Afasieconferentie
State of the Art 2026

The end of localisationism?
What brain networks teach us about aphasia

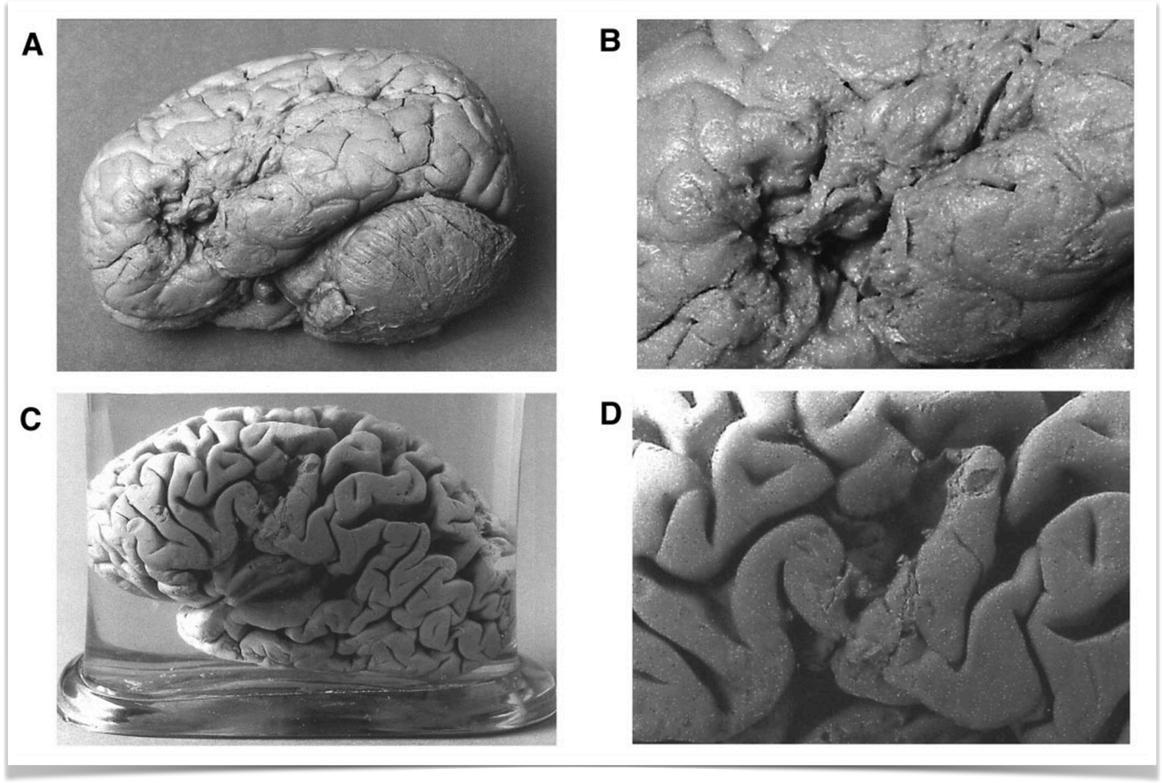
Stephanie Forkel
www.stephanieforkel.com

['stɛ.fə.ni.ˈfoː.kəl]

erc Consolidator Grant | NWO | DONDERS INSTITUTE | Radboud University | Radboudumc university medical center | MAX PLANCK INSTITUTE FOR PSYCHOLINGUISTICS | UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG 1922 2022



The birth of language localisationism



Dronkers et al., Brain 2007

https://doi.org/10.1093/brain/awab444 BRAIN 2022: 145; 801–804 | 801

BRAIN
ESSAY

Paul Broca: from fame to shame?

In 2016, the University of Bordeaux ran a competition within the local neuroscience community to find a name for its new neuroscience building. The name of Paul Broca, who was born nearby in 1824, was chosen in honour of his origins and his contributions to neuroscience. Recently, however, a debate has been ignited about the appropriateness of this choice, given Broca's endorsement of physiological anthropology. At a time when academic institutions worldwide are revising their curricula to better reflect the contributions of previously overlooked groups, how should we respond when the views of the 'founding fathers' of neurology clash with those of society today?

'Here are eight instances in which the lesion was in the posterior third of the third frontal convolution. This number seems to me to be sufficient to give strong presumptions. And the most remarkable thing is that in all the patients the lesion was on the left side. I do not dare draw conclusions from this'. (Broca, 1863)

Paul Broca was initially hesitant in 1863, but 2 years later, he was confident that *'nous parlons avec l'hémisphère gauche'* (we speak with the left hemisphere) and narrowed it down to the *troisième circonvolution frontale* (today known as the inferior frontal gyrus). This work revolutionized neuroscience in the 1860s and led not only to Broca's name becoming an eponym for this brain area, but also laid the foundations for new theories (e.g. localizationism, cerebral dominance and asymmetry), methods (lesion-symptom mapping), and disciplines (neurobiology of language, aphasiology).

During Broca's time, members of the *Société Anthropologique de Paris* were engaged in a spirited debate about the localization of function in the brain. While Broca was not the first to present evidence for speech in the left hemisphere,[1] he recognized the potential significance of his aphasia patient Louis Victor Leborgne (also known as 'Tan'), publishing a detailed clinical-anatomical description.[2] This work on Leborgne enabled Broca to identify the cortical area for speech articulation. Unanimously across languages, the opercular and triangular part of the inferior frontal gyrus is still referred to as 'Broca's area', and he joins the many scientists (e.g. Luigi Rolando, Carl Wernicke, Alexander Monro, Jan Purkinje, Richard Heschl, Franciscus Sylvius, Heinrich Sachs, Johann Christian Reil, Adolf Meyer, Moriz Probst) whose names were adopted for neuroanatomical structures. Broca went on to preserve Leborgne's brain, offering future generations the possibility to revisit the anatomy of this famous case using CT, MRI, and diffusion-weighted imaging tractography methods.[3–5] His work still resonates to this day and its impact has been solidified with the invention of cognitive neuroimaging methods and techniques (Supplementary Fig. 1).

In 2016, the University of Bordeaux and the Nouvelle-Aquitaine region launched a competition within the Bordeaux neuroscientific community to name the new building that was to house the *Institut interdisciplinaire de neurosciences* (IINS) and the *Institut des maladies neurodégénératives* (IMN). The name of Paul Broca garnered ardent support, and the building subsequently became known as the 'Centre Broca'. Born in Sainte-Foy-la-Grande (77 km east of



Figure 1 Paul Broca, born 1824 in Sainte-Foy-la-Grande (Nouvelle Aquitaine) and died 1880 in Paris. Portrait from the personal collection of Broca's great-grandson Philippe Monod-Broca, courtesy of Michel Thiebaut de Schotten.

Downloaded from https://academic.oup.com/brain/article/145/3/801/6469015 by guest on 15 June 2026

Boraud & Forkel, Brain 2022

160 years later, we are still using lesion-deficit mapping and clinical-anatomical correlations, but our concept of anatomy has fundamentally changed and so have our methods

‘The’ canonical language network

The psychic arc

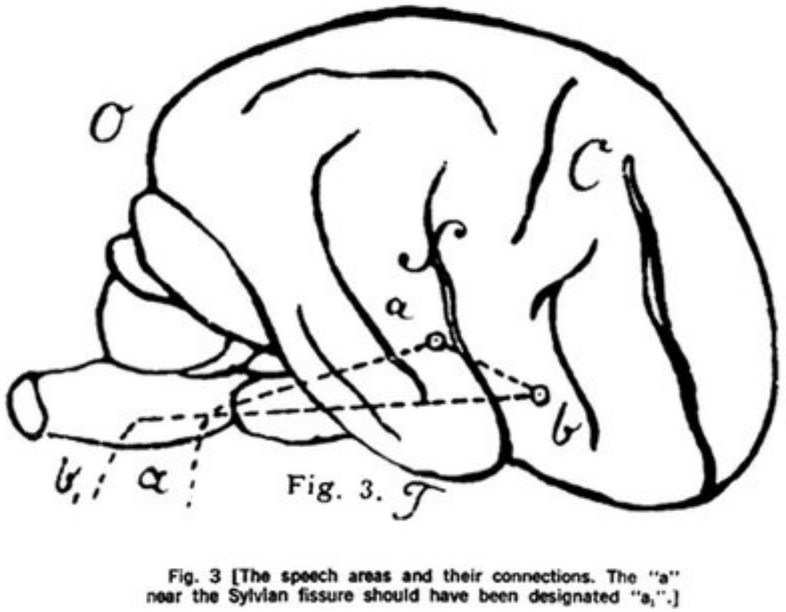
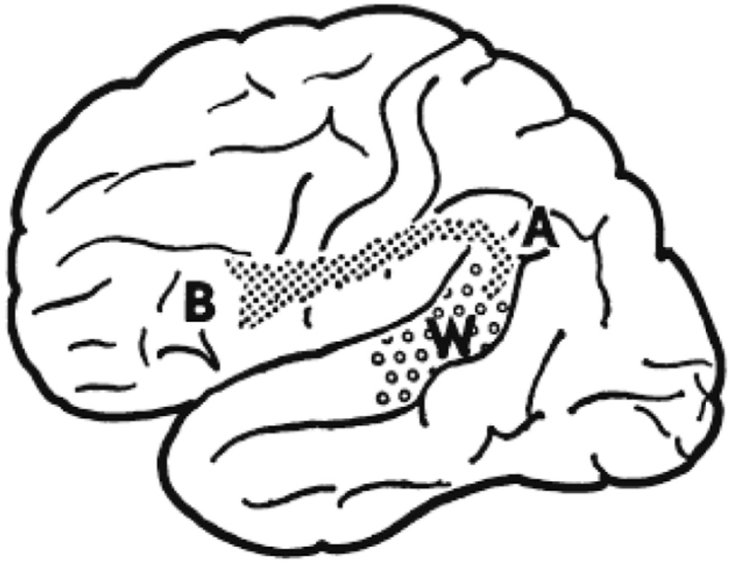


Fig. 3 [The speech areas and their connections. The "a" near the Sylvian fissure should have been designated "a_1".]

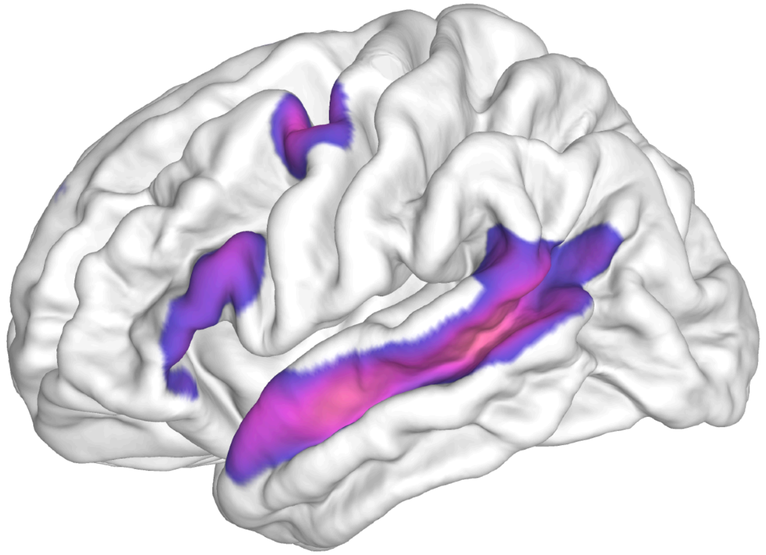
Wernicke, 1874

Arcuate fasciculus



Geschwind, 1970

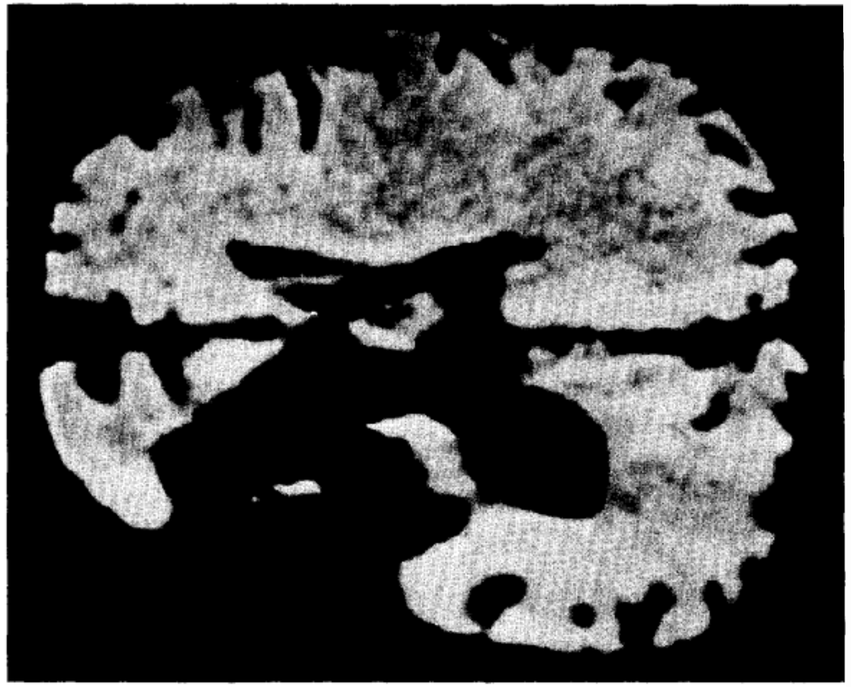
A natural kind?

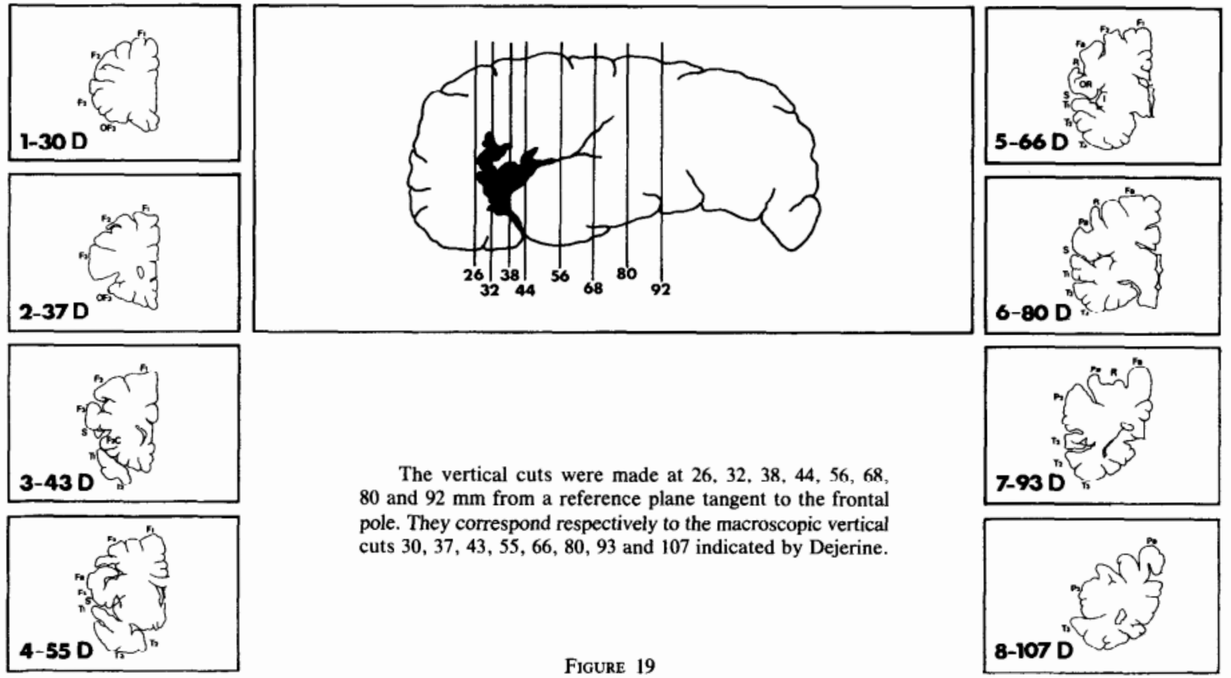


Lipkin et al., 2022

These models have guided generations of neuroscientists—and it's still where many clinical decisions begin.

The hidden anatomy of aphasia



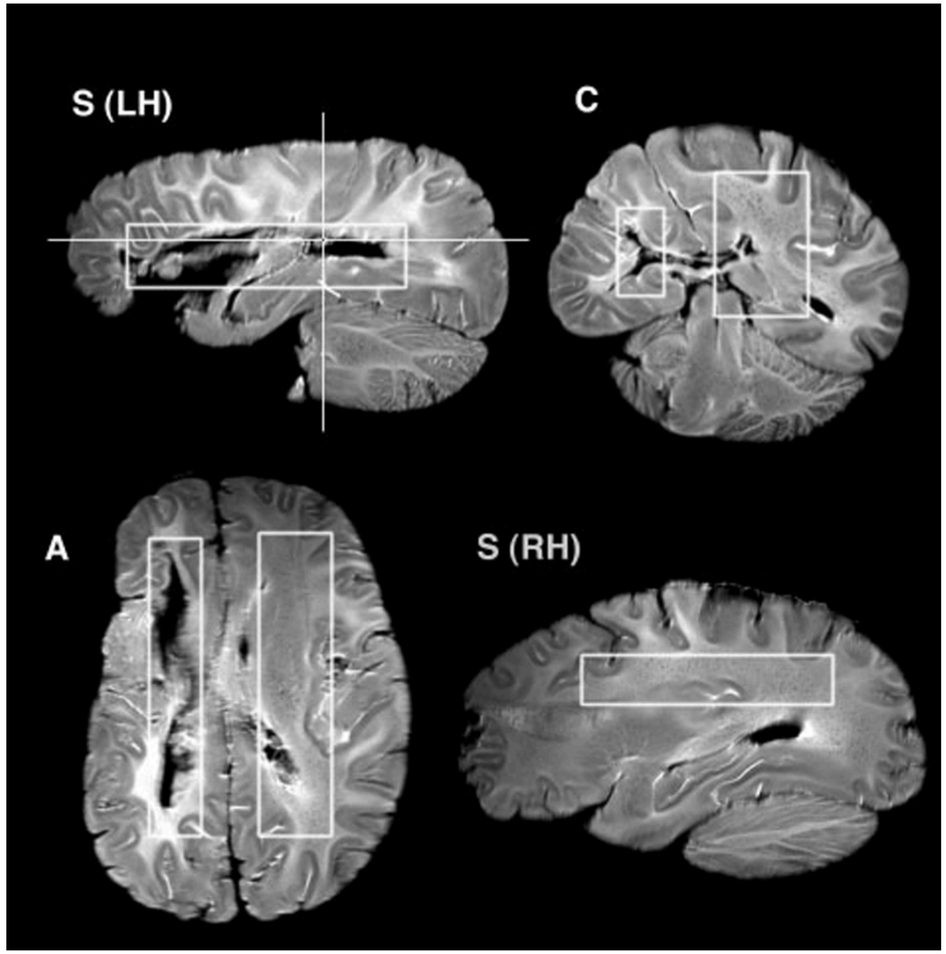


The vertical cuts were made at 26, 32, 38, 44, 56, 68, 80 and 92 mm from a reference plane tangent to the frontal pole. They correspond respectively to the macroscopic vertical cuts 30, 37, 43, 55, 66, 80, 93 and 107 indicated by Dejerine.

