Advanced Cognitive Neuroscience

Week 46: What about that other cortex? - the cerebellar one

The course plan

Week 36:
Lesson 0: What is it all about?
Class 0: Setting up UCloud and installing MNE-Python

Week 37:
No Teaching

Week 38:
Lesson 1: Workshop paradigm: Measuring visual subjective experience + MR Recordings
Class 1: Running an MEG analysis of visual responses

Week 39:
MEG workshop: Measuring and predicting visual subjective experience

Week 40:
Lesson 2: Basic physiology and Evoked responses
Class 2: Evoked responses to different levels of subjective experience

Week 41:
Lesson 3: Multivariate statistics
Class 3: Predicting subjective experience in sensor space
Deadline for feedback: Video Explainer

Week 42:
Autumn Break

Week 43:
Lesson 4: Forward modelling and dipole estimation
Class 4: Creating a forward model and fitting dipoles

Week 44:
Lesson 5: Inverse modelling: Minimum-norm estimate
Class 5: Predicting subjective experience in source space

Week 45:
Lesson 6: Inverse modelling: Beamforming
Class 6: Predicting subjective experience in source space, continued

Week 46:
Lesson 7: What about that other cortex? - the cerebellar one
Class 7: Oral presentations (part 1)
Deadline for feedback: Lab report

Week 47:
Lesson 8: Guest lecture: Laura Bock Paulsen: Respiratory analyses
Class 8: Oral presentations (part 2)

Week 48:
Lesson 9: Guest lecture: Barbara Pomiechowska: Using OPM-MEG to study brain and cognitive development in infancy
Class 9: Oral presentations (part 3)

Week 49:
Lesson 0 again: What was it all about?
Class 10: Oral presentations (part 4)

LAST TIME

Beamforming

&

Creating a glossary of terms for the course so far

Glossary of terms

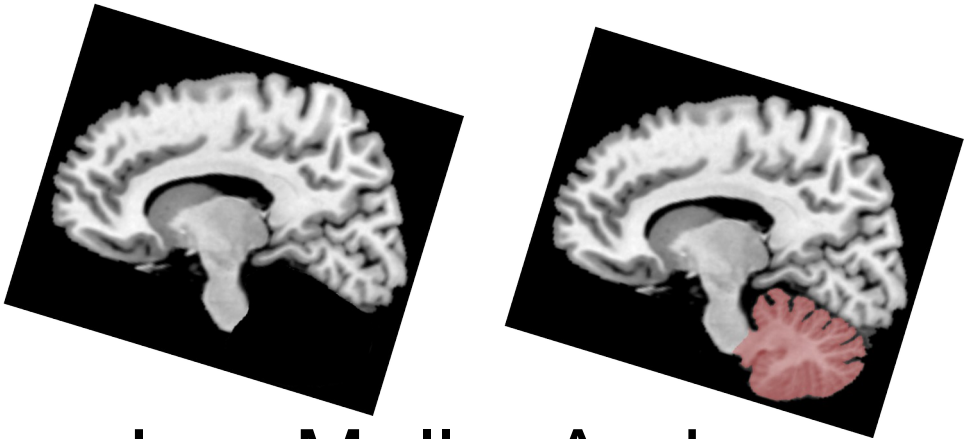
- Super-terms to create glossary around
  - Basic physiology
  - Multivariate statistics
  - Forward modelling and dipole estimation
  - Inverse modelling; MNE and beamforming

Glossary of terms

PROCEDURE

1) (10 minutes): in your study groups find all the sub-terms you think belong to each of the four super-terms
2) (10 minutes) in pairs of groups, go and write the sub-terms for each term on the whiteboard; start making internal arrows connecting them
3) (10 minutes) start connecting the sub-terms and the super-terms all across the board (mayhem will ensue)
4) (10 minutes) discussing it all together
5) Take pictures to preserve for posterity

Taking the cerebellum seriously



Lau Møller Andersen

Based on this talk: Universität Münster, December 12th 2024

AARHUS UNIVERSITY

Department of Linguistics, Cognitive Science and Semiotics

Karolinska Institutet

CFIN

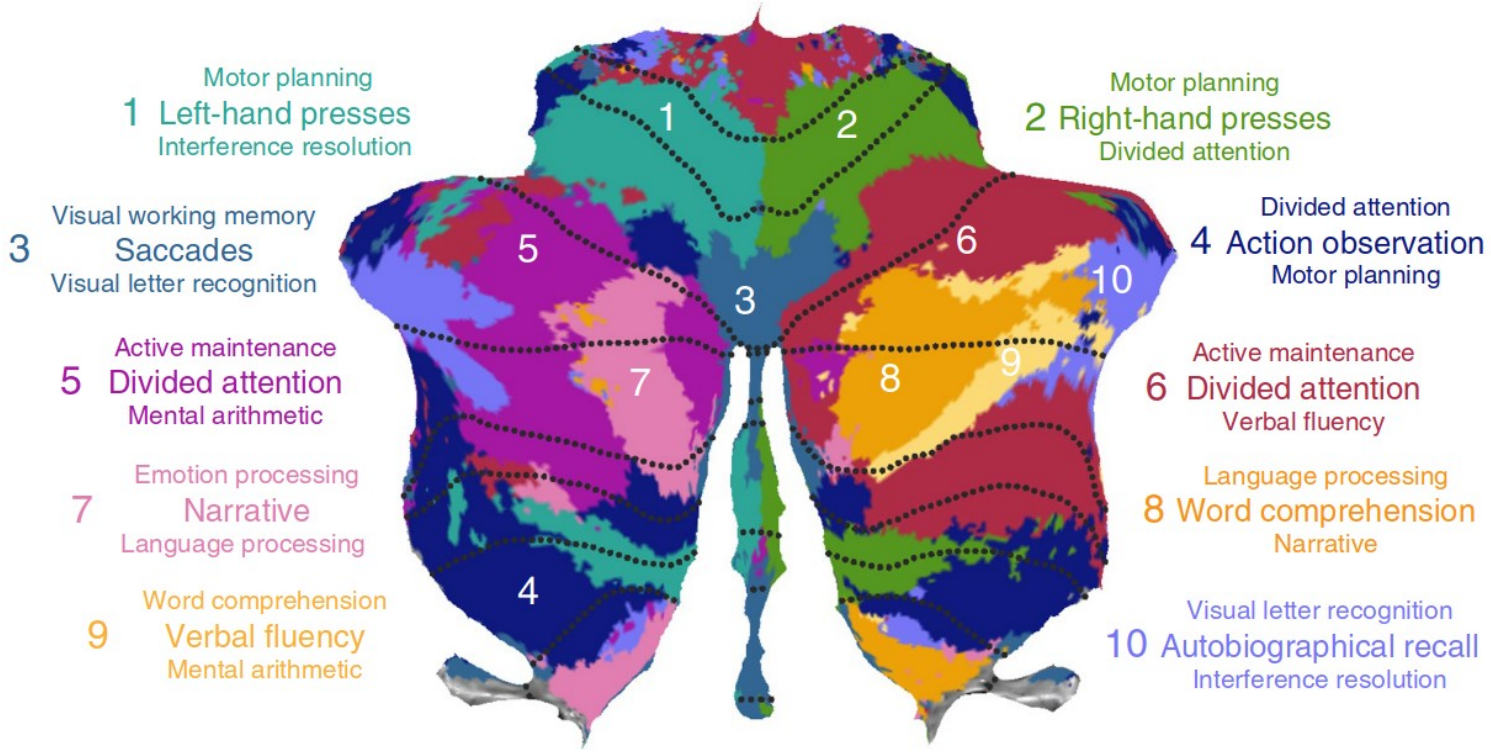
AARHUS UNIVERSITY HOSPITAL

Universität Münster

Key aspects
OBJECTIVES

1) To show that the cerebellum is integrated with the cerebrum, mid-brain and the body
   - How is timing represented in the cerebellum?
   - Cesario et al. 2020: *Your Brain Is Not an Onion With a Tiny Reptile Inside*
2) To show that it is possible to measure its activity reliably in a non-invasive manner
   - AKA: please do not cut the cerebellum from your “whole brain”-analyses

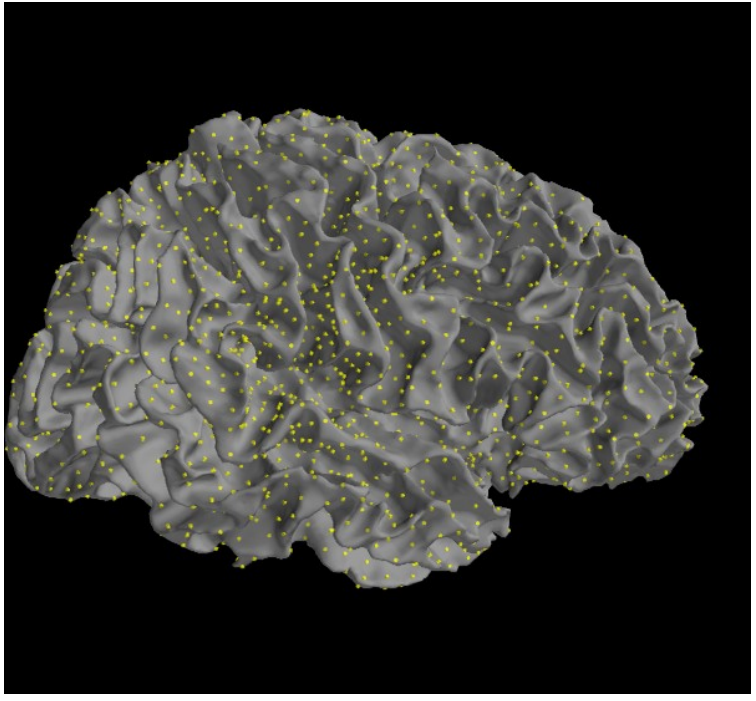
A primitive part of the brain?



(King et al. 2019)

Impossible to measure?

OR NOT MODELLED AT ALL?

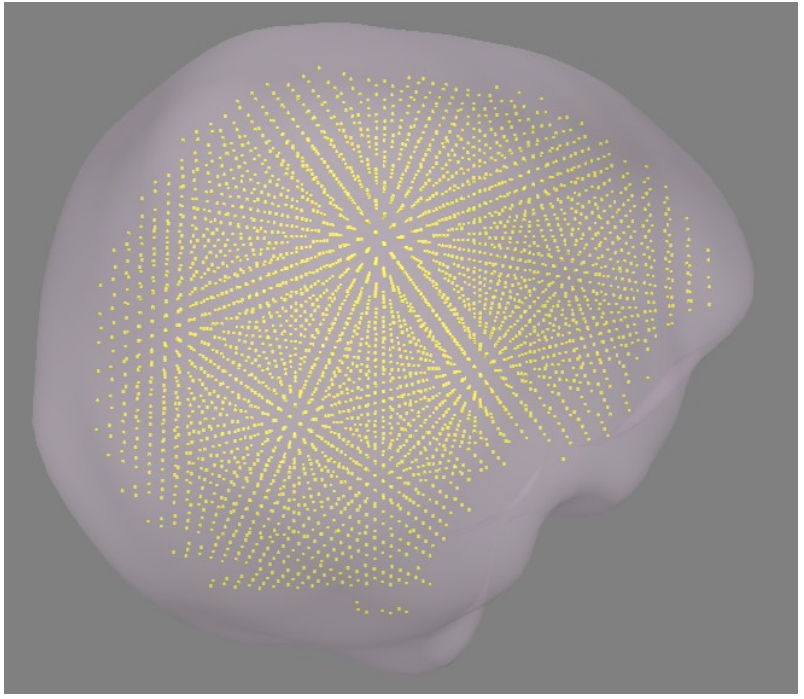


Restricted to the cortical surface

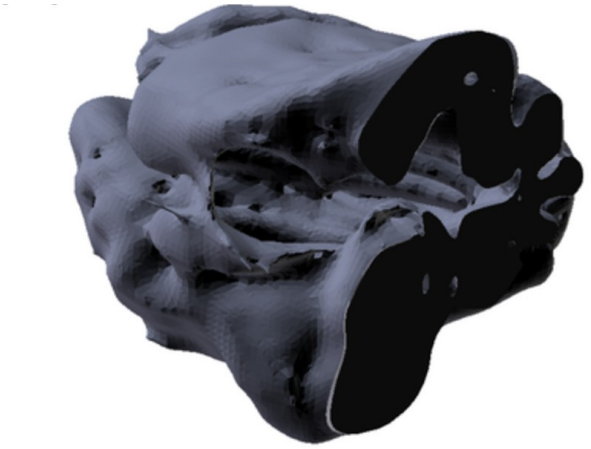
https://github.com/ualsbombe/2025_advanced_cognitive_neuroscience/blob/main/experiment/mr_processing/python/bem_processing.py

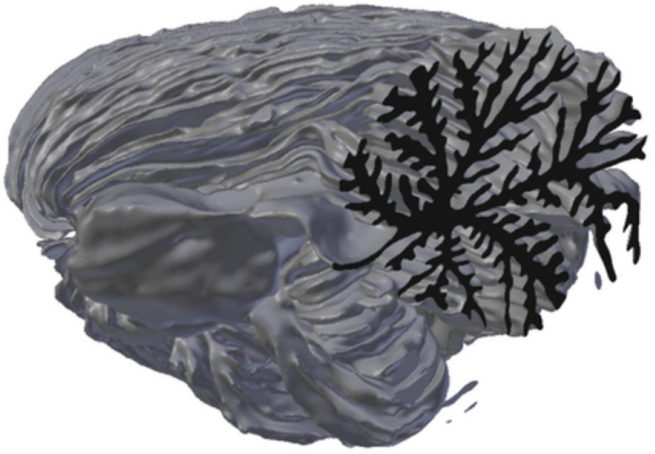
Source model – volumetric

COULD WE RESTRICT IT?



