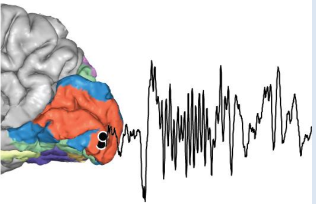
Neurohackademy
August 1, 2024

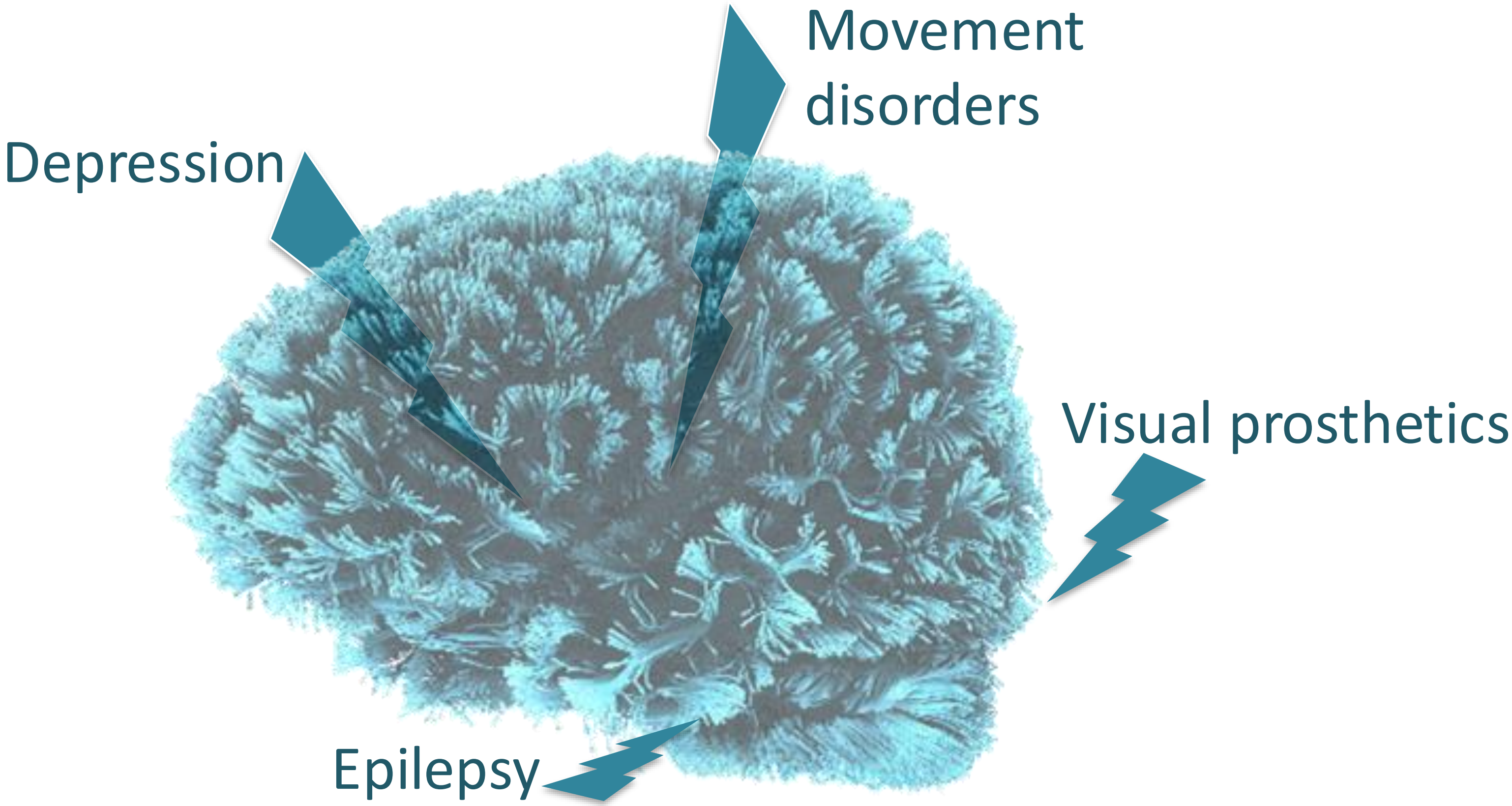
Working with multimodal data in the Brain Imaging Data Structure



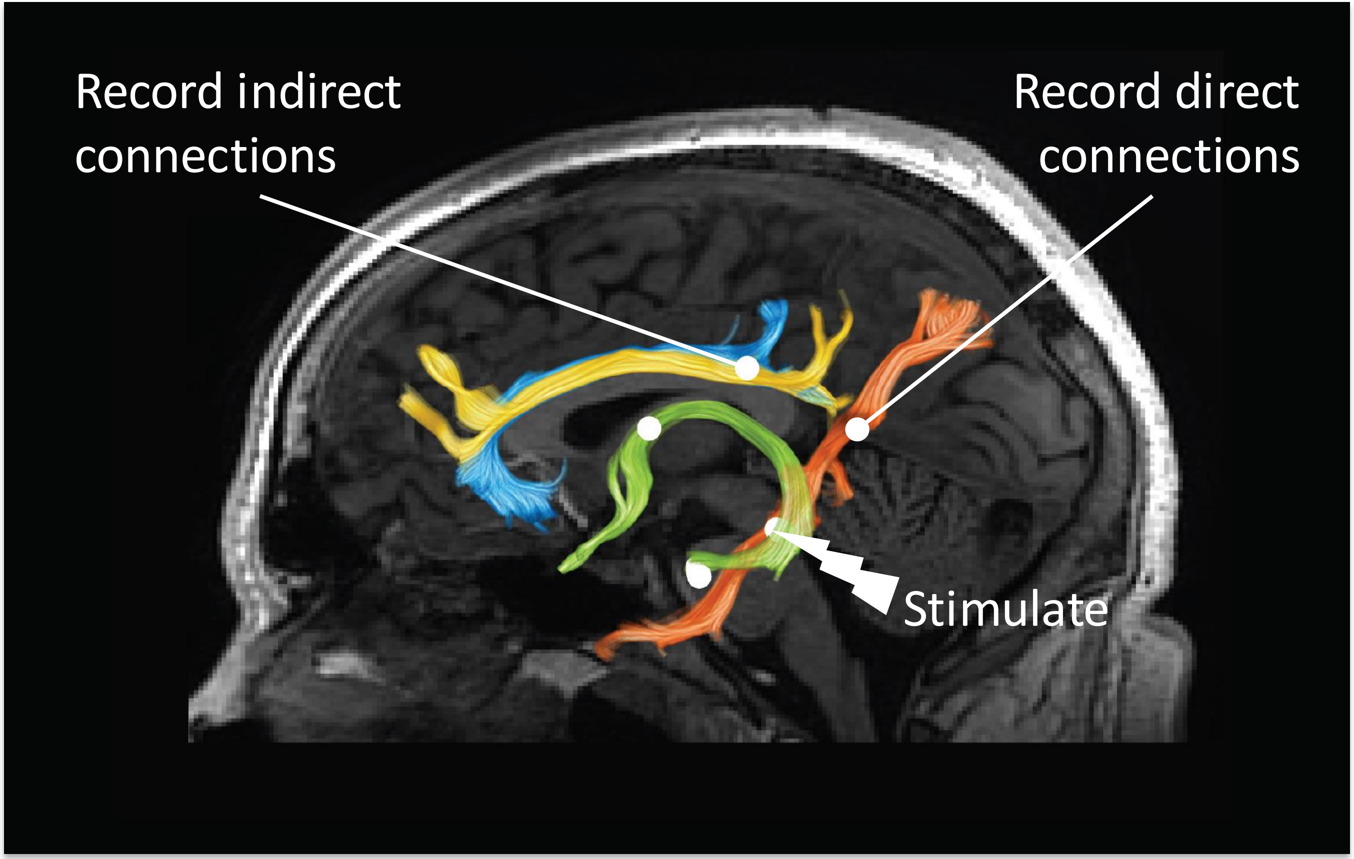
Dora Hermes

Department of Physiology and Biomedical Engineering, Mayo Clinic, Rochester, MN

Brain stimulation therapies are rapidly advancing



How does stimulation of a single site propagate through human brain networks?



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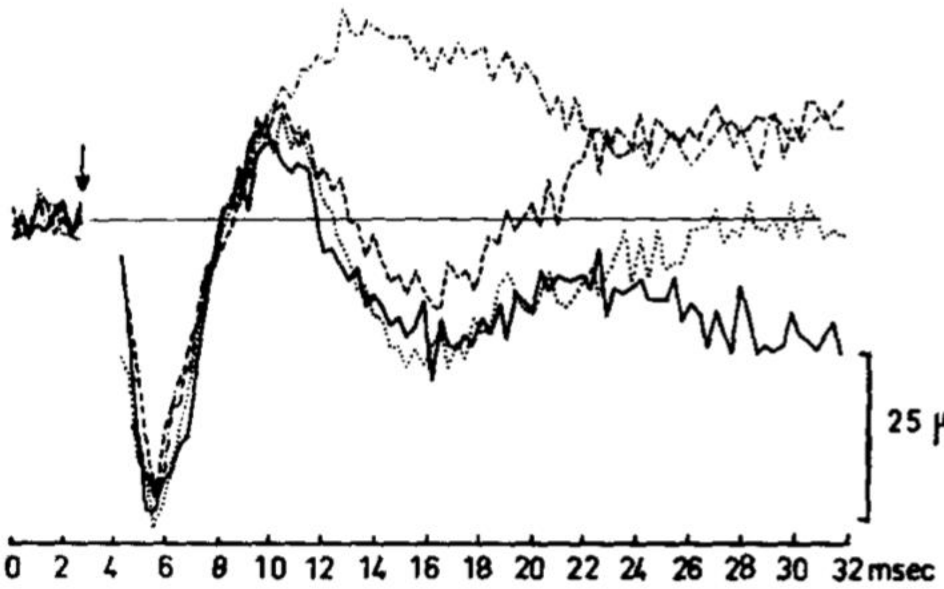
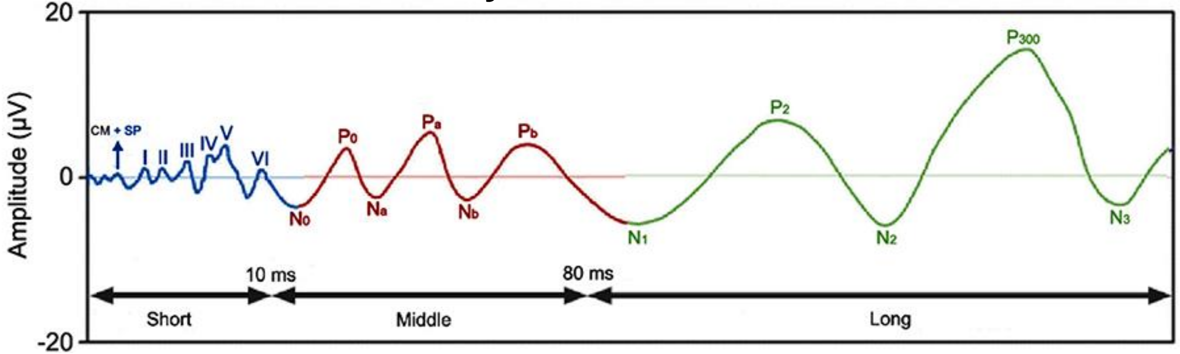


Creutzfeldt, Watanabe and Lux 1966, Electroencephalogr Clin Neurophysiol

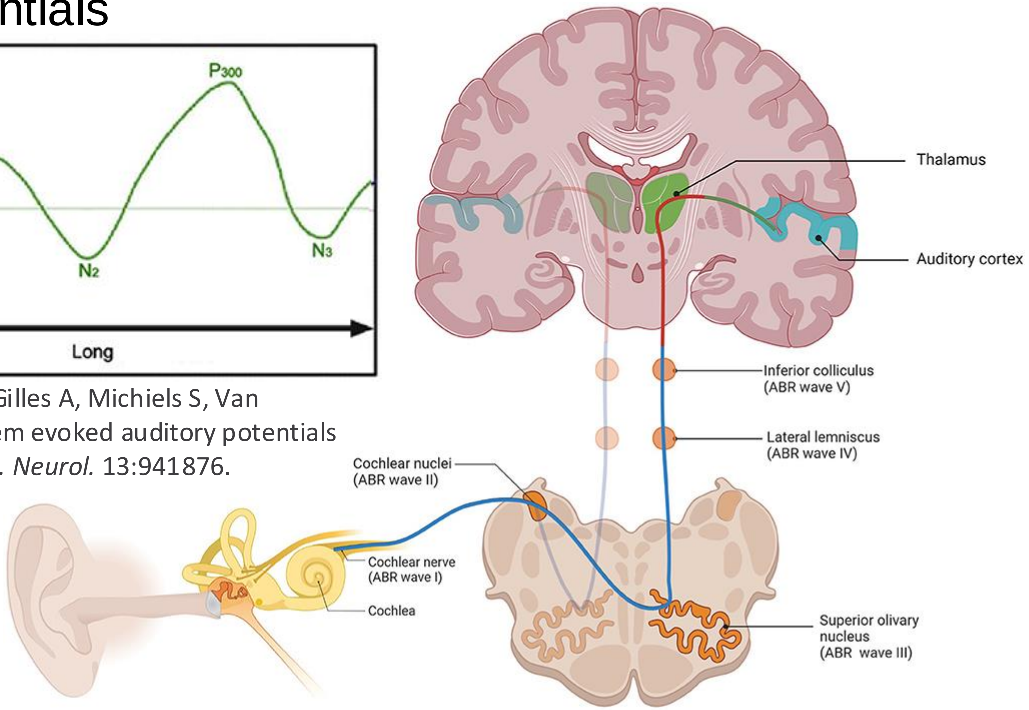
Stimulating thalamus, measuring cat cortex

How does stimulation of a single site propagate through human brain networks?