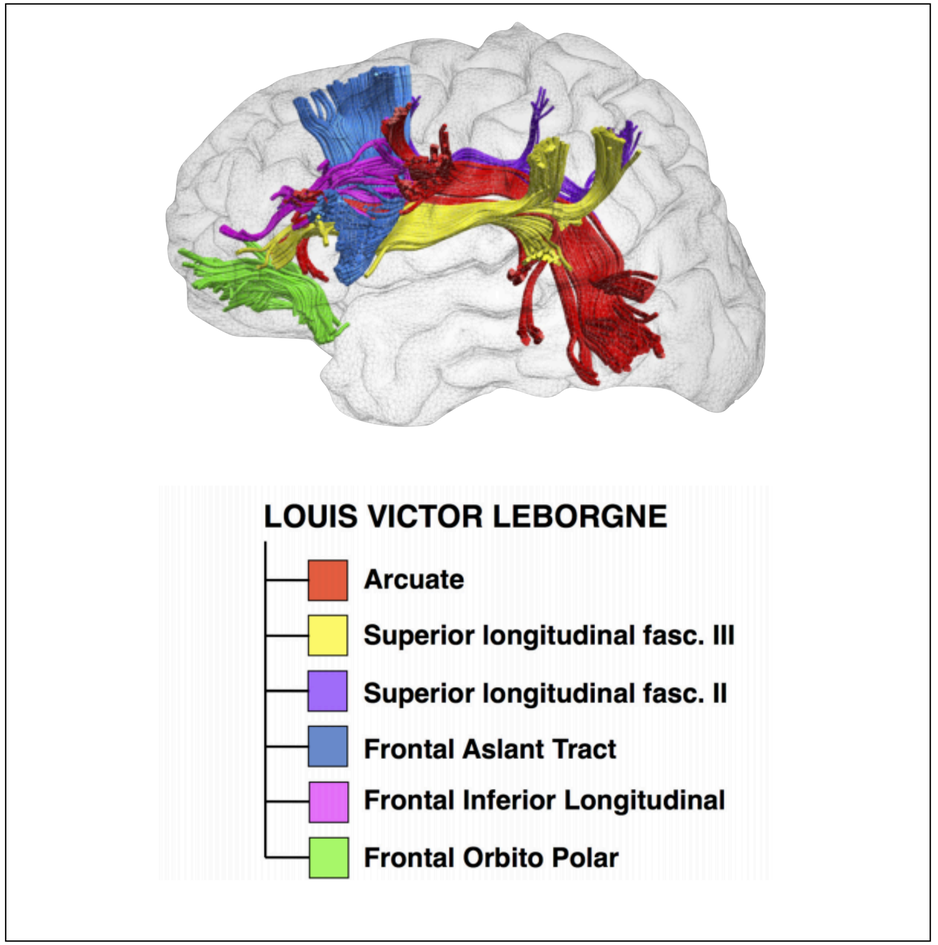
FIGURE 19

Signoret et al., Brain and Language 1984

Beyond the cortex and into the white matter

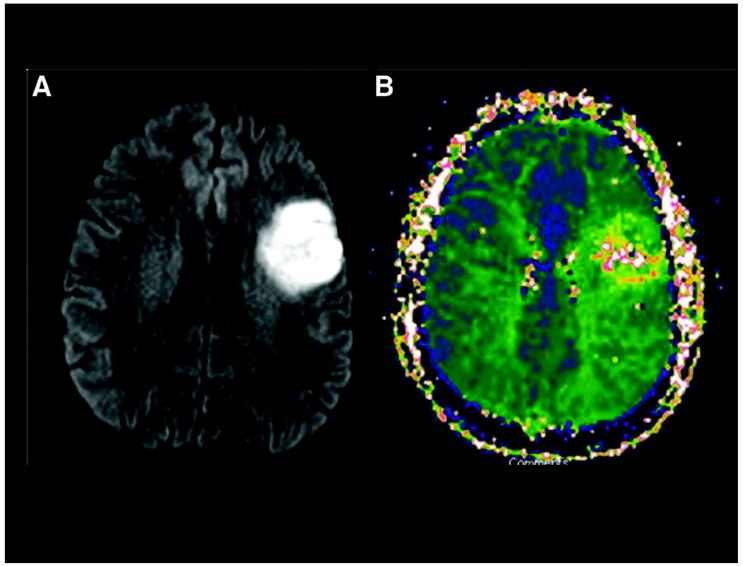


Dronkers et al., Brain 2007

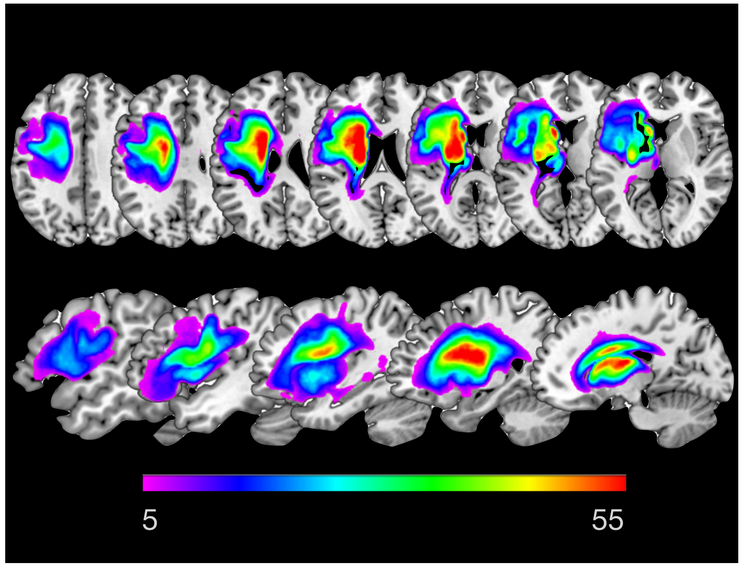


Thiebaut de Schotten et al., 2015

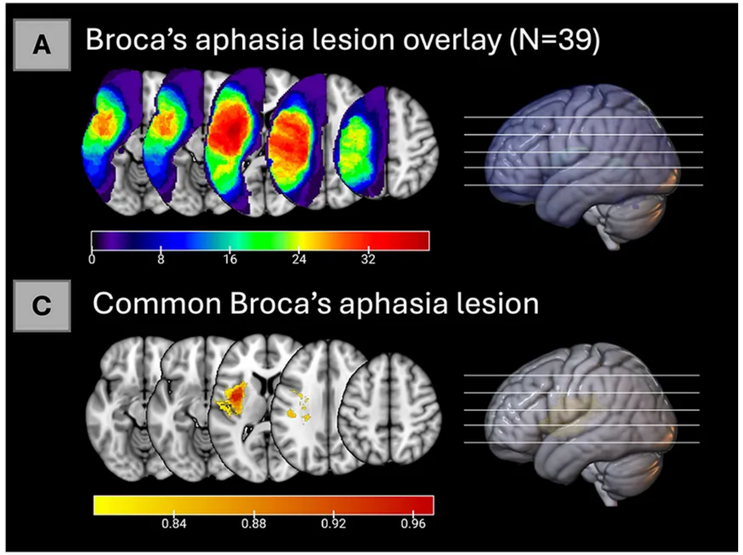
A new anatomy of ‘Broca’s aphasia’



Ochfeld et al., 2010 Stroke



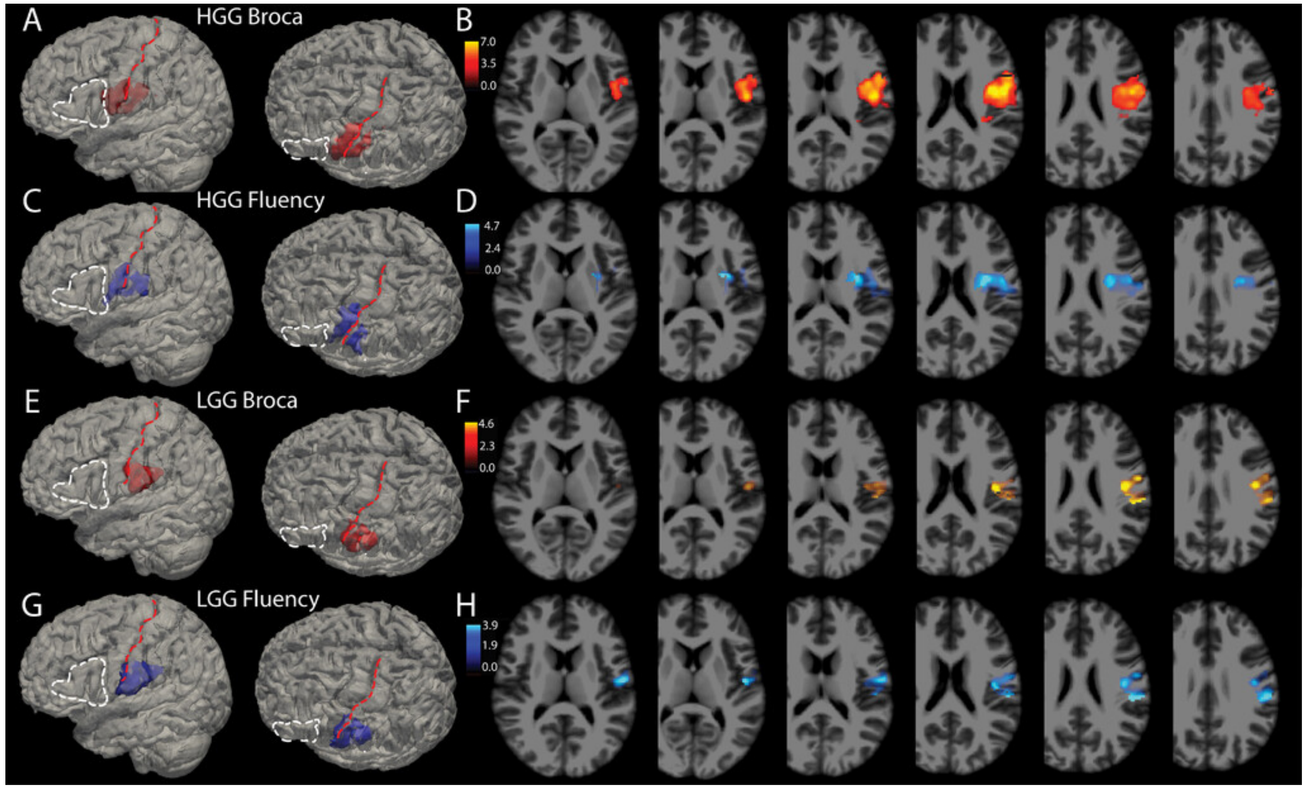
Gajardo-Vidal et al., 2021 BRAIN



Pracar et al., 2025 Frontiers in Language Sciences

Traditionally defined Broca's area showed minimal overlap,
challenging the conventional understanding of its role in chronic Broca's aphasia

Neurosurgery challenges a century-old dogma



‘Broca's aphasia does not typically arise from resections in Broca's area.

When Broca's aphasia does occur, it is typically in the early postoperative period, improves by 1 month, and is associated with resections of **v**entral sensorimotor cortex and supramarginal gyri.’

Andrews et al., 2022 JNS

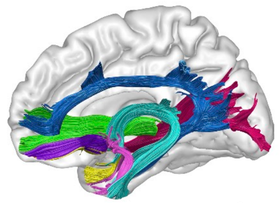
If Broca's aphasia is not explained by Broca's area, the obvious question becomes: what *does* explain it?

How do we study the human connectome?

post-mortem dissections



&



in vivo tractography

2006 | 2017 | 2018 | 2019 | 2021







Munich | Istanbul | London | Zurich | YouTube @CNSeminars

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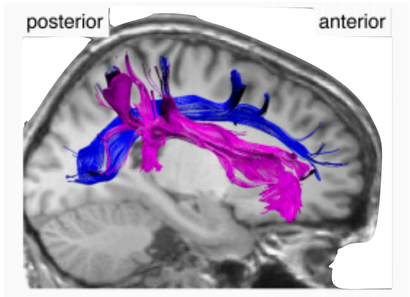
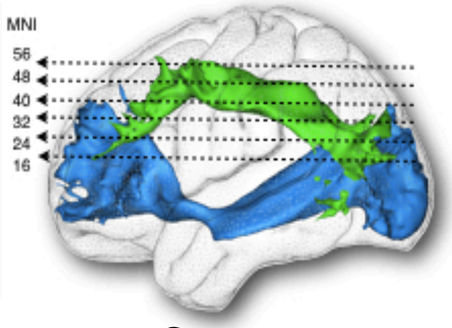
Fronto-parietal | Fronto-occipital | Occipital U-shaped | Comparative anatomy



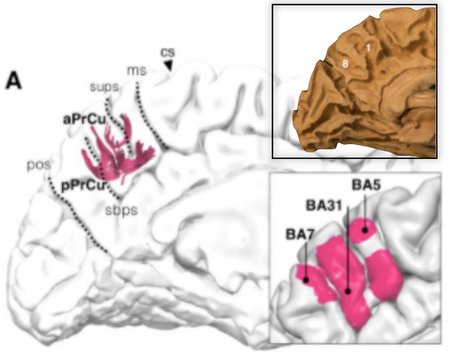
Nature Neuroscience, 2011



Cortex, 2014



Cortex, 2014



Cortex, 2018

Watch talk on YouTube

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Klingler postmortem dissections

Trigger warning

If you are squeamish…..



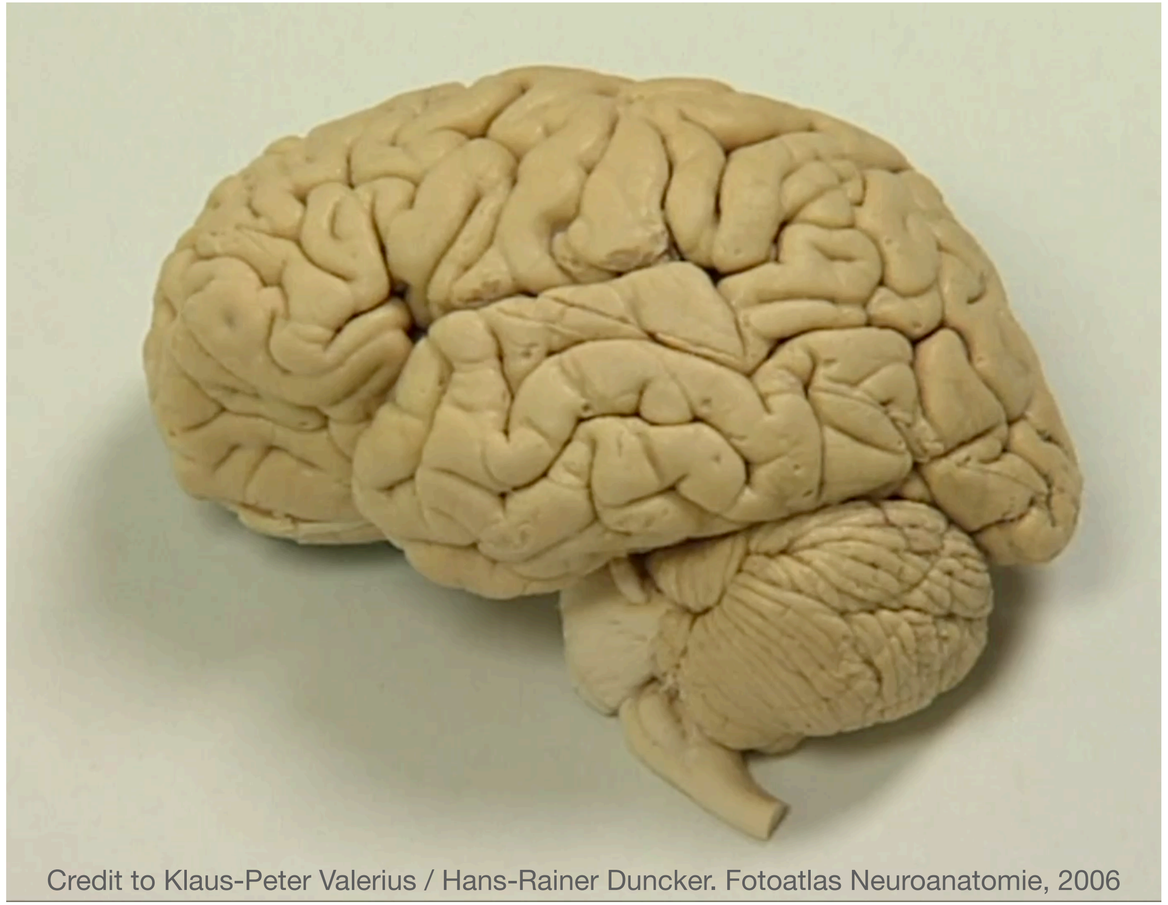
Klingler dissection technique

A special technique was developed by Joseph Klingler at the Institute of Anatomy in Basel, Switzerland, in the 1930s.

Fixation, freezing, and thawing:

- 10% formalin
- Freezing time 8h to 2M
- Temperature –5 to –80 °C

Essential to validate in vivo methods.



Credit to Klaus-Peter Valerius / Hans-Rainer Duncker. Fotoatlas Neuroanatomie, 2006

Klingler J: Atlas Cerebri Humani. Basel, S. Karger, 1956

Türe U, Yaşargil MG, Friedman AH, Al-Mefty O. Fiber dissection technique: lateral aspect of the brain. J Neurosurgery 2000

Dziedzic TA, Balasa A, Jeżewski MP, Michałowski Ł, Marchel A. White matter dissection with the Klingler technique: a literature review. Brain Struct Funct. 2021

Demirtaş OK, Güngör A, Çeltikçi P, Çeltikçi E, Munoz-Gualan AP, Doğulu FH, Türe U. Microsurgical anatomy and insular connectivity of the cerebral opercula. J Neurosurg. 2022

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Clinical usability of DWI Tractography



Brain Structure and Function (2025) 230:59
https://doi.org/10.1007/s00429-025-02921-9

CORRESPONDENCE

The scientific value of tractography: accuracy vs usefulness

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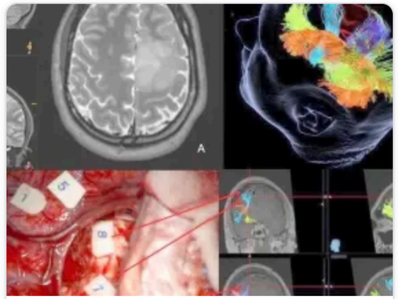
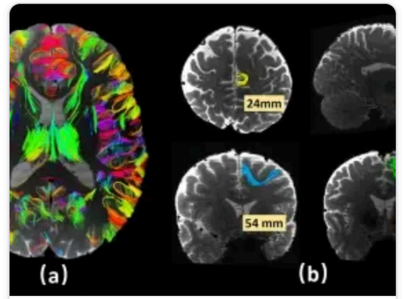
Abstract

Tractography has emerged as a central tool for mapping the cerebral white matter architecture. However, its scientific value continues to be a subject of debate, given its inherent limitations in anatomical accuracy. This concise communication showcases key points of a debate held at the 2024 Tract-Anat Retreat, addressing the trade-offs between the accuracy and utility of tractography. While tractography remains constrained by limitations related to resolution, sensitivity, and validation, its usefulness and utility in areas such as surgical planning, disorder prediction, and the elucidation of brain development are emphasized. These perspectives highlight the necessity of context-specific interpretation, anatomically informed algorithms, and the continuous refinement of tractography workflows to achieve an optimal balance between accuracy and utility.



DEBATE: is tractography accurate enough to be used to inform surgery?



Short association fiber tractography: key insights and surprising facts



A thousand ways to tailor your tractography-based connectome

OPEN ACCESS

From diffusion to tractography



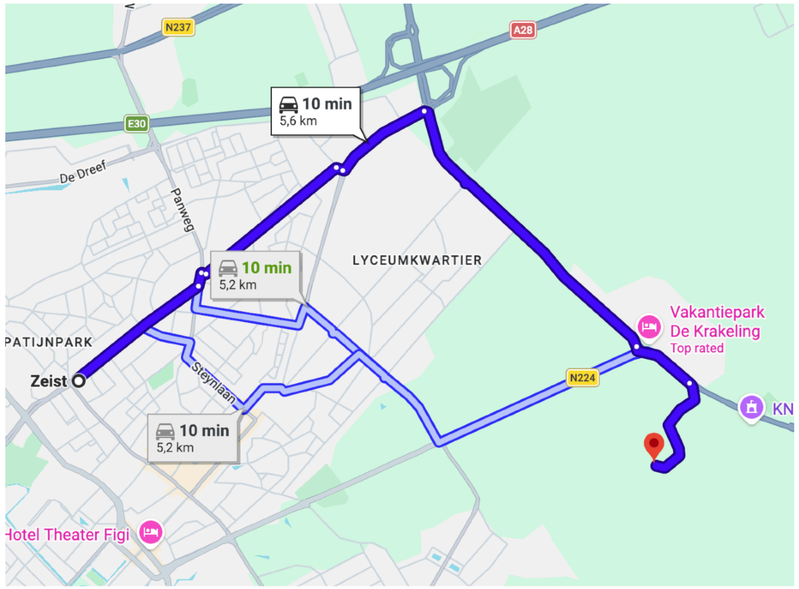
Nijmegen



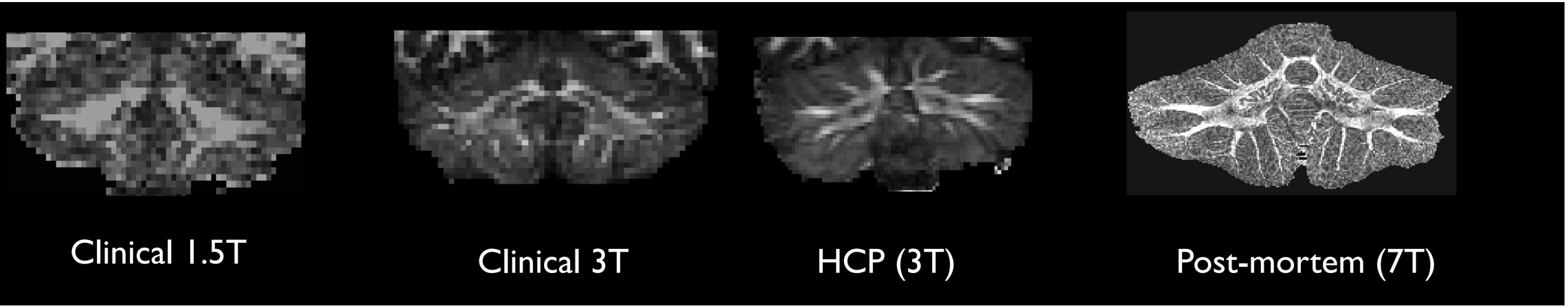
Zeist

Tractography shows the brain’s wiring









Diffusion-weighted imaging tractography

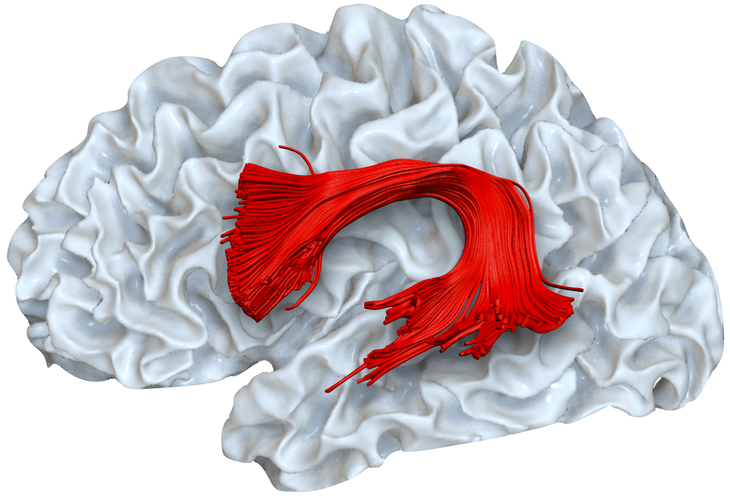


Diffusion-weighted imaging tractography



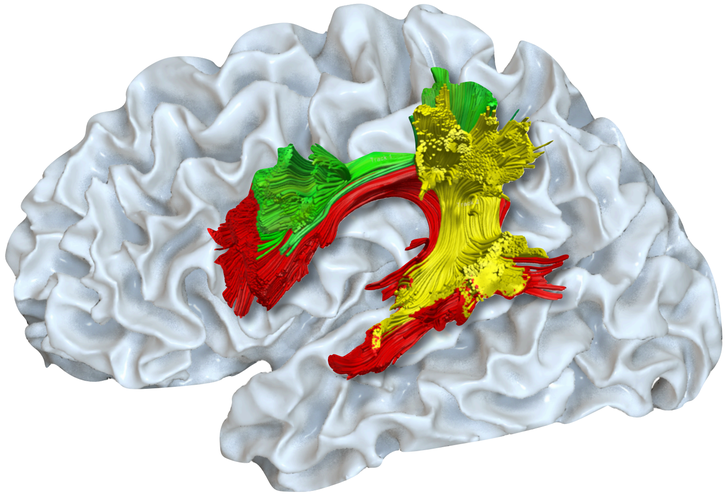
Language connectome

19th century



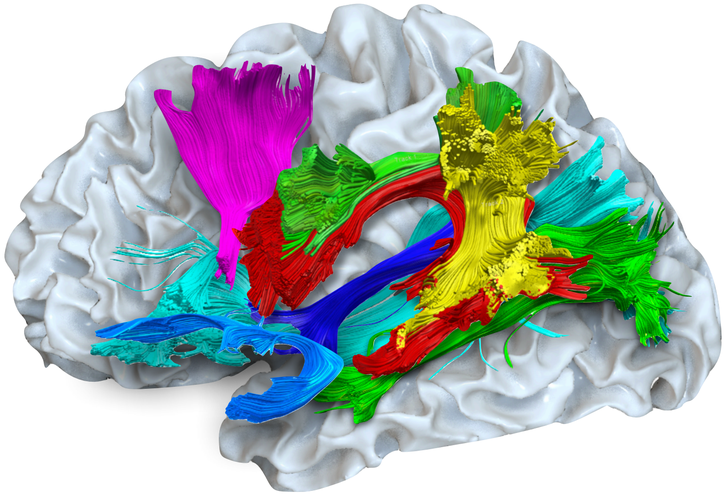
Arcuate fasciculus

Early 2000s



- Anterior segment
- Long segment
- Posterior segment

21st century



- Frontal Aslant Tract
- Uncinate fasciculus
- Temporal longitudinal fasciculus (TLF)
- Inferior fronto-occipital fasciculus (iFOF)
- Inferior longitudinal fasciculus (ILF)