Restricting cerebellar sources to the surface?

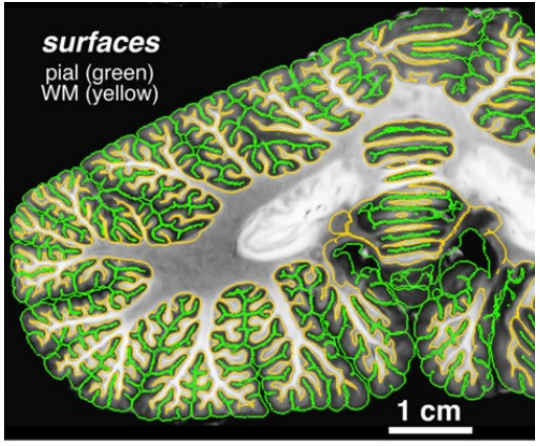




Samuelsson et al. 2020

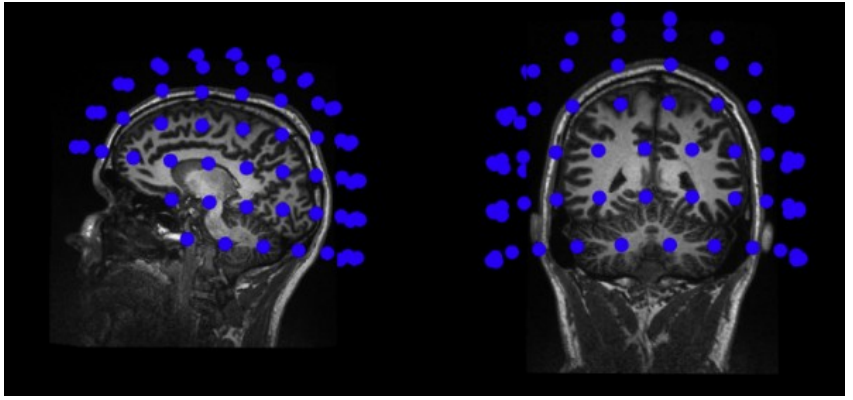
Cerebellar challenges

The cerebellar cortex is **highly convoluted** (78% of the surface of the cerebral cortex, which may lead to signal cancellation).



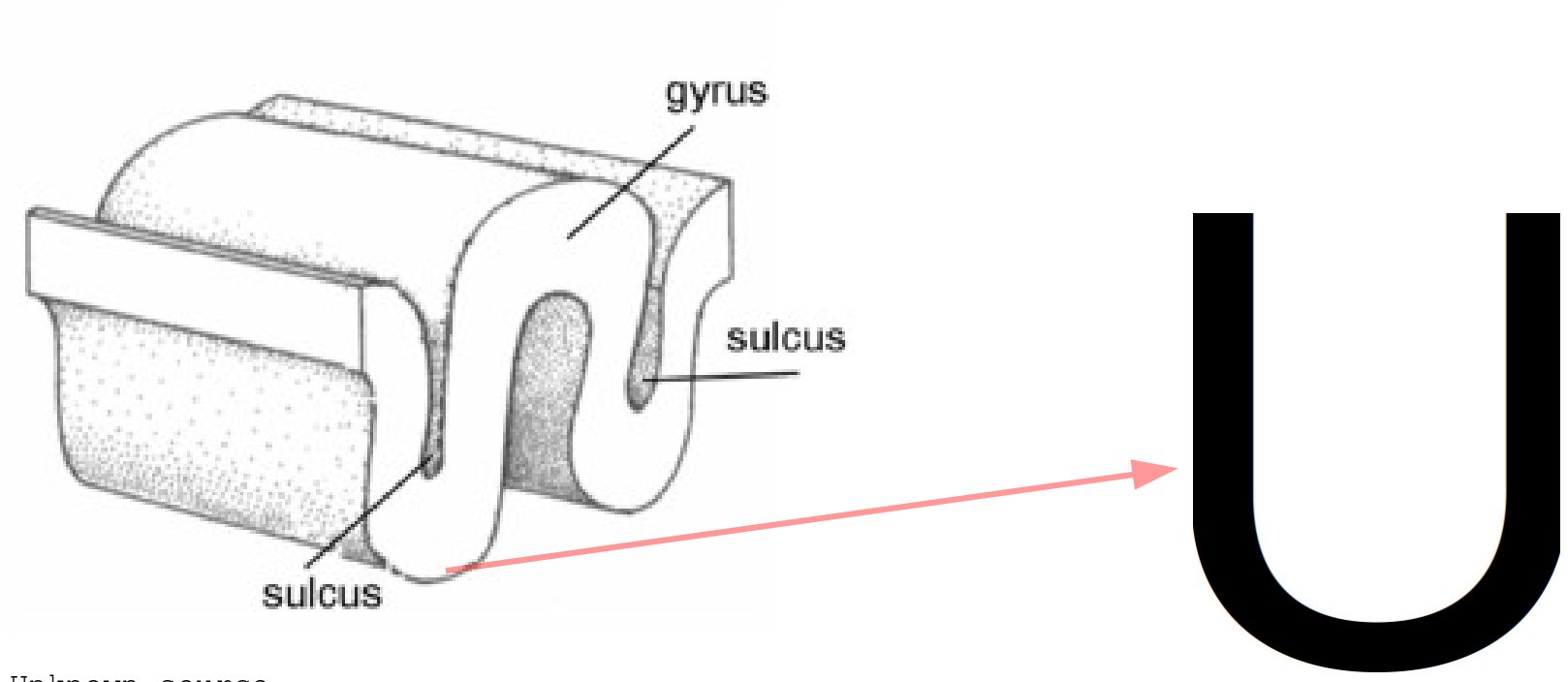
Sereno et al. 2020

The cerebellar cortex is at a **remote location** which leads to mixing at the recording sites and low SNR



Andersen, Jerbi & Dalal 2020

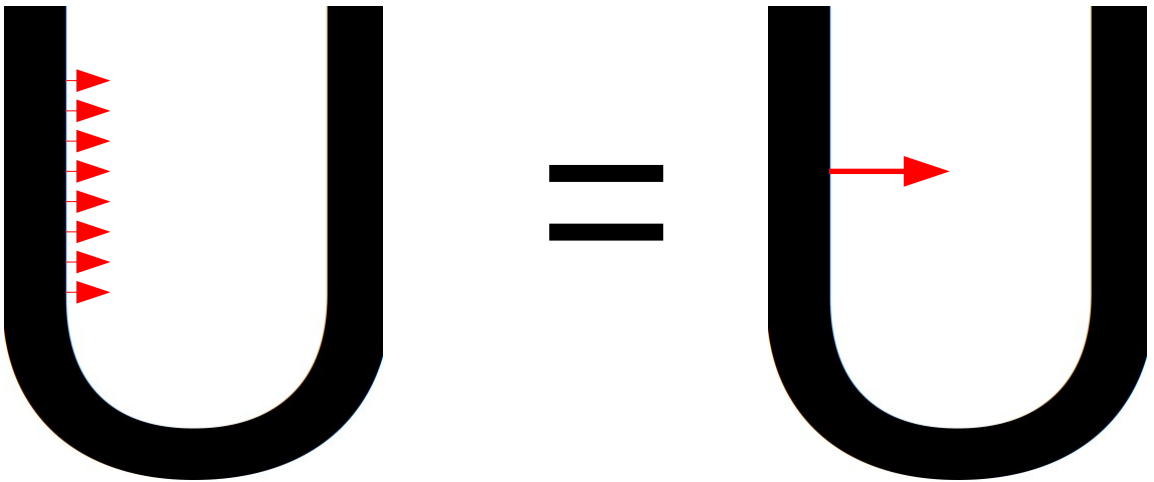
Schematic of summation/cancellation



Unknown source

Schematic of summation/cancellation

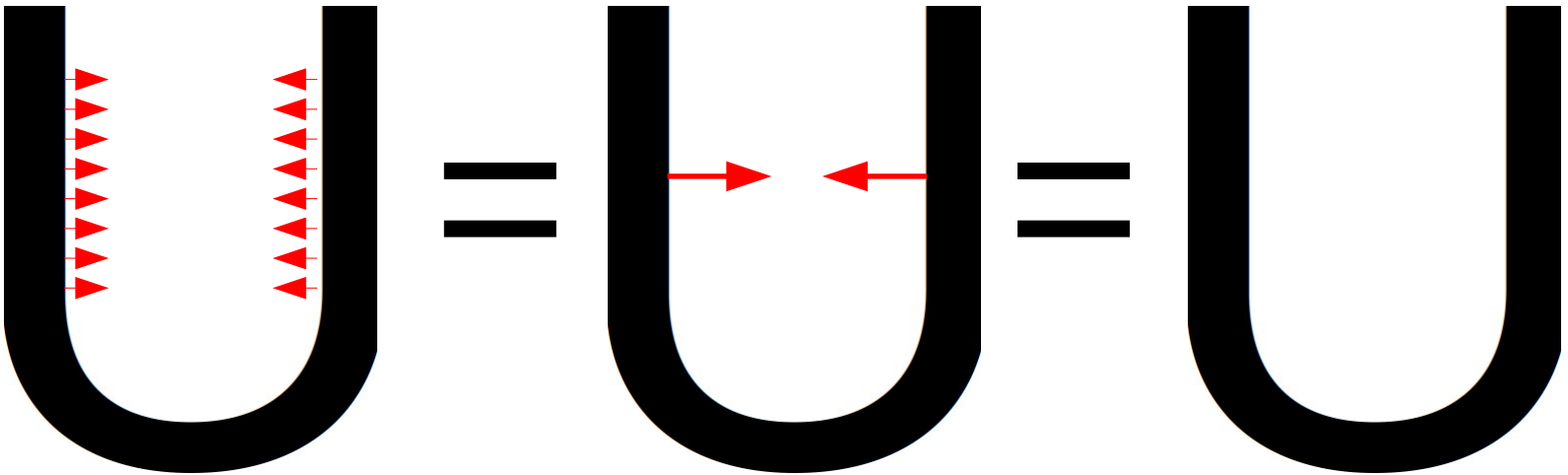
Individually considered, sources not measurable at a distance



