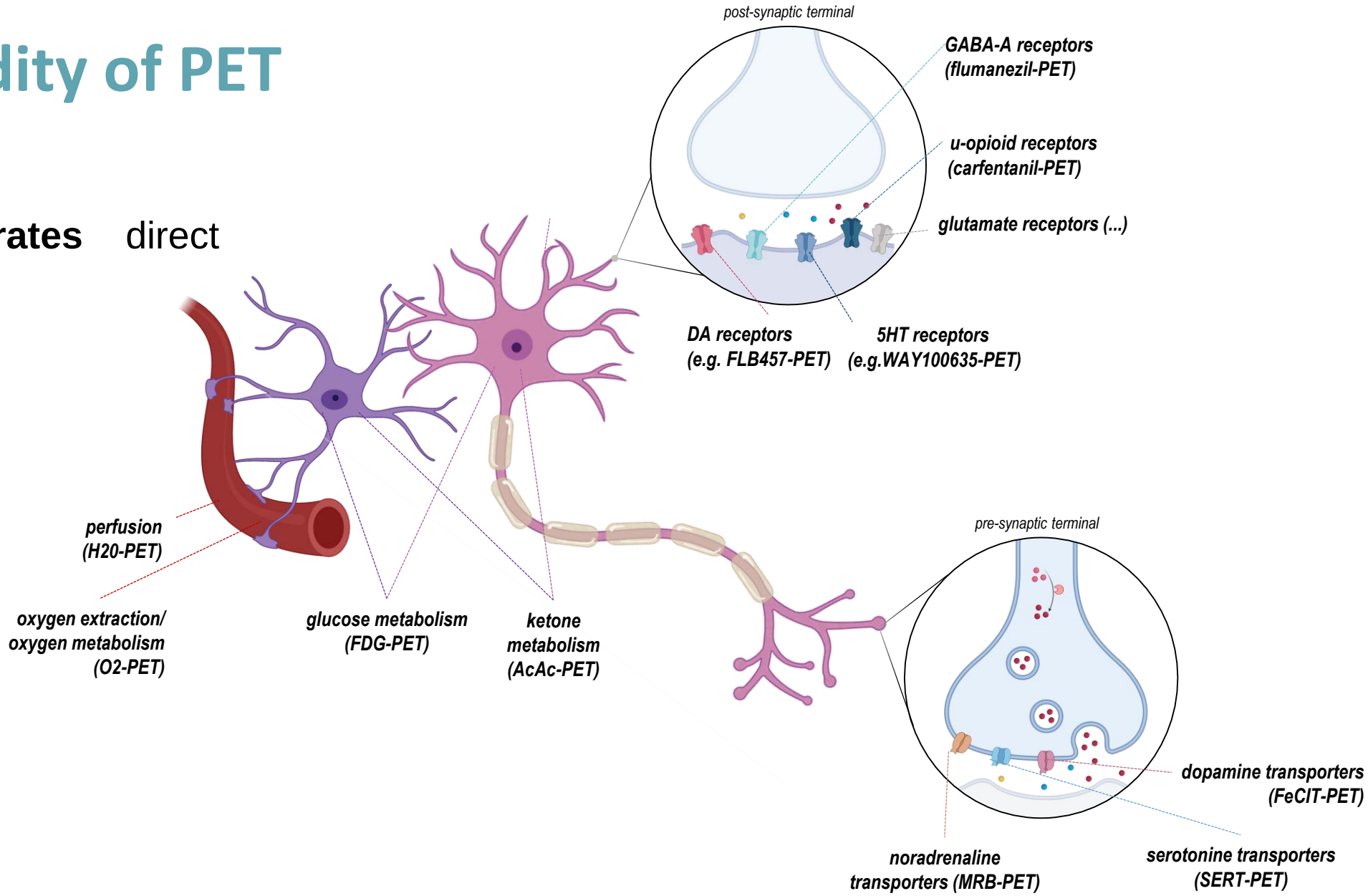


What

How

Why: validity of PET

Neuronal substrates direct



Why: validity of PET

Neuronal substrates direct

Why: validity of PET

Neuronal substrates direct

Reproducibility high **Intra-class correlation coefficient: 0.90 (Maquet et al., 1990)**