Forkel & Catani, Oxford Handbook of Neurolinguistics, 2018

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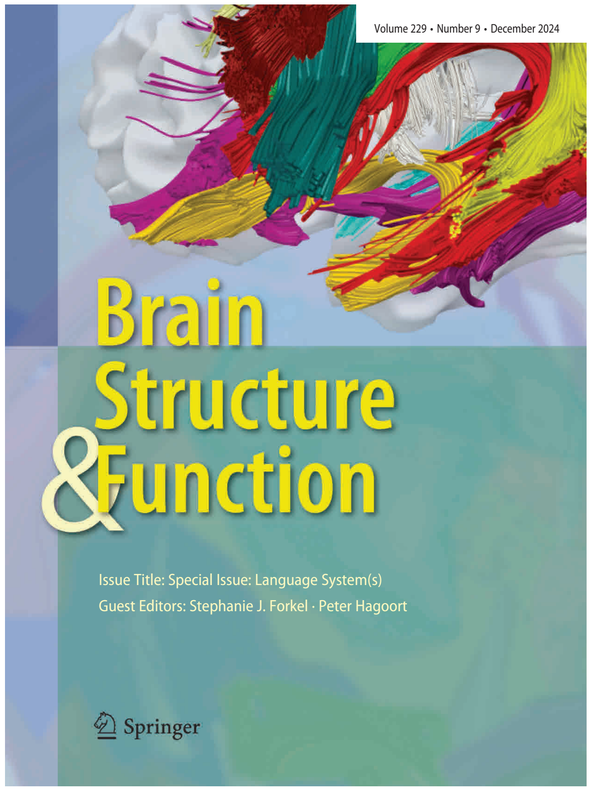
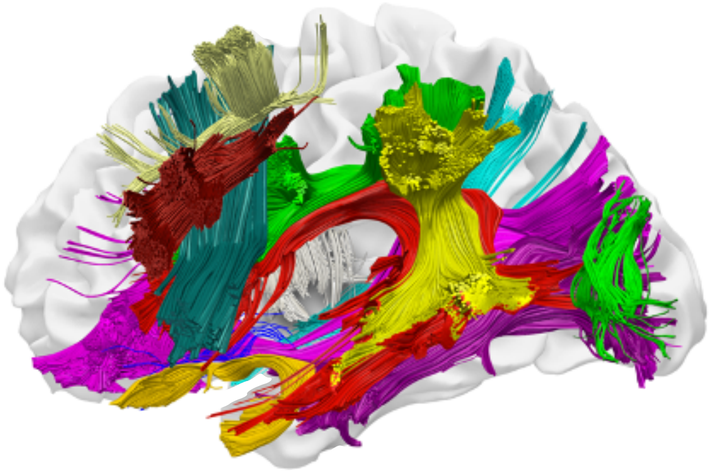
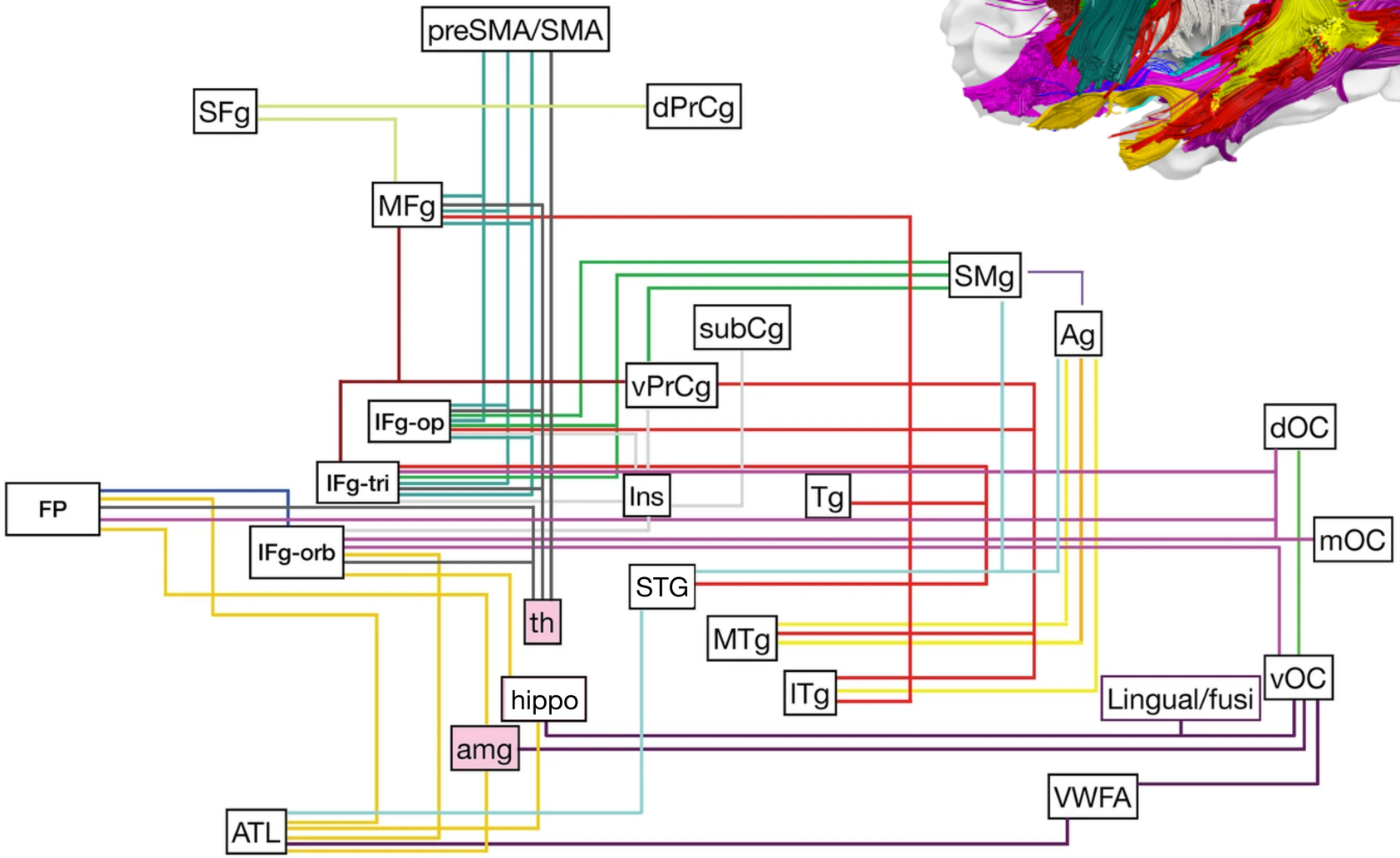
Redefining the Language system



Forkel & Hagoort, BSAF 2024





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Beyond Average



Marie Curie
Physics 1903; Chemistry 1911
Radioactivity; radium and polonium



Irène Joliot-Curie
1935 · Chemistry
Artificial radioactivity



Gerty Cori
1947 · Physiology or Medicine
Catalytic conversion of glycogen



Maria Goeppert Mayer
1963 · Physics
Nuclear shell structure



Dorothy Crowfoot Hodgkin
1964 · Chemistry
Structures of biochemical substances



Rosalyn Yalow
1977 · Physiology or Medicine
Radioimmunoassays of peptide hormones



Barbara McClintock
1983 · Physiology or Medicine
Mobile genetic elements



Rita Levi-Montalcini
1986 · Physiology or Medicine
Growth factors, including nerve growth factor



Gertrude B. Elion
1988 · Physiology or Medicine
Principles of drug treatment



Christiane Nüsslein-Volhard
1995 · Physiology or Medicine
Genetic control of embryonic development



Linda B. Buck
2004 · Physiology or Medicine
Odorant receptors and olfactory organisation



Françoise Barré-Sinoussi
2008 · Physiology or Medicine
Discovery of HIV



Elizabeth H. Blackburn
2009 · Physiology or Medicine
Telomeres and telomerase



Carol W. Greider
2009 · Physiology or Medicine
Telomeres and telomerase



Ada E. Yonath
2009 · Chemistry
Structure and function of the ribosome



May-Britt Moser
2014 · Physiology or Medicine
Grid cells and spatial navigation



Tu Youyou
2015 · Physiology or Medicine
Artemisinin therapy against malaria



Donna Strickland
2018 · Physics
Chirped pulse amplification of lasers



Frances H. Arnold
2018 · Chemistry
Directed evolution of enzymes



Andrea Ghez
2020 · Physics
Supermassive compact object at the Galactic Centre



Emmanuelle Charpentier
2020 · Chemistry
CRISPR-Cas9 genome editing



Jennifer A. Doudna
2020 · Chemistry
CRISPR-Cas9 genome editing



Carolyn Bertozzi
2022 · Chemistry
Click chemistry and bioorthogonal chemistry



Anne L'Huillier
2023 · Physics
Attosecond pulses for electron dynamics



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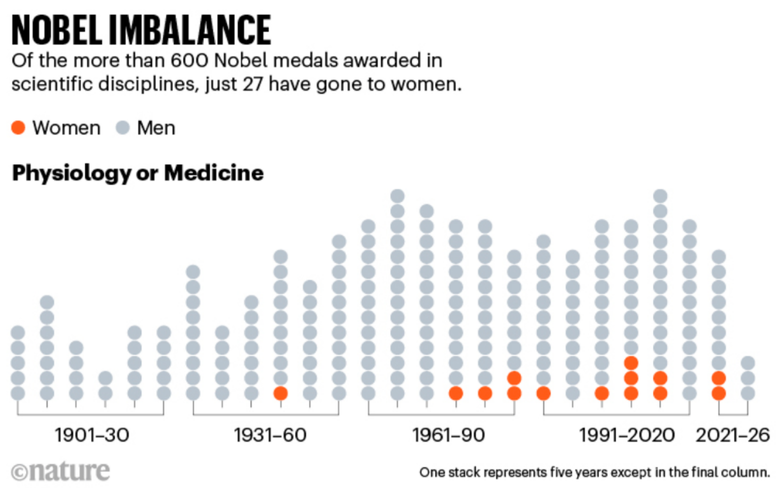
Mary E. Brunkow
2025 · Physiology or Medicine
Peripheral immune tolerance

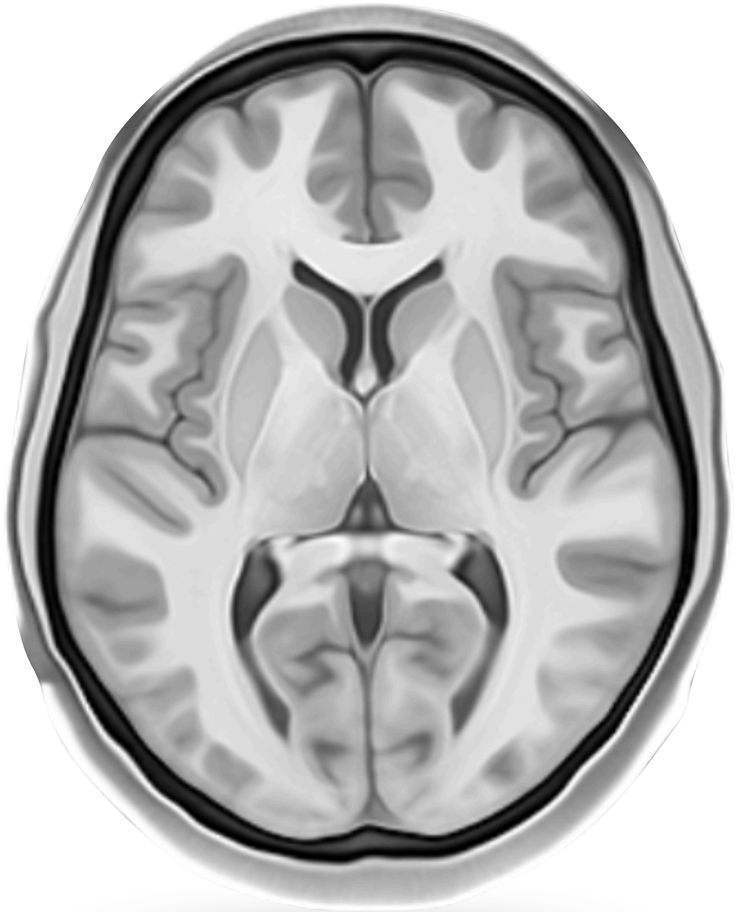
Source: NobelPrize.org

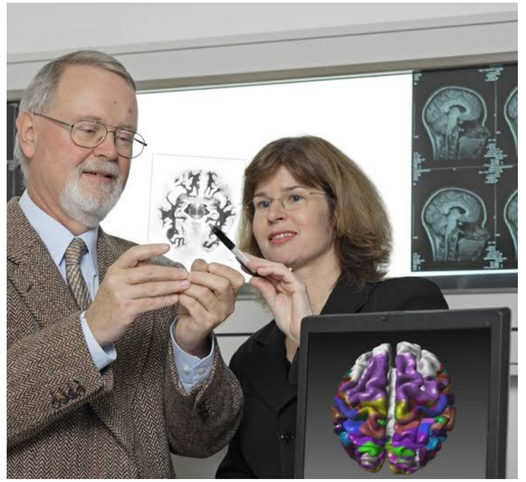




Forkel & Howells, 2014
https://www.lindau-nobel.org/professor-elizabeth-blackburn-on-unconscious-biases/

Neurovariability

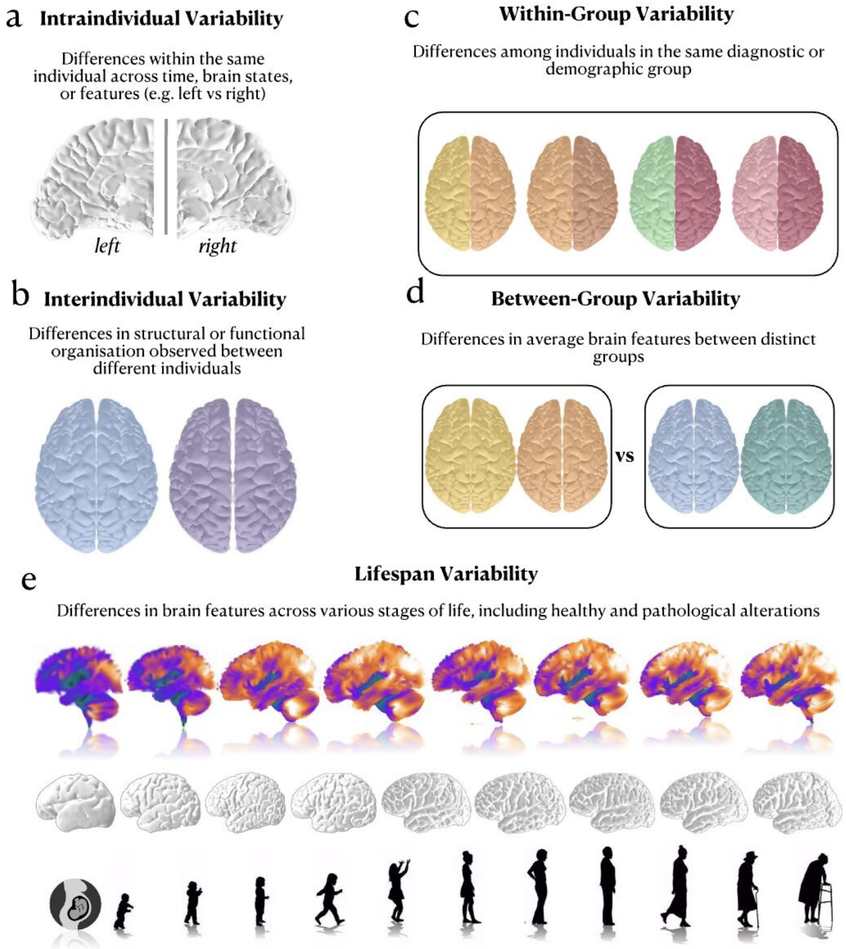




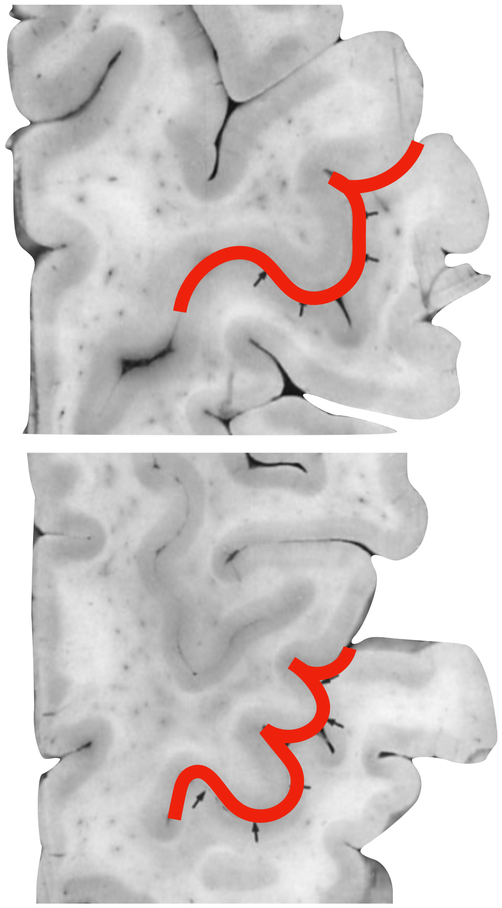
‘Rather than being ‘noise’, intersubject variability is invaluable for understanding principles of brain evolution and ontogenetic development, and for interpreting statistical maps in task-based functional neuroimaging studies.’