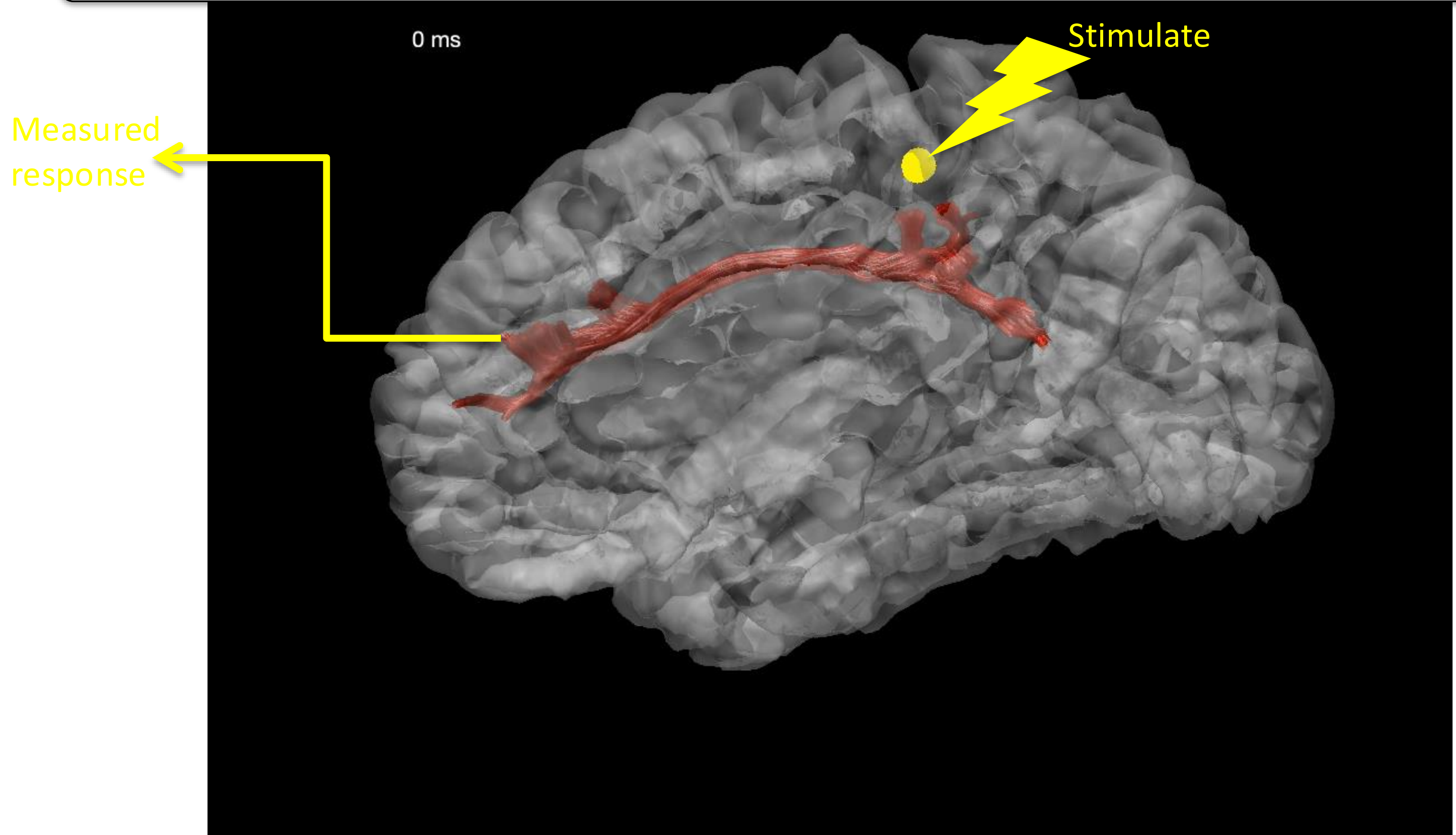
Brainstem Auditory Evoked Potentials



Jacxsens L, De Pauw J, Cardon E, van der Wal A, Jacquemin L, Gilles A, Michiels S, Van Rompaey V, Lammers MJW and De Hertogh W (2022) Brainstem evoked auditory potentials in tinnitus: A best-evidence synthesis and meta-analysis. *Front. Neurol.* 13:941876.



Single pulse electrical stimulation to measure cortico-cortical evoked potentials (CCEPs)



Outline:
Multimodal integration and the Brain Imaging Data Structure

1. Integrating iEEG single pulse stimulation with dMRI atlases to quantify the speed of neural signal propagation across development

V Blooijs*, VD Boom*, VD Aar, Huiskamp, Castegnaro, Demuru, Zweiphenning, Van Eijsden, Miller, Leijten, Hermes, *Nature Neuroscience* 2023

2. Integration iEEG single pulse stimulation with dMRI to understand direct and indirect connectivity in the human limbic system

Miller, Müller, Valencia, Huang, Gregg, Worrell, Hermes. Canonical Response Parameterization: Quantifying the structure of responses to single-pulse intracranial electrical brain stimulation. *PLOS Computational Biology* 2022

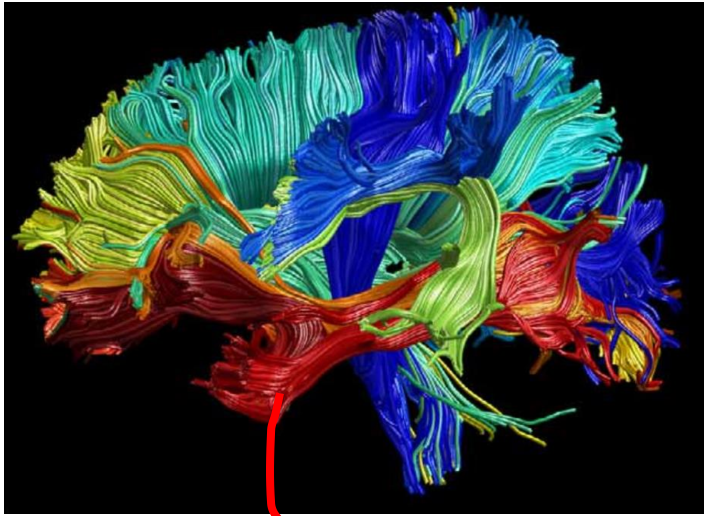
Ojeda Valencia, Gregg, Huang, Lundstrom, Brinkmann, Pal Attia, Van Gompel, Bernstein, In, Huston, Worrell, Miller, Hermes, *JNeurosci* 2023

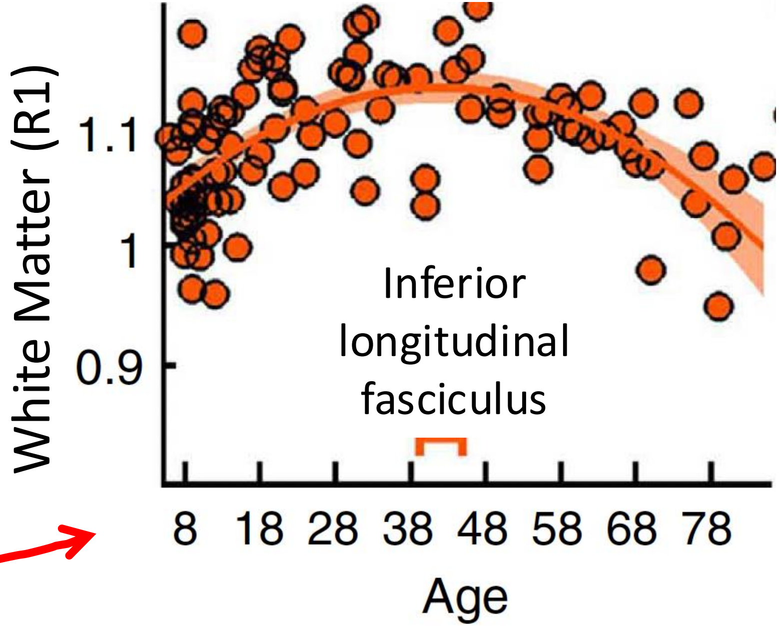
3. DEMO: iEEG data in BIDS for network mapping

What is a typical speed of neural signal propagation?

Structural connections develop up to age 30-40

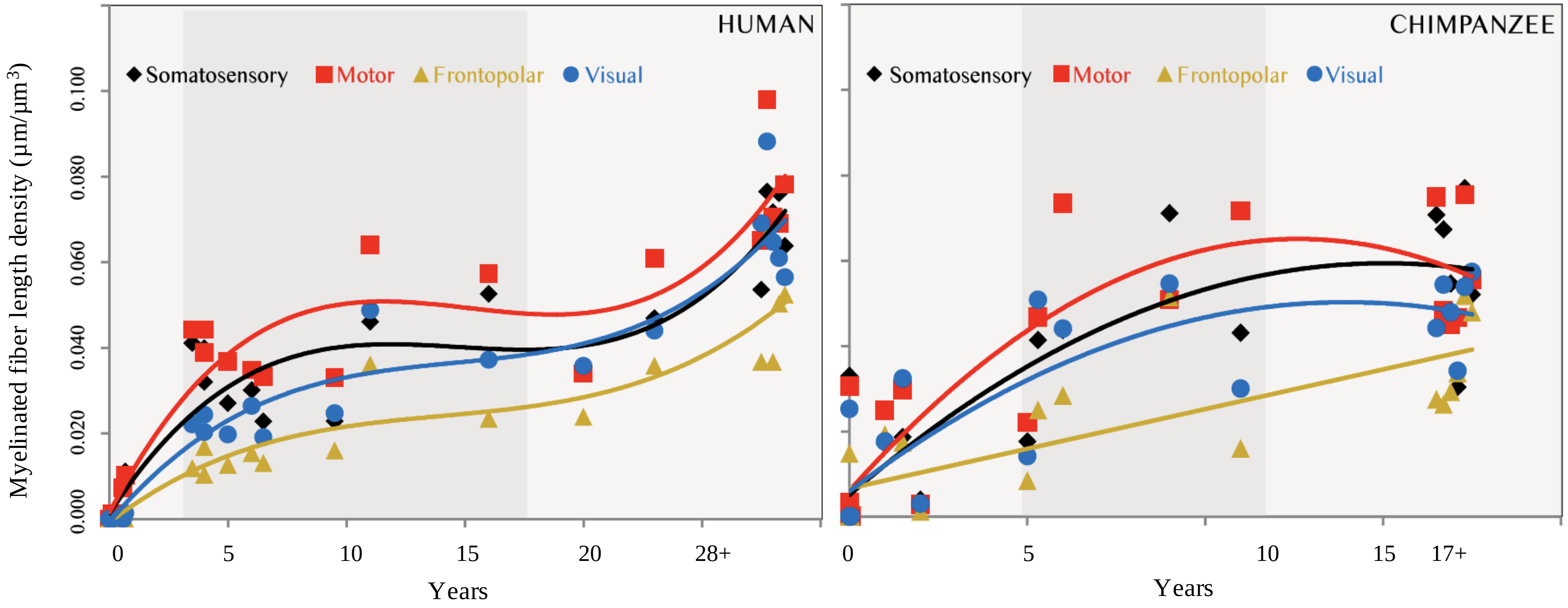
Yeatman, Wandell, Mezer, 2014 Nature Communications



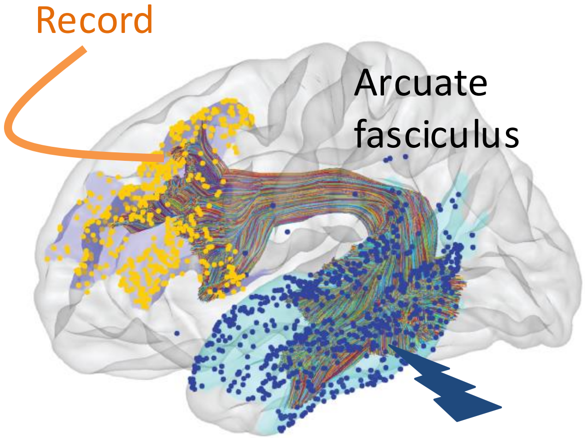


What is a typical speed of neural signal propagation?