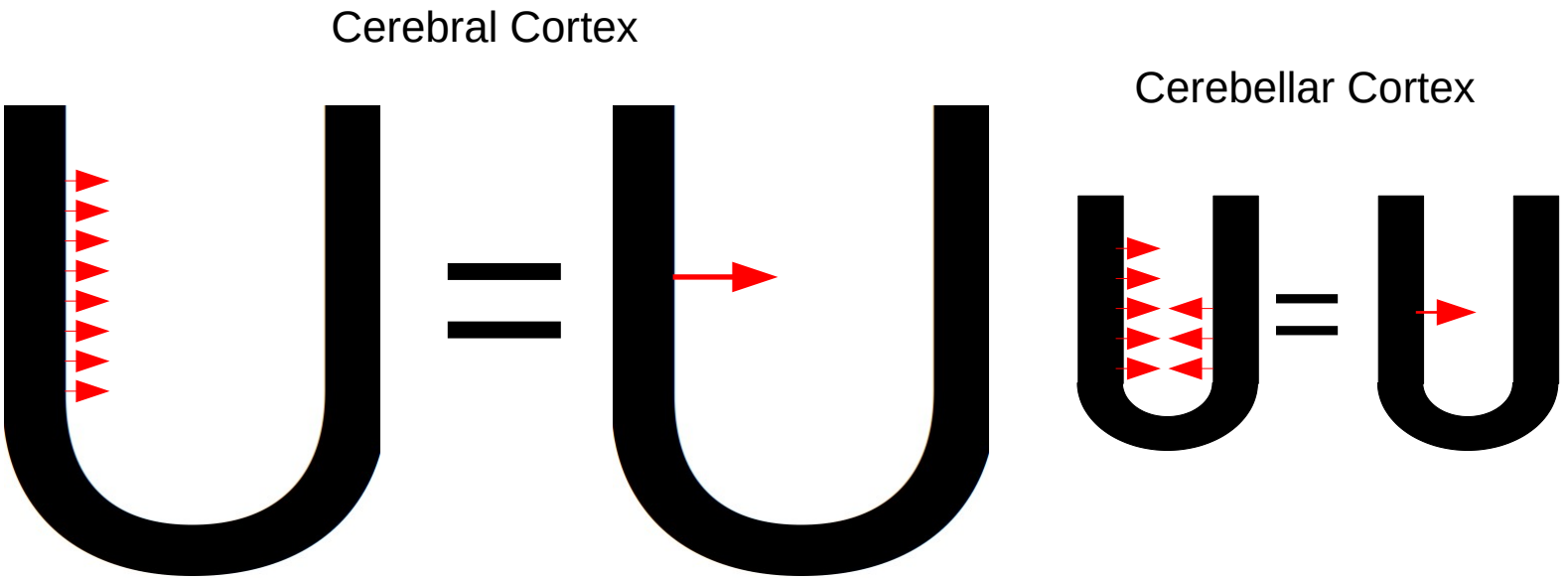
But the sum is...

Schematic of summation/cancellation

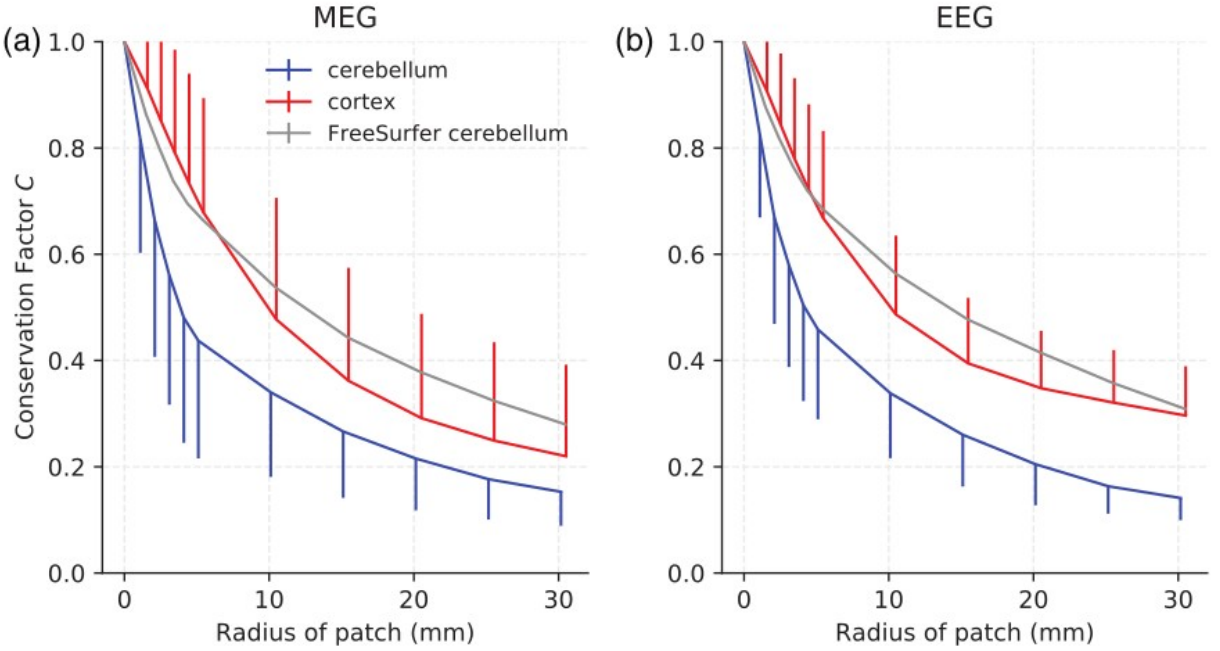
Sources may cancel one another



Schematic of summation/cancellation



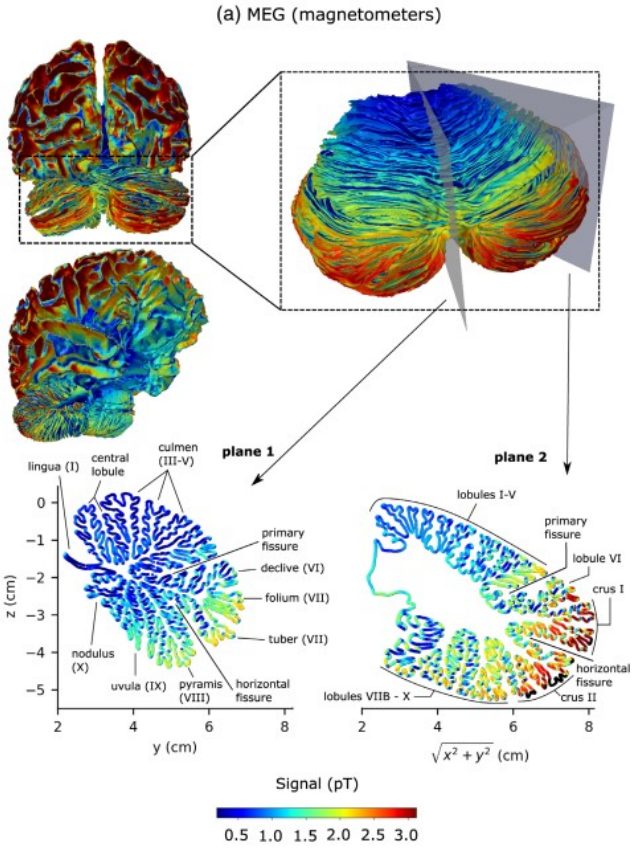
FreeSurfer overestimates the cerebellar signal ...



Advice (for now):
use volumetric source models

Samuelsson et al. 2020

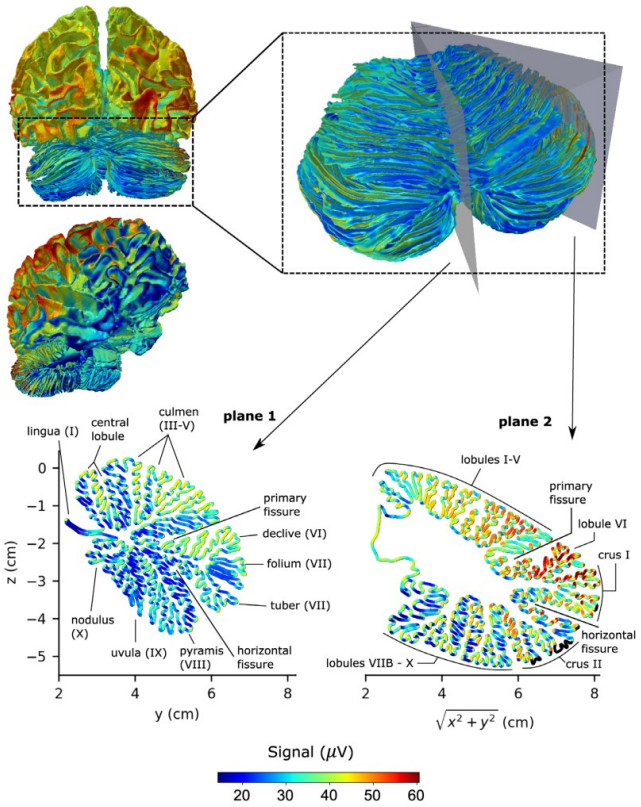
... but cerebellum is within the sensitivity range of MEG



100 nAm dipoles ≈ patch with 10 mm radius and C = 0.3 (conservation factor)

Samuelsson et al. 2020

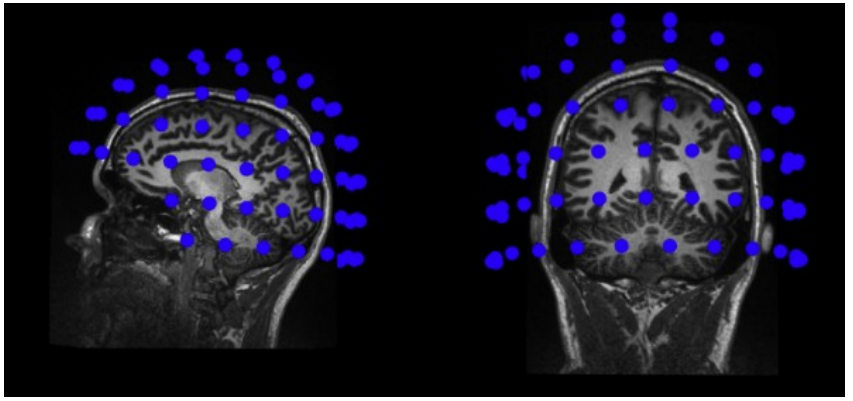
and EEG



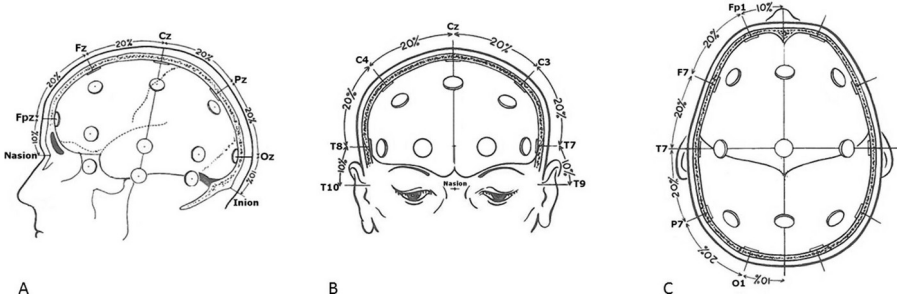
100 nAm dipoles ≈ patch with 10 mm radius and C = 0.3 (conservation factor)

Samuelsson et al. 2020

... but we haven't covered it



Andersen, Jerbi & Dalal 2020



(Jasper 1958)

So we basically know very little about the cerebellum, and there aren’t many MEG/EEG studies around.

INDEPENDENT RESEARCH FUND DENMARK

WHAT WILL I BE DOING?

Optically pumped magnetometers
OPM

Respiratory analyses

Deep brain stimulation
(DBS)
and sensing

MEG: Elekta Neuromag Triux®

WHAT HAVE I ALREADY DONE?