Zilles & Amunts TICS 2013

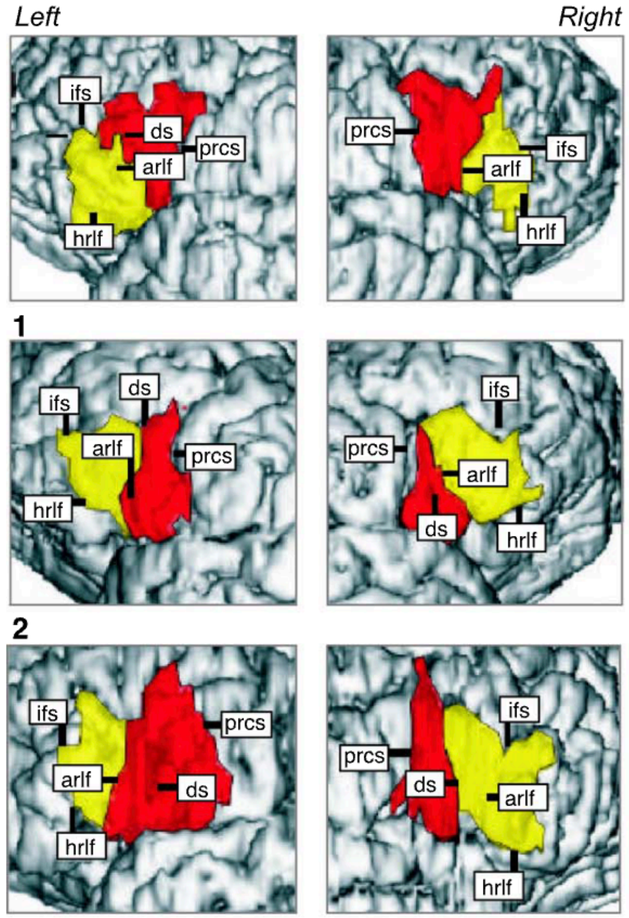
The magnitude of neurovariability



Forkel et al., BSAF 2026

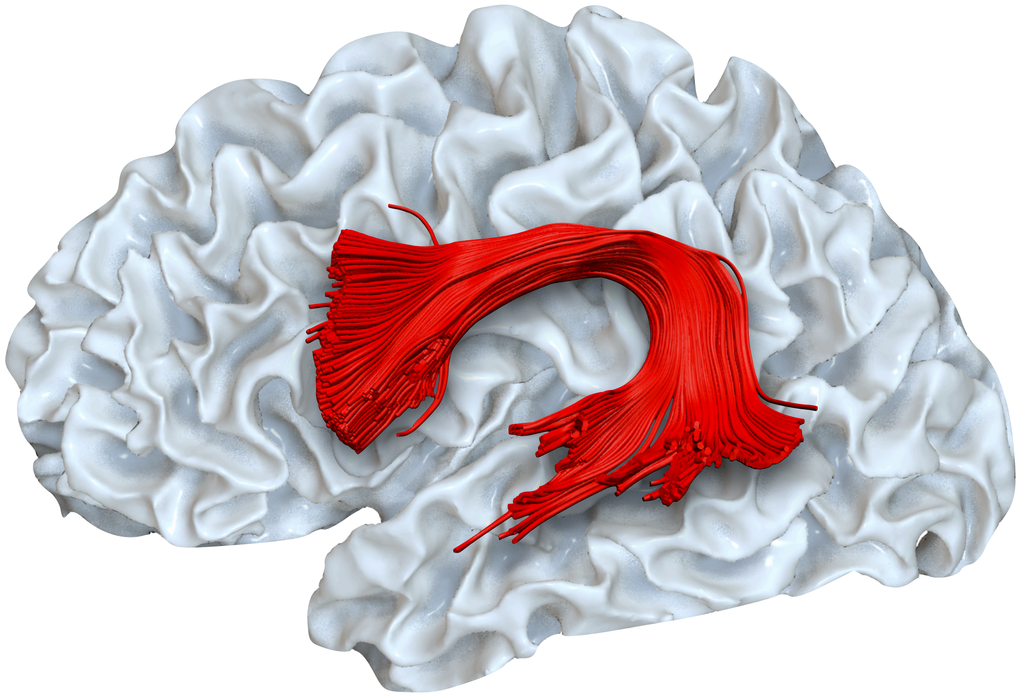


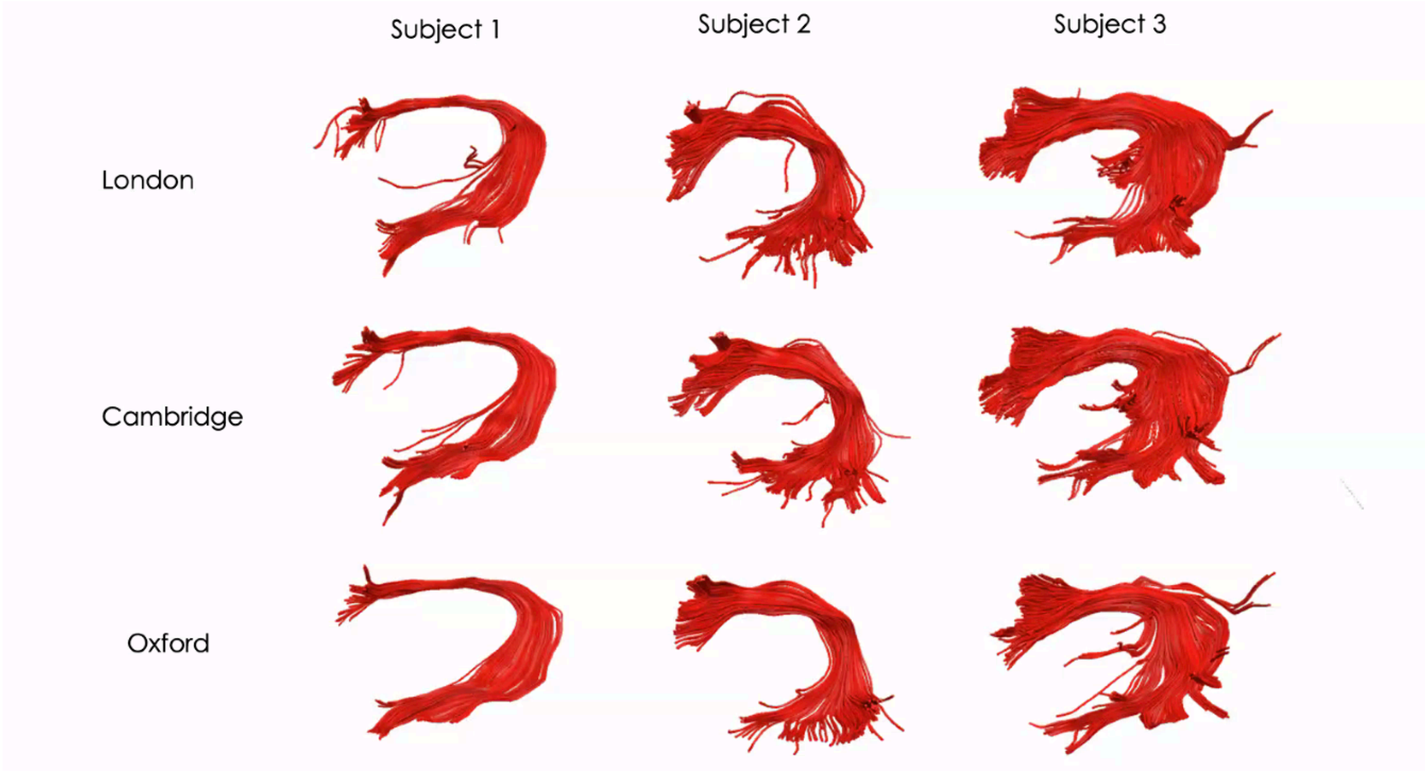
Yousry et al., 1997



Uylings et al., 2005; Amunts et al., 2004

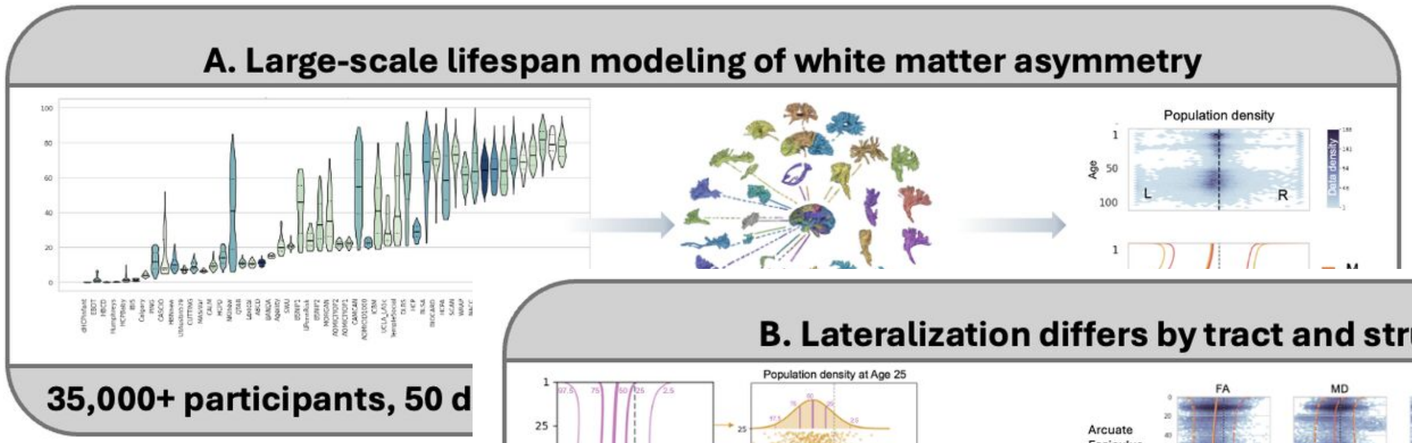
There is no canonical language brain

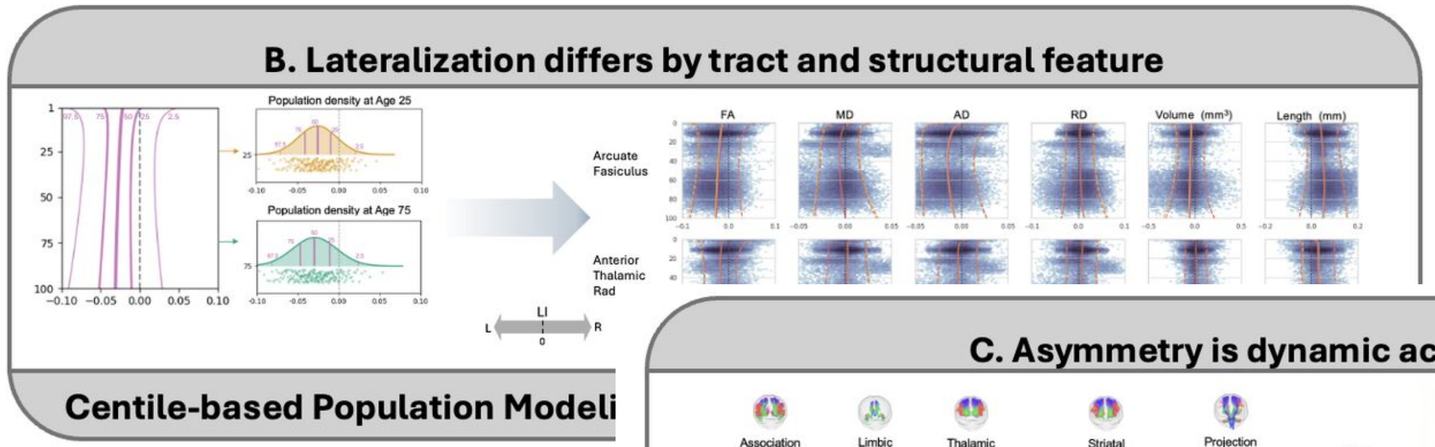


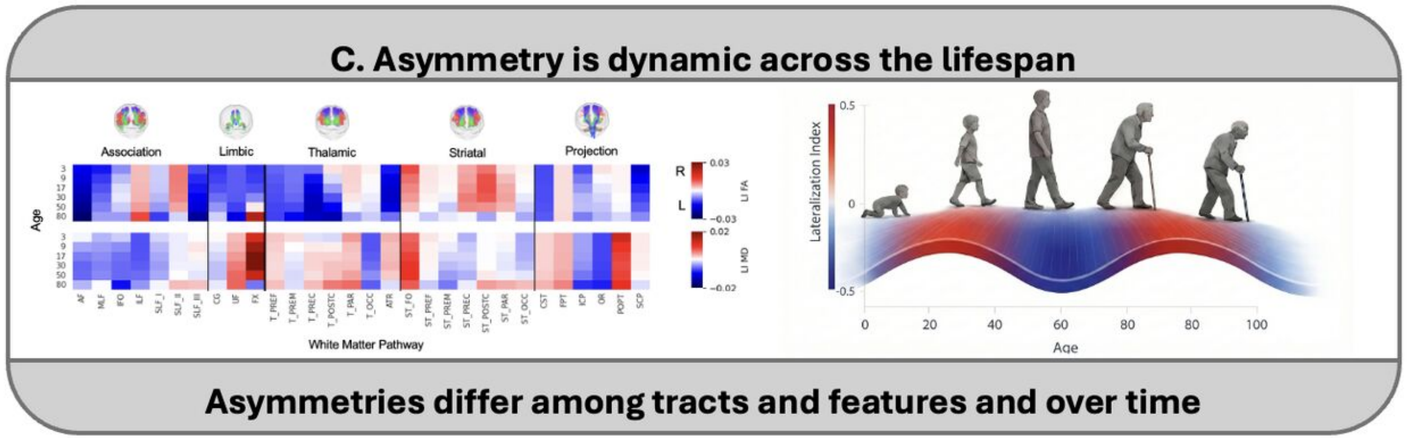


Dell'Acqua et al. 2025 *Brain Structure and Function* "The Tractographer's Dilemma"

Language networks change across the lifespan







Bogdanov et al., HBM 2026

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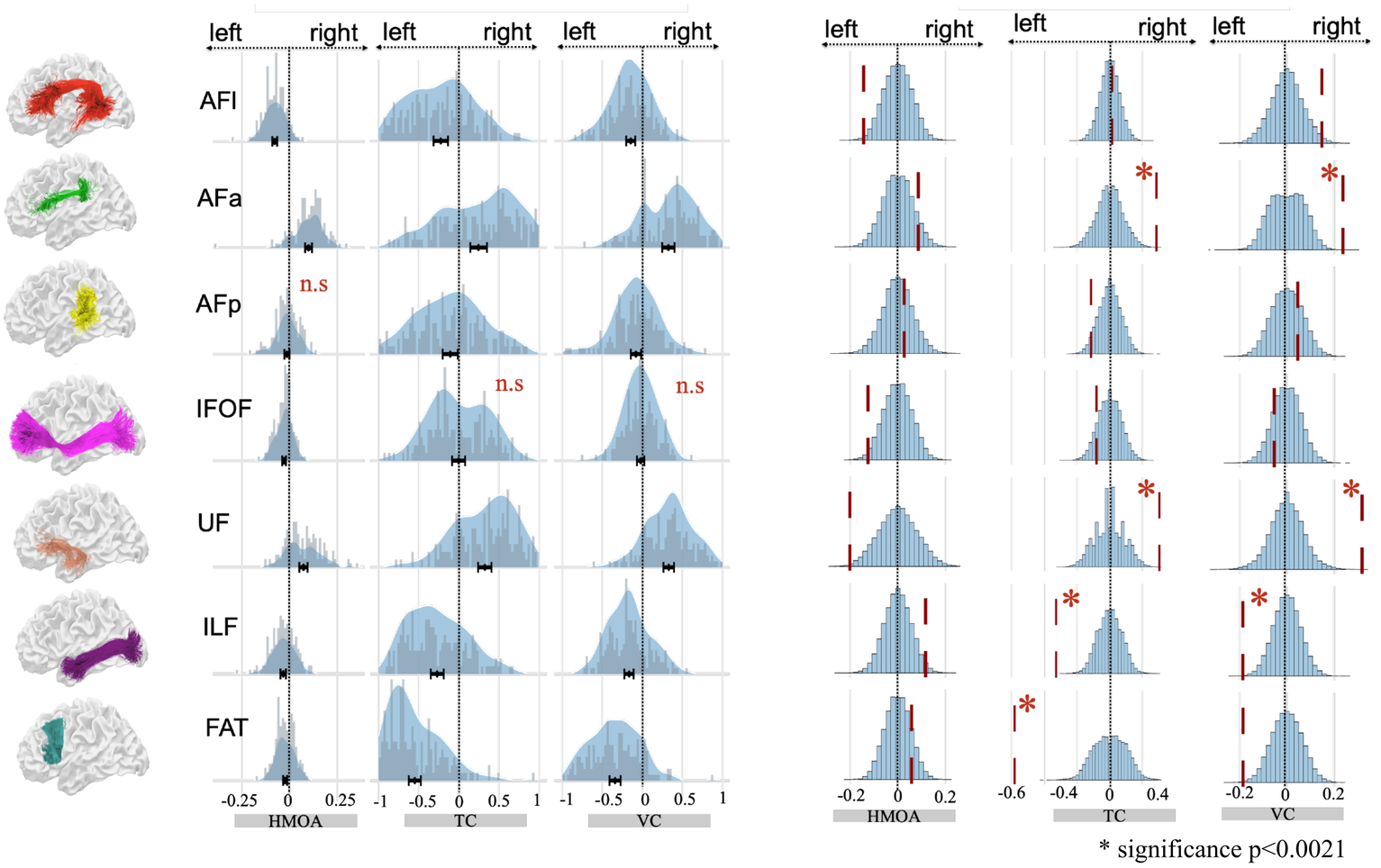
Laterlisation and variabiliy patterns

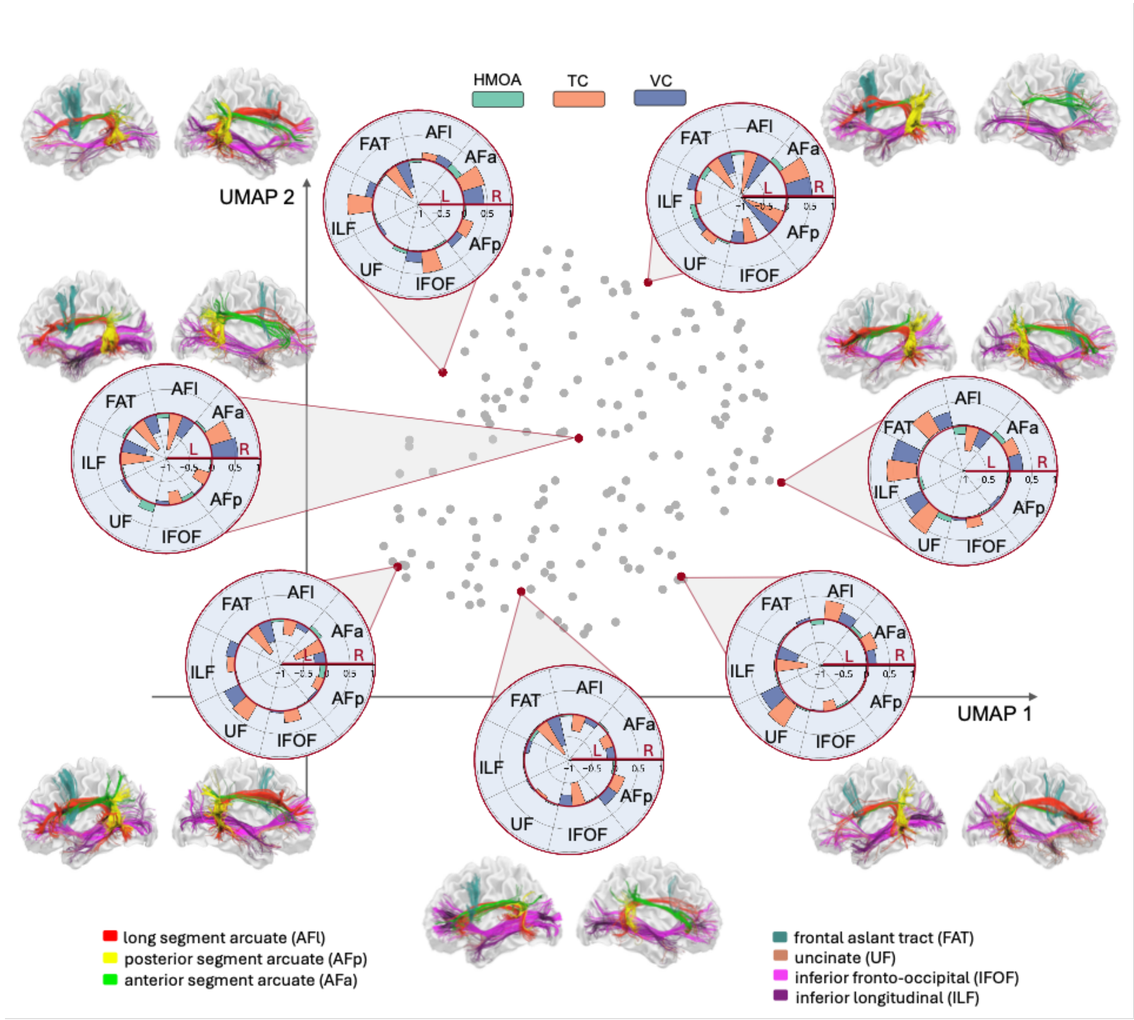


Dulyan et al., *under revision*

The language connectome is **neither uniformly left-lateralised nor anatomically fixed**, but rather a probabilistic system with tract-specific asymmetries and variability patterns.