Human brains have prolonged myelination compared to other primates *(Miller ea 2012 PNAS).*



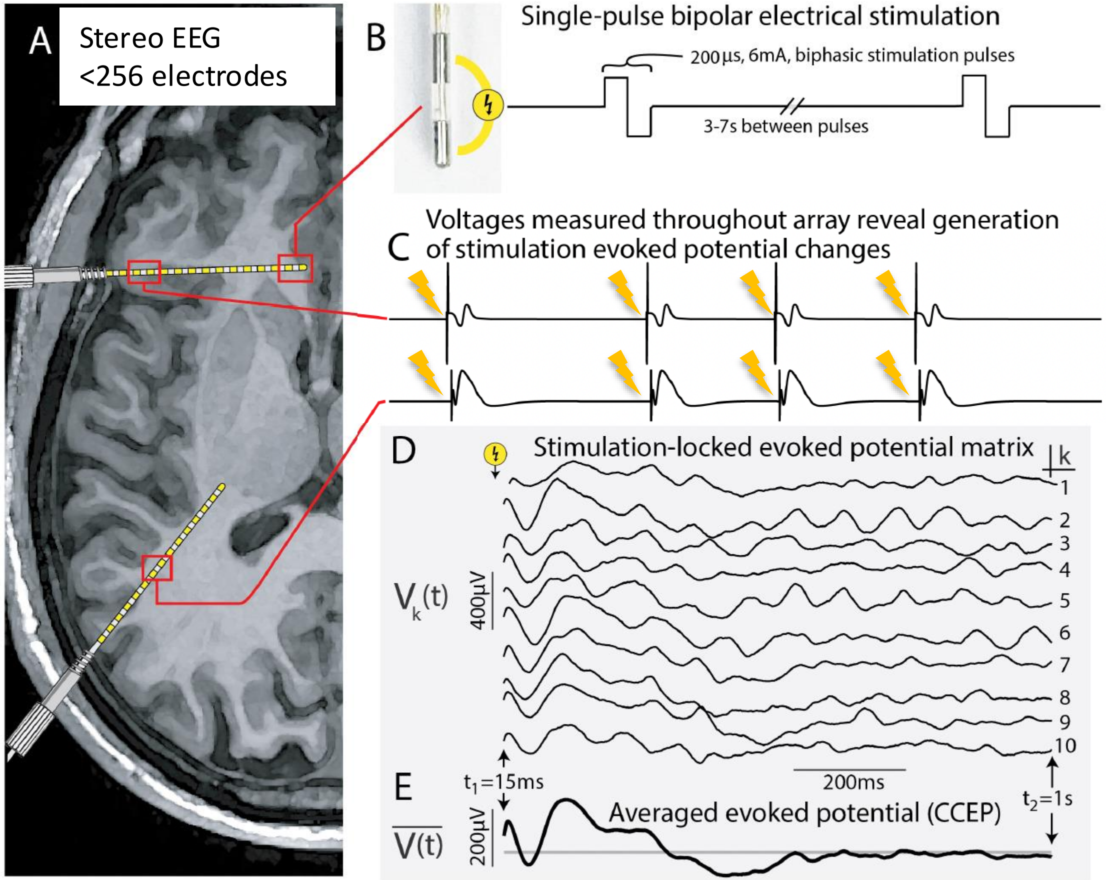
What is a typical transmission speed along the arcuate fasciculus?



1.  ~2 m/s
2.  ~5 m/s
3.  ~25 m/s
4.  ~100 m/s

Created with BioRender.com

Single pulse electrical stimulation to measure cortico-cortical evoked potentials (CCEPs)



Brief electrical pulses at different electrode pairs

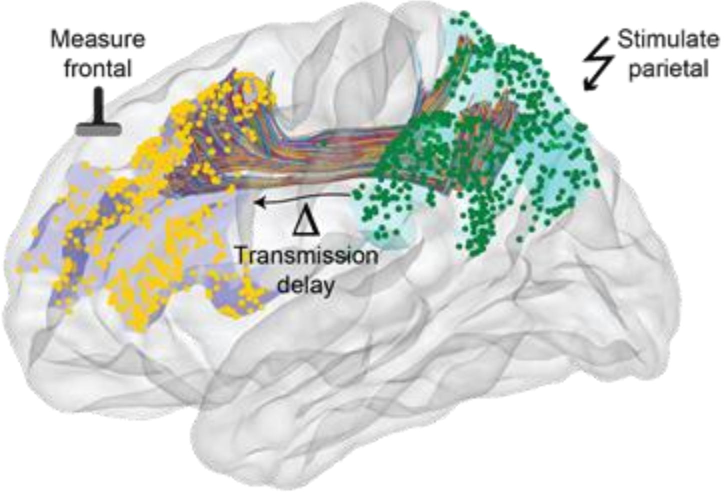
Connected areas show stimulation evoked potentials

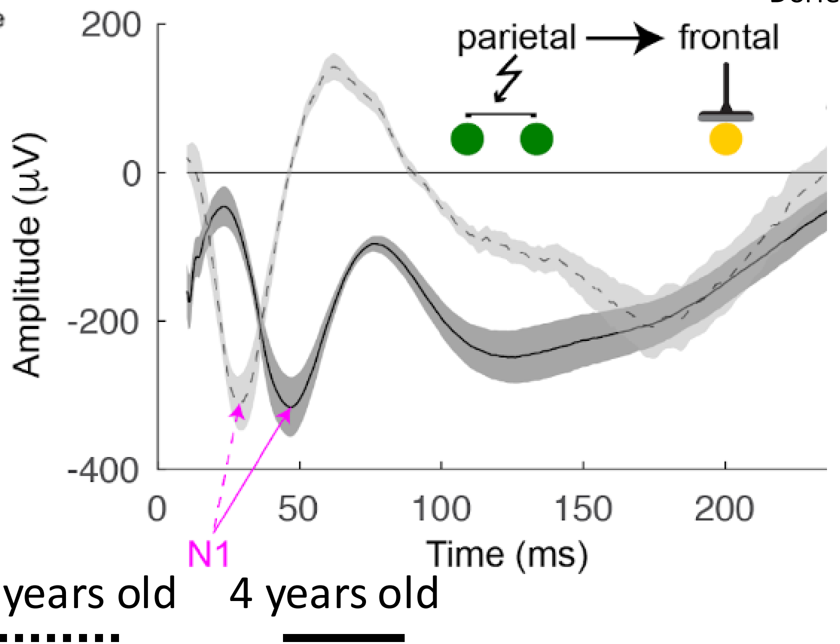
Average pulses in one site by one stimulation pair

Miller, Mueller, Ojeda Valencia, Huang, Gregg, Worrell, Hermes, 2023, *PLOS Computational Biology*

Stimulation driven responses in the human brain: Conduction delays

- ECoG electrodes in 74 patients





Dorien v Blooijs

Max vd Boom

Frans Leijten
(UMC Utrecht)

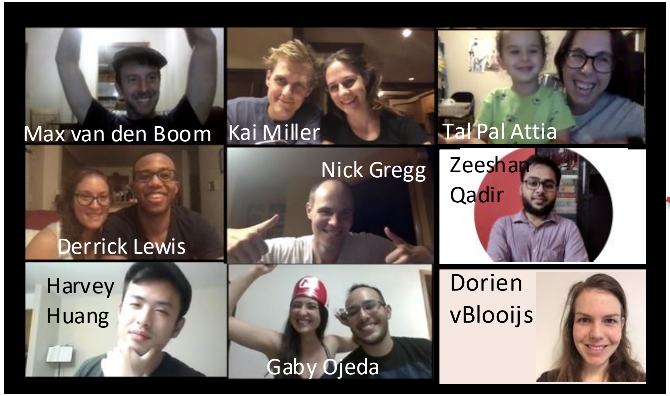
Single pulse stimulation with 10 monophasic, 1ms pulses of 4-8mA, alternating polarity

D v Blooijs*, MA vd Boom*, JF vd Aar, GJM Huiskamp, G Castegnaro, M Demuru, WJEM Zweiphenning, P van Eijsden, K. J. Miller, F.S.S. Leijten, D. Hermes (2023) *Nature Neuroscience*,
* These authors contributed equally

Intracranial EEG (iEEG): how to scale?

One center: ~10-20 patients a year
Neurologist present during stimulation

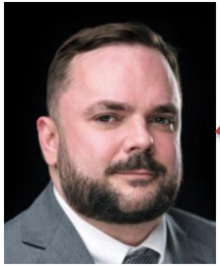
Multimodal Neuroimaging Lab (Mayo Clinic)



Frans Leijten (UMC Utrecht)

Clinical Collaborators, BNEL lab

Greg Worrell Nick Gregg Brian Lundstrom



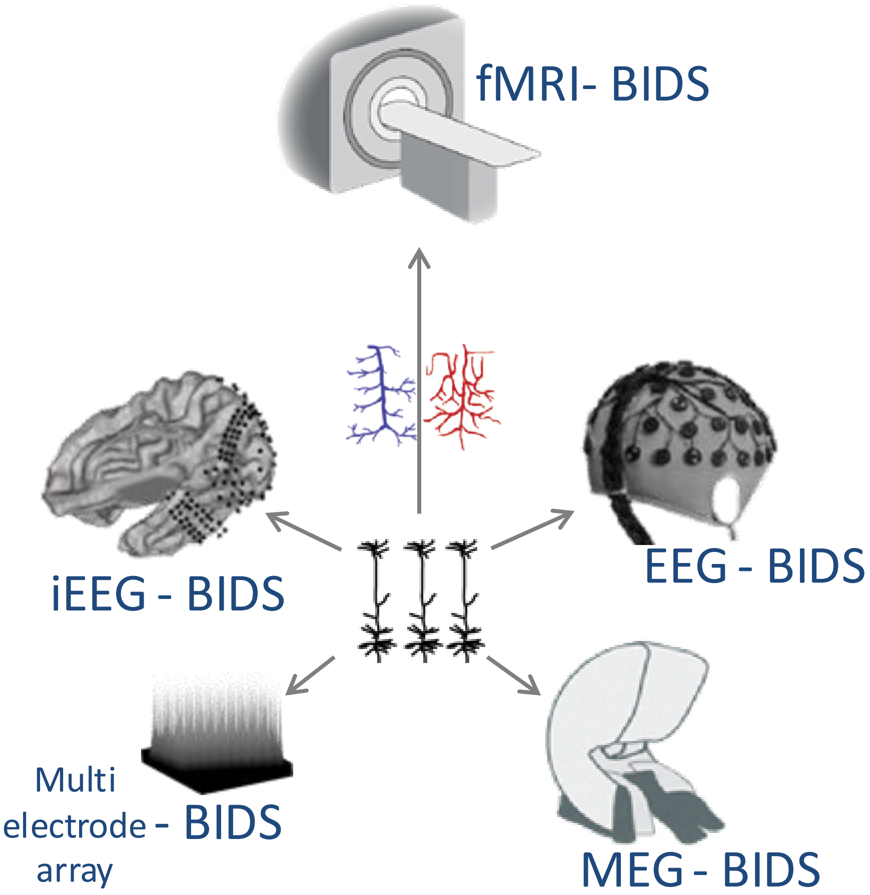
Peter Brunner (WashU)

Intracranial EEG (iEEG): how to scale?

Multiple centers (Mayo, UMC Utrecht, WashU)
Centers who have done this for a long time (Leijten, UMC Utrecht)
Harmonize data collection (BCI2000, Brunner, WashU)
Neurologists to ensure safety of electrical stimulation

Harmonizing iEEG data curation within and across centers

Harmonizing human neuroimaging data, practically



BIDS
BRAIN IMAGING DATA STRUCTURE

Shared data structure for neuroimaging data.
Machine and human readable.
Community effort.

iEEG- ... Data

Christophe ... lhoff[2], S ... fer Bouchard[4], Sasha D'Ambros ... evinsky[7] ... deen Flinker[7], Brett L. Foster ..., Iris G ... , Aysegul Gunduz[12], Liberty H ... ney[14], M ... ight[16], Jean-Philippe Lachaux[17] ... opher L ... Lundstrom[19], Kai J. Miller[20], J ... t Ooste ... ou[23], Gio Piantoni[24], Andrea Pi ... , Nick F. ... , Nicole C. Swann[29], François Tadel[6,28], Bradley Voytek[29], Brian A. Wandell[8], Jonathan Winawer[10], Kirstie Whitaker[30], Lyuba Zehl[31], Dora Hermes[17,32,*]

Chris Gorgolewski

Chris Holdgraf

Human and machine-readable data in iEEG-BIDS

```
a
iEEGBIDSdataset/
├── sub-01
│   ├── anat
│   │   ├── sub-01_T1w.nii.gz
│   │   └── sub-01_T1w.json
│   └── ieeg
│     b ├── sub-01_task-visual_run-01_ieeg.eeg
│       ├── sub-01_task-visual_run-01_ieeg.vmrk
│       ├── sub-01_task-visual_run-01_ieeg.vhdr
│       ├── sub-01_task-visual_run-01_ieeg.json
│       │
│       │     {
│       │       "TaskName": "visual",
│       │       "Manufacturer": "Tucker Davis ...",
│       │       "TaskDescription": "visual ...",
│       │       "SamplingFrequency": 1000,
│       │          ...
│       │     }
│     c ├── sub-01_task-visual_run-01_channels.tsv
│       │
│       │     name  type   units  low_cutoff  high_cutoff  notch
│       │     O01   ECOG   mV     300         0.1          n/a
│       │     O02   ECOG   mV     300         0.1          n/a
│       │     ...
│     d ├── sub-01_task-visual_run-01_events.tsv
│       │
│       │     onset     duration  trial_type  stim_file
│       │     17.8533   0.5       5           stimuli/...
│       │     18.35564  0.5       8           stimuli/...
│       │     18.85764  0.5       2           stimuli/...
│       │     ...
│     e ├── sub-01_electrodes.tsv
│       │
│       │     name  x   y    z    size
│       │     O01   19  -39  -16  4
│       │     O02   23  -40  -19  4
│       │     ...
│       ├── sub-01_coordsystem.json
│       │     {
│       │      "iEEGCoordinateSystem": "ACPC",
│       │      "iEEGCoordinateUnits": "mm",
│       │      "IntendedFor": "..._T1w.nii.gz",
│       │      ...
│       │     }
│     f └── sub-01_photo.jpg
│
├── sub-02
│
├── stimuli
│   └── stim01.png
├── participants.tsv
├── dataset_description.json
└── README
```

bids-validator 🎉

iEEG timeseries data

Events: e.g. visual, electrical stimulation

Electrode positions and MRI

More info:
https://bids.neuroimaging.io/

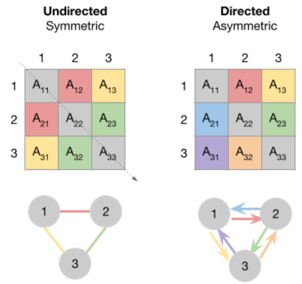
A standard that applies across modalities