How I stumbled upon the cerebellum

ELSEVIER

NeuroImage

Volume 184, 1 January 2019, Pages 78-89

Somatosensory responses to nothing: An MEG study of expectations during omission of tactile stimulations

Lau M. Andersen, Daniel Lundqvist

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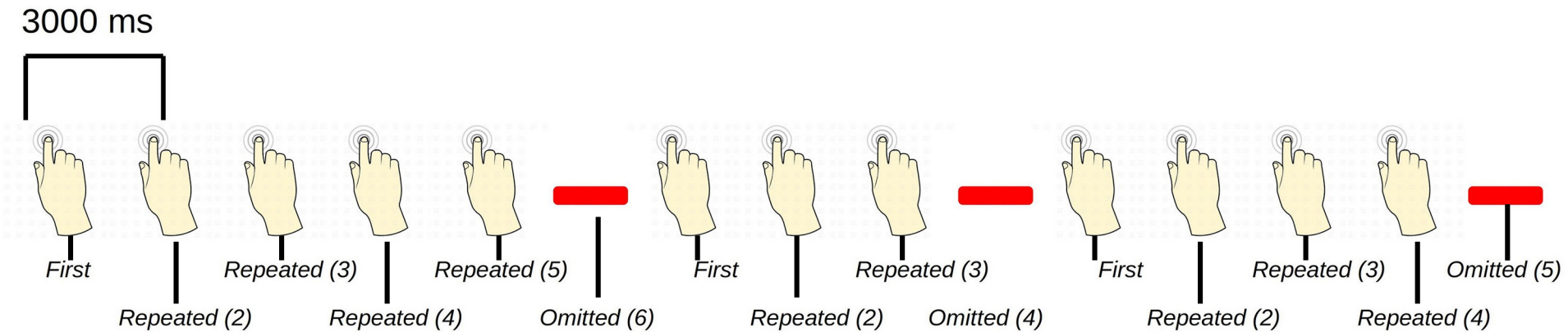
https://doi.org/10.1016/j.neuroimage.2018.09.014

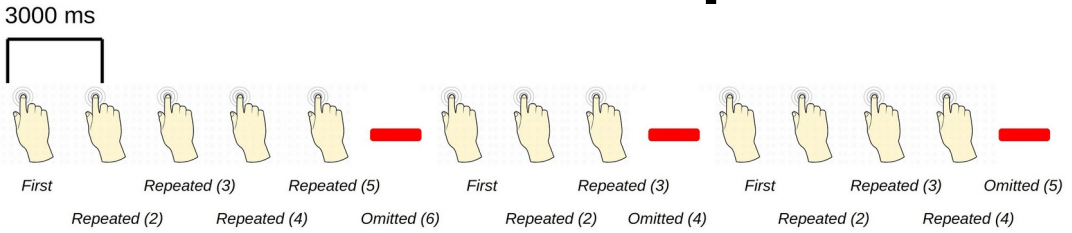
Paradigm



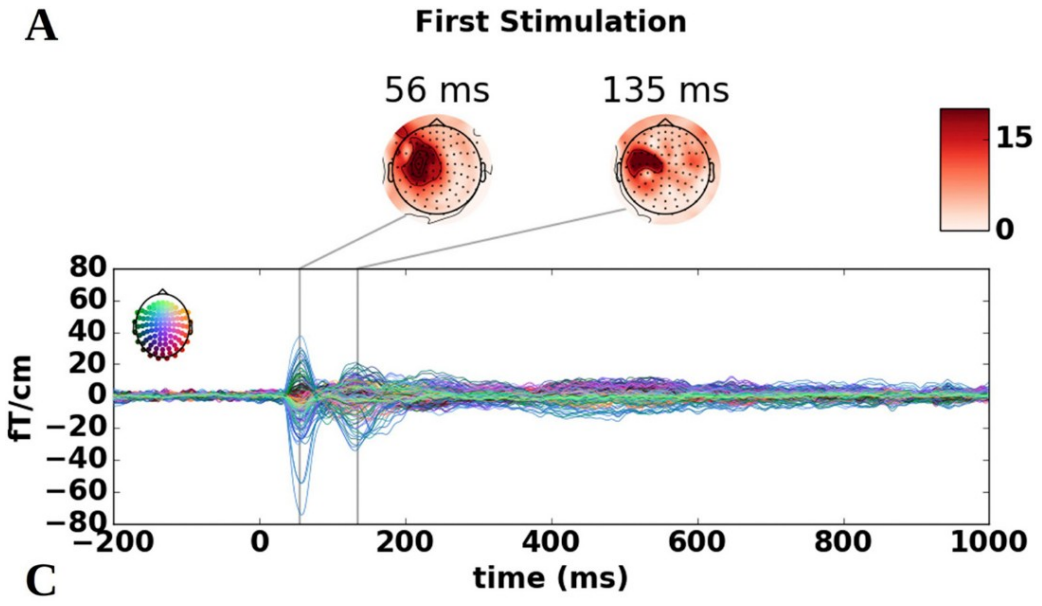
20 subjects
200 first and repeated stimulation
200 omissions

Andersen & Lundqvist 2019

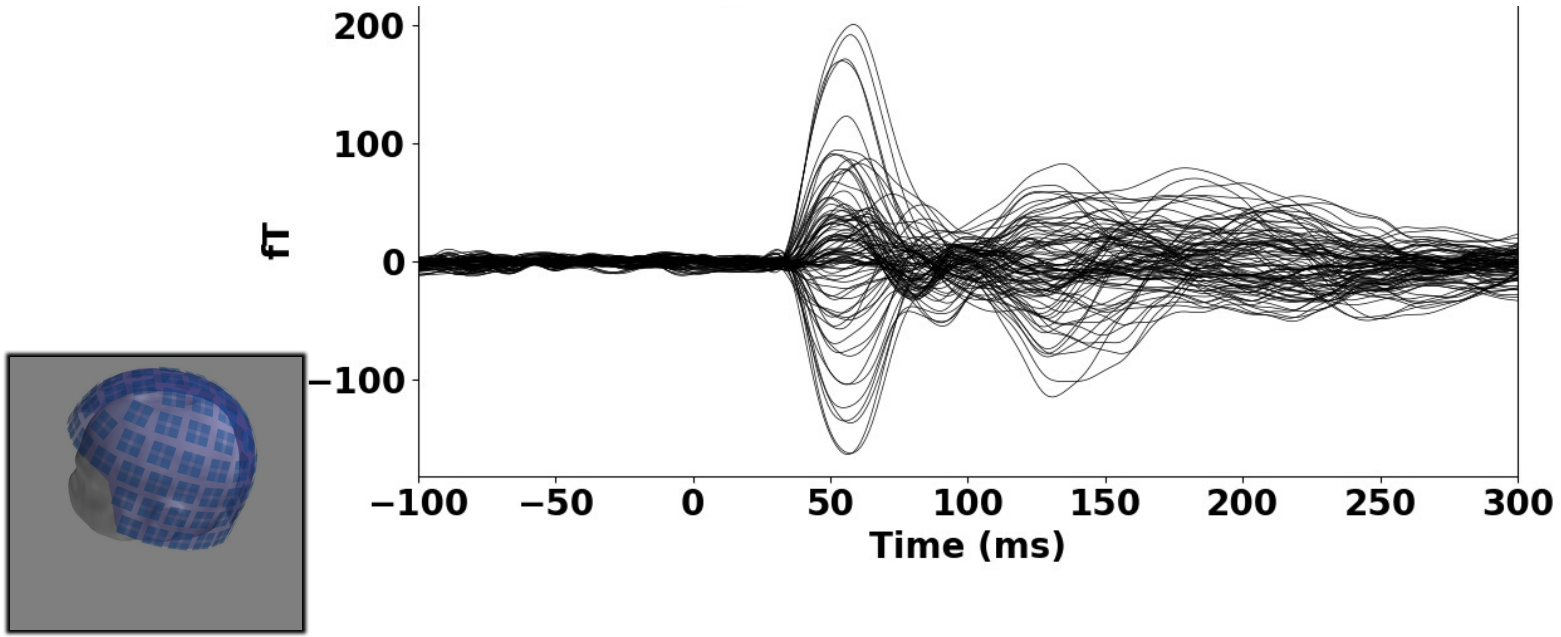
Evoked responses from paradigm



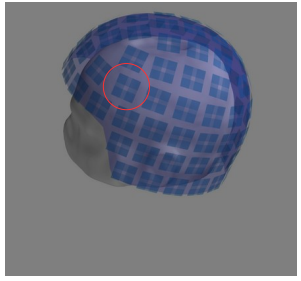
Andersen & Lundqvist 2019

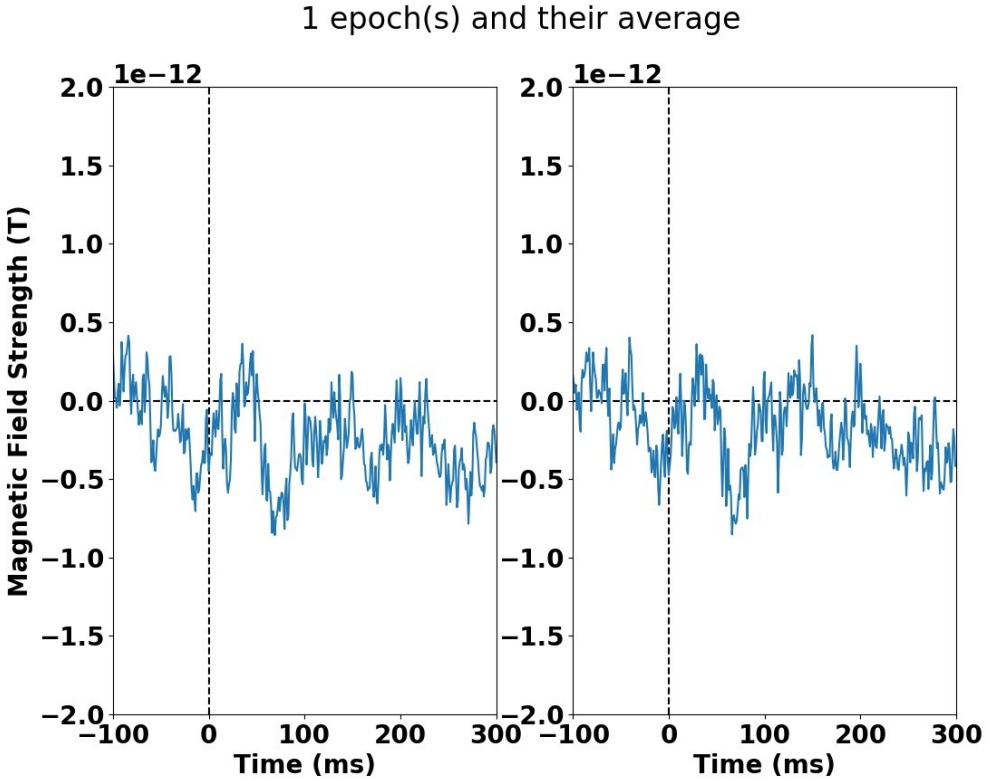


What do signals look like?