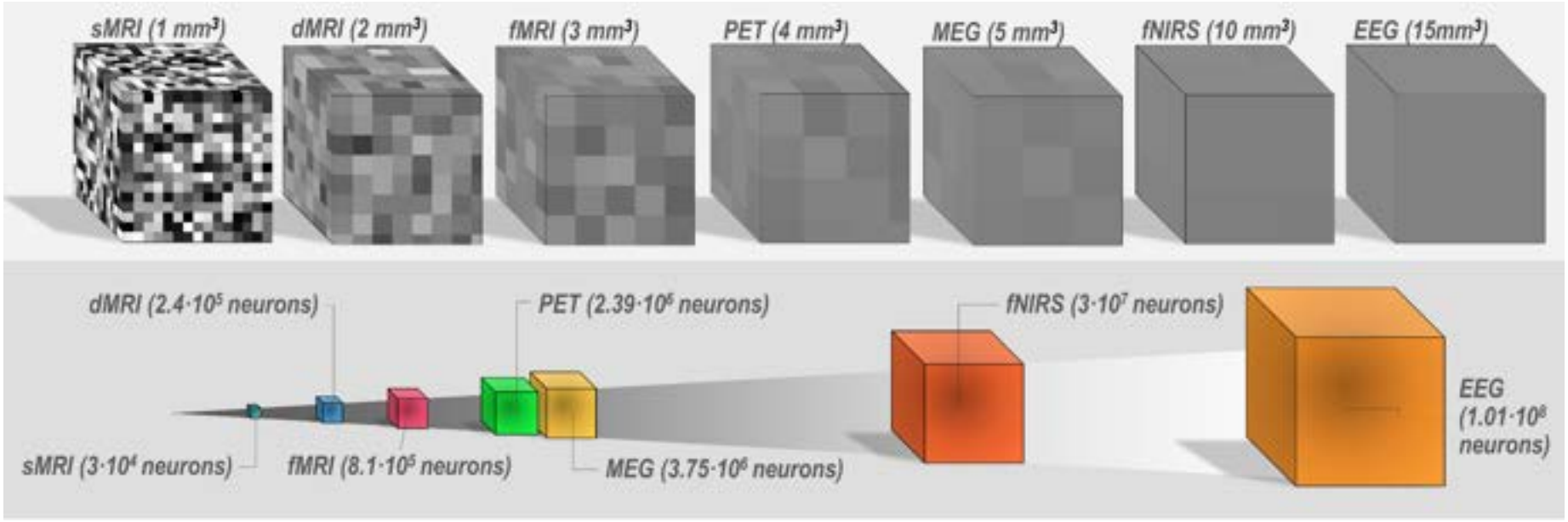
Courtesy of Igor Yakushev, MD, PhD

Why: validity of PET

Neuronal substrates direct

Reproducibility high

Spatial resolution 4.3 mm



Courtesy of Igor Yakushev, MD, PhD

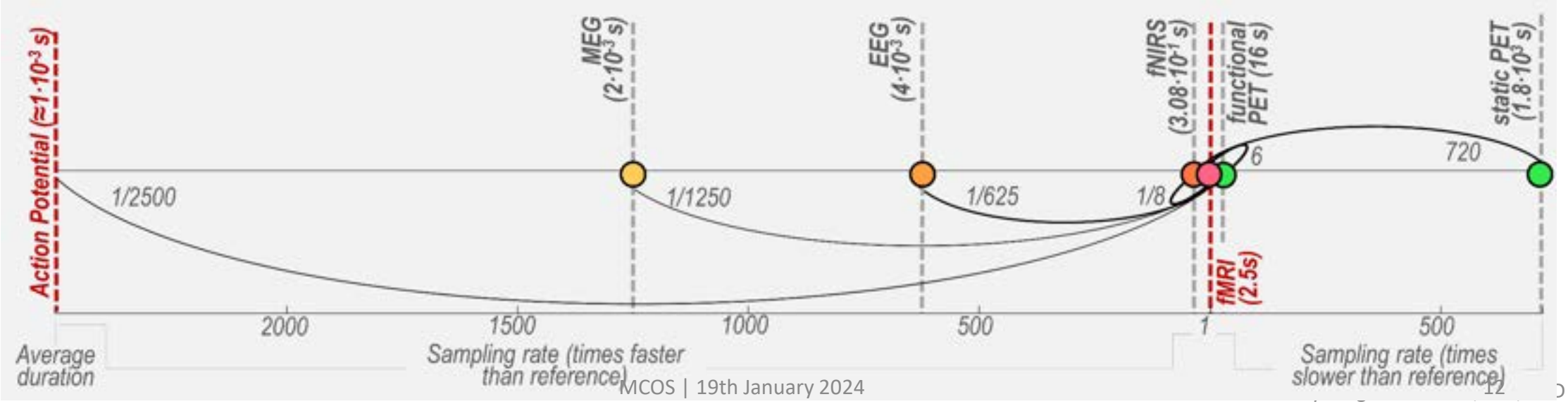
Why: validity of PET

Neuronal substrates direct

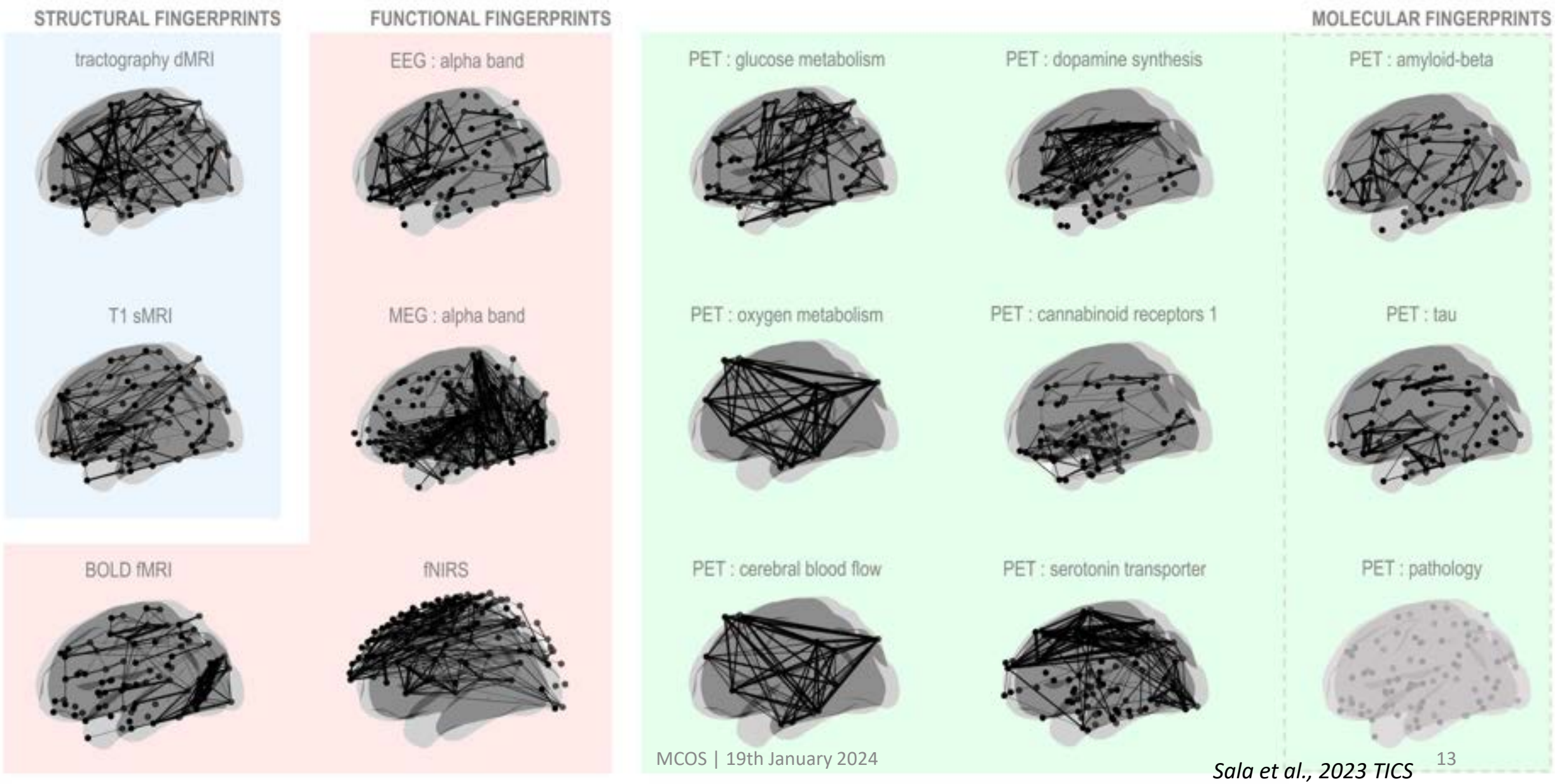
Reproducibility high

Spatial resolution 4.3 mm

Temporal resolution seconds to minutes

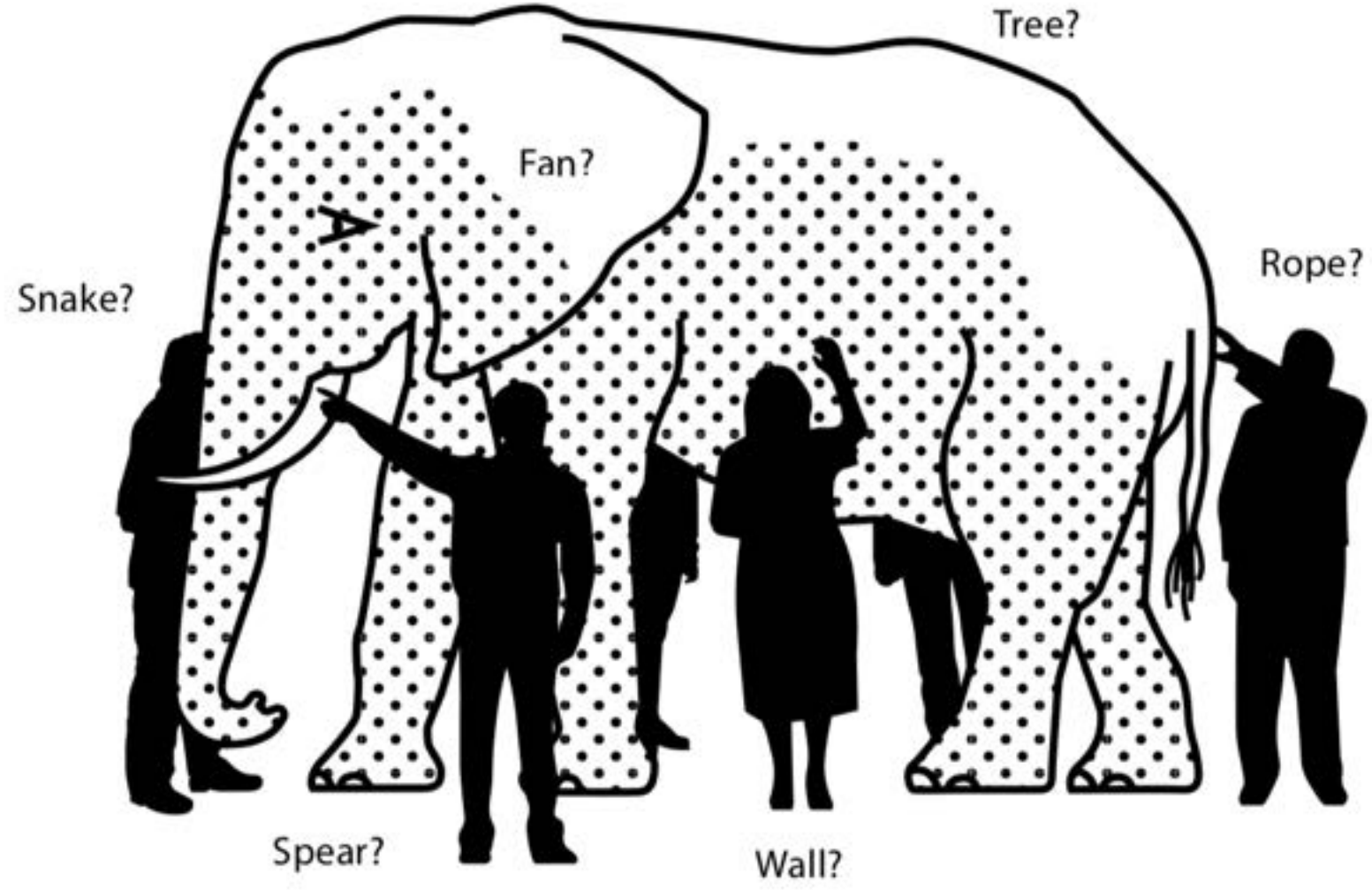


Why: accurate models of brain function



Sala et al., 2023 TICS

Why: accurate models of brain function

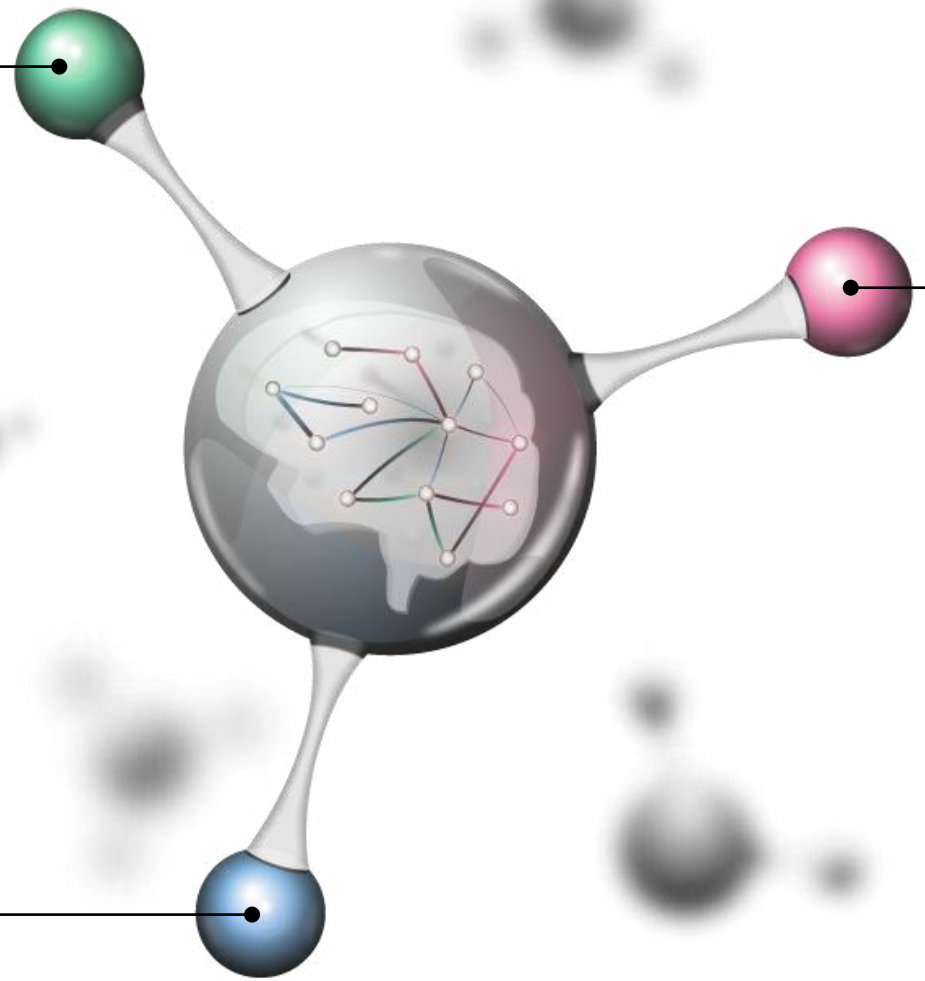


Outline

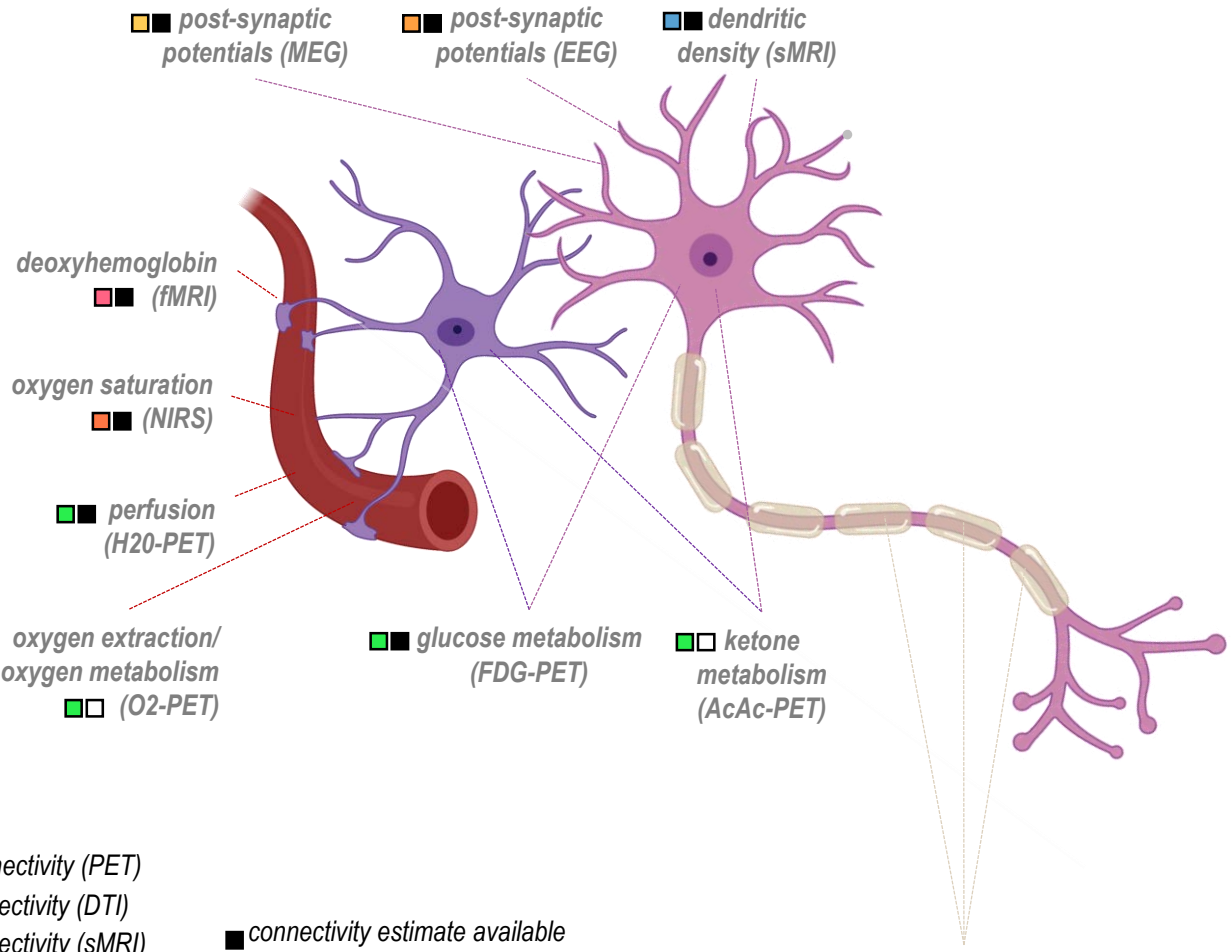
Why

What

How



Types of PET connectivity: neural activity



- molecular connectivity (PET)
- structural connectivity (DTI)
- structural connectivity (sMRI)
- functional connectivity (fMRI)
- functional connectivity (EEG)
- functional connectivity (MEG)
- functional connectivity (NIRS)

- connectivity estimate available
- connectivity estimate possible
- radiopharmaceutical advancements needed