BIDS: https://bids.neuroimaging.io/
bids-starter-kit: https://bids-standard.github.io/bids-starter-kit/
BIDS validator: https://bids-standard.github.io/bids-validator/

Feel free to post an issue or contribute

https://bids.neuroimaging.io/get_involved.html#extending-the-bids-specification

Examples of what we are working on:



- BEP017: Generic BIDS connectivity data schema
- BEP21: Electrophysiology derivatives and annotations
  - Artifacts: HED-SCORE https://github.com/bids-standard/bids-examples/pull/324
  - Stimuli: https://github.com/bids-standard/bids-specification/issues/153

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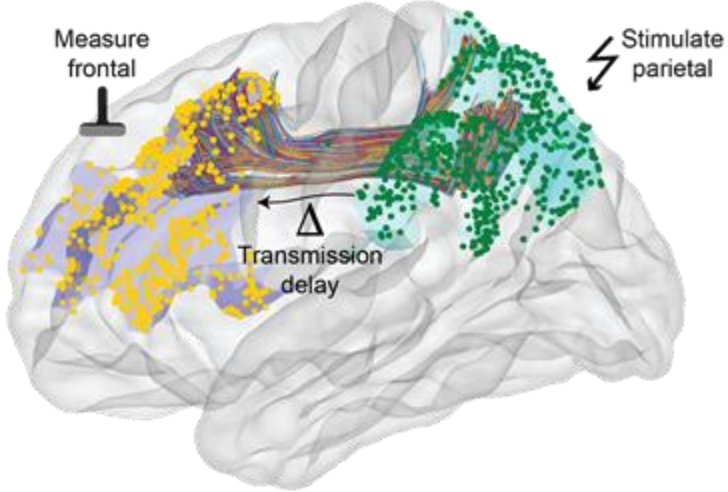
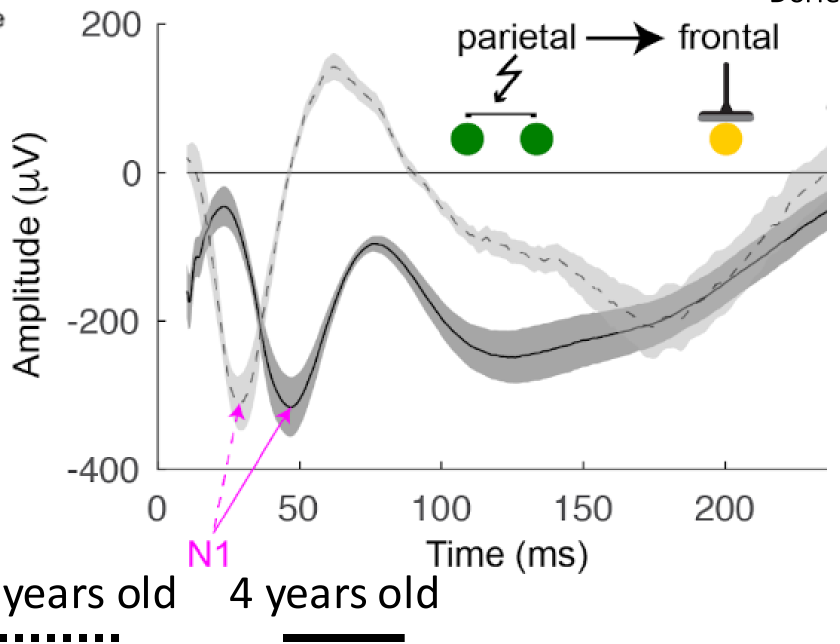
BIDS

BRAIN IMAGING DATA STRUCTURE

Stimulation driven responses in the human brain: Conduction delays

- ECoG electrodes in 74 patients





Single pulse stimulation with 10 monophasic, 1ms pulses of 4-8mA, alternating polarity

D v Blooijs*, MA vd Boom*, JF vd Aar, GJM Huiskamp, G Castegnaro, M Demuru, WJEM Zweiphenning, P van Eijsden, K. J. Miller, F.S.S. Leijten, D. Hermes (2023) *Nature Neuroscience*,
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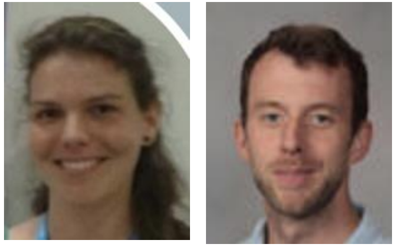

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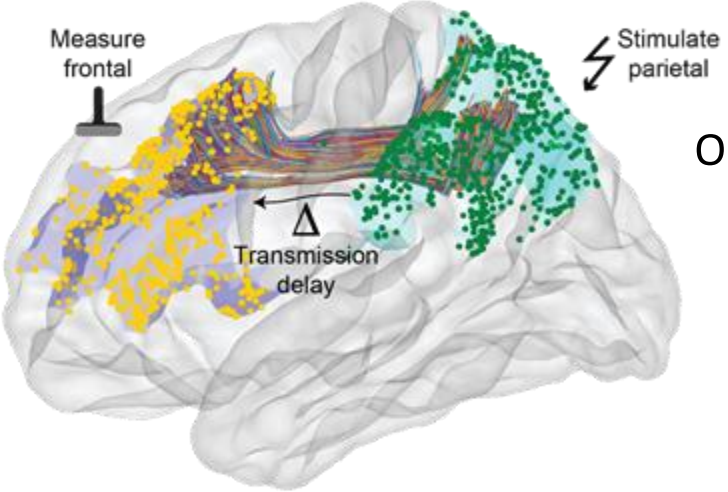

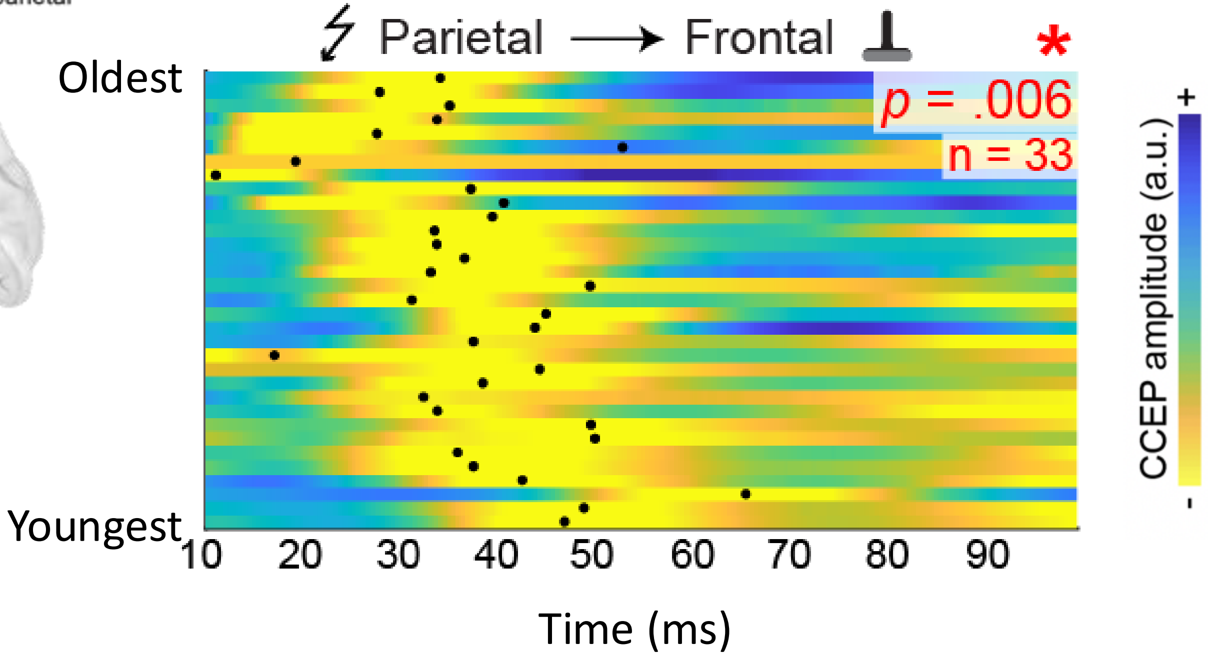

D v Blooijs*, MA vd Boom*, JF vd Aar, GJM Huiskamp, G Castegnaro, M Demuru, WJEM Zweiphenning, P van Eijsden, K. J. Miller, F.S.S. Leijten, D. Hermes (2023) *Nature Neuroscience*,
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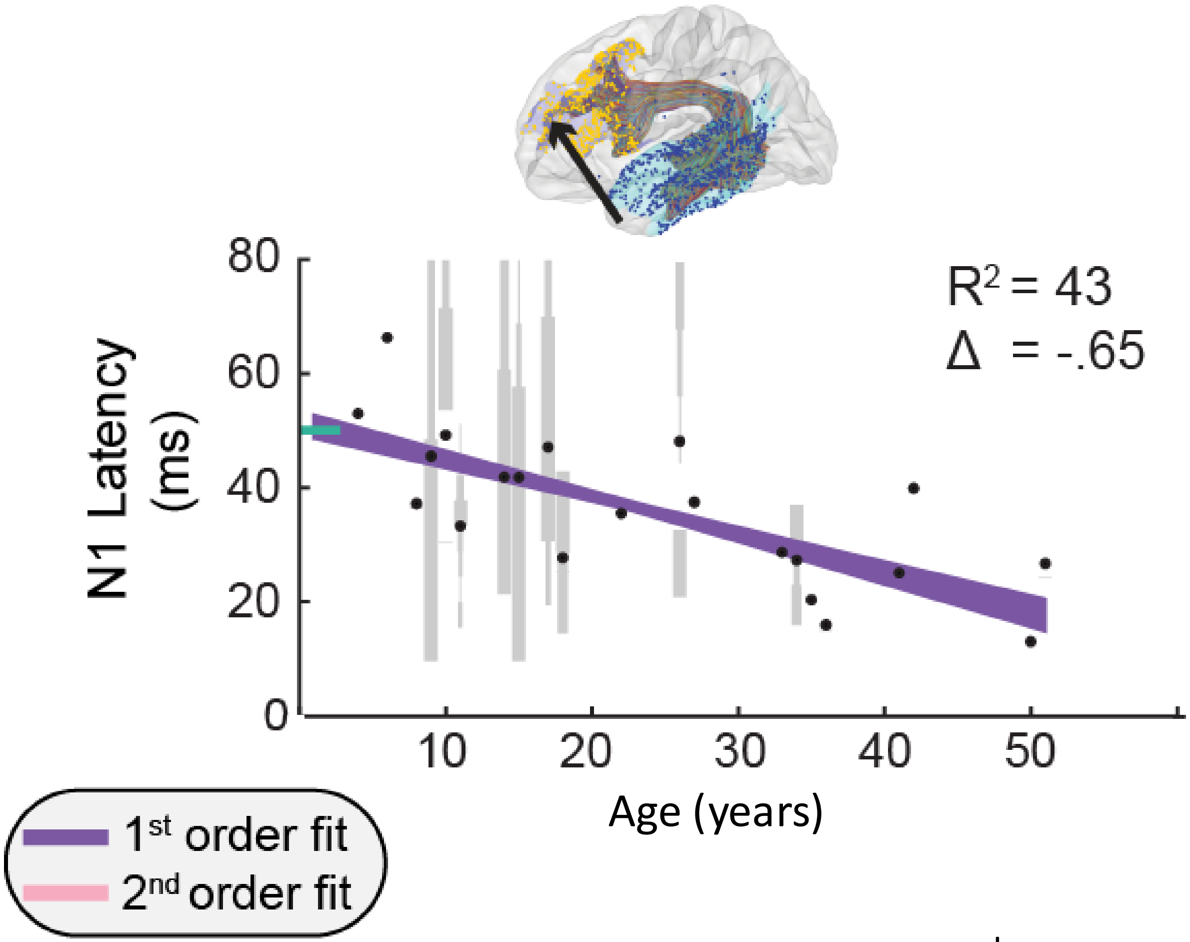
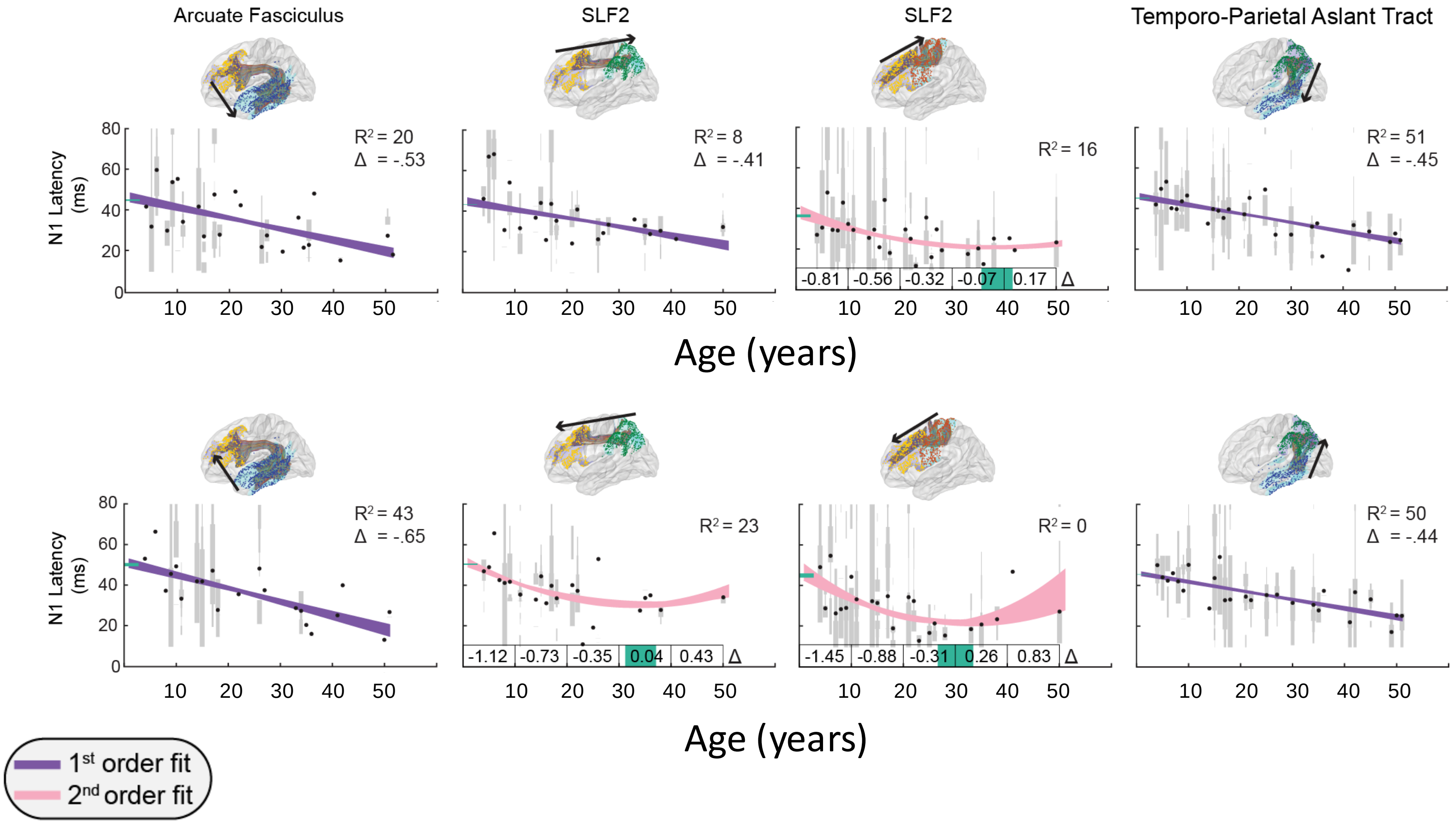
Conduction delays decrease with development