AVERAGES 101





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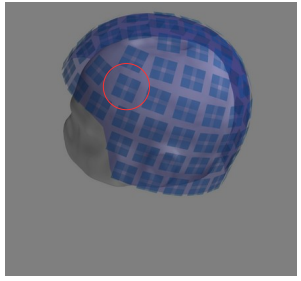

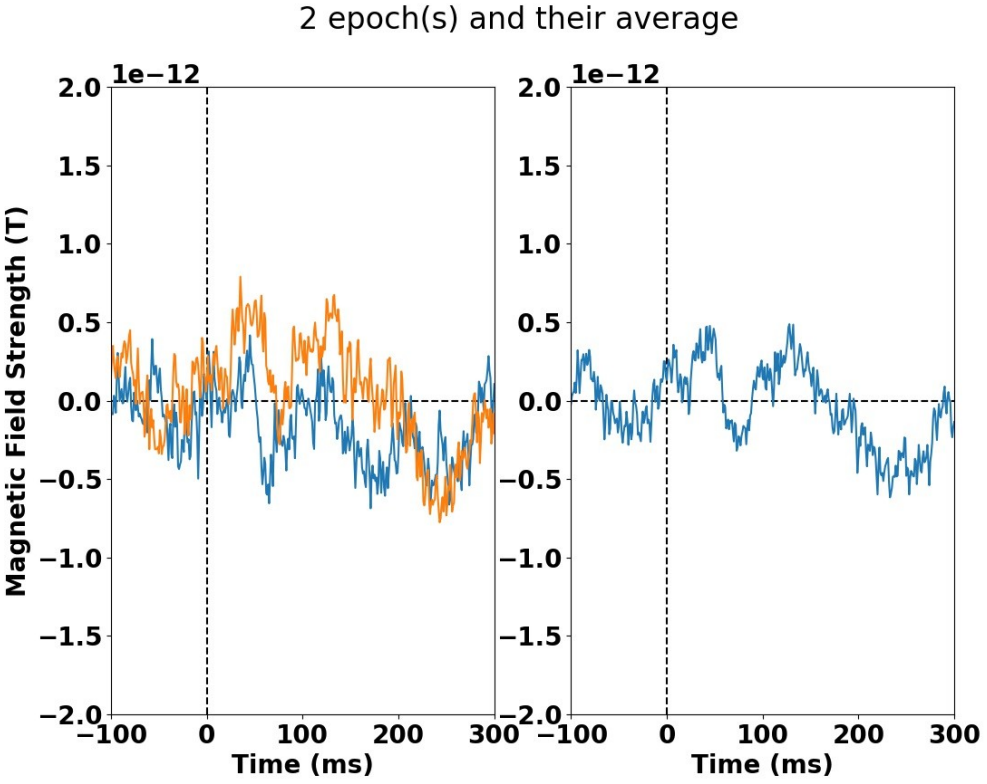

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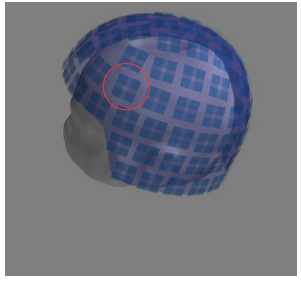
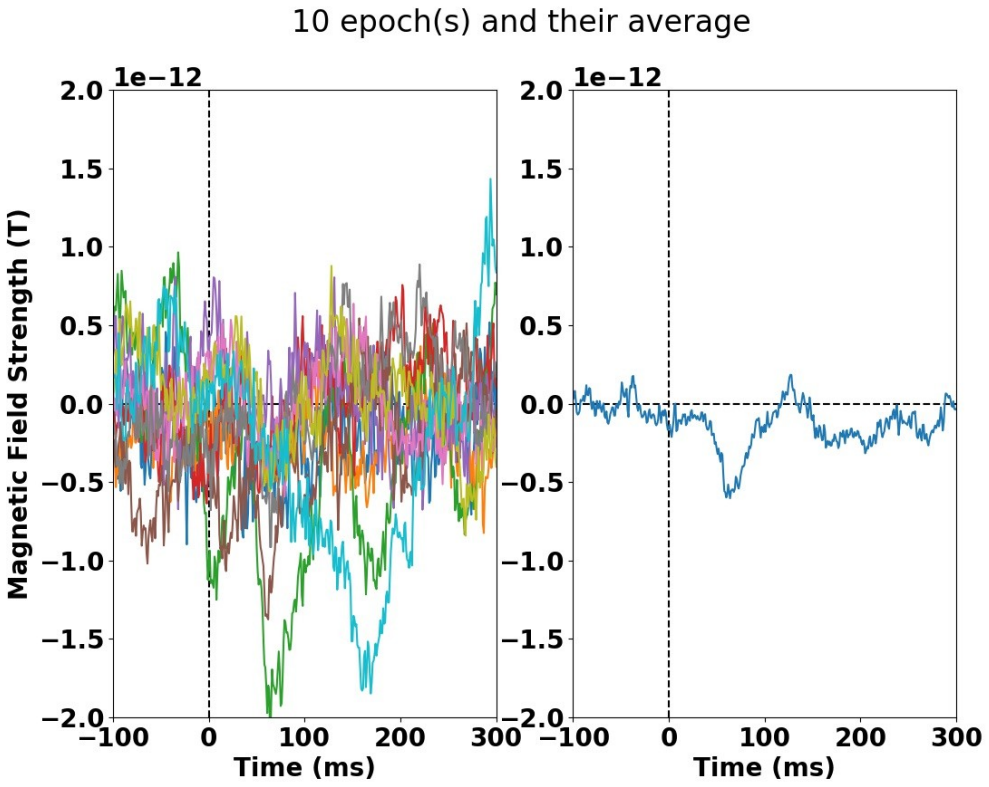
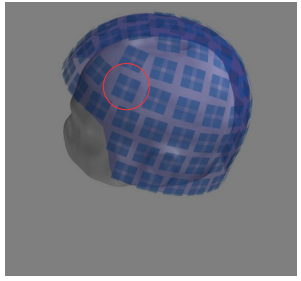
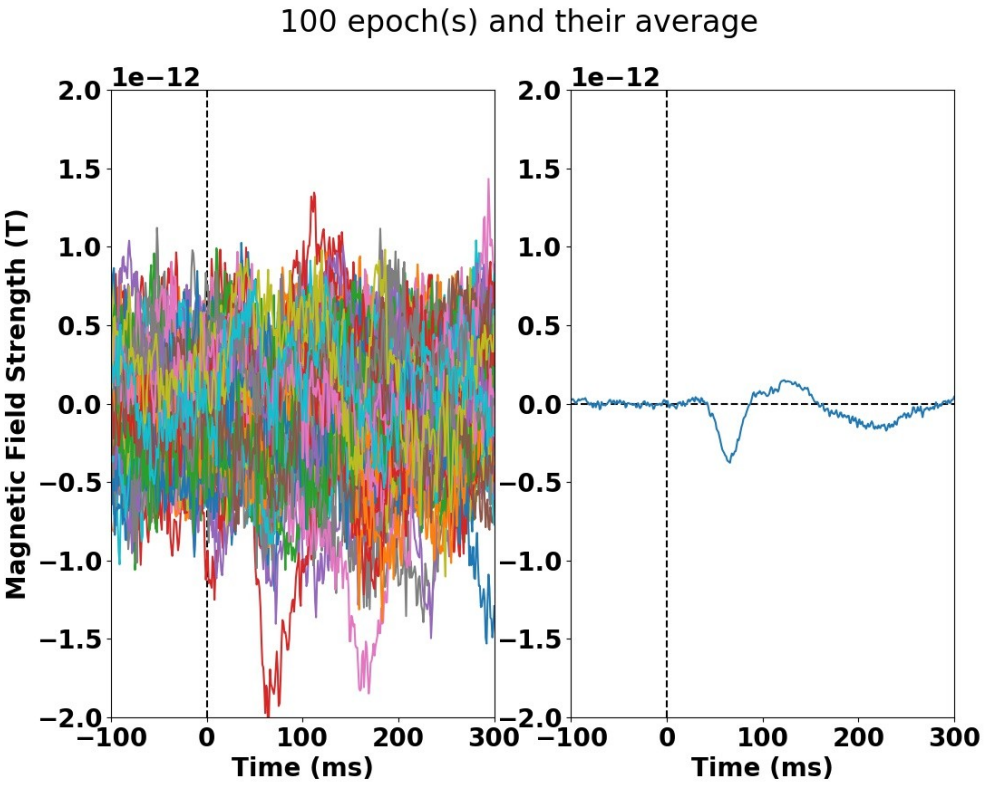