OPEN ACCESS

Laterlisation and variabiliy patterns



Dulyan et al., *under revision*

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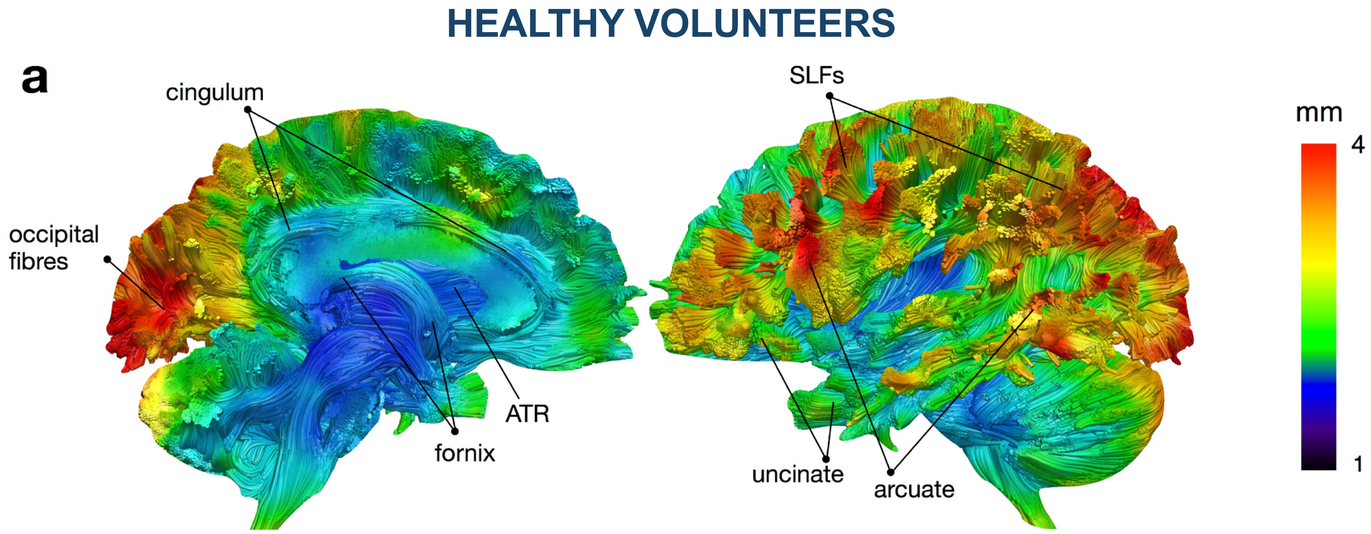
Inter-individual variability

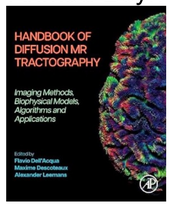


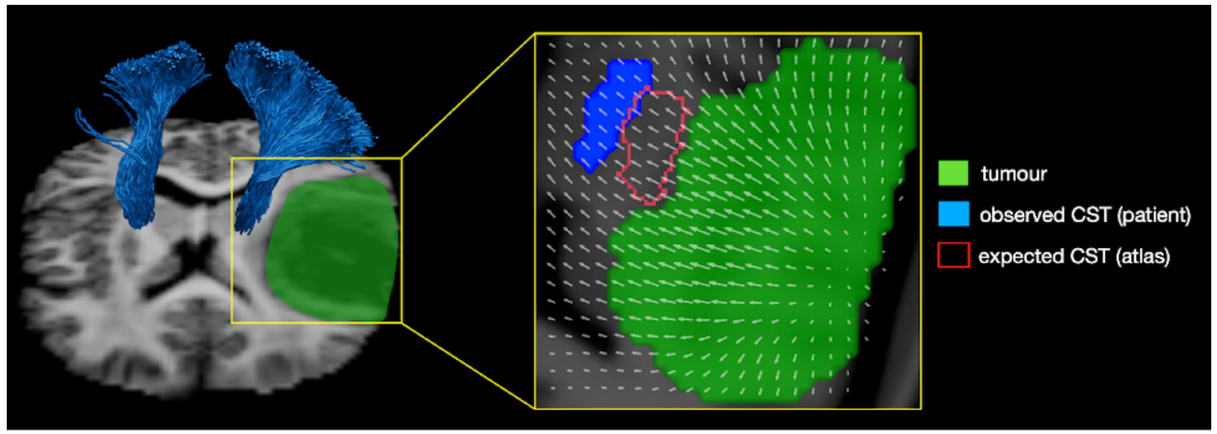


Croxson, Forkel et al., 2018



Ahmad Beyh

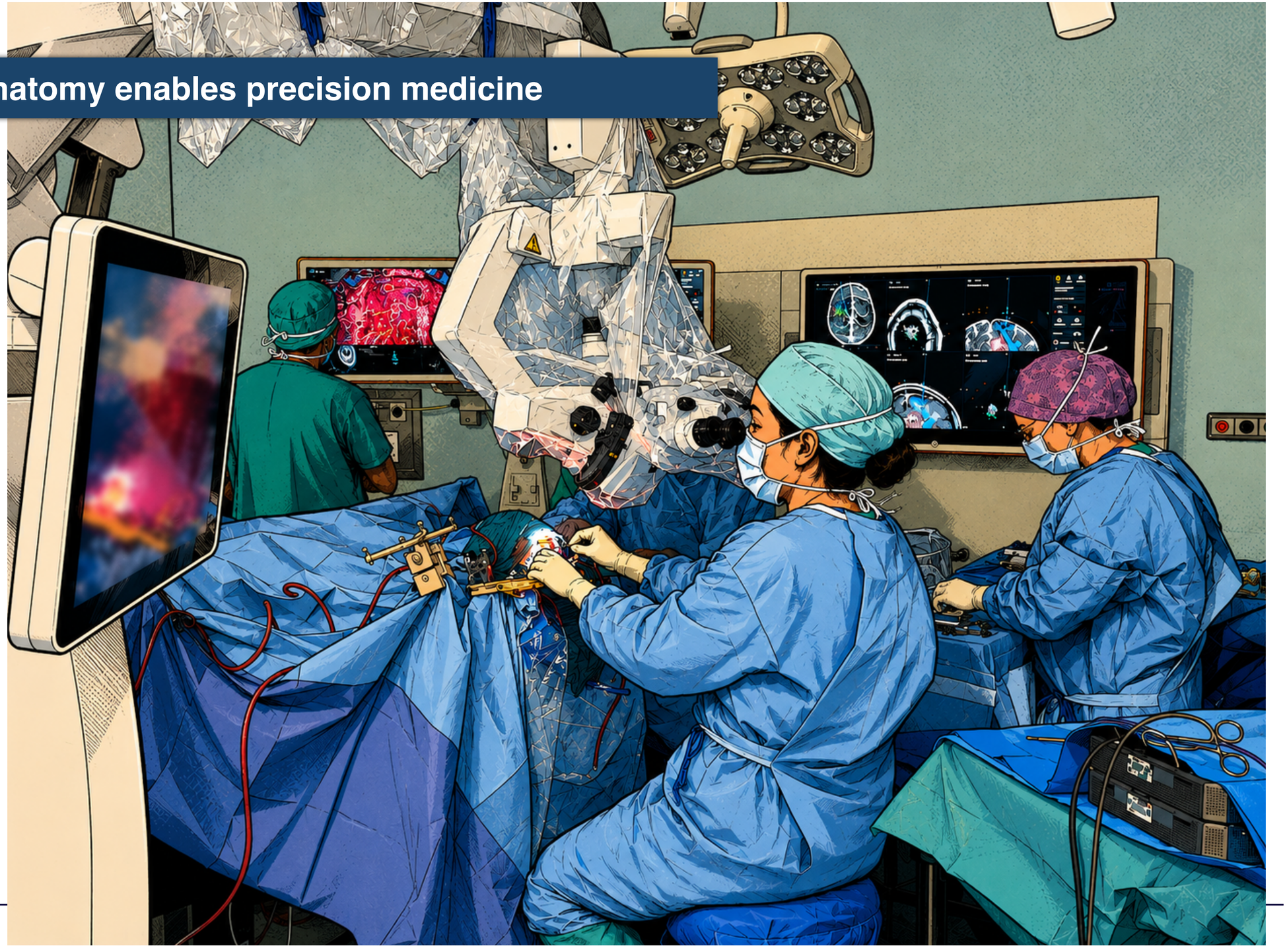




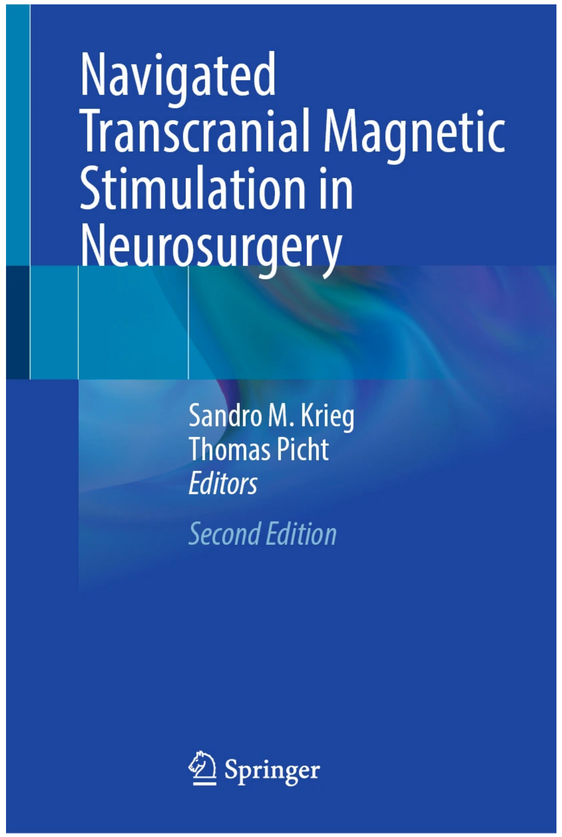
Forkel et al., *Handbook of Diffusion MRI Tractography, 2025*

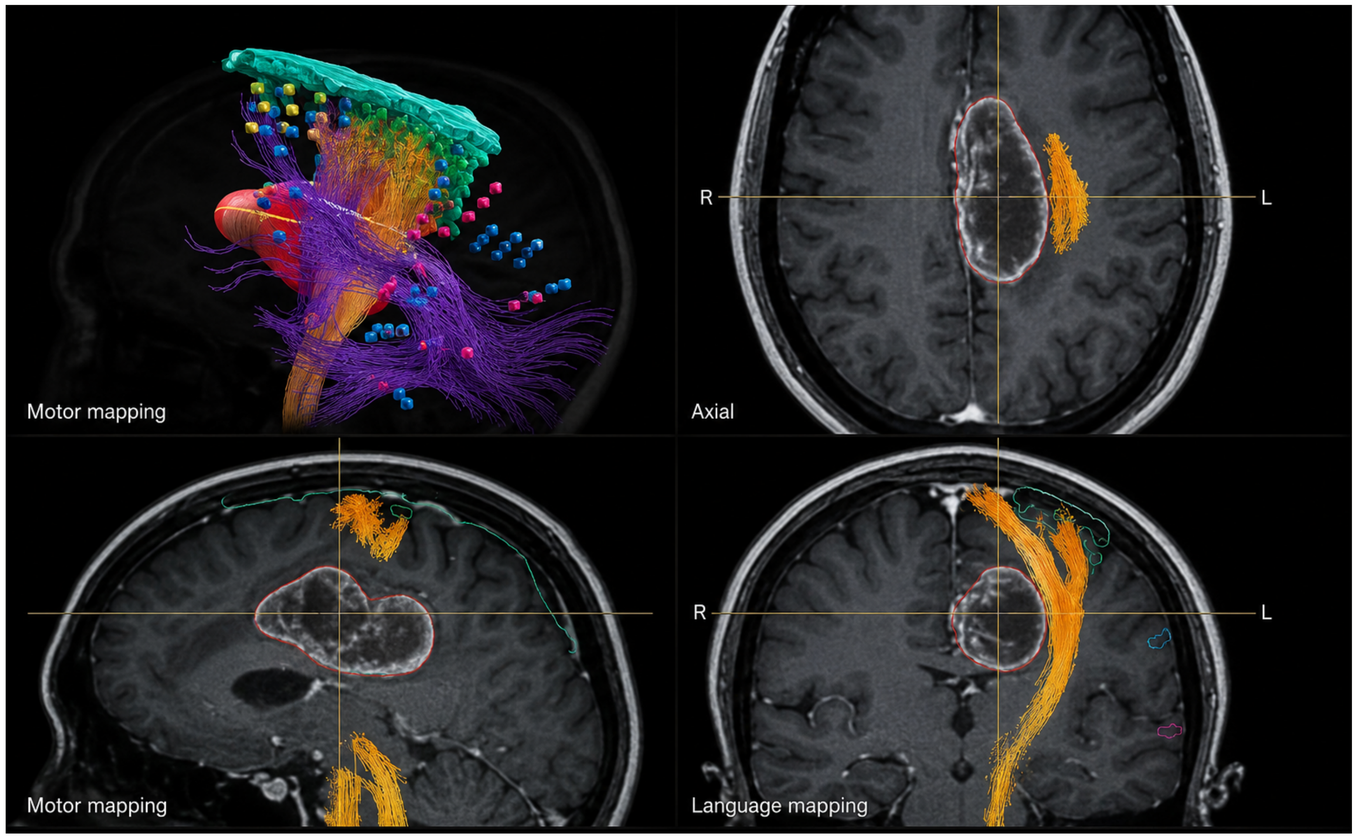
Watch talk on YouTube

Precision anatomy enables precision medicine



Combining nTMS and tractography for intraoperative mapping





Beyh, A., Ohlerth, A.-K., & Forkel, S. J. (2025). Harnessing advanced tractography in neurosurgical practice.

Ohlerth, A.-K., Lavrador, J. P., Vergani, F., & Forkel, S. J. (2025). Combining nTMS and tractography for language mapping.

Clinical usability of DWI Tractography

Overview of subcortical brain regions with sensorimotor, language/cognitive functions and tasks.

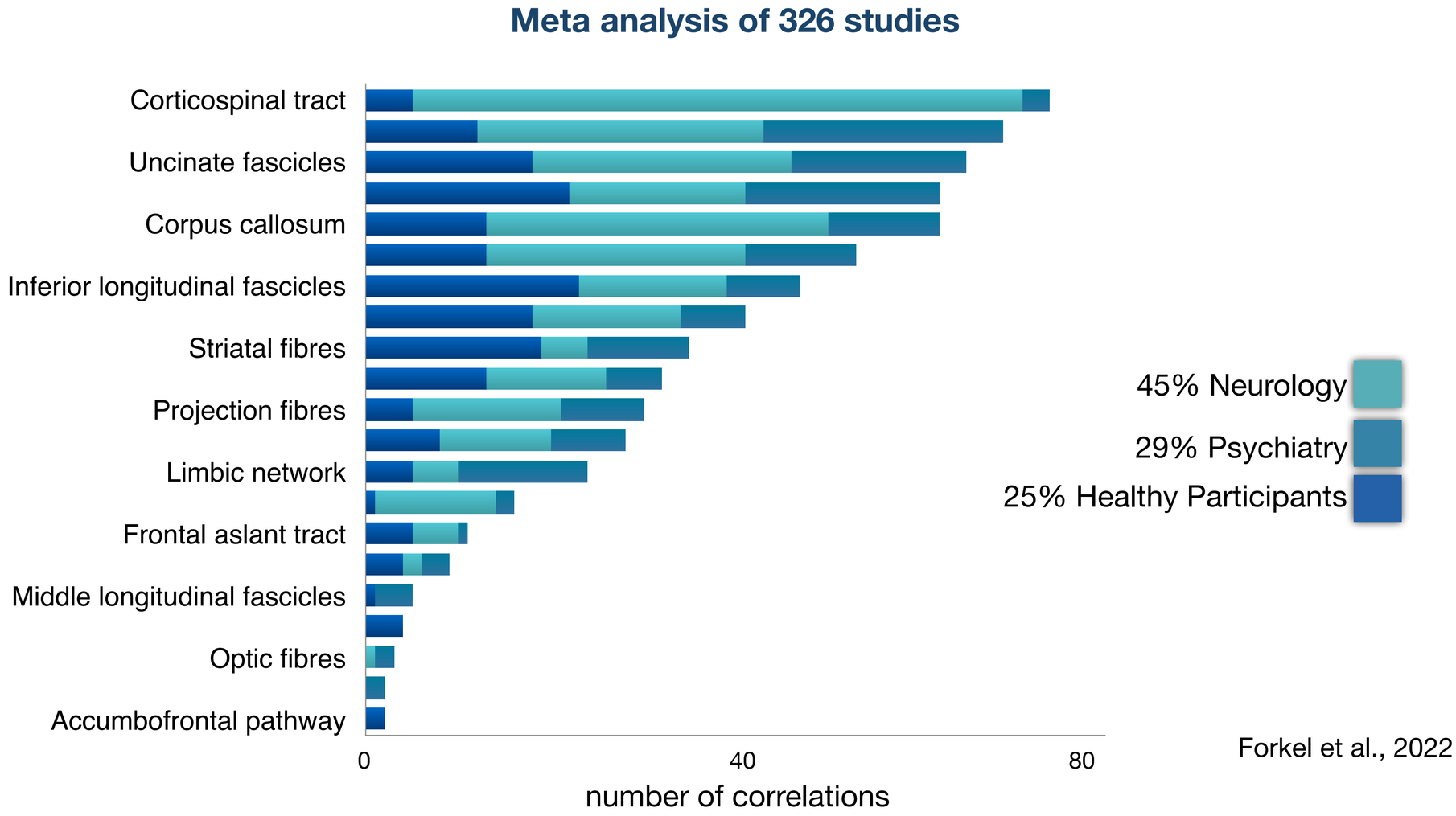
Subcortical level—tracts	Function	Task	Hemisphere
Frontal Aslant Tract	Initiation of speech, motor speech	Verbal fluency, sentence completion, spontaneous speech	L+R
Corticospinal tract	Motor speech	Verbal diadochokinesis, word repetition	L+R
Arcuate fasciculus	Phonology	(Non) word repetition	L
Superior longitudinal fasciculus	Visuospatial	Line bisection	R
Inferior frontal occipital fasciculus	Word retrieval Semantics, reading	Naming	L
		Semantic judgment and association	L+R
	Visuospatial	Line bisection	R
Inferior Longitudinal Fasciculus	Reading, phonology, semantics	Reading, (non) word repetition, semantic judgment, association, object naming	L
Uncinate fasciculus	Word/proper name retrieval, semantics, phonology, face naming/recognition	Object naming/proper noun naming, semantic judgment, famous face naming, (non) word repetition	L

Satoer, D., Dulyan, L., & Forkel, S. J. (2025). Cerebral Asymmetries: Handbook of Clinical Neurology

Variability in anatomy



Henrietta Howells



Forkel et al., 2022

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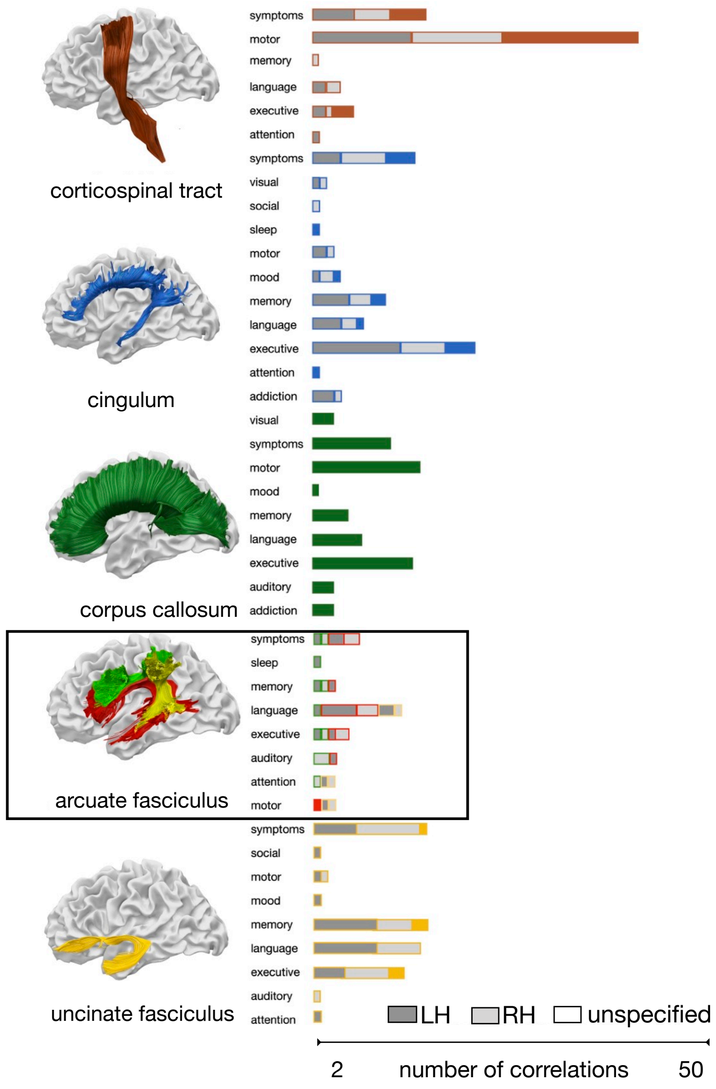
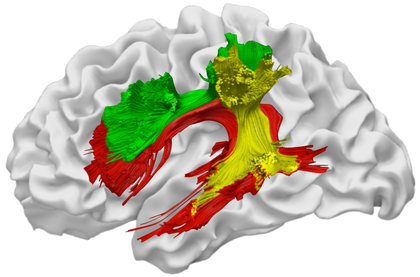
One Track – Many Functions





arcuate fasciculus

anterior segment
long segment
posterior segment

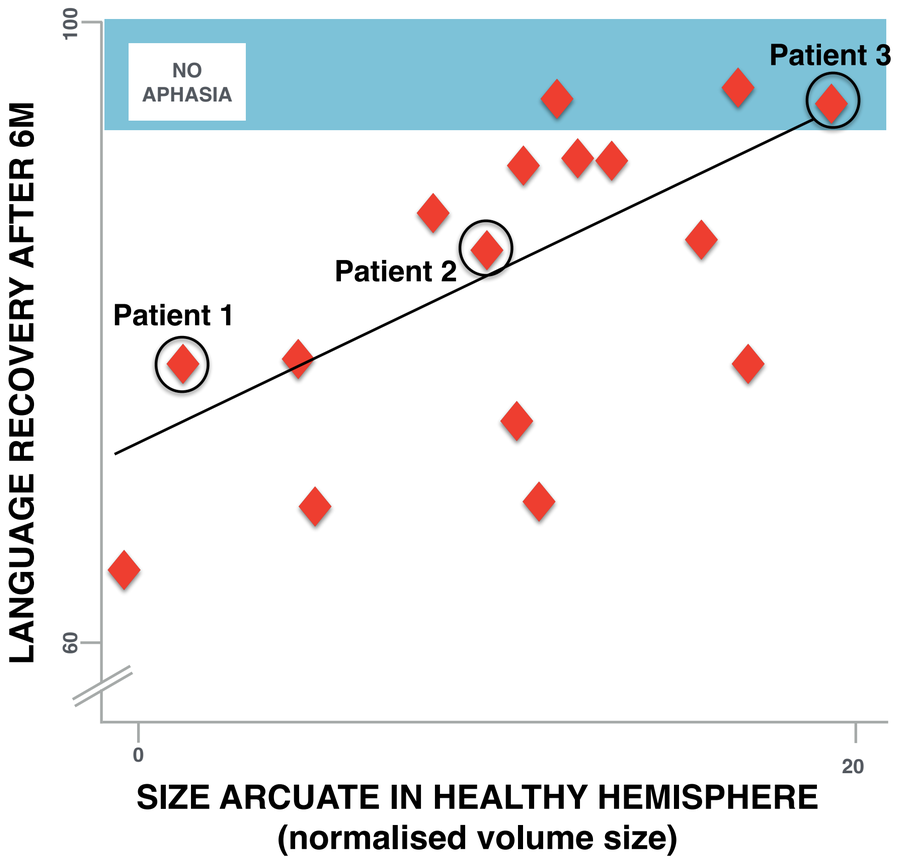


Forkel et al., 2022

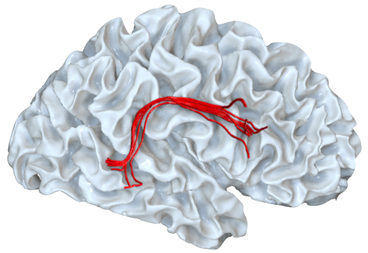
OPEN ACCESS

Anatomical variability doubles the prediction of recovery

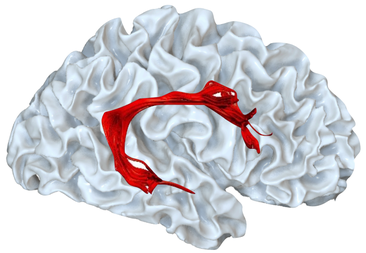
LH STROKE PATIENTS



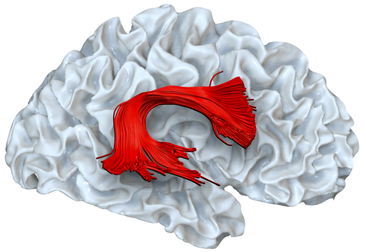
RH HEALTHY HEMISPHERE



Patient 1 (59 yrs man)