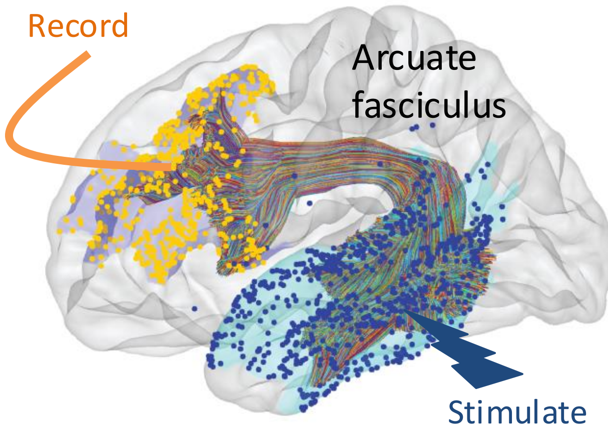
Robust regression

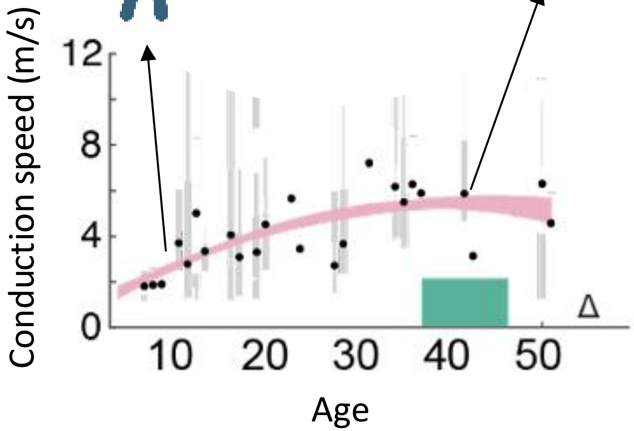
Leave one out cross-validation for R^2

Conduction delays decrease with development



What are neurotypical transmission speeds along the arcuate fasciculus?





Estimated fiber length in each subject:

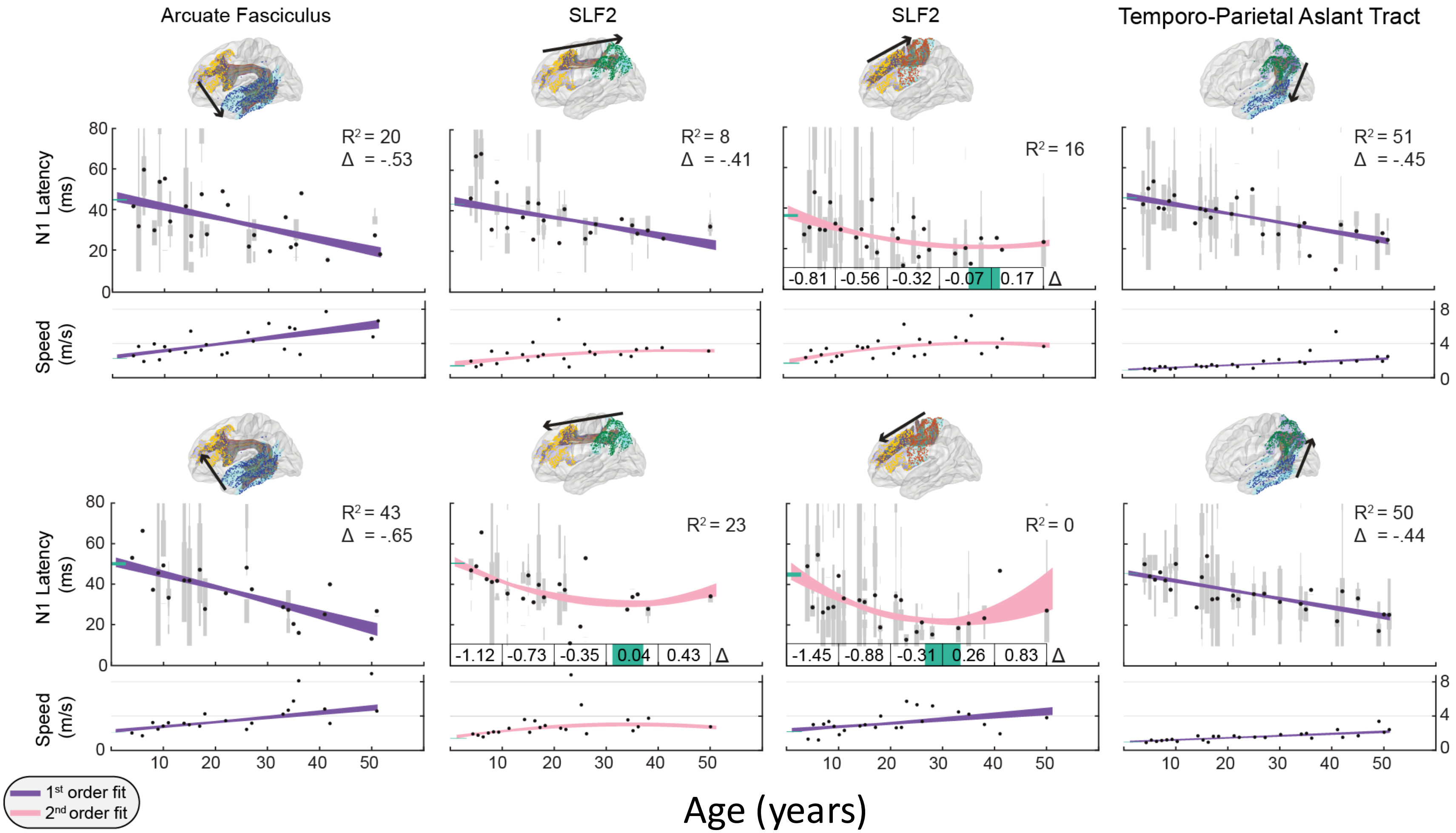
- Yeh atlas → subject space

  https://brain.labsolver.org/hcp_trk_atlas.html

- Calculate conduction speeds

Images with help of Biorender
Line drawings with help of Chat GPT

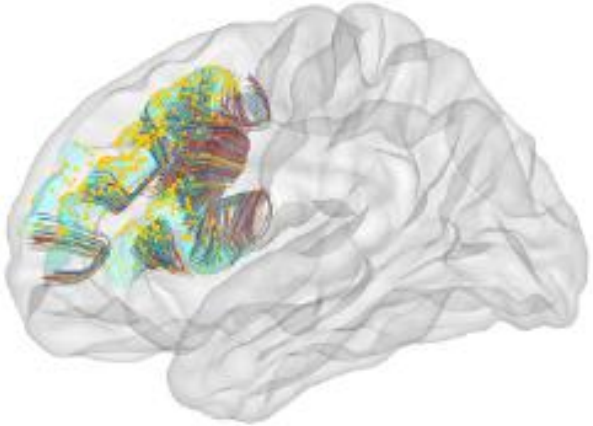
Conduction speed increases with development in association fibers



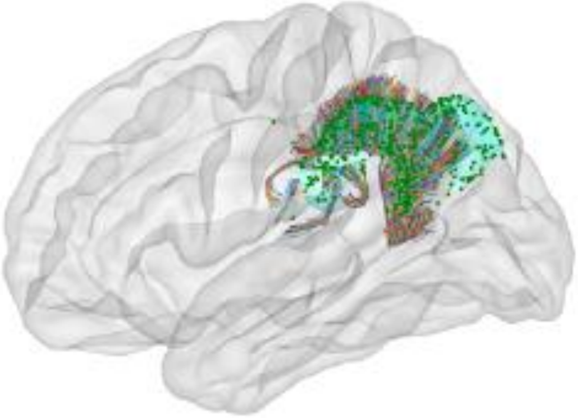
Do short range connections develop in the same manner?