Sala et al., 2023 TICS

Types of PET connectivity: neural activity - basics

Journal of Cerebral Blood Flow and Metabolism
13:5–14 © 1993 The International Society of Cerebral Blood Flow and Metabolism
Published by Raven Press, Ltd., New York

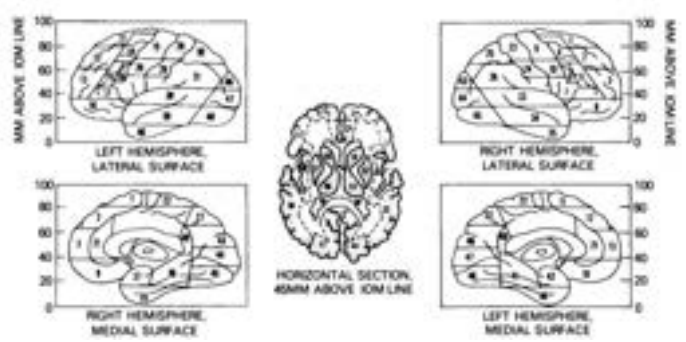
Functional Connectivity: The Principal-Component Analysis of Large (PET) Data Sets

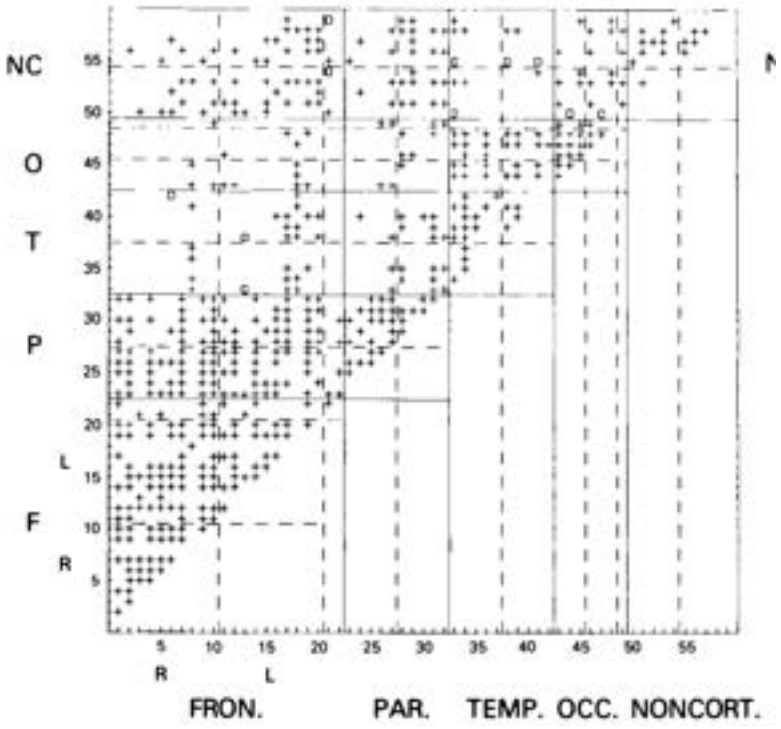
K. J. Friston, C. D. Frith, P. F. Liddle, and R. S. J. Frackowiak

however, can be linked at two levels: (i) A unifying concept is provided by coherence [$\sigma(w)$]. Coherence is a measure of the correlation at a particular frequency (w) (Cox and Miller, 1980). Consequently, coherence and functional connectivity at a frequency w [$fc(w)$] are directly related:

$$fc_{ij}(w) = \sigma_{ij}(w) = |g_{ij}(w)|^2 / g_{ii}(w) \cdot g_{jj}(w)$$

where $g_{ij}(w)$ is the cross-spectral density and $g_{ii}(w)$ and $g_{jj}(w)$ are the autospectral densities of the neurophysiological processes in question. Equation (4)

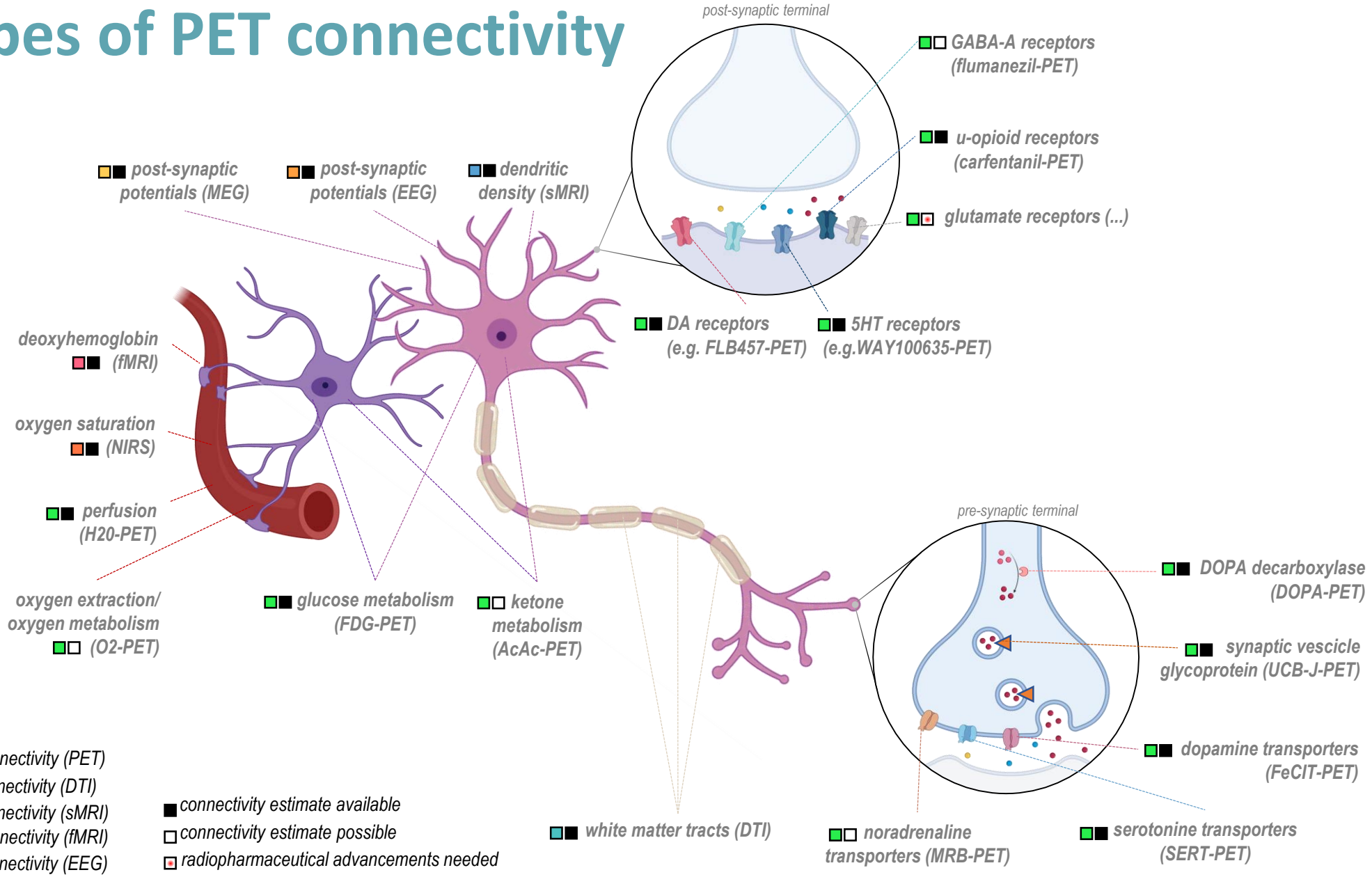




PET connectivity ≈ functional connectivity

Horwitz et al 1984, J Cereb Blood Flow Metab

Types of PET connectivity



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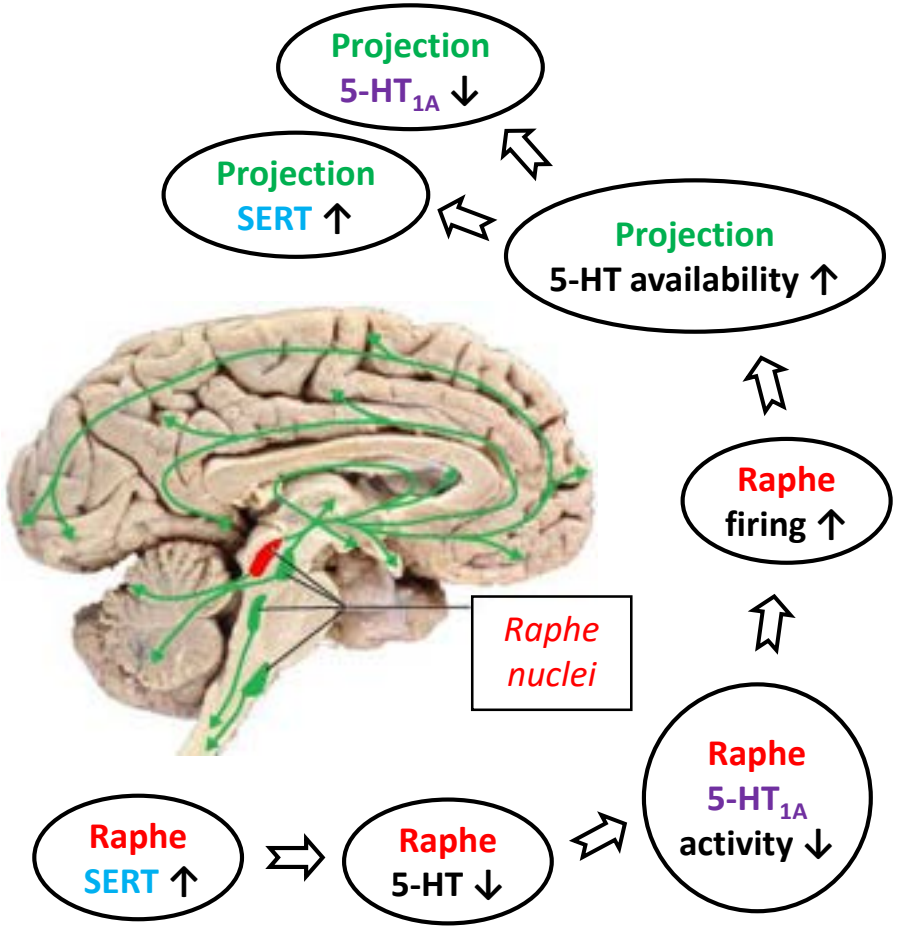
Sala et al., 2023 TICS

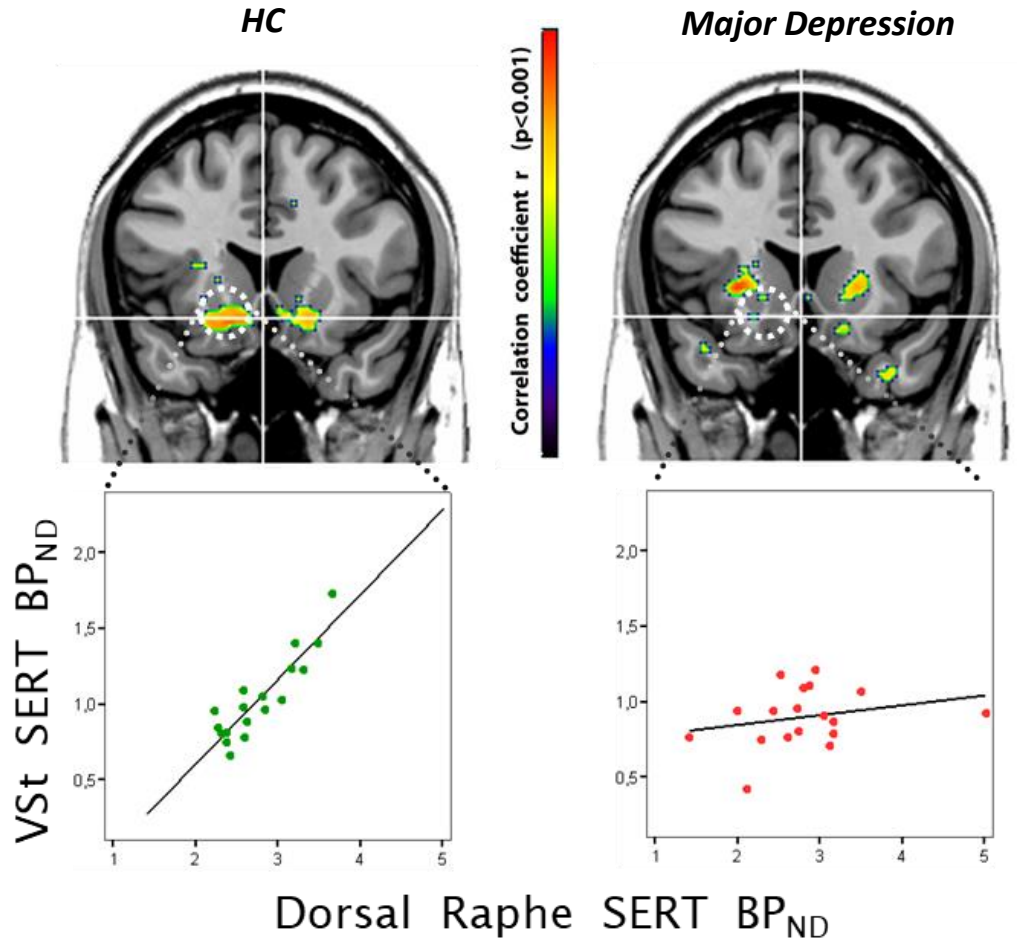
Types of PET connectivity: neurotransmission - basics