Patient 2 (81 yrs woman)



Patient 3 (87 yrs woman)

NHS
Guy's and St Thomas'
NHS Foundation Trust

BRAIN
A JOURNAL OF NEUROLOGY
Volume 137 Part 7 July 2014
www.brain.oxfordjournals.org



OXFORD OPEN

F1000 Research

Forkel et al., 2014

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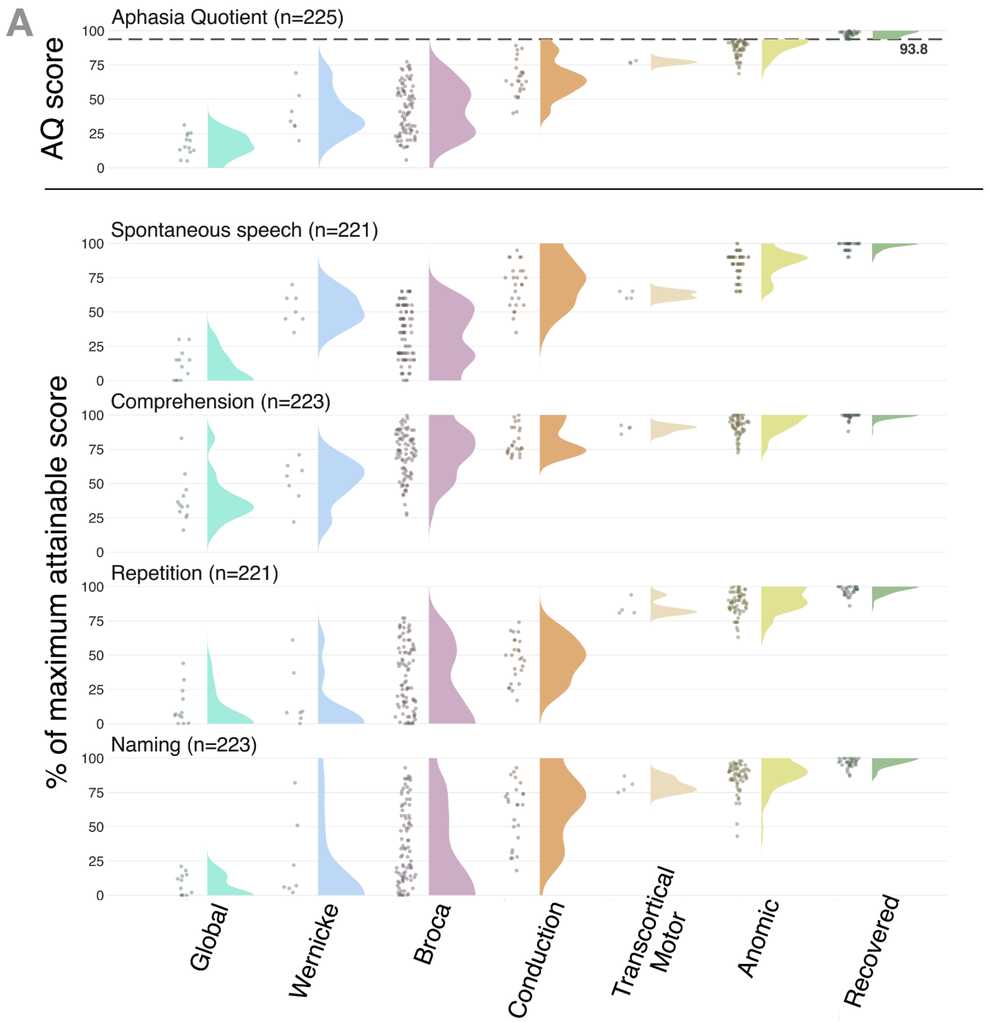
Do clinical syndromes reflect biological organisation?



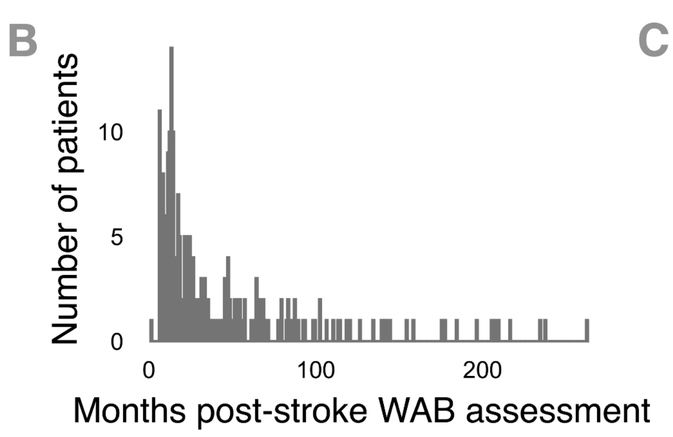
nature › scientific data › data descriptors › article

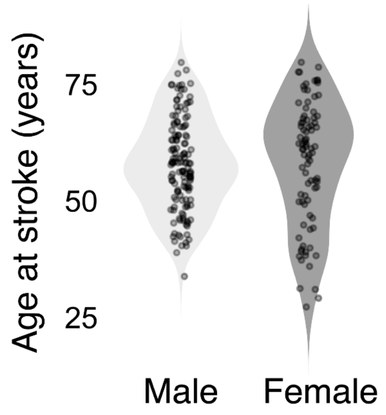
Data Descriptor | Open access | Published: 09 September 2024

The Aphasia Recovery Cohort, an open-source chronic stroke repository

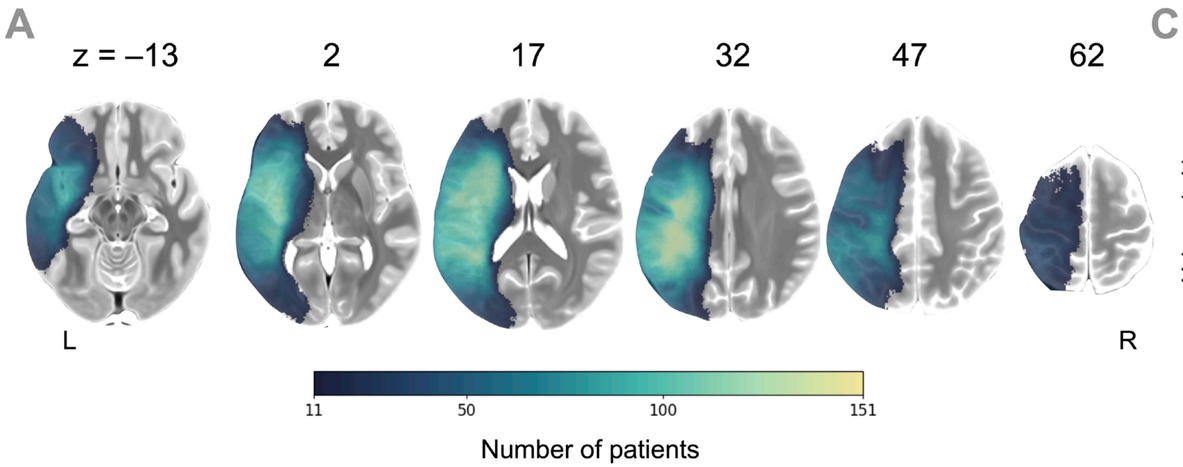
Makayla Gibson, Roger Newman-Norlund, Leonardo Bonilha, Julius Fridriksson, Gregory Hickok, Argye E. Hillis, Dirk-Bart den Ouden & Christopher Rorden

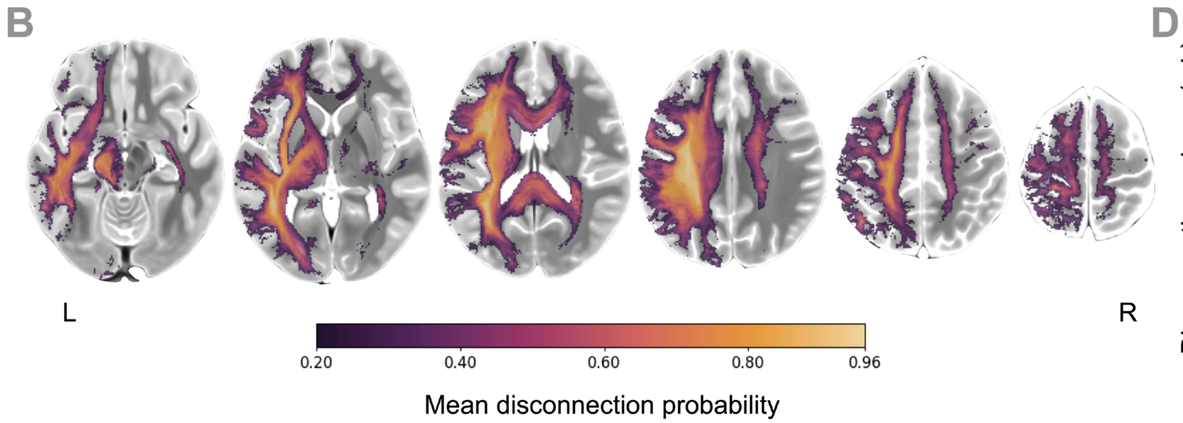
Scientific Data **11**, Article number: 981 (2024) | Cite this article

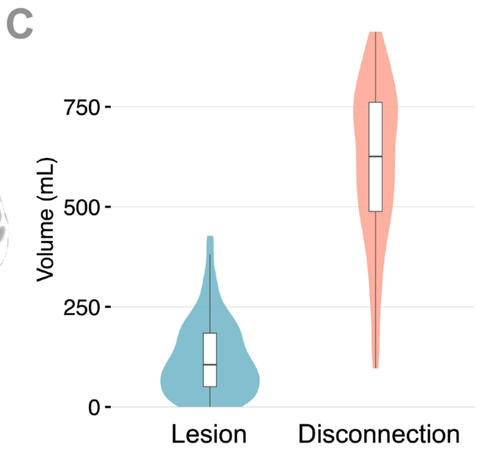


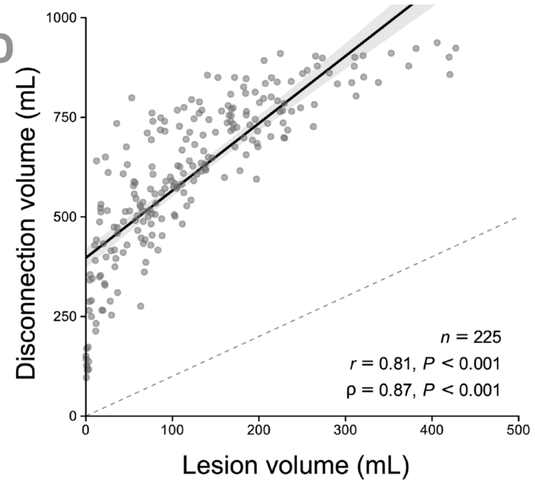


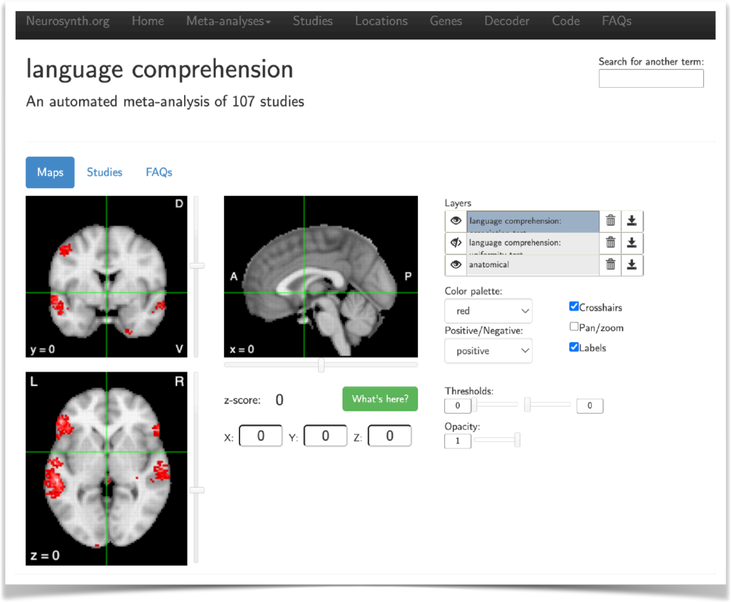
A lesion's network impact extends beyond its boundaries