The cranium only has limited space, axon diameters vary from <1μm to 10+ μm

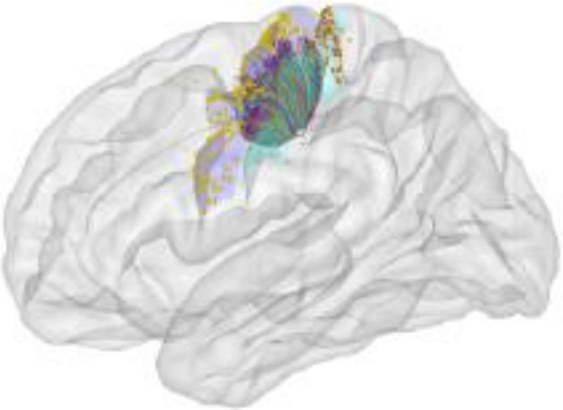
Frontal U-fibers



Parietal U-fibers

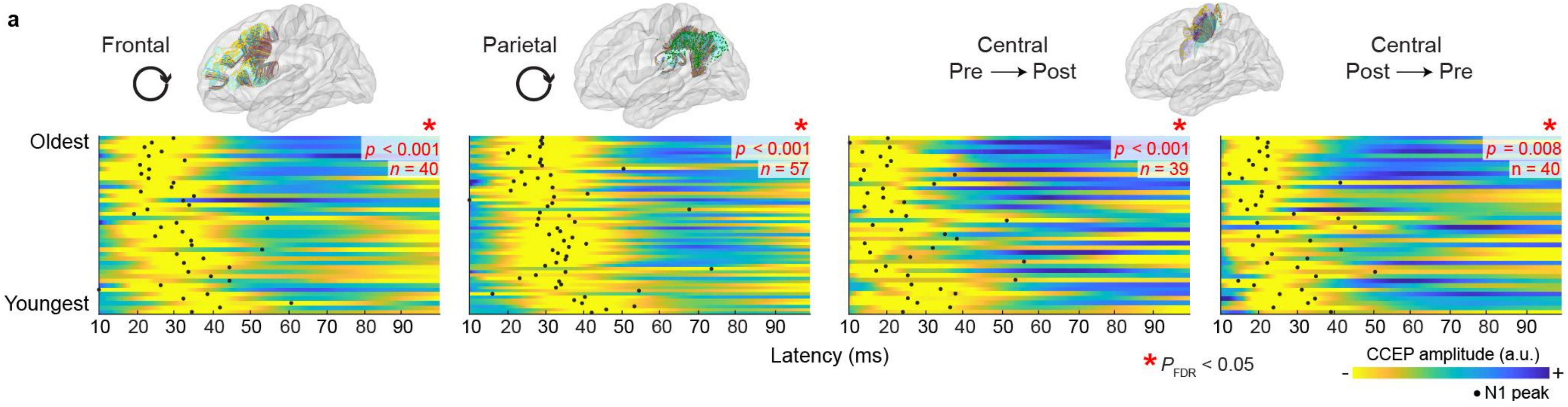


Central U-fibers



Excluding measured electrodes within 13 mm of stimulated pair

Latency decreases with development in U-fibers



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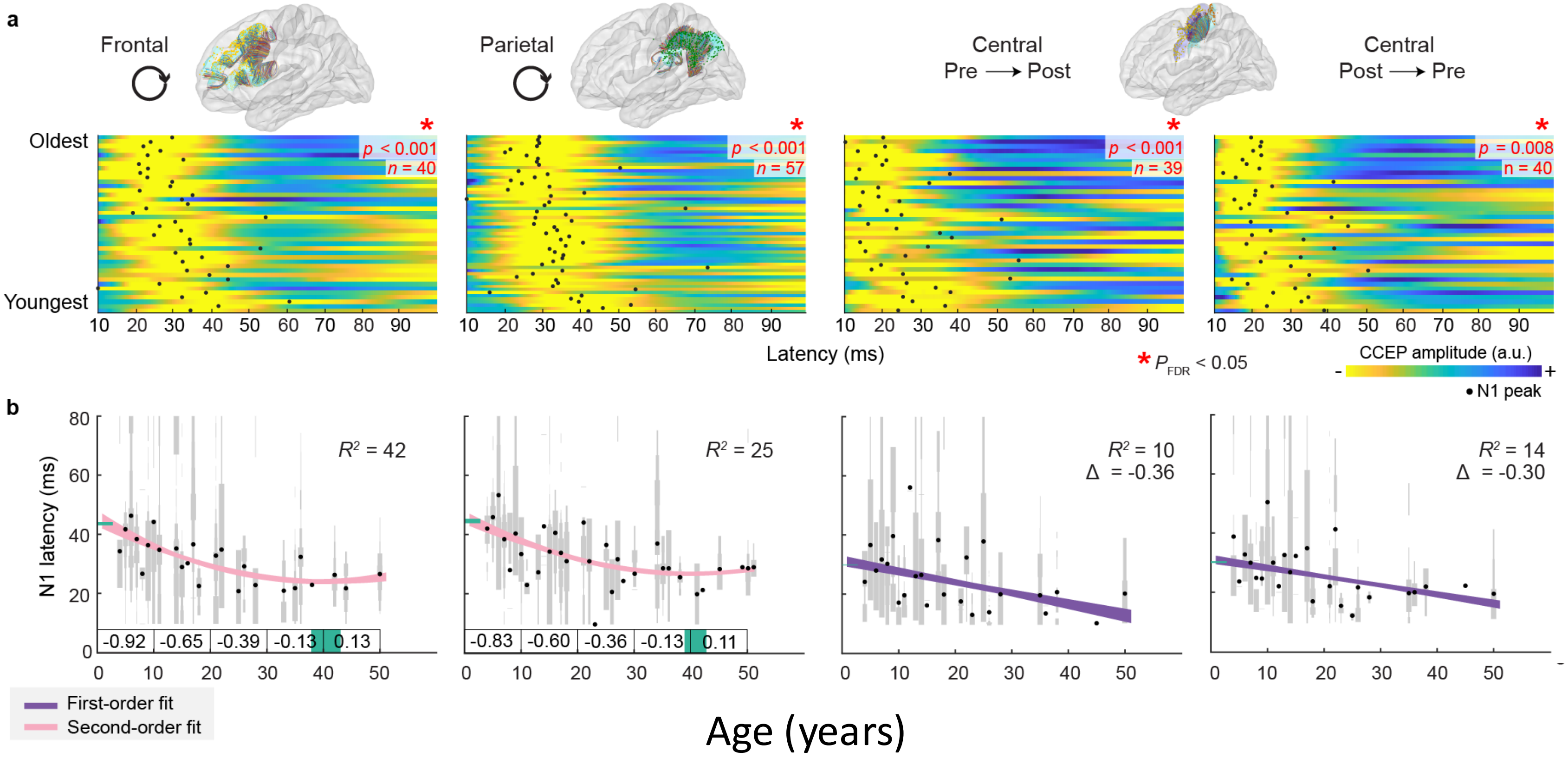

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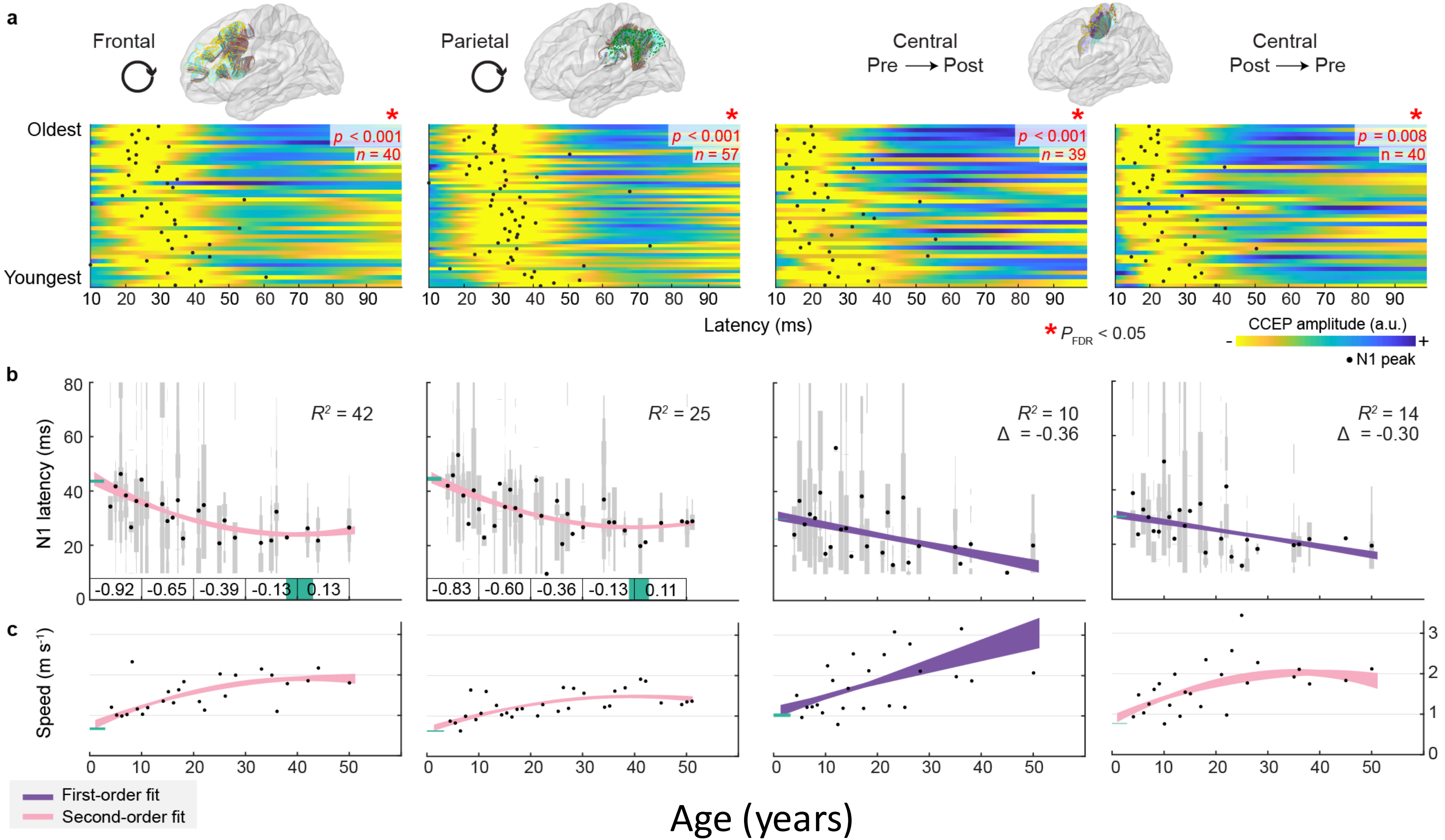

Age (years)

1. Integrating iEEG single pulse stimulation with dMRI atlases to quantify the speed of neural signal propagation across development

V Blooijs*, VD Boom*, VD Aar, Huiskamp, Castegnaro, Demuru, Zweiphenning, Van Eijsden, Miller, Leijten, Hermes, *Nature Neuroscience* 2023

- Adult transmission speeds are ~2x faster than kids
- This developmental trajectory is comparable to that measured with diffusion MRI, and likely driven by microstructural changes in e.g. myelin and axon diameter
- U-fibers were slower compared to large cortico-cortical connections
- Sensorimotor connections mature before frontal and parietal connections
- Timescales of neural signal propagation change across the life-span

Continued data collection and BIDS curation to understand differences between more rapidly developing projection fibers, callosal fibers and slowly developing cingulum bundle – data will be made available with publications!

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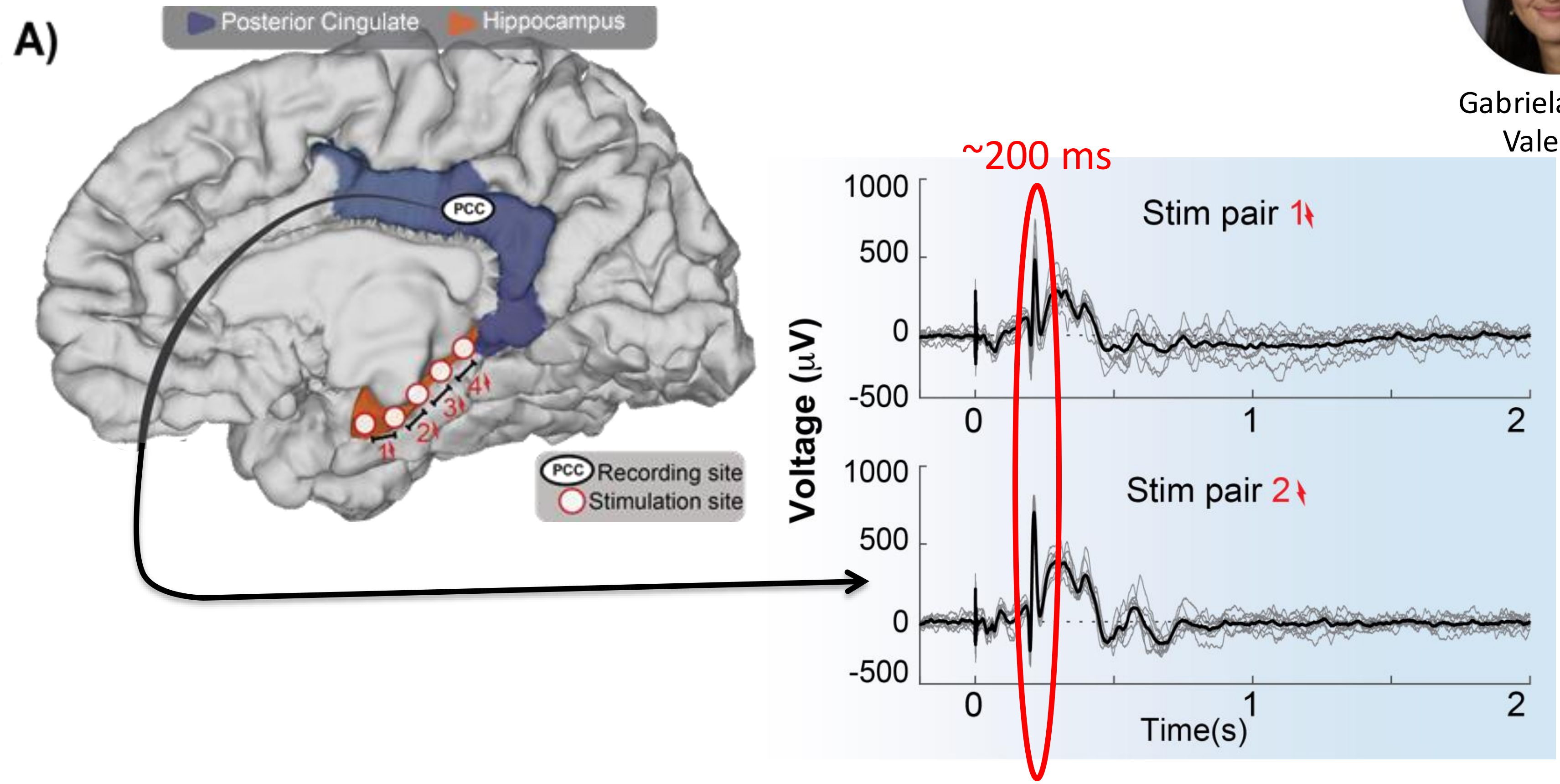
3. DEMO: iEEG data in BIDS for network mapping