Courtesy of Andreas Hahn

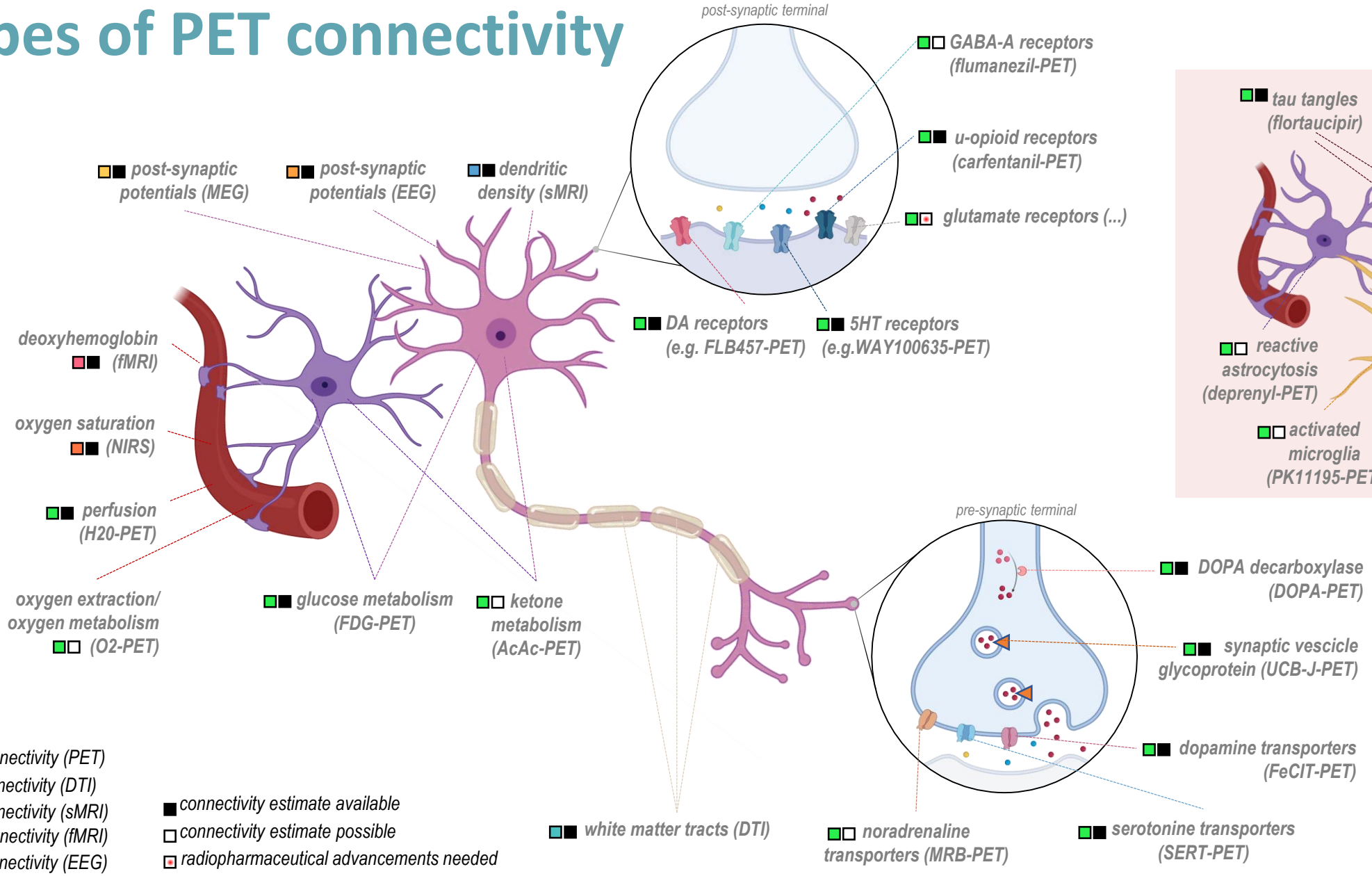
More on humanbrainmapping.org - OHBM 2021 Meeting

Symposium: PET Imaging of Brain Connectivity: Hype or Future?



Hahn et al 2014, Hum Brain Mapp

Types of PET connectivity



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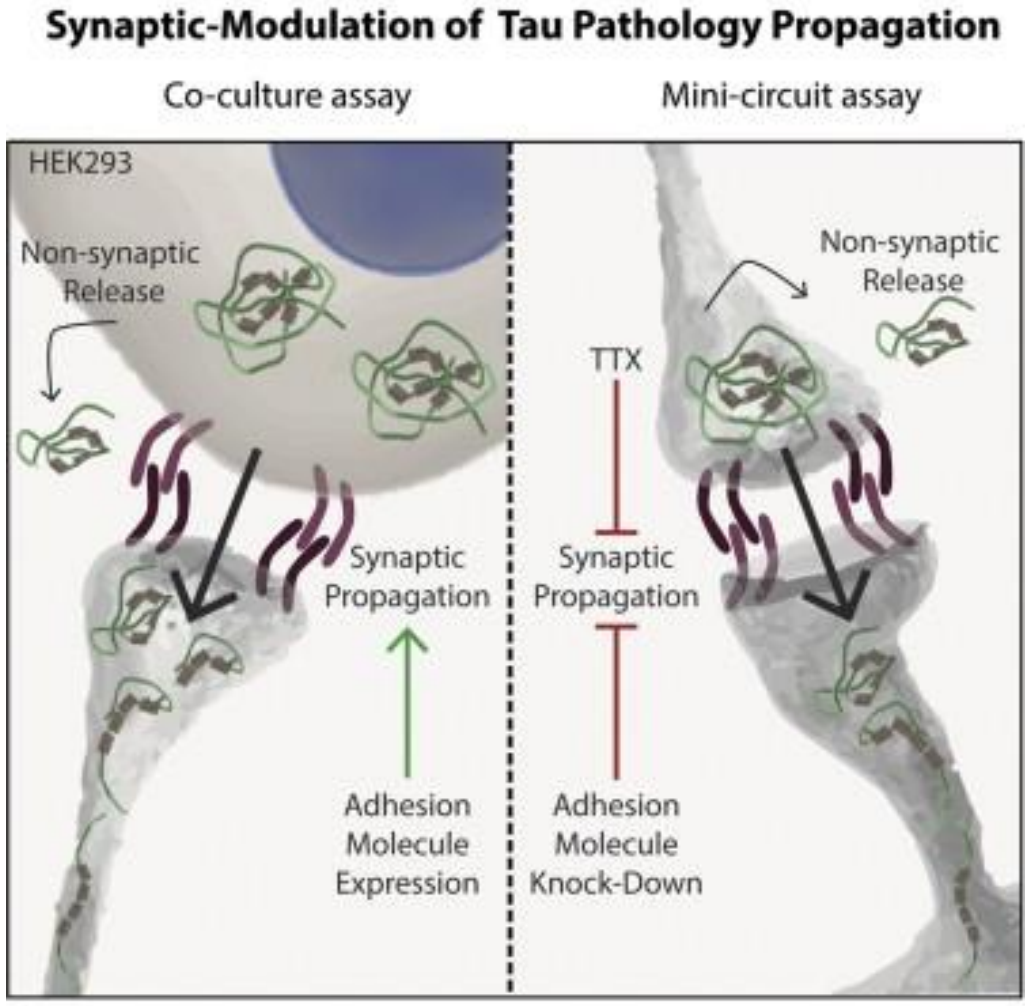
functional connectivity (NIRS)

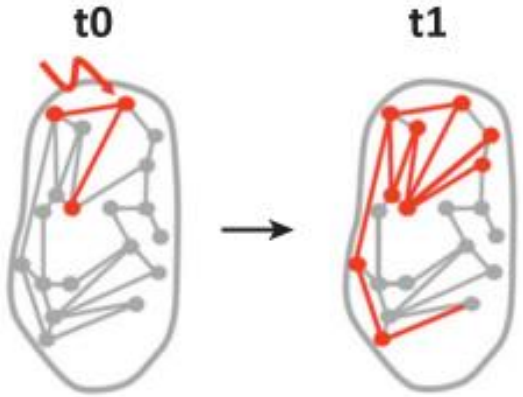
connectivity estimate available
connectivity estimate possible
radiopharmaceutical advancements needed