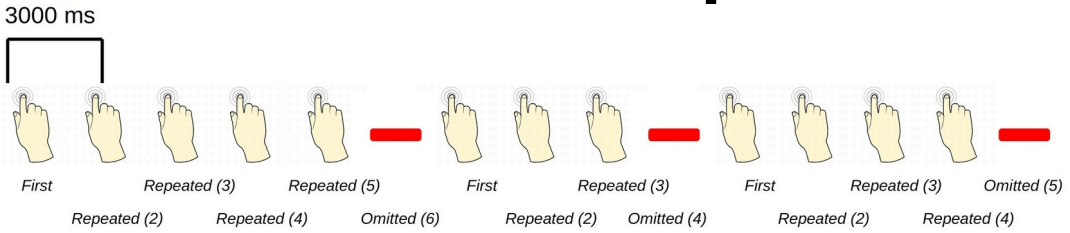


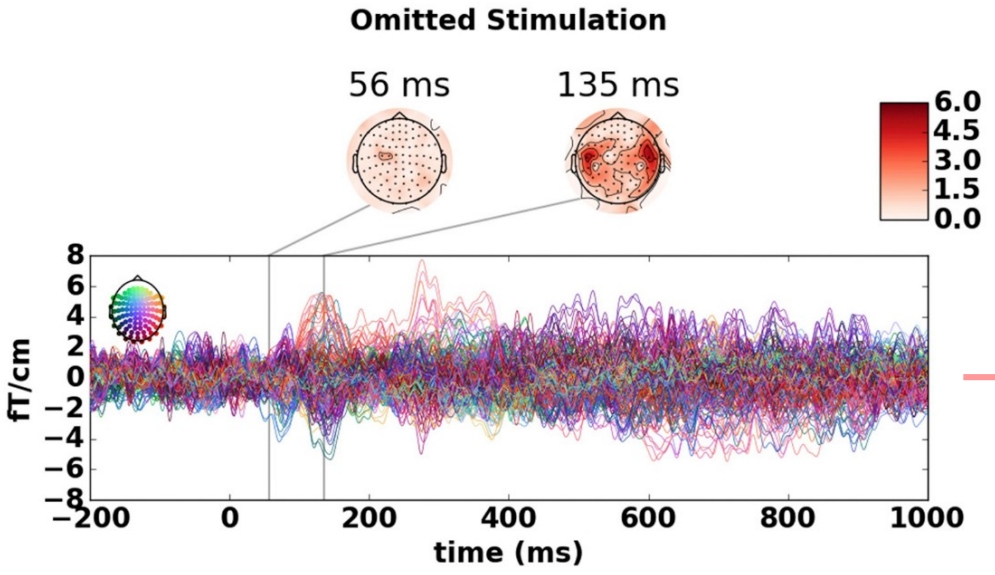
AVERAGES 101





Evoked responses from paradigm

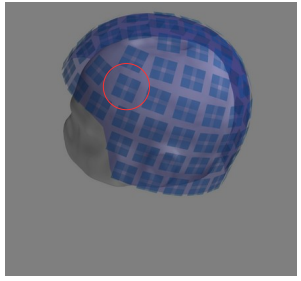


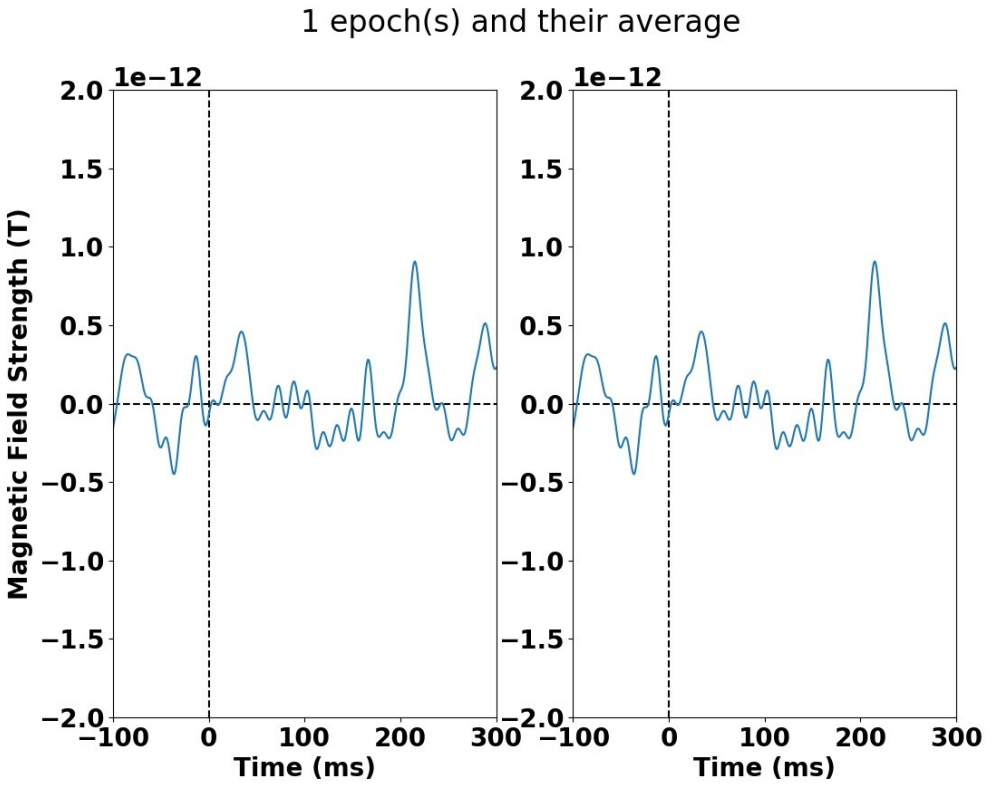


Andersen & Lundqvist 2019

135 ms

AVERAGES 101- jittered 50 ms





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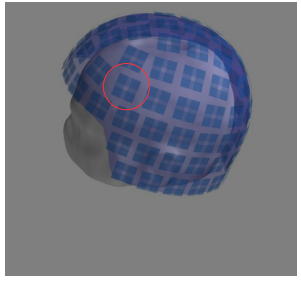
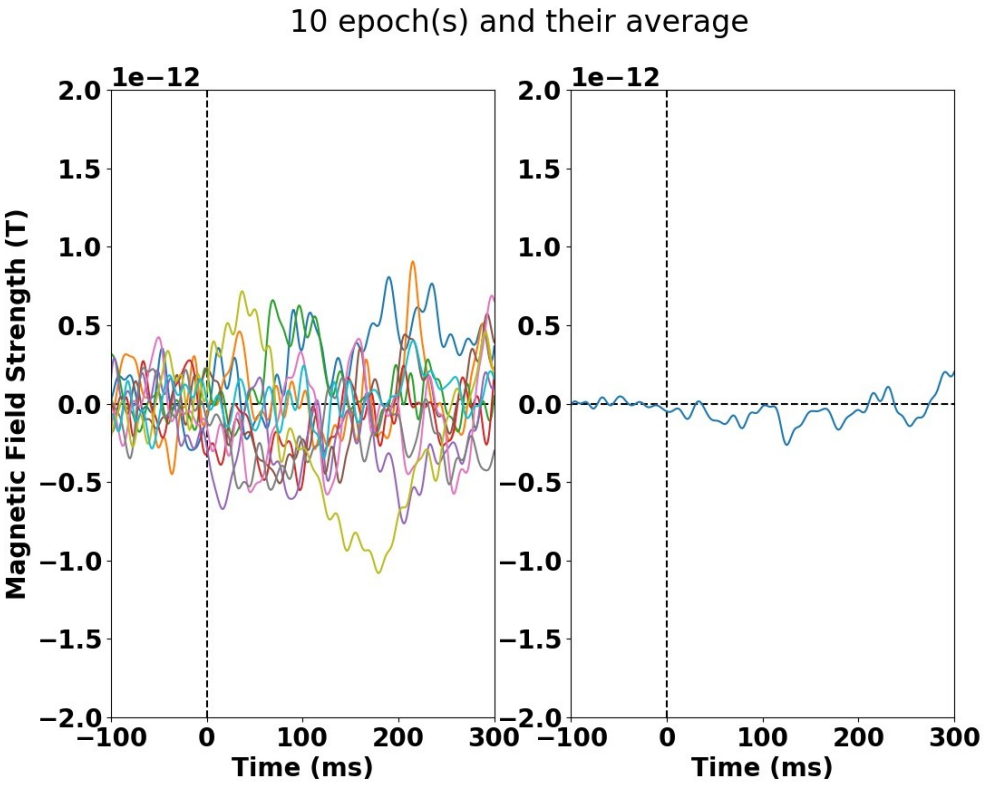
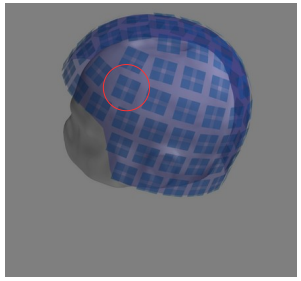
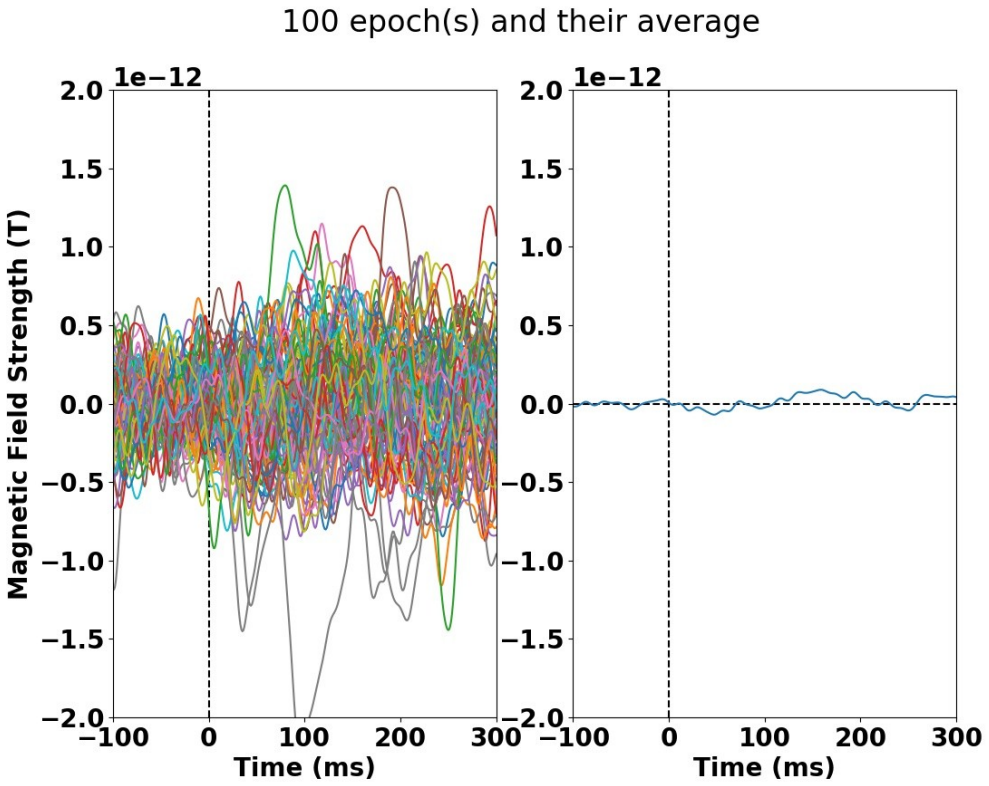




AVERAGES 101- jittered 50 ms

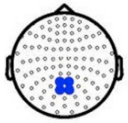


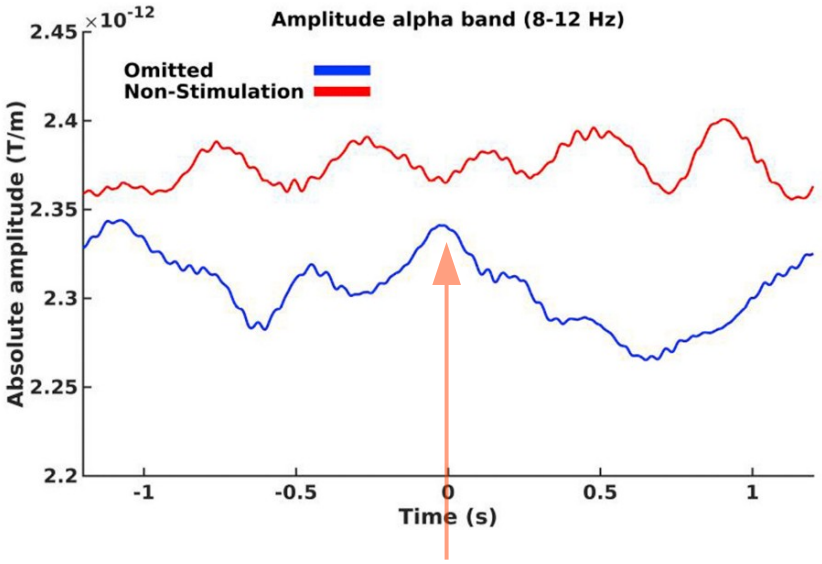


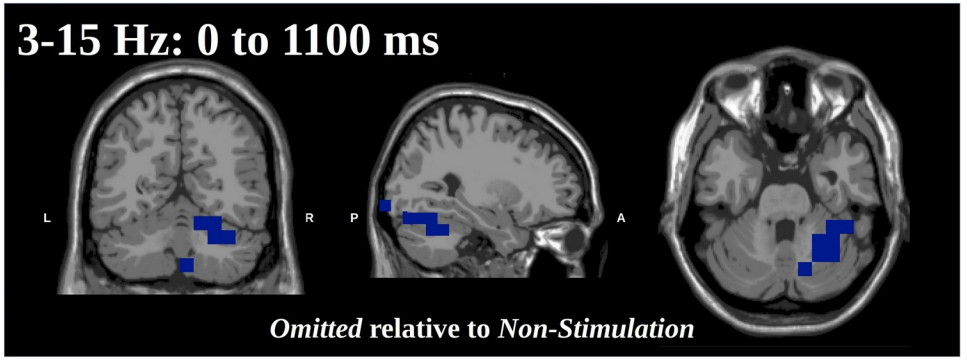
What is time zero for the omissions?

Non-stimulation differences

Andersen & Lundqvist 2019

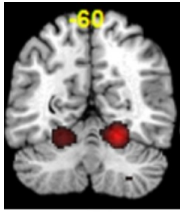






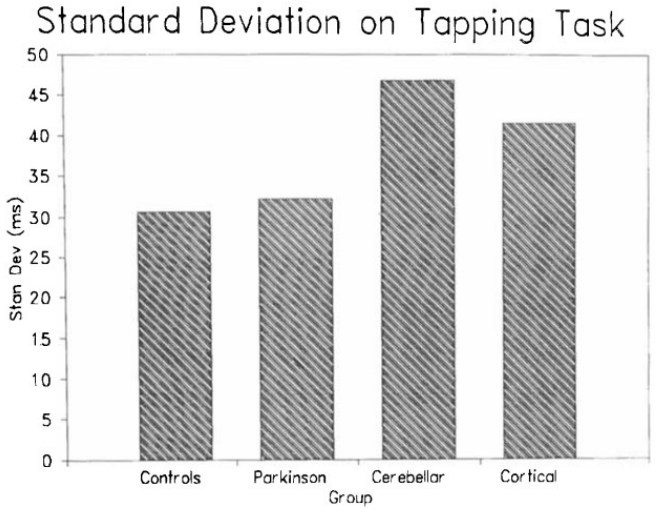
Tonic difference – no time dependency

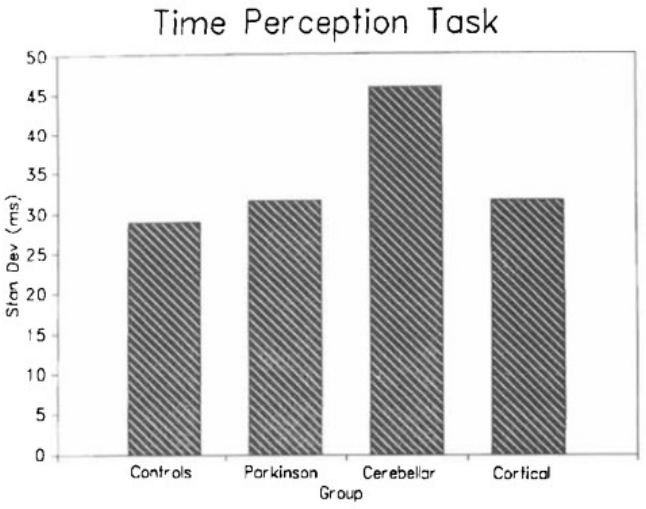
but anything to be made from this peak?!