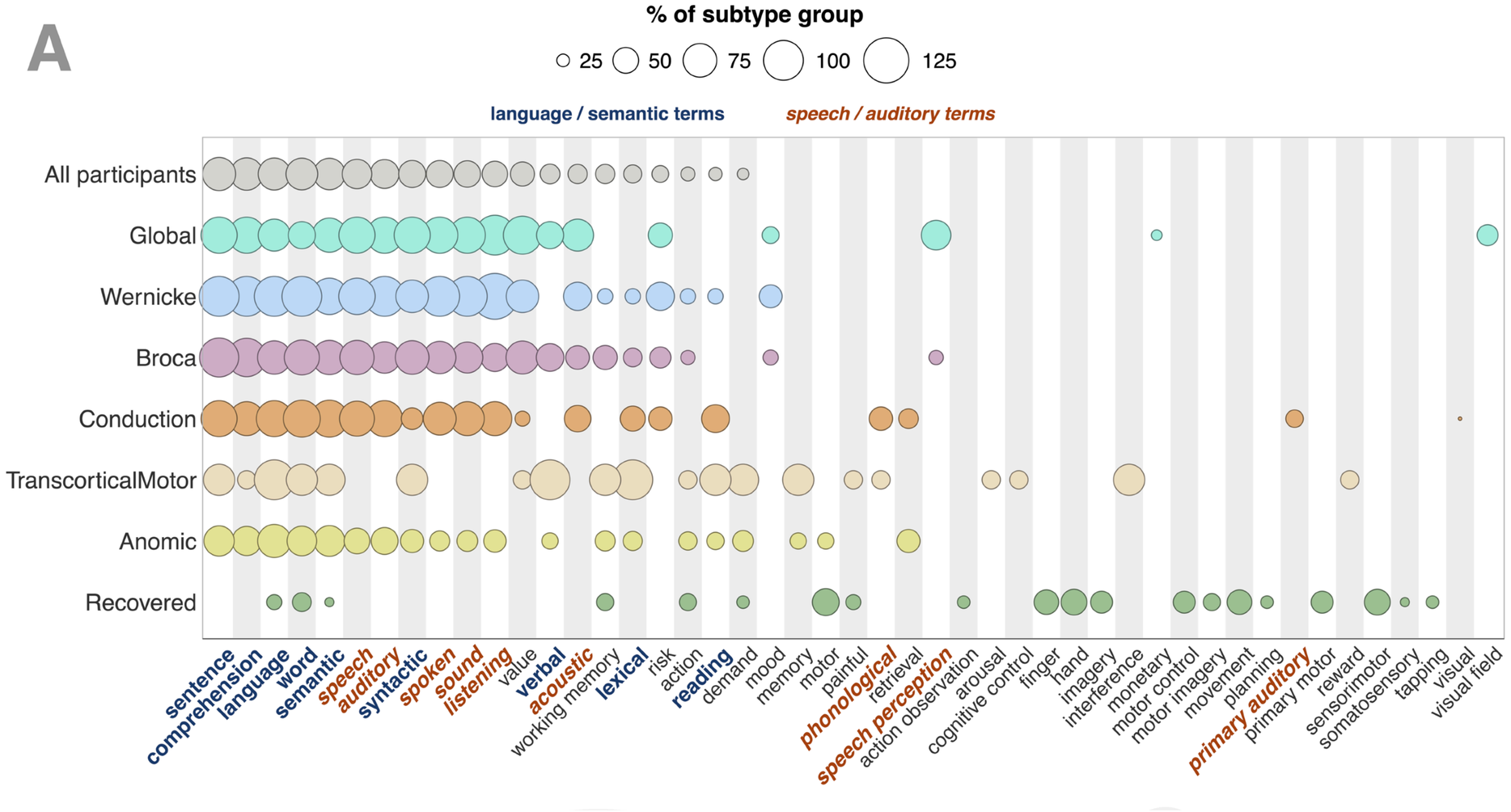






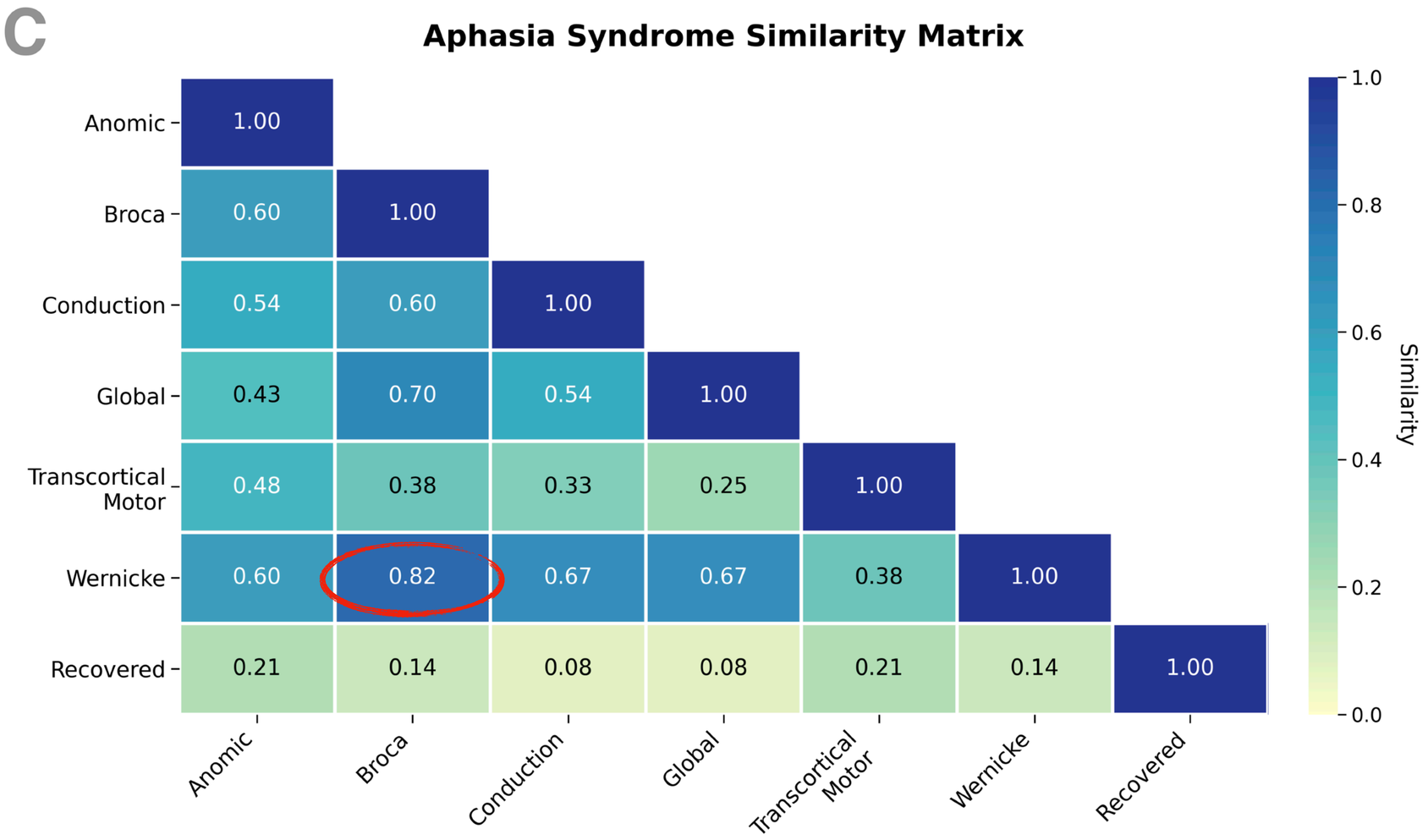
Tulner et al., Academy of Aphasia 2026

Full functional lesion profiles



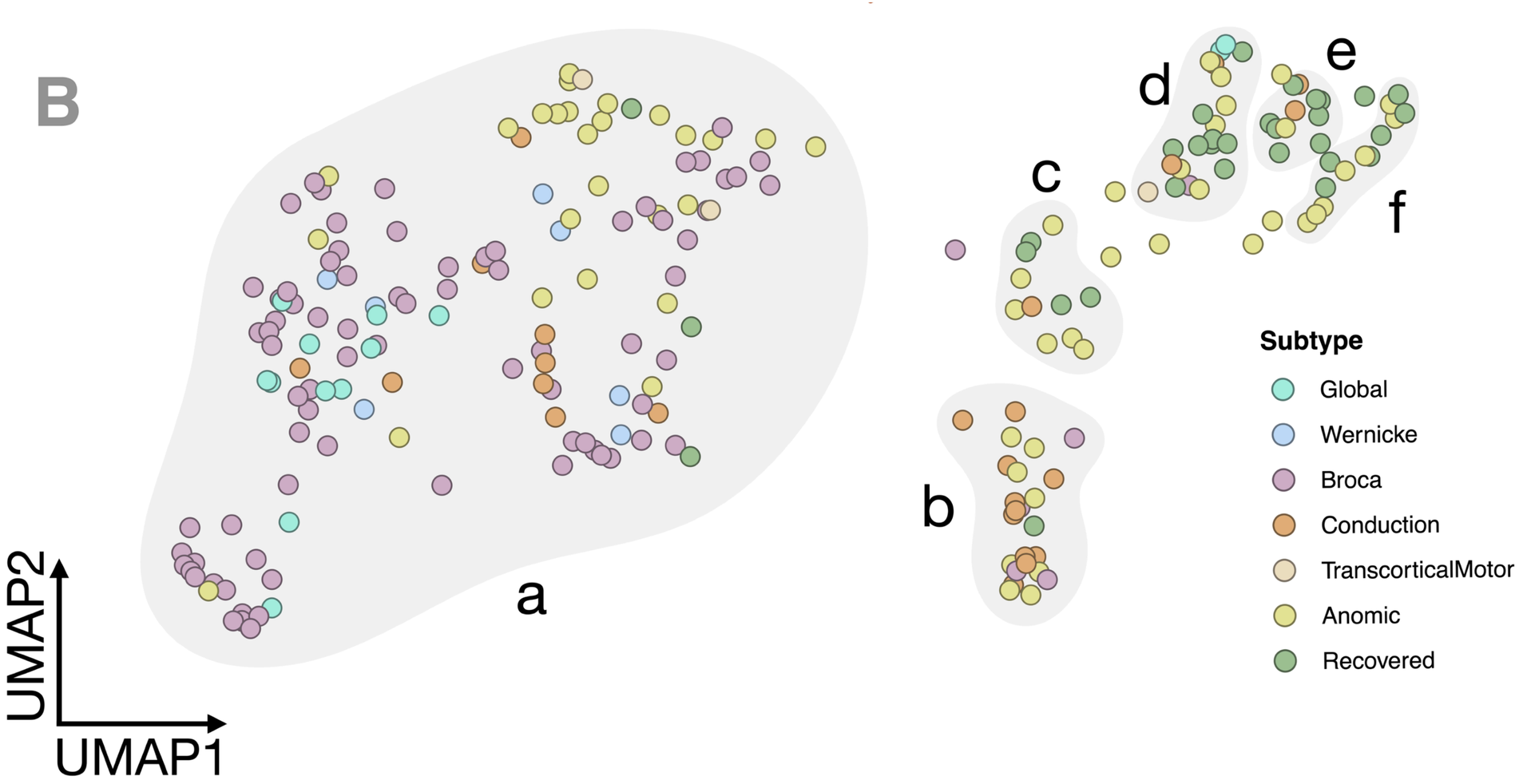
Tulner et al., Academy of Aphasia 2026

Broca’s and Wernicke’s labels conceal substantial overlap



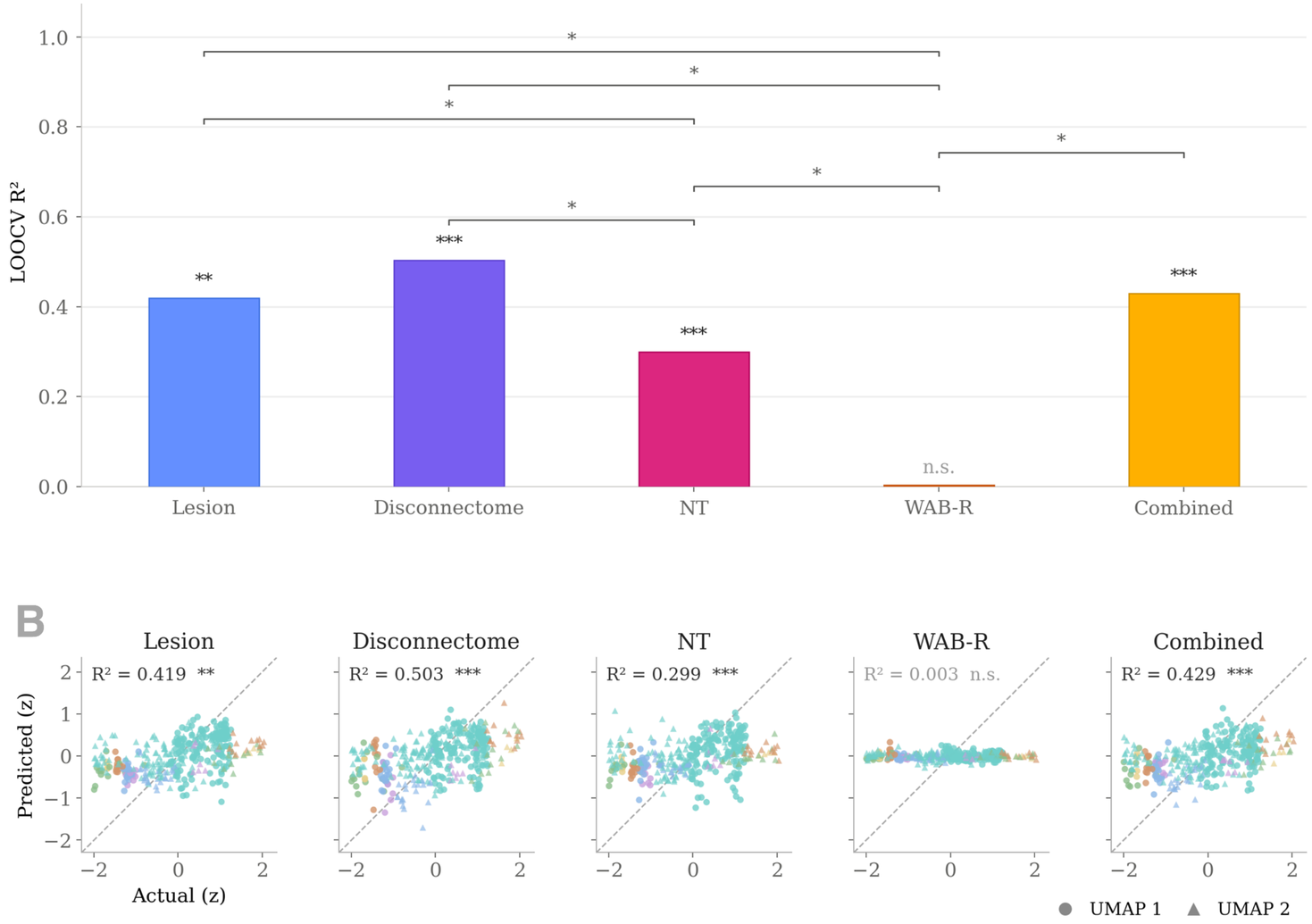
Tulner et al., Academy of Aphasia 2026

Biological groupings cross diagnostic boundaries



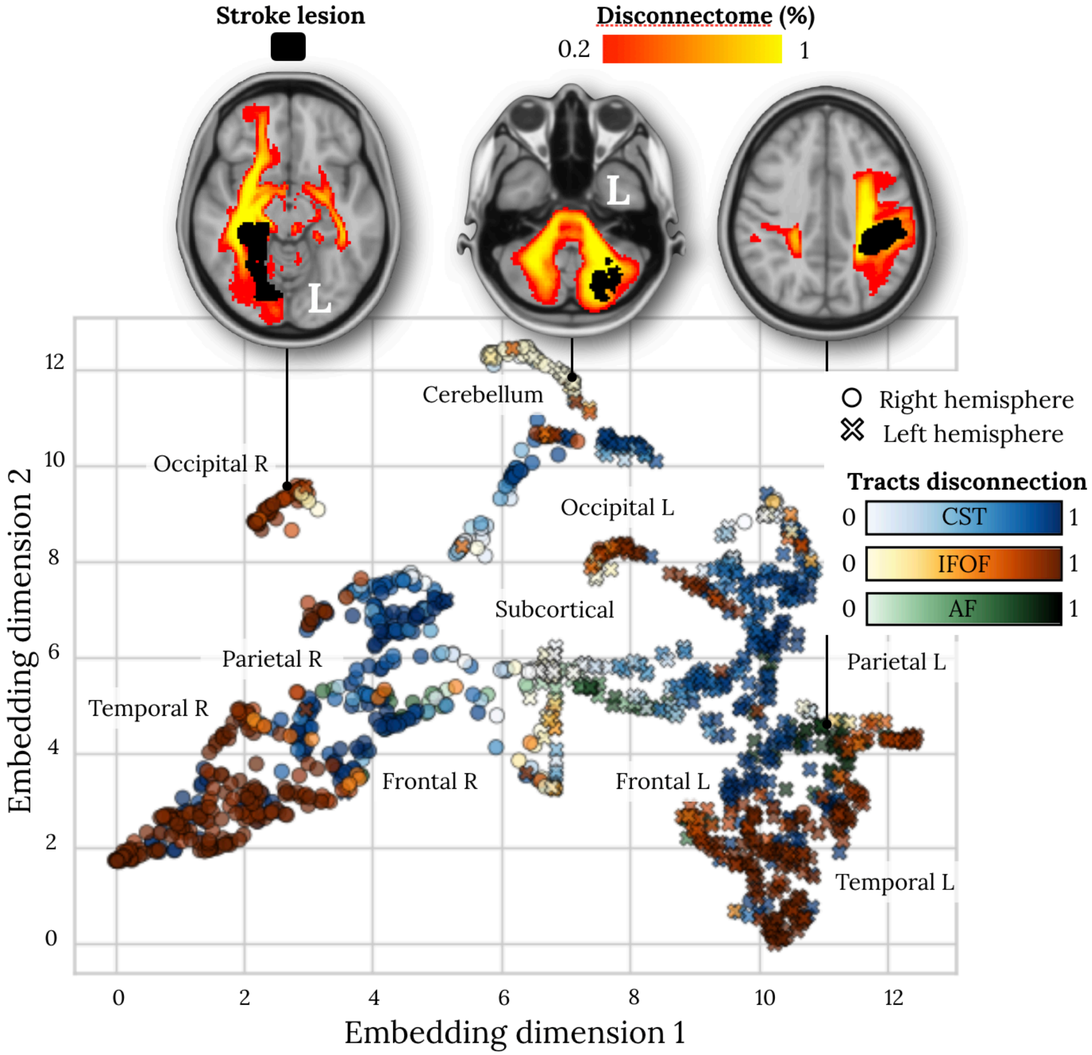
Tulner et al., Academy of Aphasia 2026

What explains the organisation of these profiles?



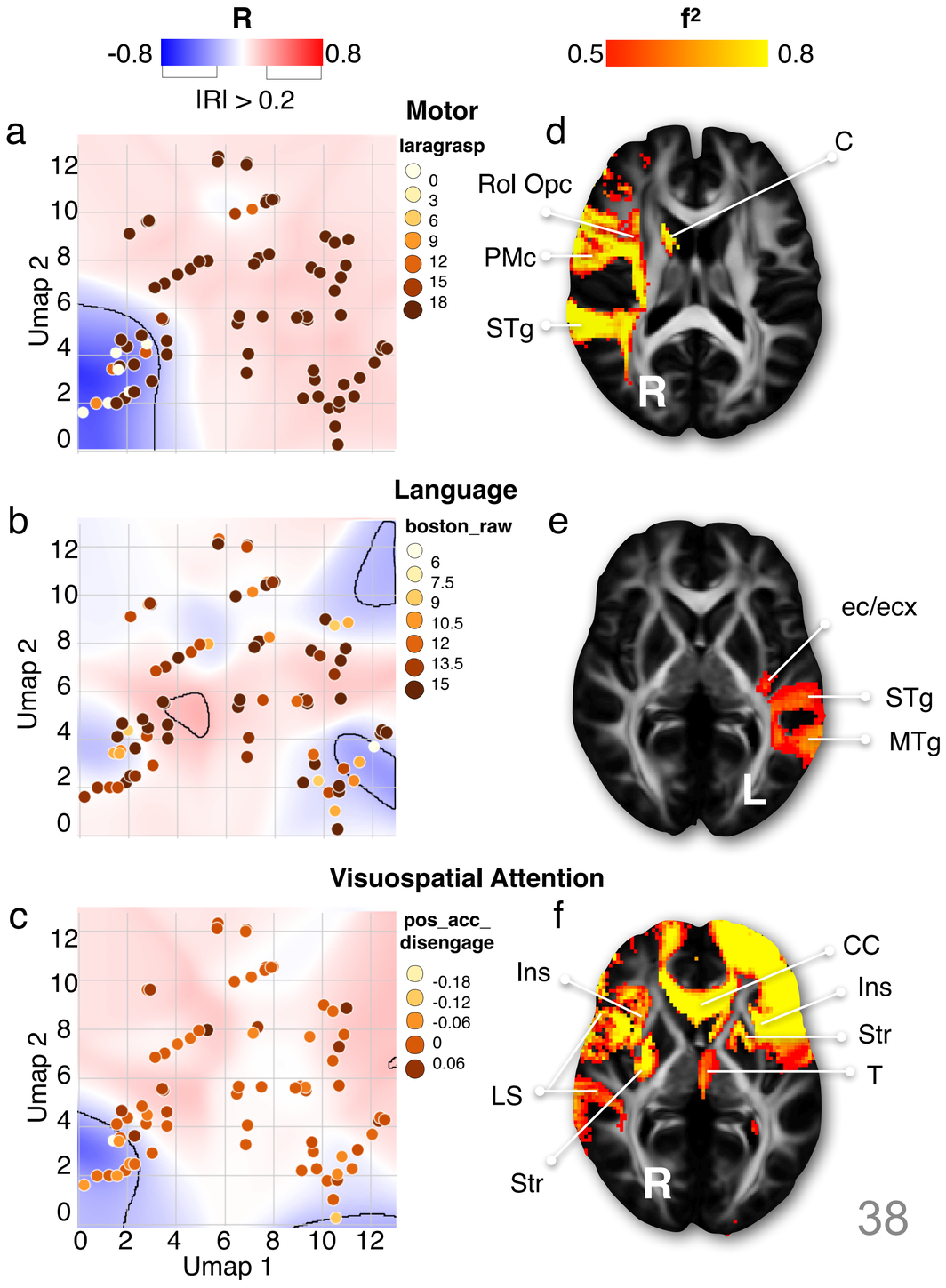
Tulner et al., Academy of Aphasia 2026

Predicting long-term cognition after stroke

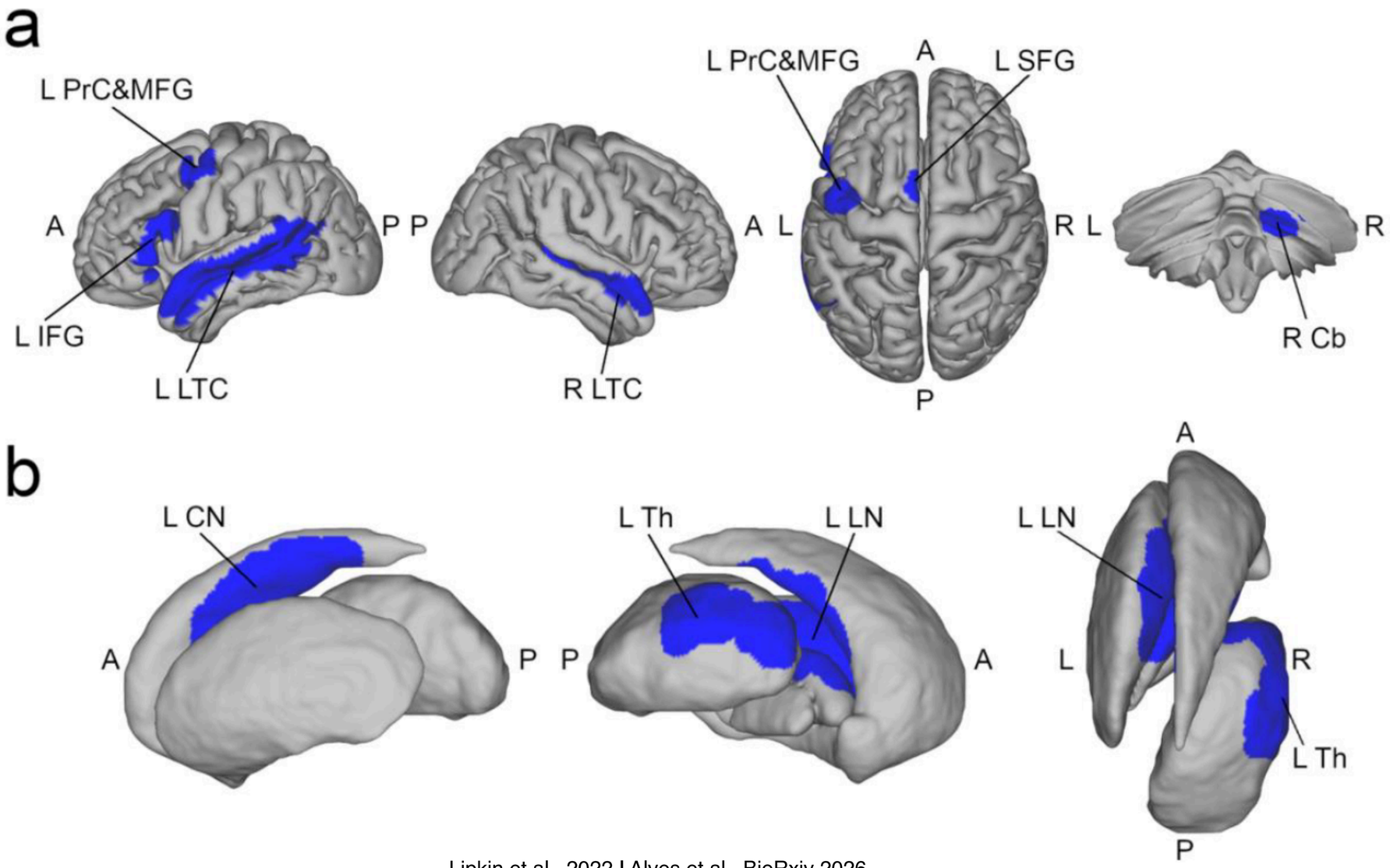


Original framework: Talozzi et al. **Brain (2023)**

Out-of-sample validation: Hope et al. **Brain (2024)**



Language engages distributed cortical and subcortical networks



Lipkin et al., 2022 I Alves et al., BioRxiv 2026

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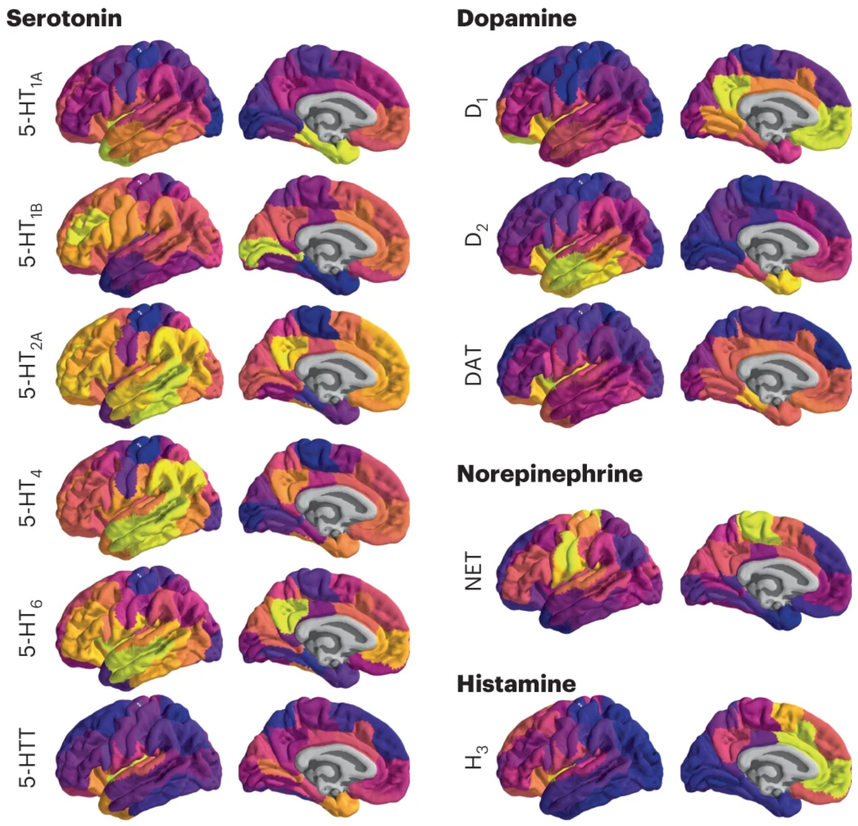
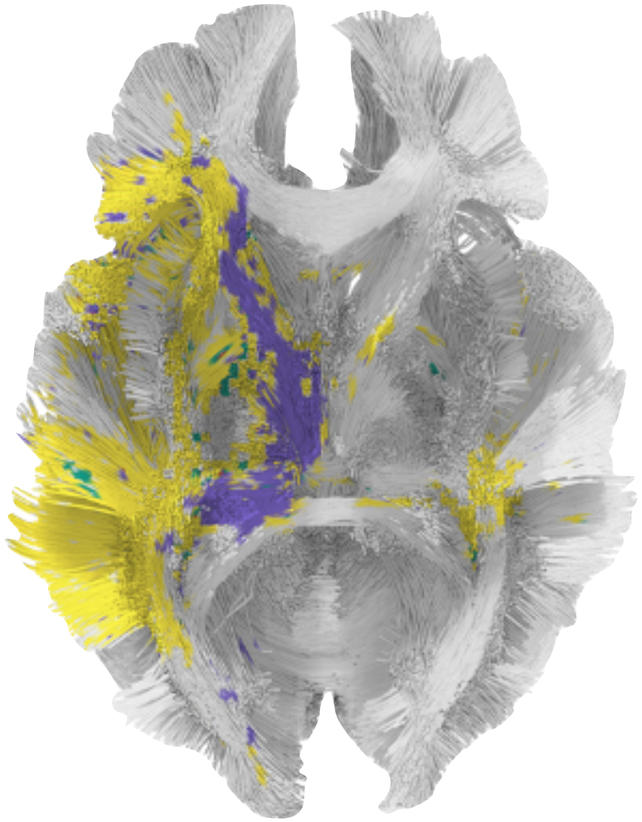
The language network has a neurochemical architecture