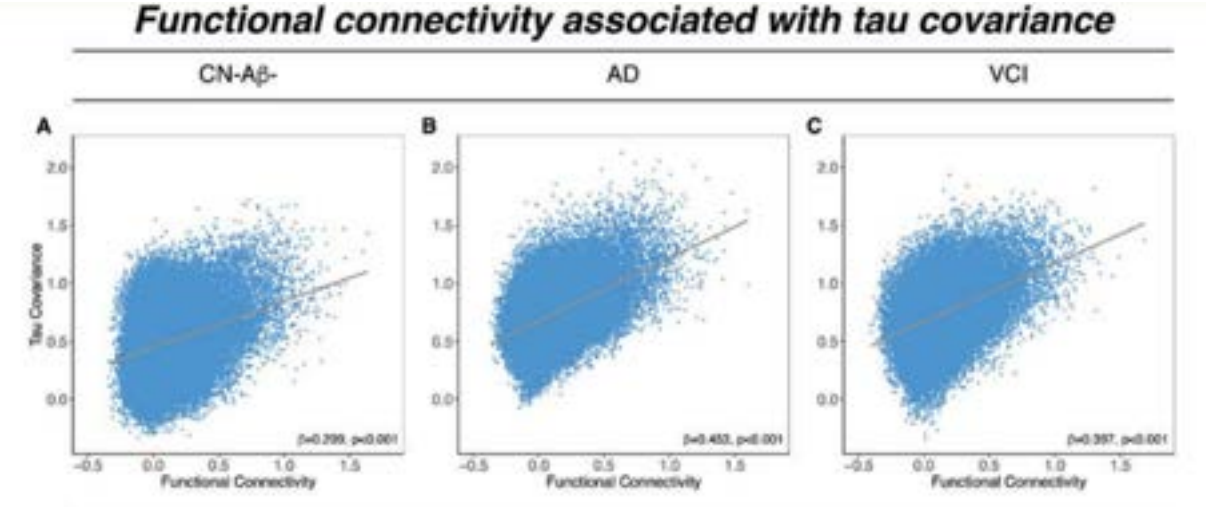
Sala et al., 2023 TICS

Types of PET connectivity: proteinopathies - basics



Calafate et al 2015, Cell Reports

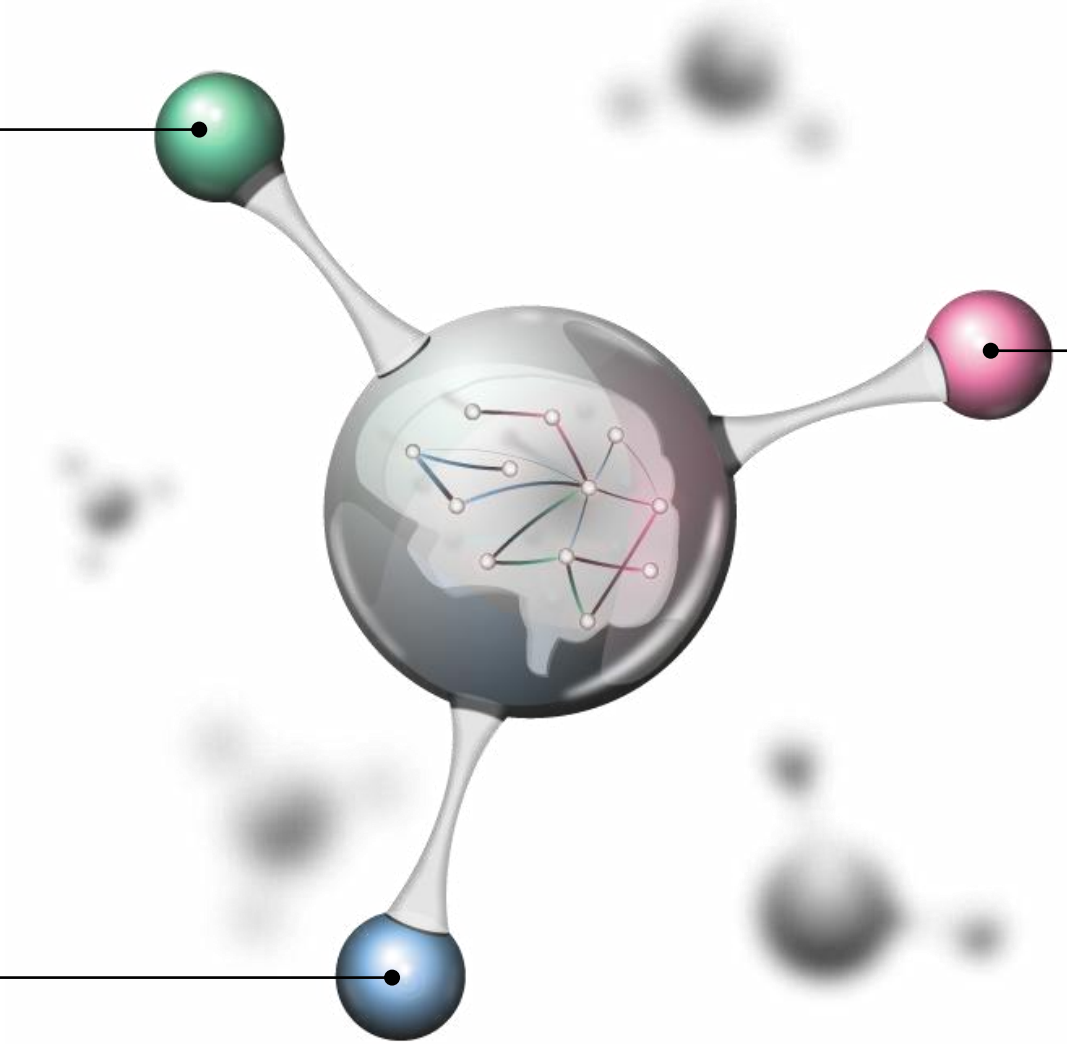




Franzmeier et al., 2019 Brain

Outline

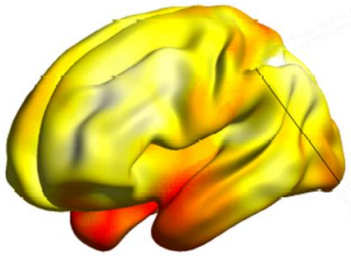
Why



What

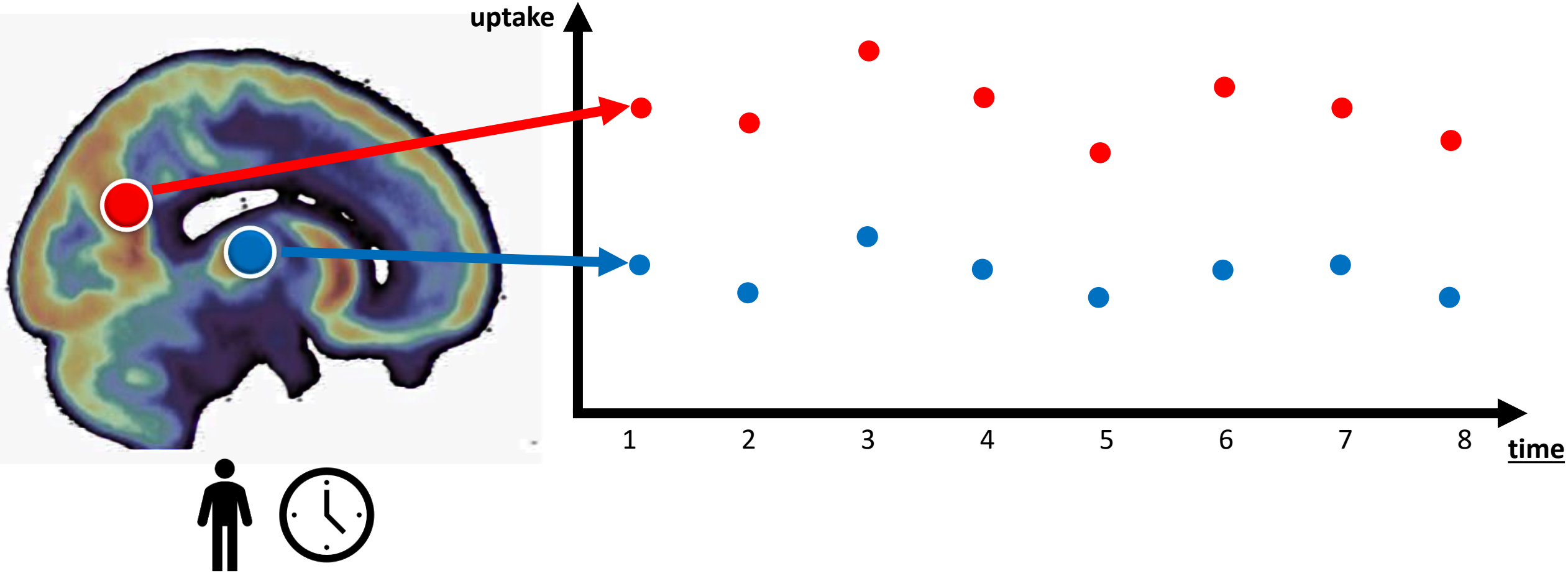
How

Summary: Methods

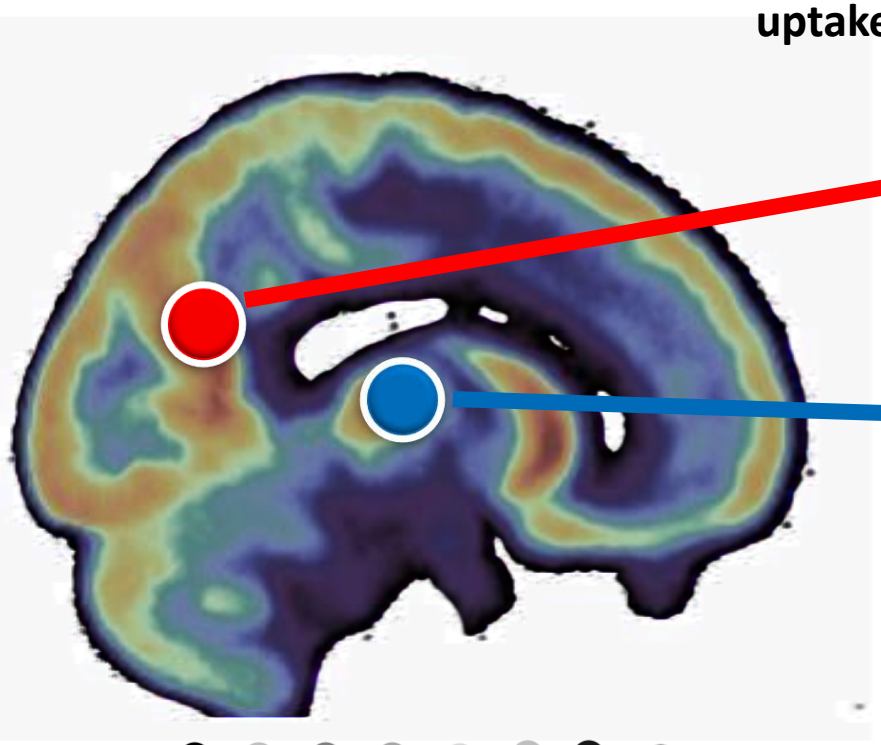


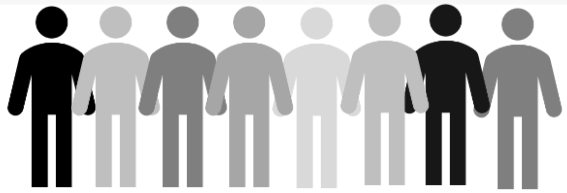
Method	Starting point	Endpoint	Unit	User Intervention
Seed-based inter-regional correlation	ROI (Seed)	Connectivity map of the seed	ROI -> voxel	Seed (atlas, granularity), Metrics
Independent Component Analysis	Whole-brain	Components (Resting-State Networks)	voxel -> voxel	Algorithm, Number & Selection of Components
Principal Component Analysis	Whole-brain	Components (Patterns)	voxel -> voxel	Algorithm, Number & Selection of Components
ROI-to-ROI Correlation	ROIs (Circuit to whole-brain)	Graph / Connectome	ROI -> ROI	ROIs (coverage, atlas, granularity), Metrics