The limbic memory subsystem shows a unique waveform

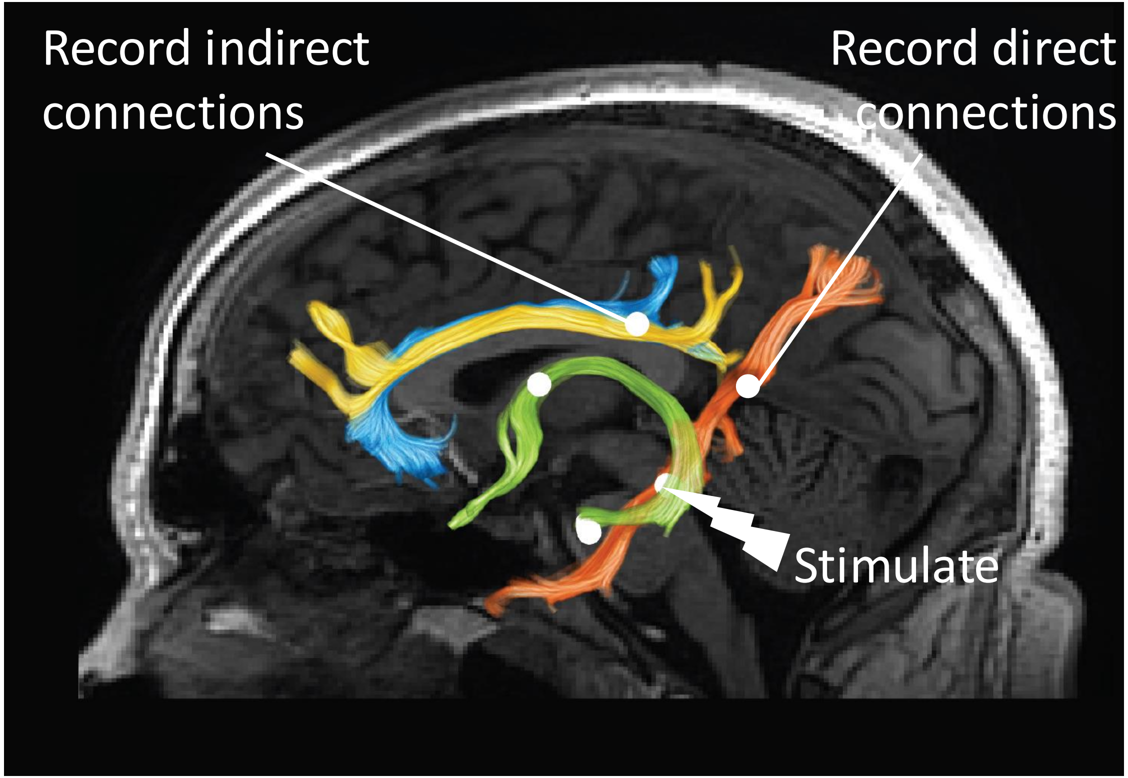
Gabriela Ojeda Valencia



Ojeda Valencia, Gregg, Huang, Lundstrom, Brinkmann, Pal Attia, Van Gompel, Bernstein, In, Huston, Worrell, Miller, Hermes, *JNeurosci*, 2023

Anatomical connections between Hippocampus and PCC

Trace the network



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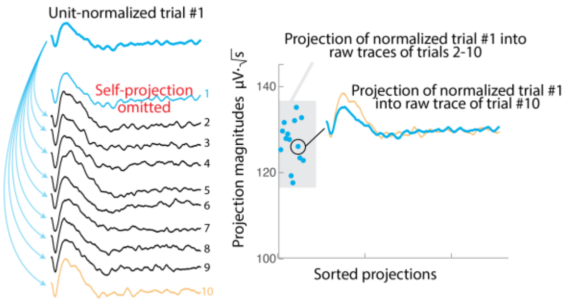
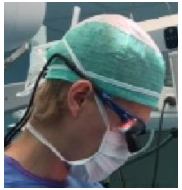
Miller, Müller, Valencia, Huang, Gregg, Worrell, Hermes. Canonical Response Parameterization: Quantifying the structure of responses to single-pulse intracranial electrical brain stimulation. *PLOS Computational Biology* 2022

Canonical response parameterization (CRP)



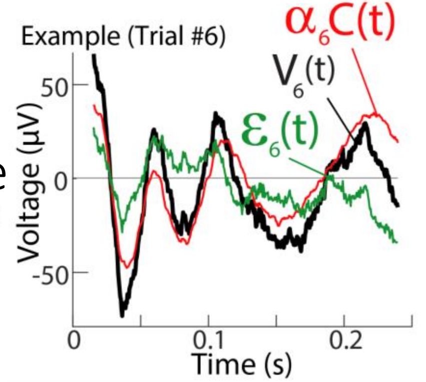
Cross projection magnitudes enable us to identify reliable responses

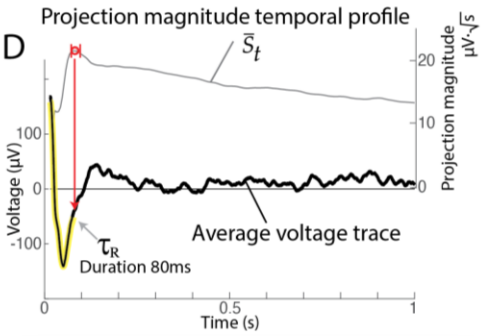
$$V_k(t) = \alpha_k C(t) + \varepsilon_k(t)$$



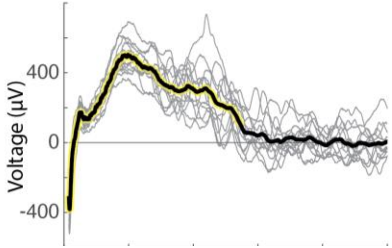
Kai Miller
(Mayo Clinic)

We can parameterize single trials





Temporal profiles of projection magnitudes identify response durations



$\bar{S}_{\tau_R}$ (µV·√s)	τ_R (s)	α' (µV)	$\alpha/\sqrt{\varepsilon^T\varepsilon}$	$1-\frac{\varepsilon^T\varepsilon}{V^TV}$
228	0.54	322	4.55	0.95

Parameterization is a powerful tool, allowing full statistical description of arbitrary shapes

Miller, Mueller, Ojeda Valencia, Huang, Gregg, Worrell, Hermes, 2023, Canonical Response Parameterization, *PLOS Comp Biol*

Canonical response parameterization (CRP)

Python code:

https://github.com/bnelair/best_toolbox

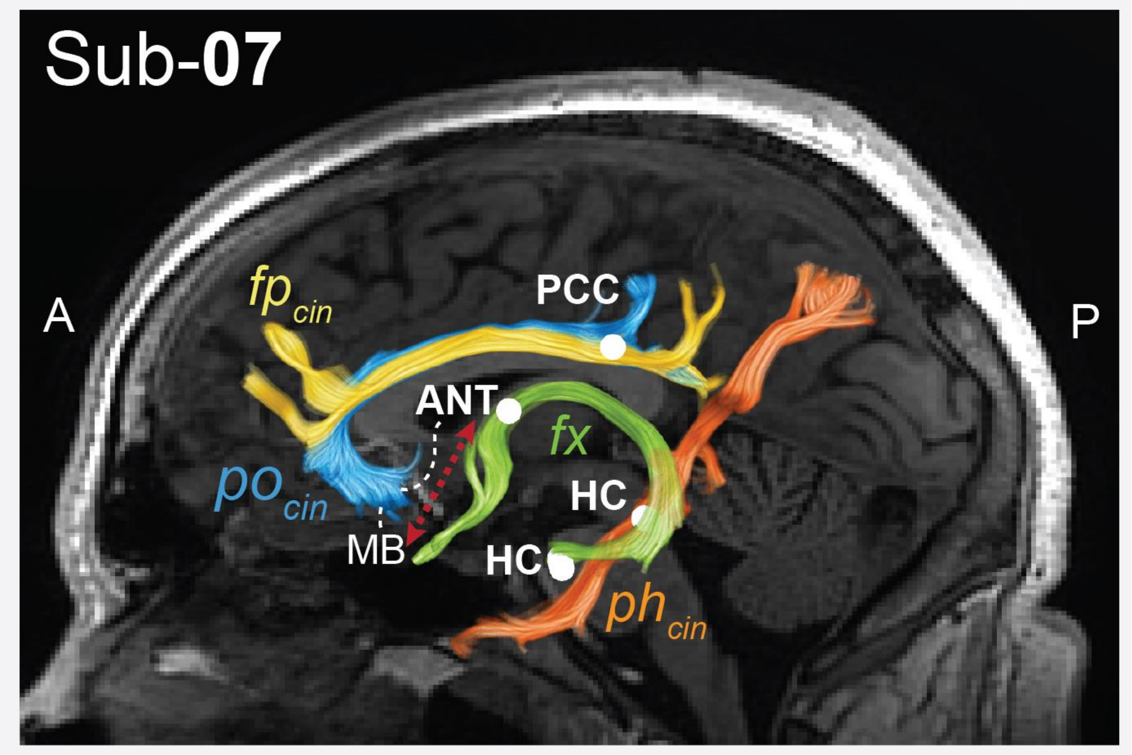
https://github.com/bnelair/best_toolbox/blob/master/best/erp/crp.py

https://best-toolbox.readthedocs.io/en/latest/erp.crp.html

Miller, Mueller, Ojeda Valencia, Huang, Gregg, Worrell, Hermes, 2023, Canonical Response Parameterization, *PLOS Comp Biol*

Anatomical connections between Hippocampus and PCC

Trace the network

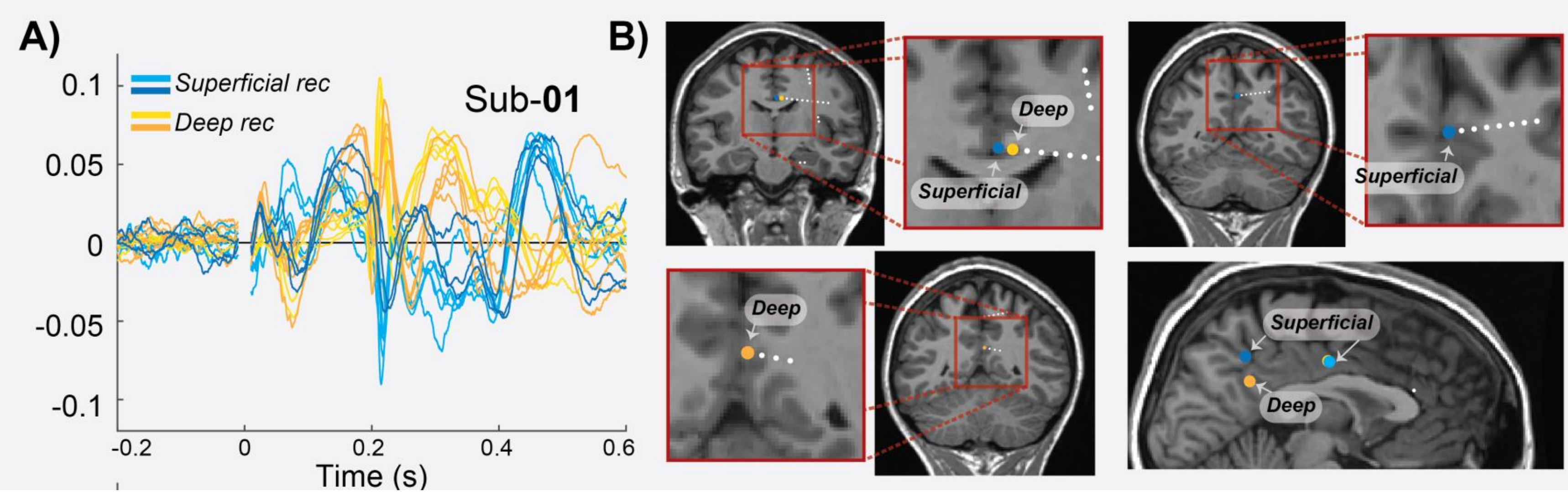


Canonical Response Parameterization (CRP) *(Miller et al., 2023)* to characterize CCEPs within the limbic network without prior assumptions on latency, polarity and form.

Hippocampal-PCC connections are stronger than Amygdala-PCC connections.