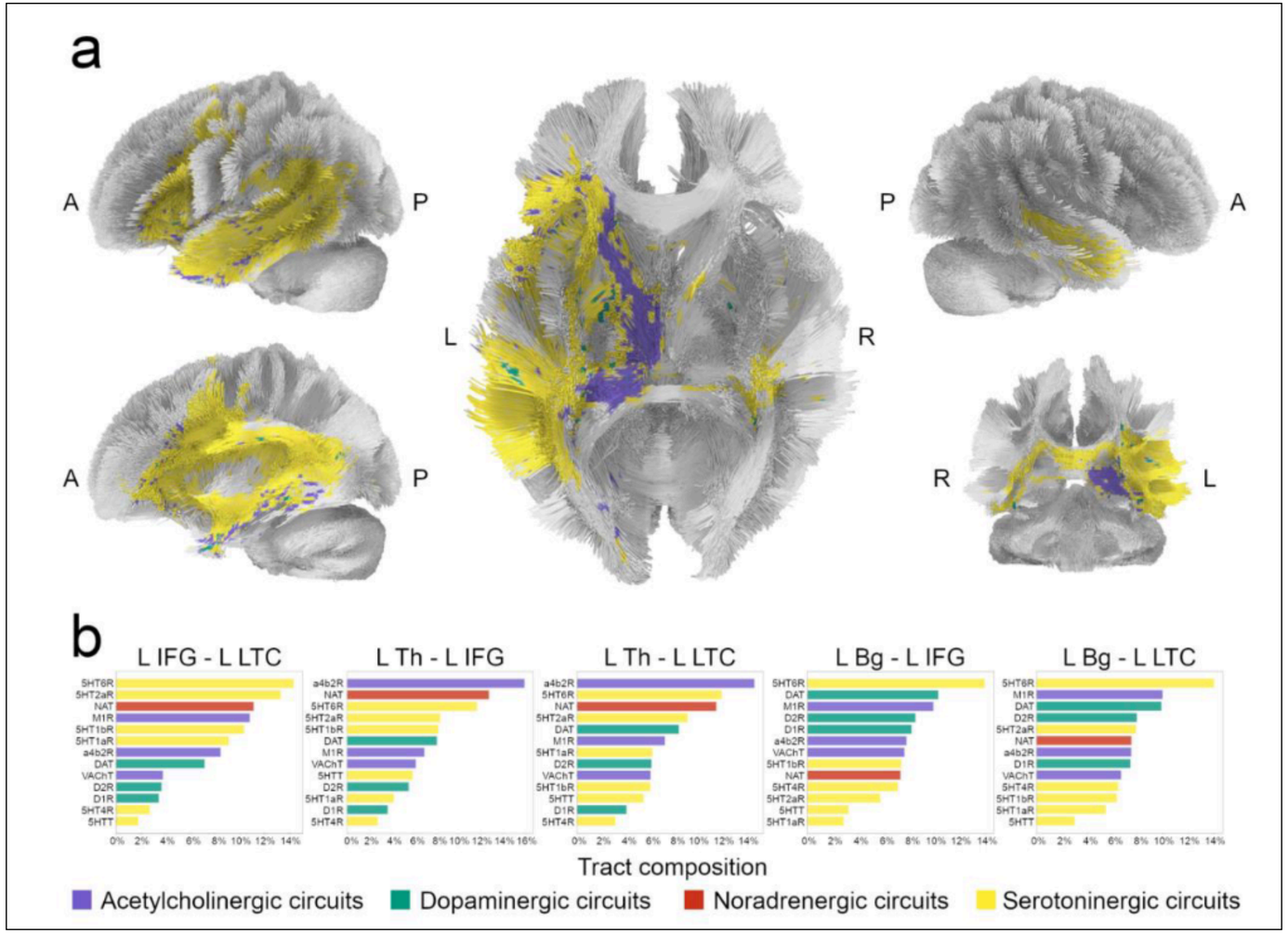
FUNCTIONNECTOME

Nozais et al., Comms Bio 2021
Nozais et al., Comms Bio 2022
Nozais et al., BSAF 2023



Alves et al., Comms Bio 2022 | Hansen et al., Nat Neuro 2022 | Alves et al., Nat Comms 2025

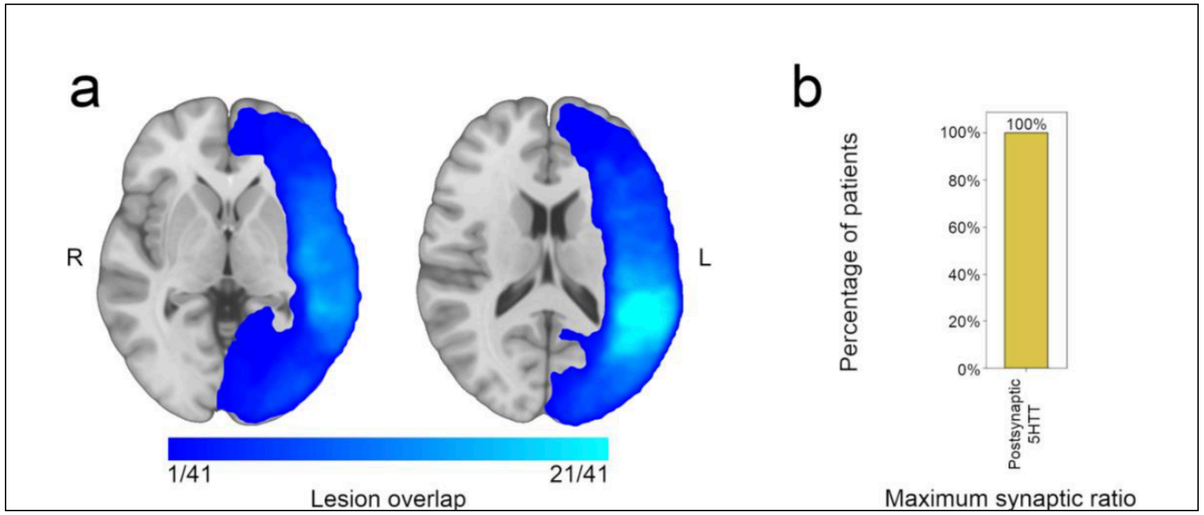
The language network has a neurochemical architecture



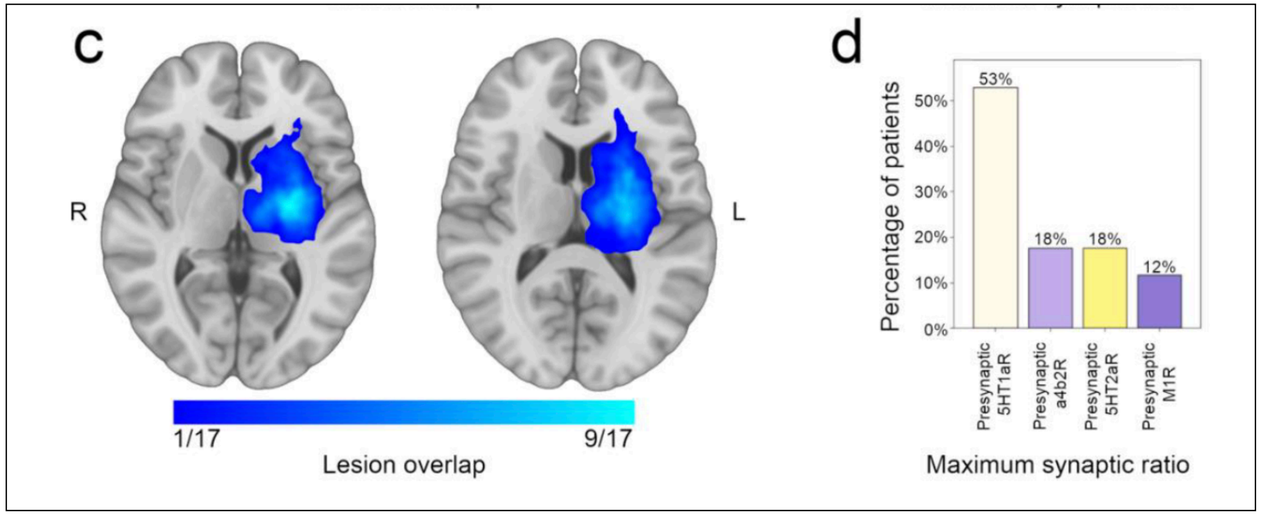
Alves et al., BioRxiv 2026

Neurochemical fingerprints of stroke

CORTICAL LESIONS



SUBCORTICAL LESIONS



Alves et al., BioRxiv 2026

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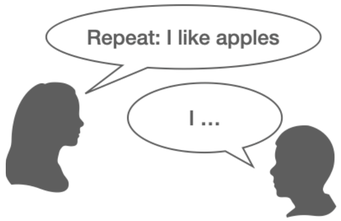
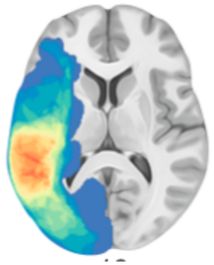
Towards personalised neuropharmacology

Patient with aphasia

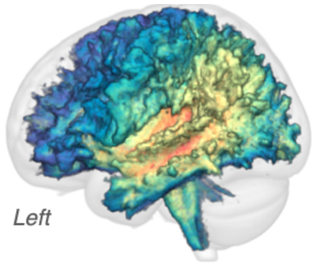


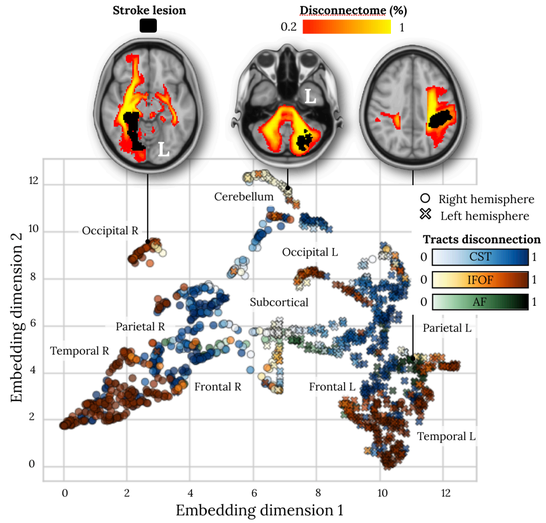
Repetition is impaired

MRI

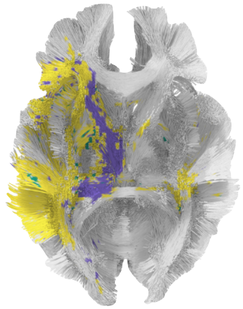


Disconnection





Recovery is not only a matter of where the lesion is, but which biological systems it disrupts.

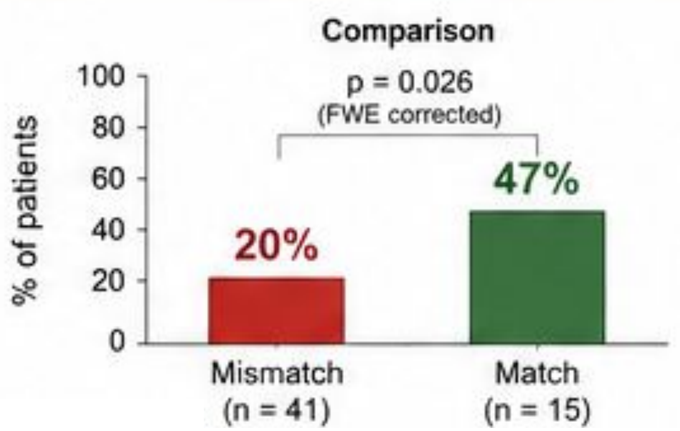


Neuro-T

SSRI

Donepezil

Neuropharmacology



Talozzi et al., 2023 I Hope et al. 2024 I Alves et al., 2025 I Alves et al., BioRxiv 2026

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Language as an emergent property

October 21, Hybrid,
Registration: https://www.stephanieforkel.com/erc-sa-october



Day 1, Wednesday 21st October (full day, CPD pending)

Venue: Seminar room 2. Emthonjeni Centre, University of the Witwatersrand, 1 Jan Smuts Avenue, Johannesburg

08:45–09:00
Arrival and coffee

09:00–09:10
Institutional Welcome — Prof Sumaya Laher, Wits Head of School of Human & Community Development

09:10–09:20
Welcome and objectives — Local Organiser, Prof Aline Ferreira Correia, Associate Professor, Department of Psychology, Wits

09:20–09:50
Speech-language assessment in South Africa: current practice and the Aclickia survey — Dr Nancy Barber, Lecturer in the Department of Speech Language Therapy at Wits

09:50–10:20
Ethical considerations for Global North and Global South collaborations — Prof Aline Ferreira Correia, Associate Professor, Department of Psychology, Wits

10:20–10:40
Understanding aphasia among isiXhosa-speaking adults: Lessons from research and clinical practice — Dr Carol Legg, Lecturer, Speech and Language Pathology, University of Cape Town

10:40–11:00
Coffee break

11:00–11:45
Mapping the directional flow of the language network — Dr Irene Bellin, Donders Institute, Netherlands

11:45–12:30
The multilingual brain: A critical review of cognitive advantages — Prof Kate Cockcroft, NeuRL (Neuroscience Research Laboratory) co-director, Wits

12:30–13:30
Lunch break

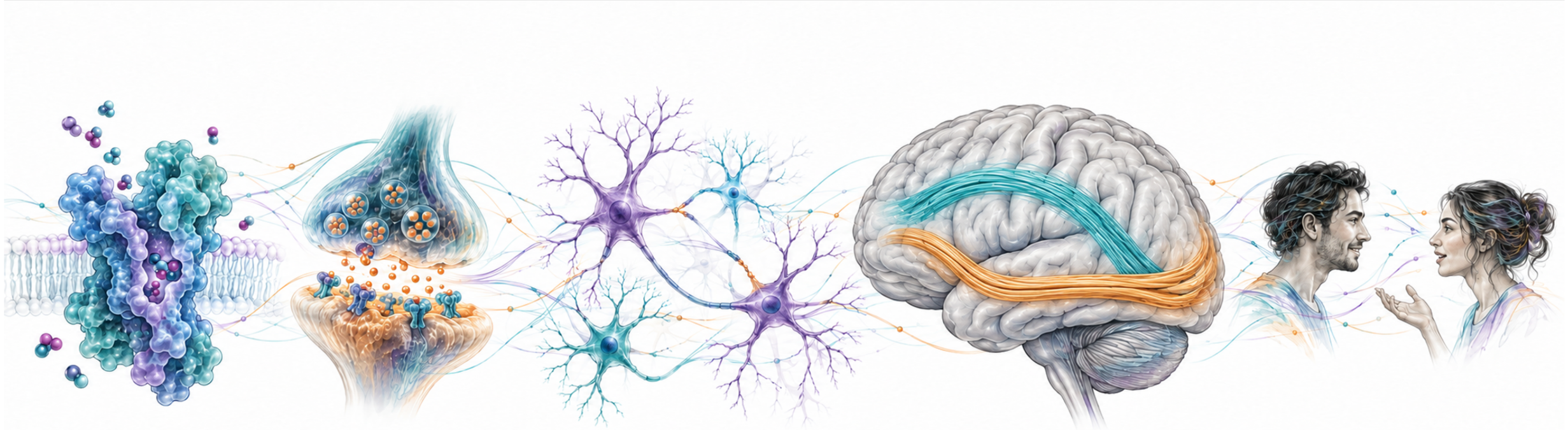
13:30–14:30
Towards a new neurobiology of language — Prof Stephanie Forkel, Donders Institute / Max Planck Institute, the Netherlands

14:30–16:20
Panel: Research opportunities in neurosciences

- Opportunities through the ERC Implementing Arrangement — European Research Council (ERC) Executive Agency representative

erc Consolidator Grant

Interactions across scales support language

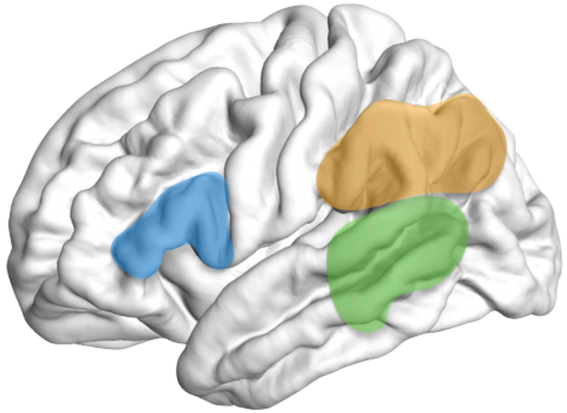


Molecules	Synapses	Neural circuits	Brain networks	Communication
Receptors and transmitters	Signalling and plasticity	Excitability and coordination	Connectivity and dynamics	Meaning in context

Language emerges from a multiscale, distributed, and individually variable biological system

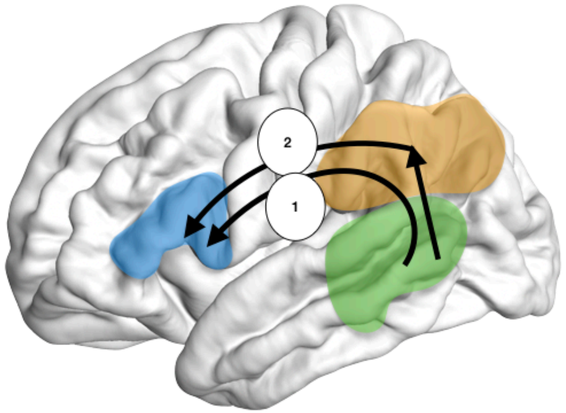
erc Consolidator Grant

Language as an emergent property



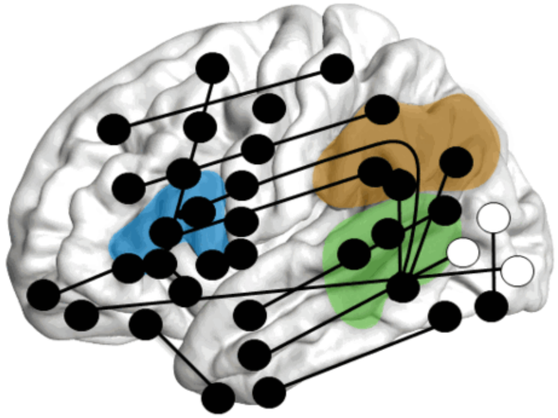
Modular model

- “Broca’s area’
- ‘Geschwind’s area’
- ‘Wernicke’s area’



Hierarchical model

1. Direct processing route
2. Indirect processing route



Integrative model

- Inactive
- Active



Thiebaut de Schotten & Forkel, 2022

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Conclusion

- Language depends on interactions across distributed networks, with regional specialisation embedded within this organisation.
- A focal lesion can disrupt an extended network, affecting communication beyond the damaged tissue.
- Individual network organisation helps explain variability in impairment and the capacity for recovery.
- Aphasia syndromes do not map neatly onto biological profiles: understanding each patient requires behaviour, lesion anatomy, and connectivity.



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