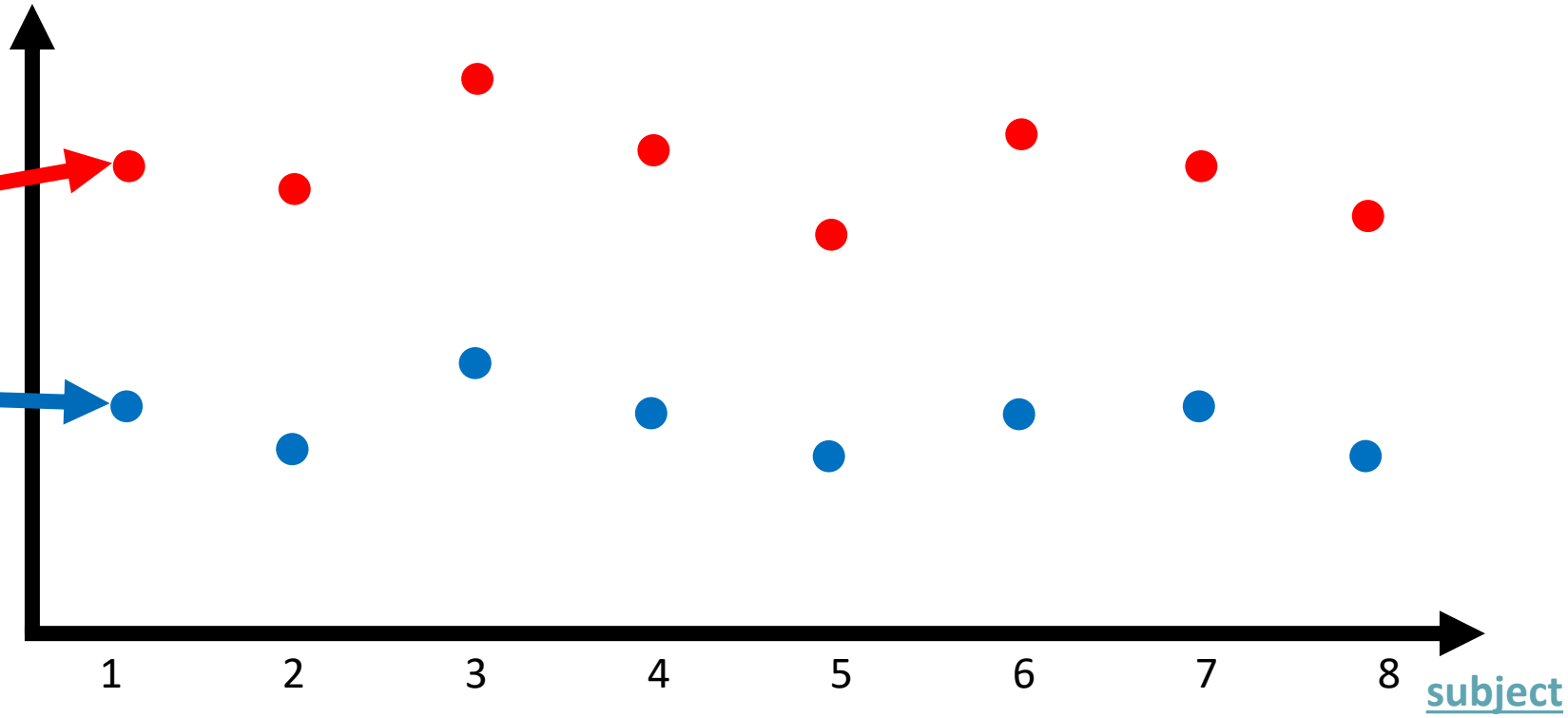
Approaches: intra-subject



Approaches: inter-subject

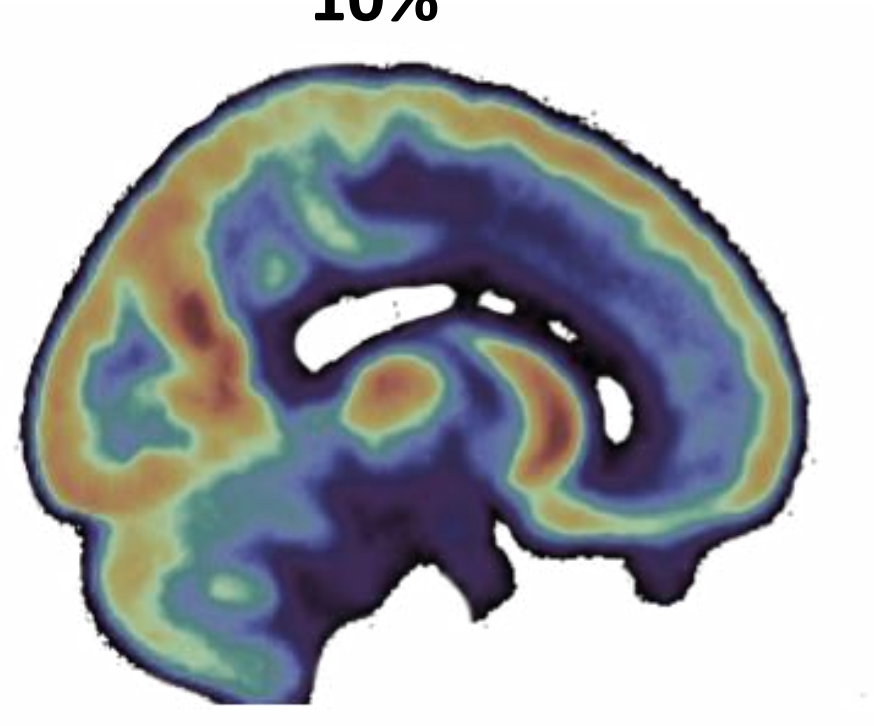


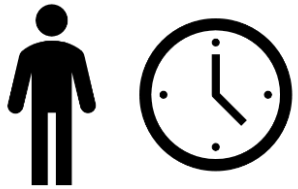




Approaches: equivalent?

10%





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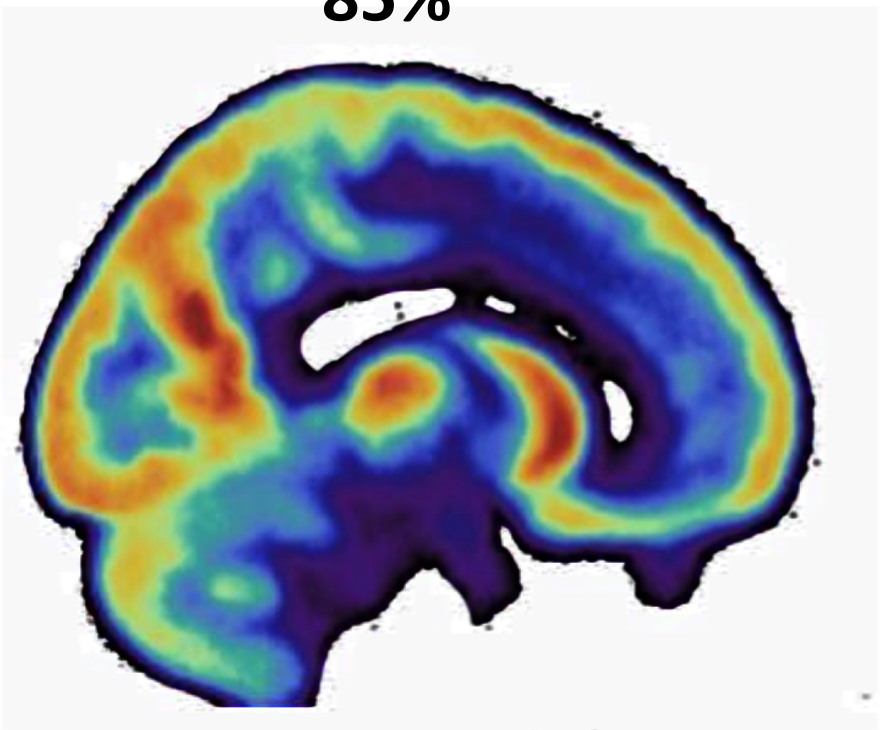
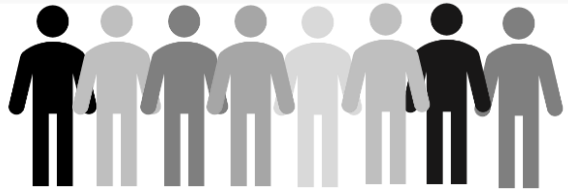
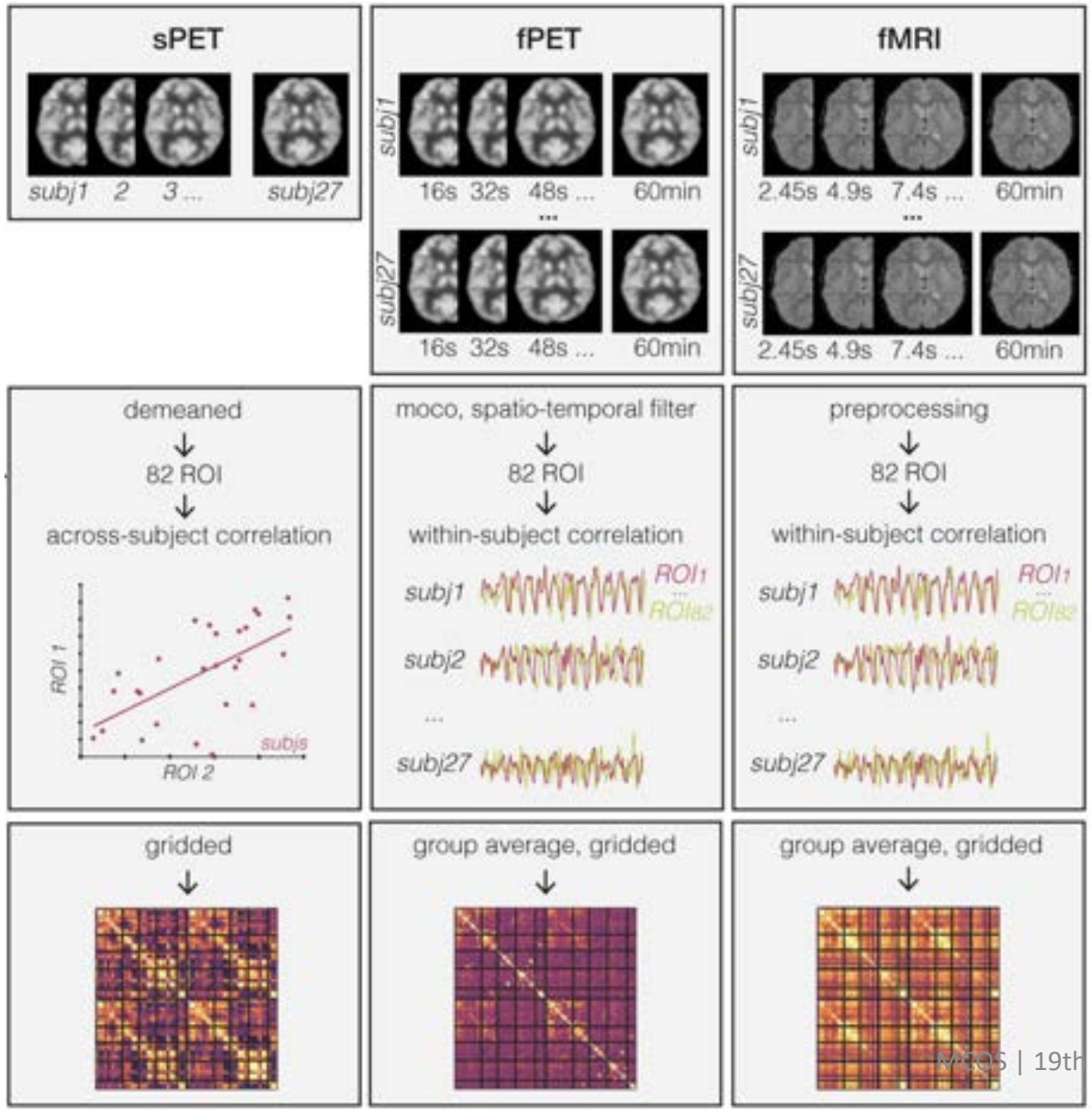




Approaches: equivalent?



Sharna Jamadar

Metabolic and Hemodynamic Resting-State Connectivity of the Human Brain: A High-Temporal Resolution Simultaneous BOLD-fMRI and FDG-fPET Multimodality Study

Sharna D Jamadar ✉, Phillip G D Ward, Emma X Liang, Edwina R Orchard, Zhaolin Chen, Gary F Egan

Cerebral Cortex, Volume 31, Issue 6, June 2021, Pages 2855–2867, https://doi.org/10.1093/cercor/bhaa393

Static versus Functional PET: Making Sense of Metabolic Connectivity

Arianna Sala ✉, Aldana Lizarraga, Isabelle Ripp, Paul Cumming, Igor Yakushev

Cerebral Cortex, bhab271, https://doi.org/10.1093/cercor/bhab271

Resting-State FDG-PET Connectivity: Covariance, Ergodicity, and Biomarkers. Response to Commentary by Sala et al.; Static versus Functional PET: Making Sense of Metabolic Connectivity Get access ›