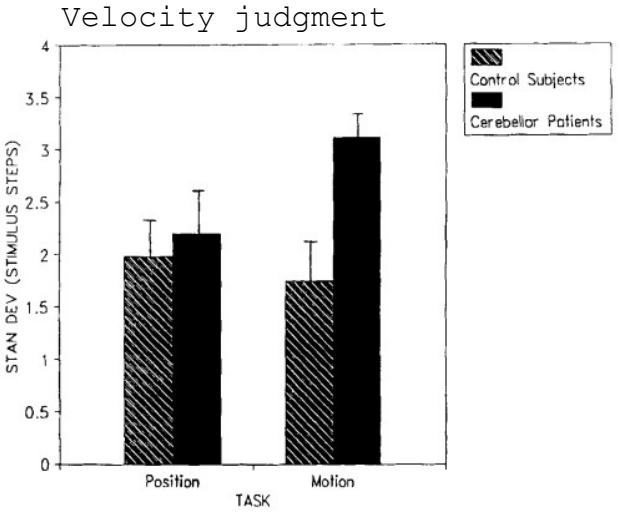


Keren-Happuch et al. 2014

Cerebellum and timing



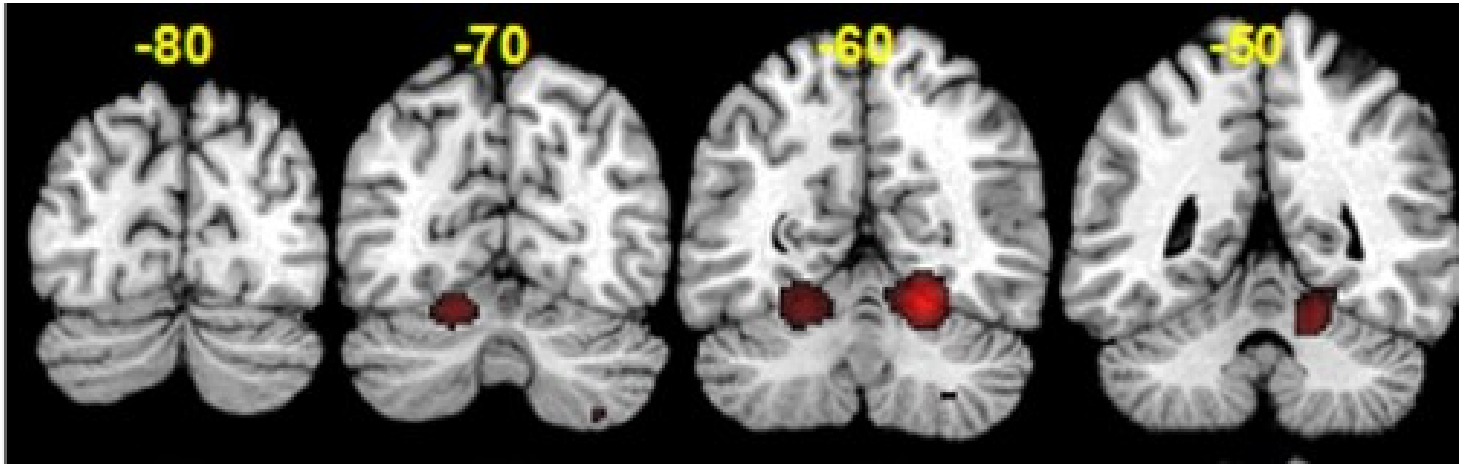




Ivry 1993

Meta-analysis of 36 fMRI and PET timing studies

Timing



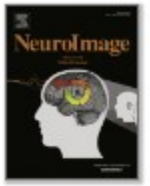
Keren-Happuch et al. 2014

INTERPRETATION

Something is clocking when stimuli should appear?

Is it the cerebellum?

NeuroImage
Volume 238, September 2021, 118202



The cerebellar clock: Predicting and timing somatosensory touch

Lau M. Andersen [a, b, c], Sarang S. Dalal [a]

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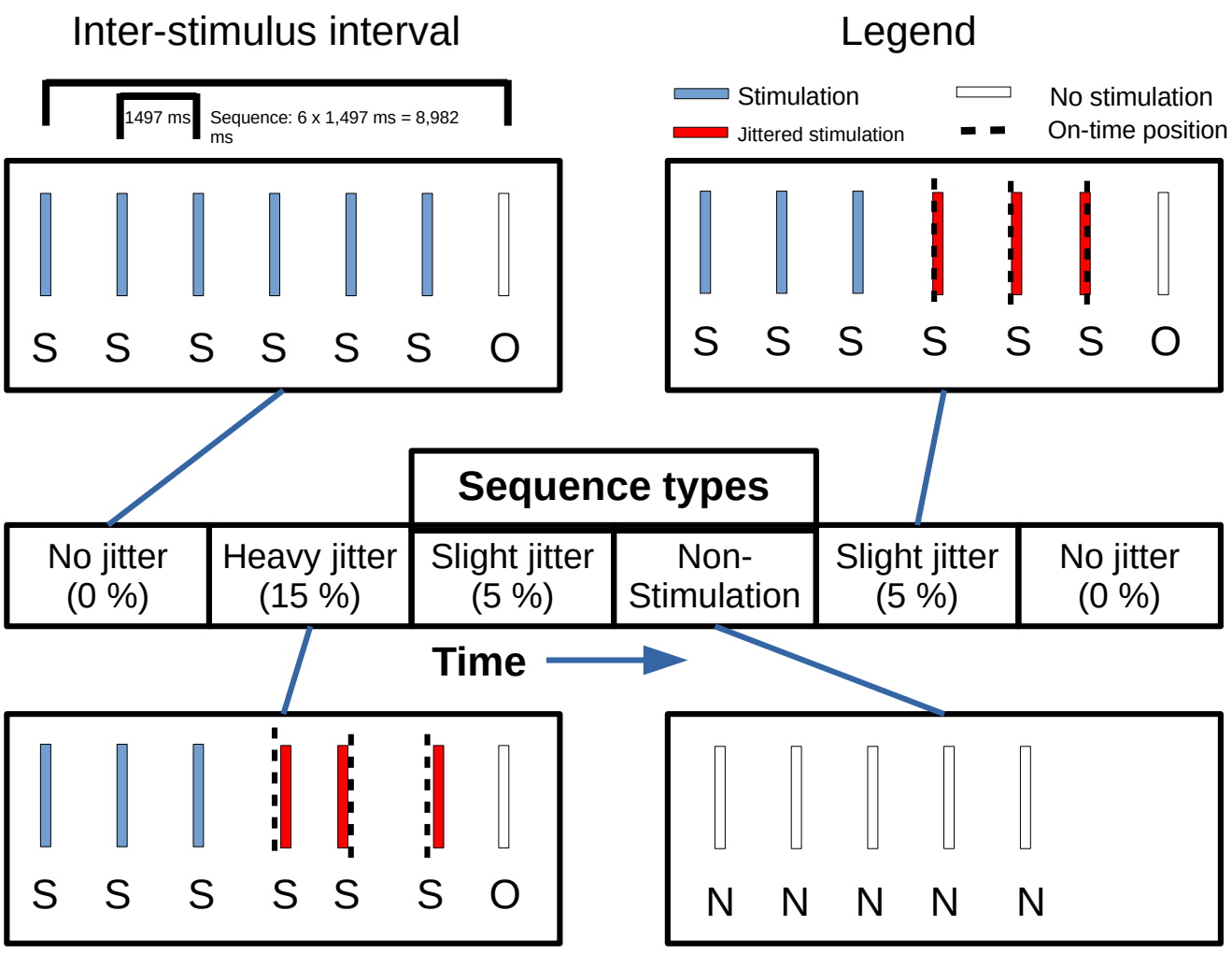
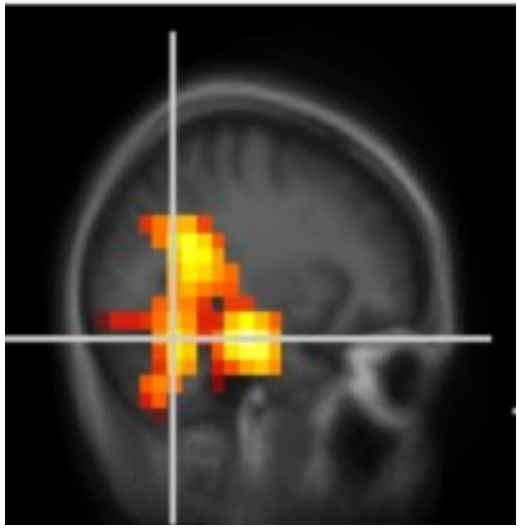
https://doi.org/10.1016/j.neuroimage.2021.118202

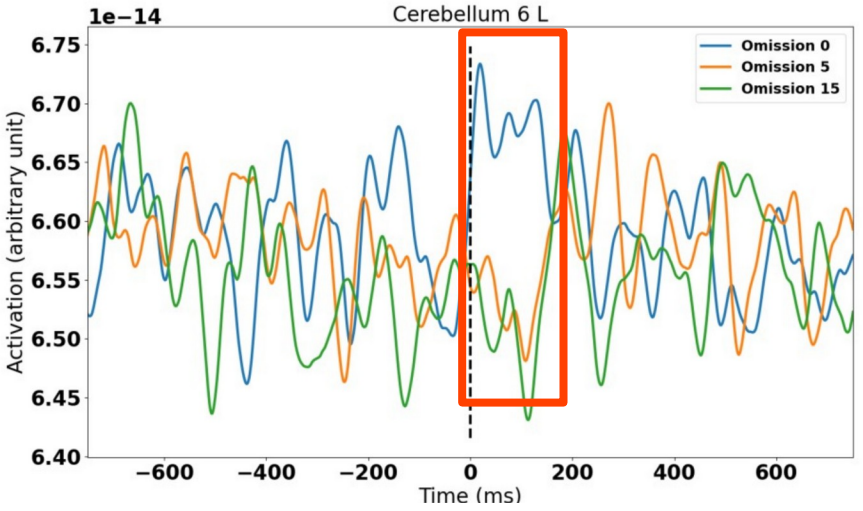


30 subjects
450 first and repeated stimulation
150 omissions of each kind

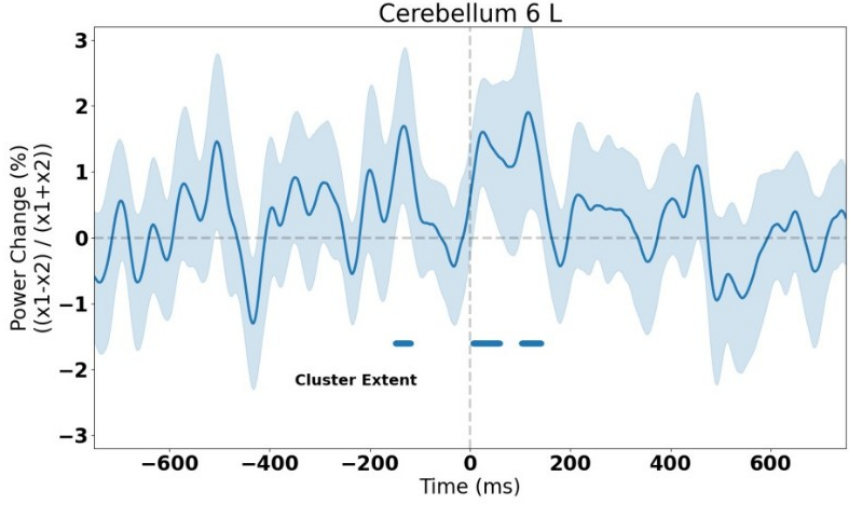
Andersen & Dalal, *2021*



Regular
Jittered ± 75 ms
Jittered ± 225 ms



Beta band (14-30 Hz)



Andersen and Dalal 2022

INTERPRETATION

The cerebellum builds expectations that are temporally sensitive

Are these expectations functionally relevant?