Ojeda Valencia, Gregg, Huang, Lundstrom, Brinkmann, Pal Attia, Van Gompel, Bernstein, In, Huston, Worrell, Miller, Hermes, *JNeurosci*, 2023
Miller, Müller, Valencia, Huang, Gregg, Worrell, Hermes. Canonical Response Parameterization: Quantifying the structure of responses to single-pulse intracranial electrical brain stimulation. *PLOS Computational Biology* 2022

Tracing the memory subsystem of the limbic network: Endpoints in PCC

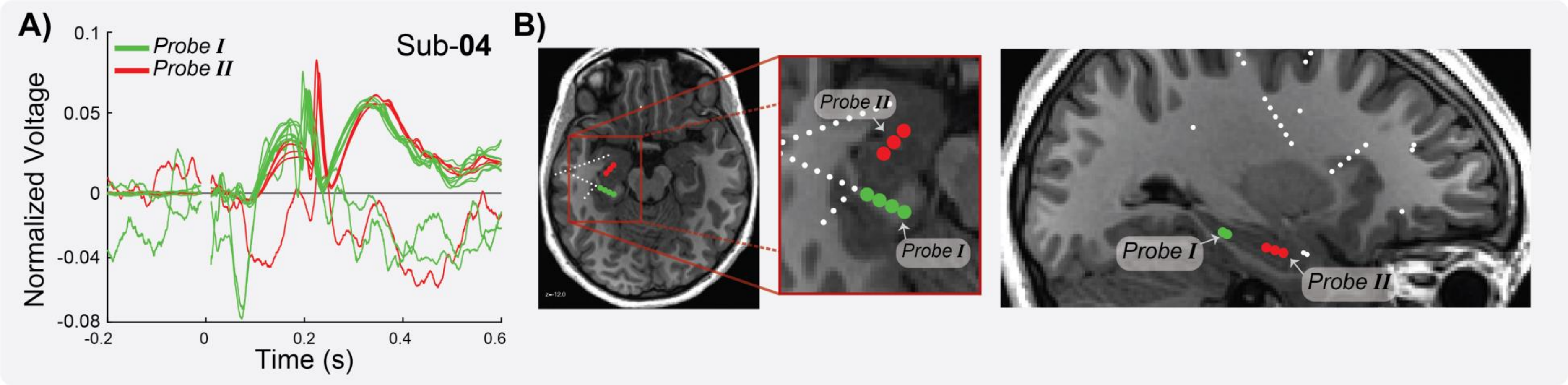


Maintain single electrode evoked responses without bias using adjusted common average re-referencing (CARLA)

Huang, Ojeda Valencia, Gregg, Osman, Montoya, Worrell, Miller, Hermes . CARLA: Adjusted common average referencing for cortico-cortical evoked potential data. arXiv preprint arXiv:2310.00185. 2023 Sep 29.

Ojeda Valencia, Gregg, Huang, Lundstrom, Brinkmann, Pal Attia, Van Gompel, Bernstein, In, Huston, Worrell, Miller, Hermes, *JNeurosci*, 2023

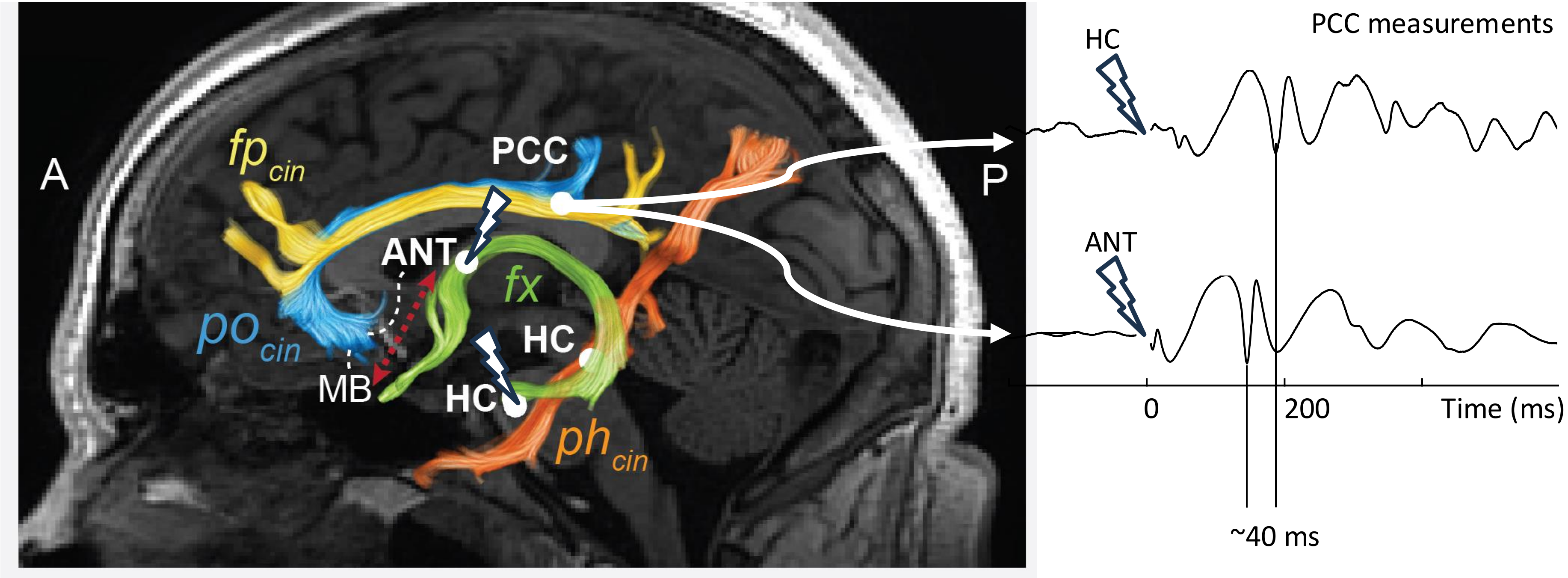
Tracing the memory subsystem of the limbic network:
Stimulating more posterior in the hippocampus results in an earlier response



Ojeda Valencia, Gregg, Huang, Lundstrom, Brinkmann, Pal Attia, Van Gompel, Bernstein, In, Huston, Worrell, Miller, Hermes, *JNeurosci*, 2023

Tracing the memory subsystem of the limbic network:

- dMRI in two patients, all data in BIDS: https://openneuro.org/datasets/ds004696
- Preprocessed with qsiprep, analyses in dsiStudio (to obtain all cingulum bundles)
- Move electrode positions to the dMRI space!
- Limbic HAP wave: Hippocampus → Anterior nucleus of thalamus → Posterior cingulate cortex



Ojeda Valencia, Gregg, Huang, Lundstrom, Brinkmann, Pal Attia, Van Gompel, Bernstein, In, Huston, Worrell, Miller, Hermes, *JNeurosci*, 2023

Tracing the memory subsystem of the limbic network:

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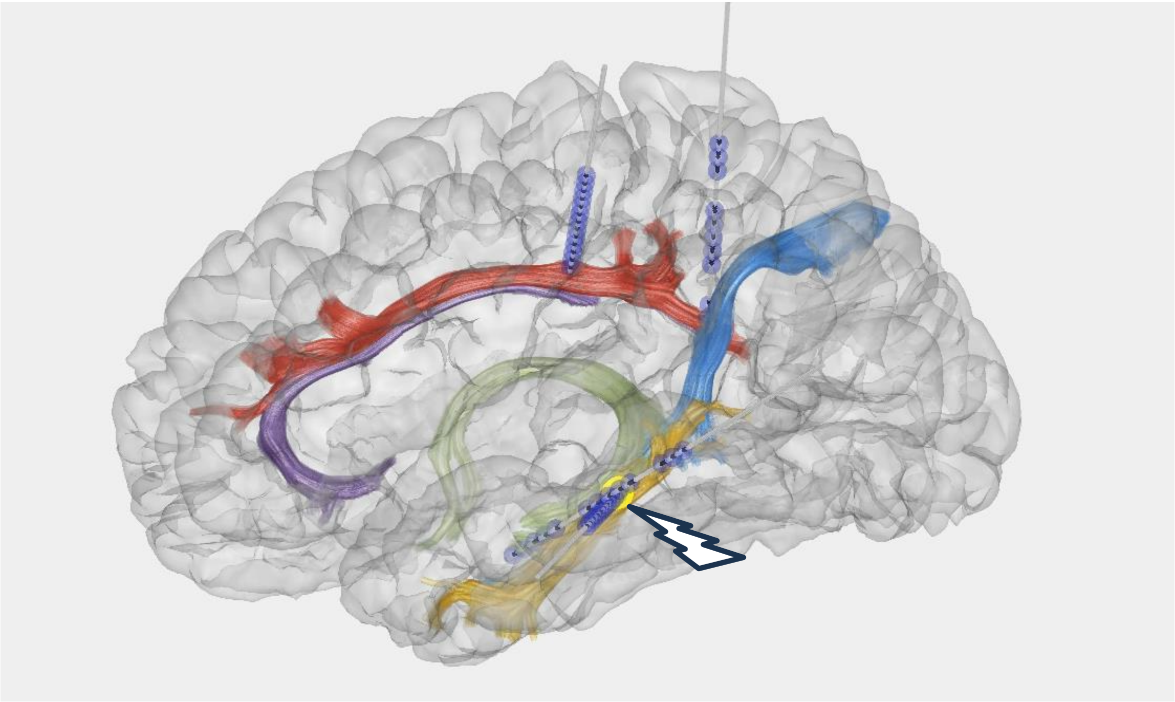


Ojeda Valencia, Gregg, Huang, Lundstrom, Brinkmann, Pal Attia, Van Gompel, Bernstein, In, Huston, Worrell, Miller, Hermes, *JNeurosci*, 2023

2. Integration iEEG single pulse stimulation with dMRI to understand direct and indirect connectivity in the human limbic system

Ojeda Valencia, Gregg, Huang, Lundstrom, Brinkmann, Pal Attia, Van Gompel, Bernstein, In, Huston, Worrell, Miller, Hermes, *JNeurosci* 2023

- Not all evoke potentials are related to direct connections
- Some indirect connections have strong evoked potentials, does this perhaps relate to network excitability?
- Analysis techniques should be suitable for the measured responses. The canonical response parameterization (CRP technique) is waveform agnostic.

Take home points

- Transmission speeds show a long developmental trajectory that matches neuroimaging findings
- Speeds increase >2-fold from childhood to adulthood, likely driven by microstructural changes in the white matter
- Stimulation evoked responses as biomarkers for brain circuits: the limbic-HAP-wave propagates along the limbic memory subsystem
- Integration of iEEG with imaging helps understand direct and indirect pathways of neural signal propagation

Electrical stimulation evoked potentials can be used as brain circuit biomarkers that characterize development, myelination and signal propagation across cognitive networks

For all published manuscripts described in this talk, accompanying de-identified data in the Brain Imaging Data Structure (BIDS) + code are shared such that all the main figures from the manuscripts can be reproduced *(please contact me or post a GitHub issue if you have any issues)*

Outline:
Multimodal integration and the Brain Imaging Data Structure

1. Integrating iEEG single pulse stimulation with dMRI atlases to quantify the speed of neural signal propagation across development

V Blooijs*, VD Boom*, VD Aar, Huiskamp, Castegnaro, Demuru, Zweiphenning, Van Eijsden, Miller, Leijten, Hermes, *Nature Neuroscience* 2023

2. Integration iEEG single pulse stimulation with dMRI to understand direct and indirect connectivity in the human limbic system

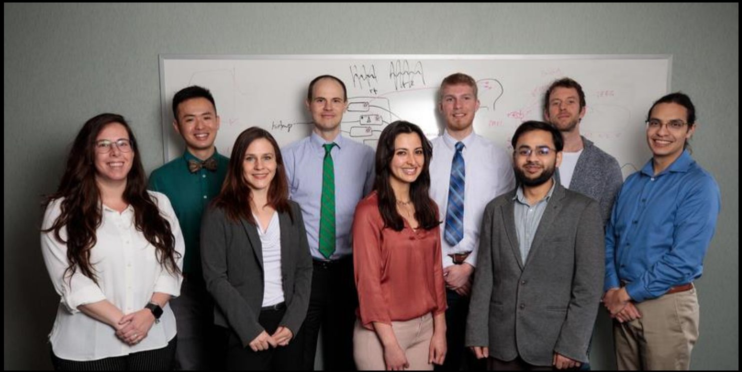
Miller, Müller, Valencia, Huang, Gregg, Worrell, Hermes. Canonical Response Parameterization: Quantifying the structure of responses to single-pulse intracranial electrical brain stimulation. *PLOS Computational Biology* 2022

Ojeda Valencia, Gregg, Huang, Lundstrom, Brinkmann, Pal Attia, Van Gompel, Bernstein, In, Huston, Worrell, Miller, Hermes, *JNeurosci* 2023

3. DEMO: iEEG data in BIDS for network mapping

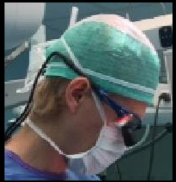
Acknowledgements

Multimodal Neuroimaging Lab



iEEG teams at Mayo Clinic and UMC Utrecht

Collaborators



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Funding: NIMH & NSF-CRCNS: R01-MH122258, NEI R01-EY035533, NEI R01-EY023384, Mayo Clinic

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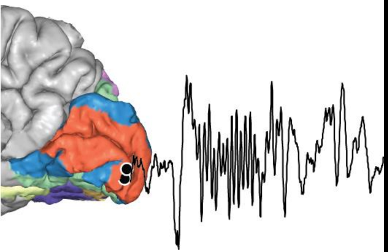

Thank you!

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Multimodal Neuroimaging Lab

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