Sharna D Jamadar ✉, Gary F Egan

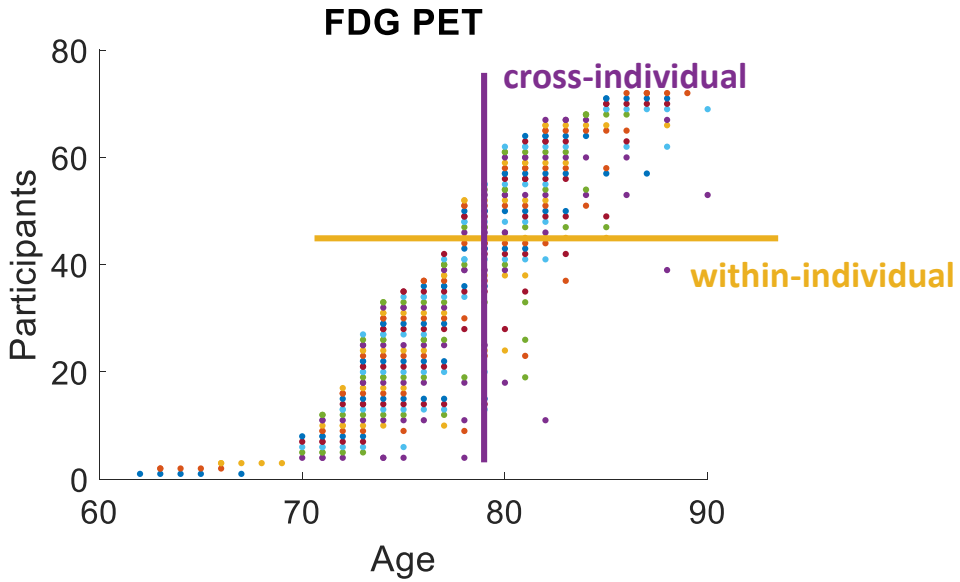
Cerebral Cortex, Volume 32, Issue 9, 1 May 2022, Pages 2054–2055, https://doi.org/10.1093/cercor/bhab316

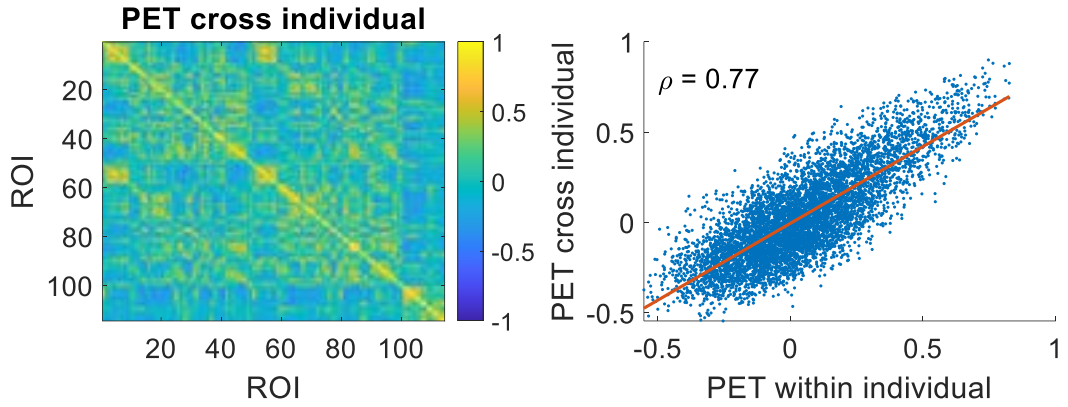
Approaches: equivalent?

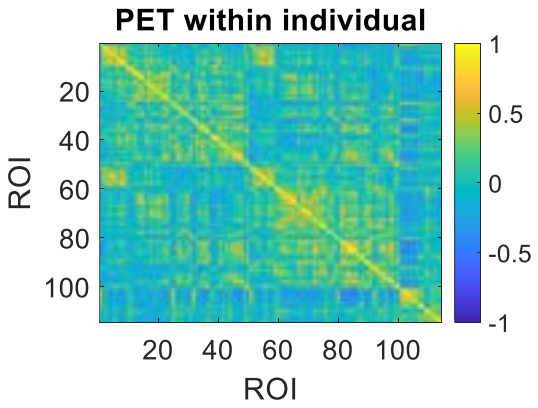
Xin Di

ADNI dataset

FDG-PET: n= 72 healthy controls (5-9 scans available)

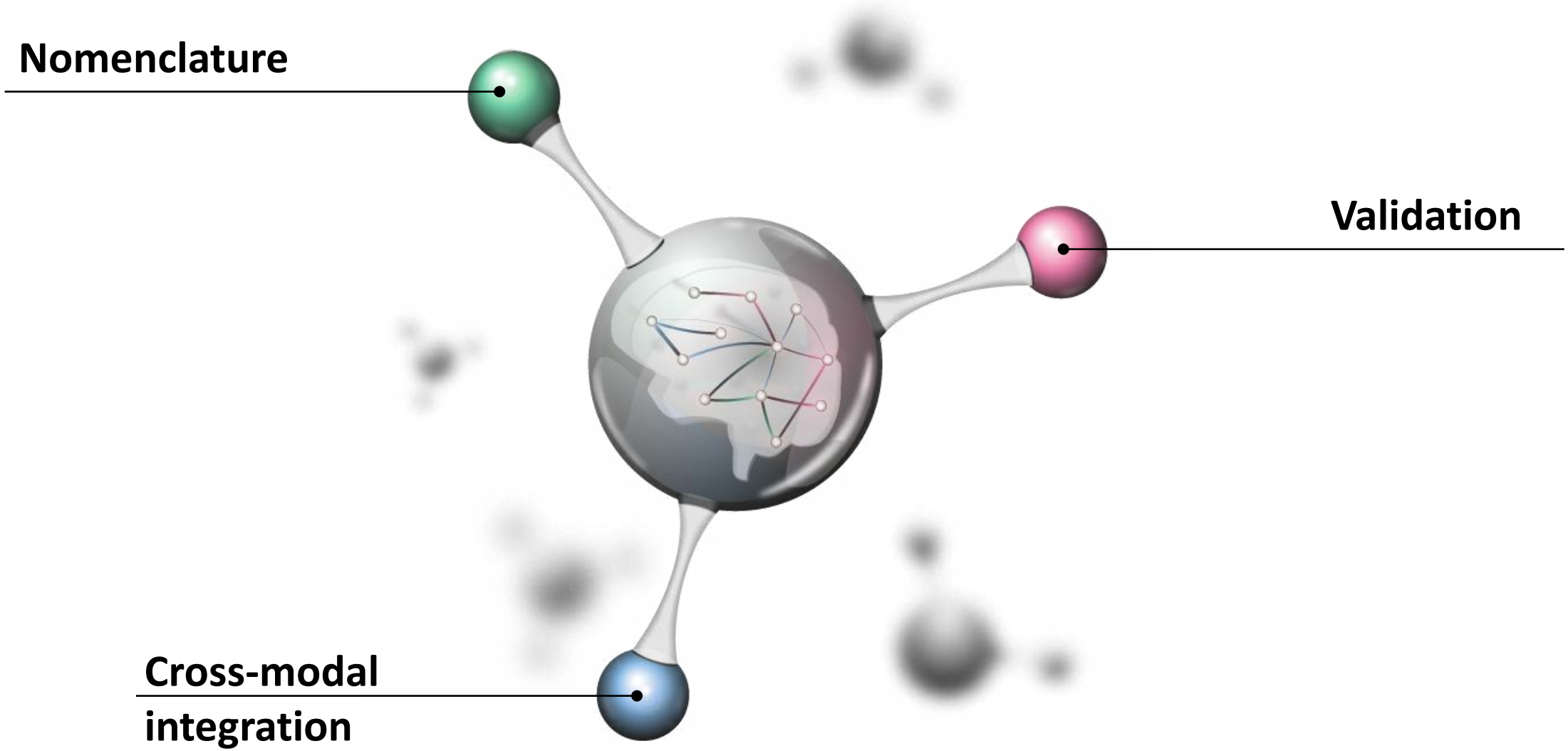






Courtesy of Xin Di, PhD

Molecular connectivity: what is left to do?



Molecular connectivity: what is left to do?

Nomenclature

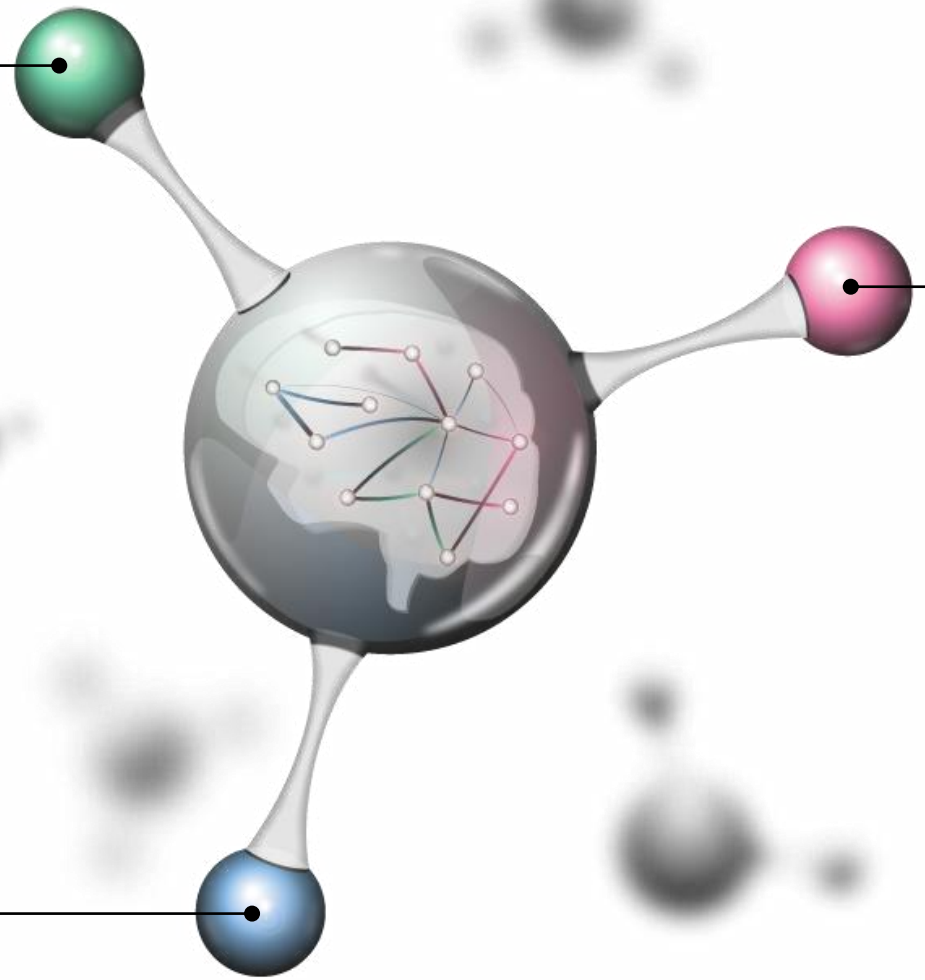
Consensus meeting

Validation

dal integration

Molecular connectivity: what is left to do?

Nomenclature

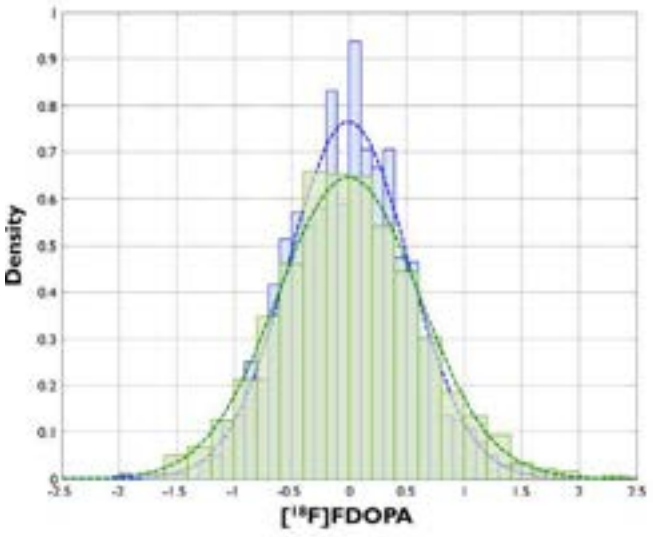


Validation

Cross-modal integration

Validation

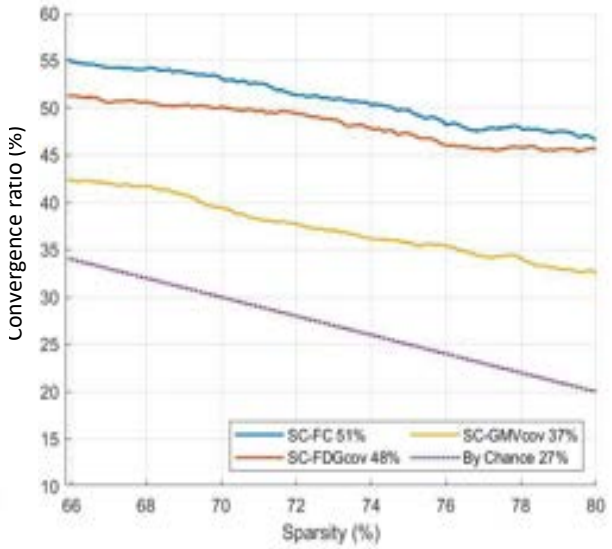
Robust, precise and reproducible



Veronese et al., 2019, Sci Rep

Mattia Veronese

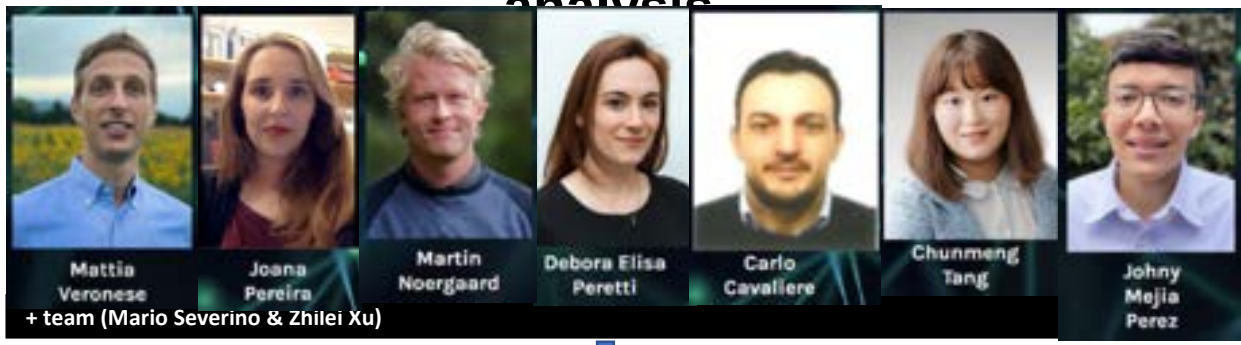
Matches gold-standard



Lizarraga et al., 2023, J Cereb Blood Flow Metab

Igor Yakushev

Systematic review & gap analysis

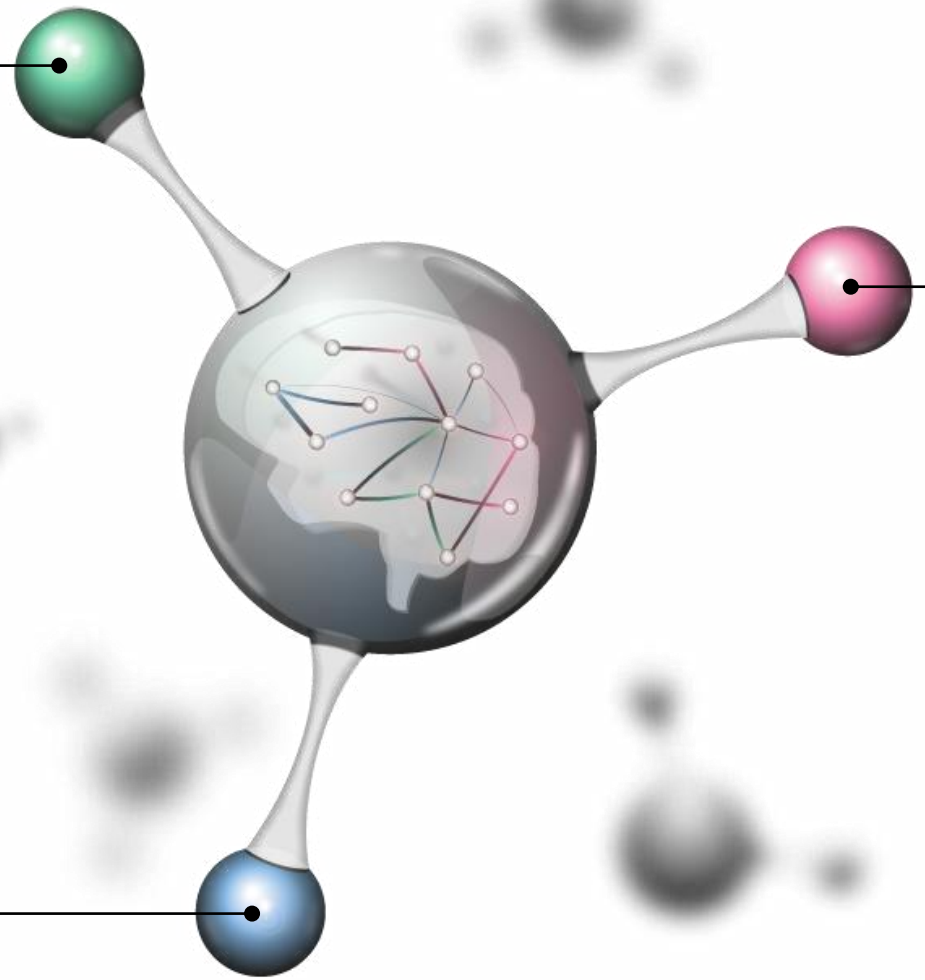


Design of validation studies

Best methodological practices

Molecular connectivity: what is left to do?

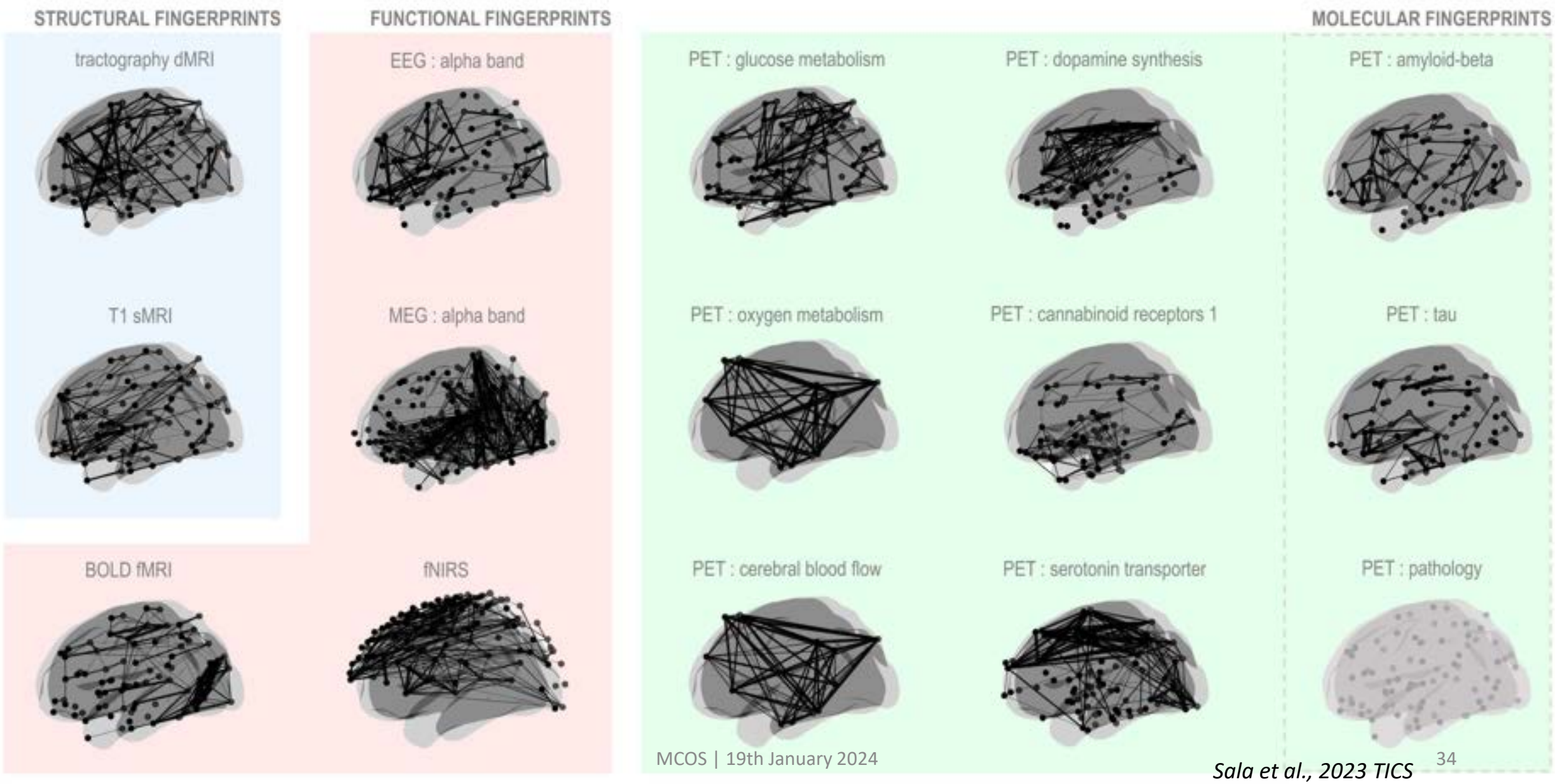
Nomenclature



Validation

Cross-modal integration

Cross-modal integration



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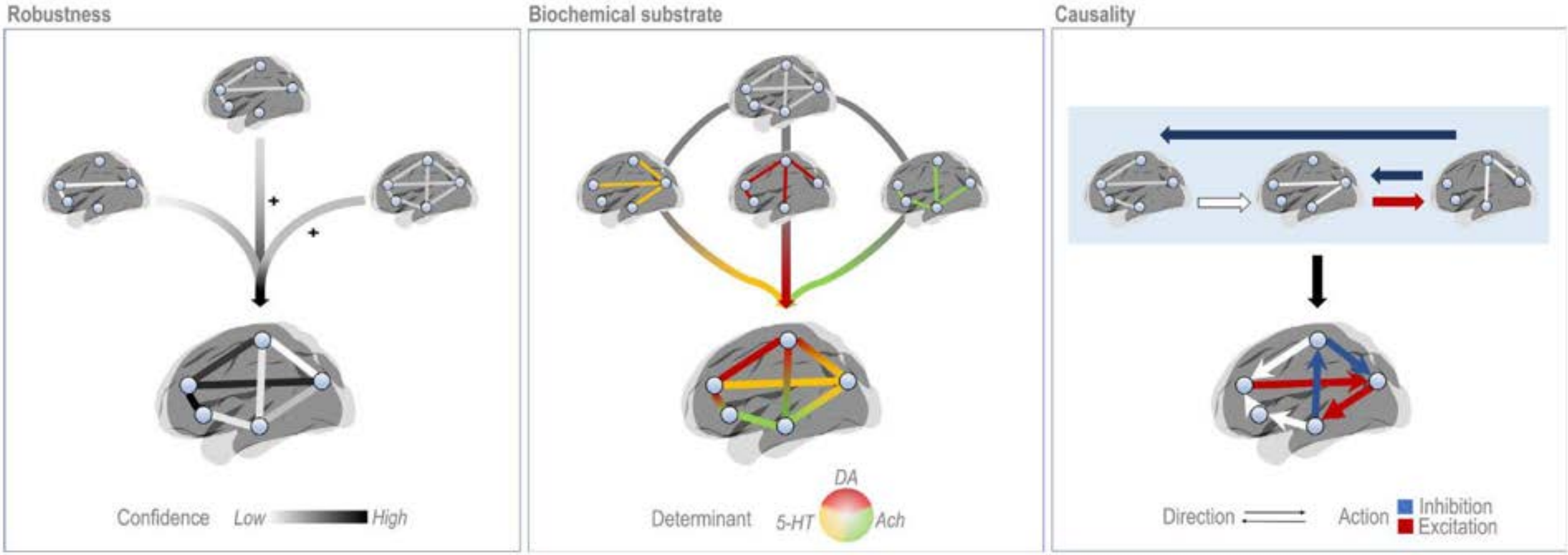
Cross-modal integration



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