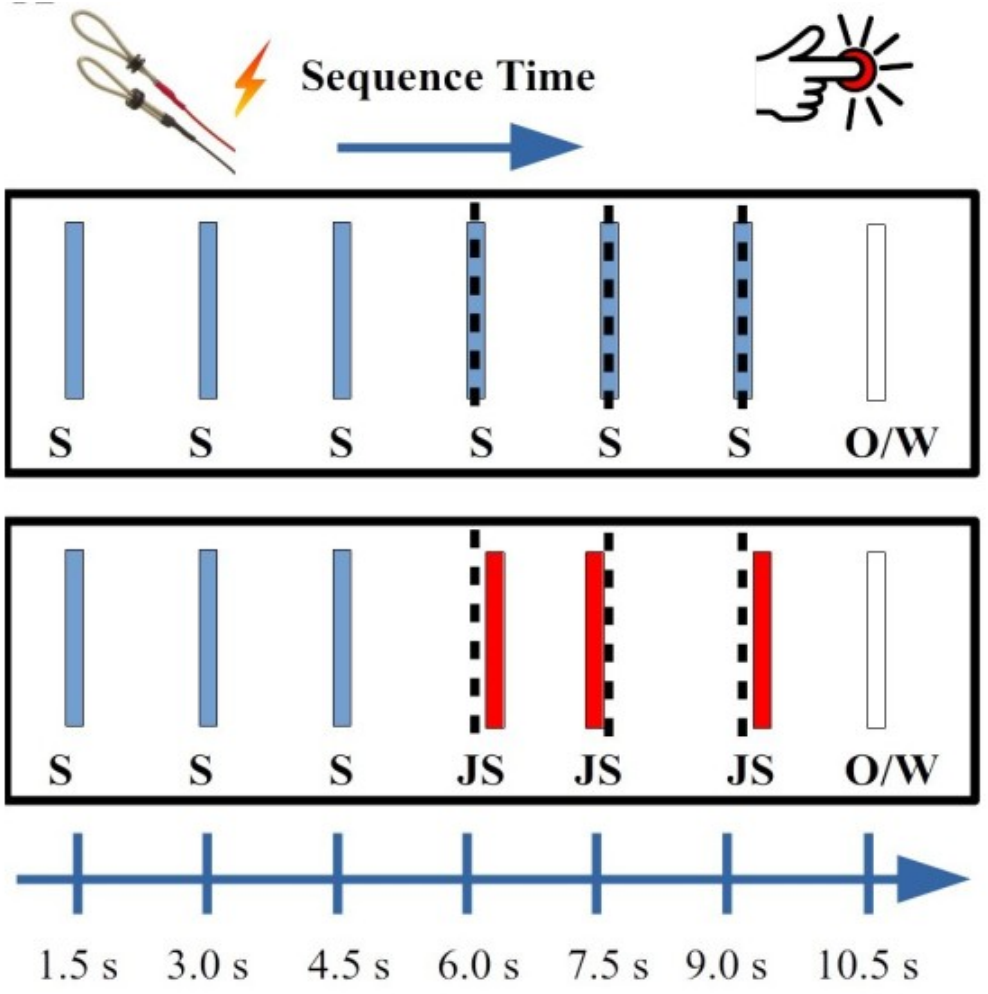
eNeuro

Research Article: New Research
Cognition and Behavior

Detection of Threshold-Level Stimuli Modulated by Temporal Predictions of the Cerebellum

Lau M. Andersen[1,2,3] and Sarang S. Dalal[1]

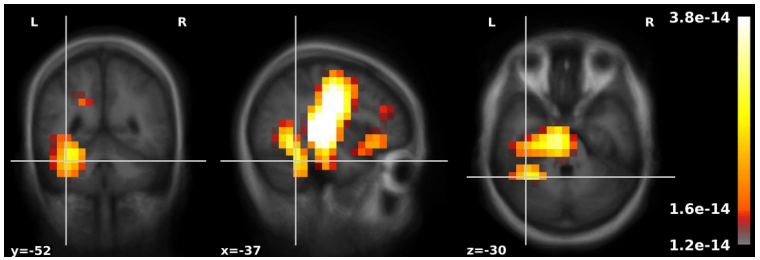
[1]Center of Functionally Integrative Neuroscience (CFIN), Aarhus University, Aarhus C 8000, Denmark, [2]Aarhus Institute of Advanced Studies (AIAS), Aarhus University, Aarhus C 8000, Denmark, and [3]Department for Linguistics, Cognitive Science and Semiotics, Aarhus University, Aarhus C 8000, Denmark

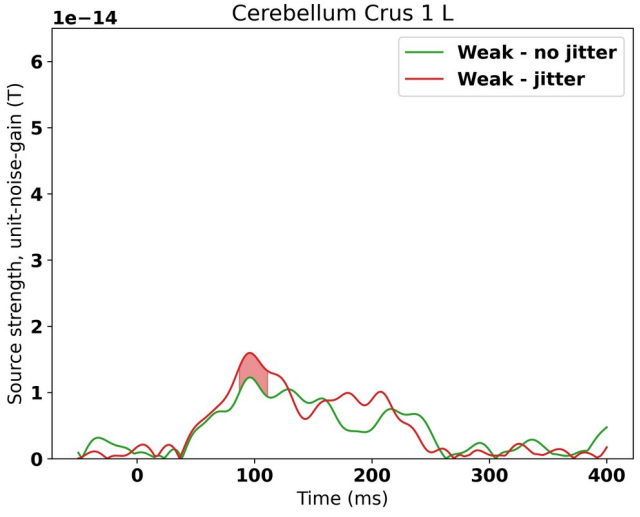


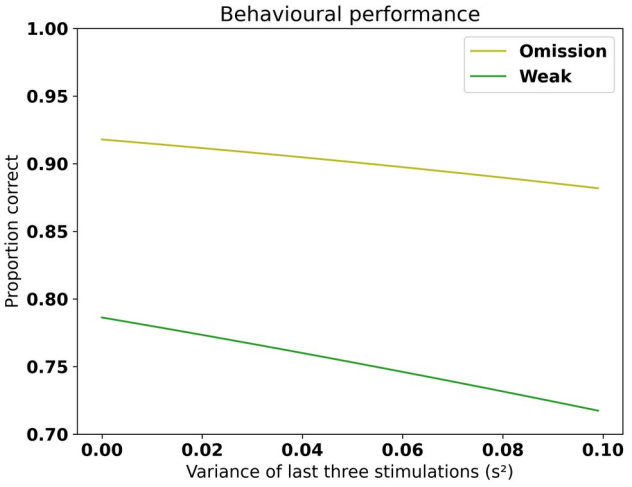
30 subjects

n trials:

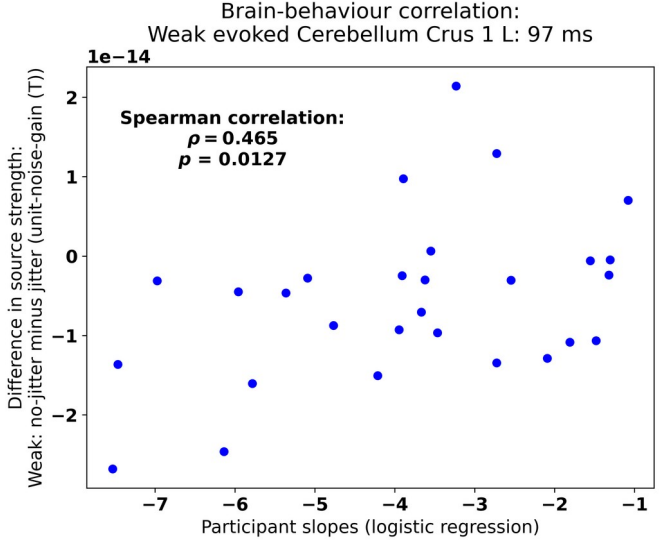
- 75 Weak Jittered
- 75 Weak regular
- 75 Omission jittered
- 75 Omission regular







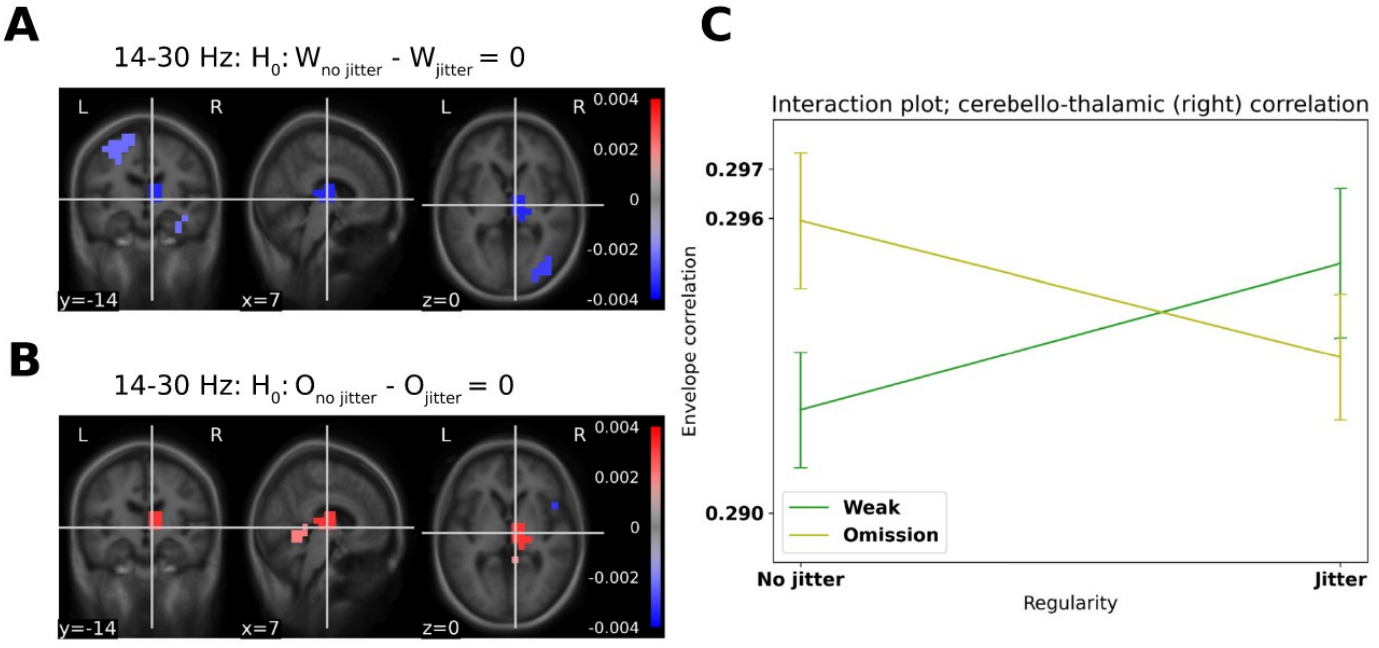
$$\sigma^2_{\text{STIMULATION}} = \sum_{i=4}^{n=6} \left(t^{(i)}_{\text{ACTUAL}} - t^{(i)}_{\text{EXPECTED}}\right)^2,$$
$$\text{with: } t^{(i)}_{\text{EXPECTED}} = 1,497\,\text{ms} \times i$$



Andersen & Dalal, 2024

Beta band connectivity

-100 ms to 100 ms

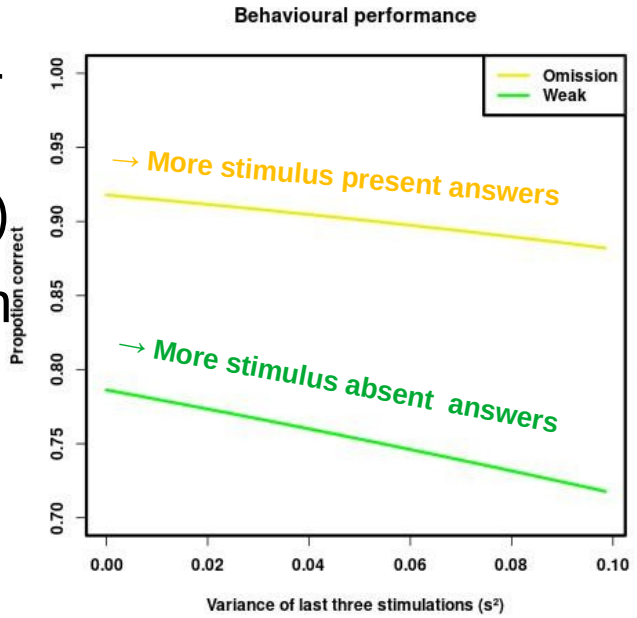


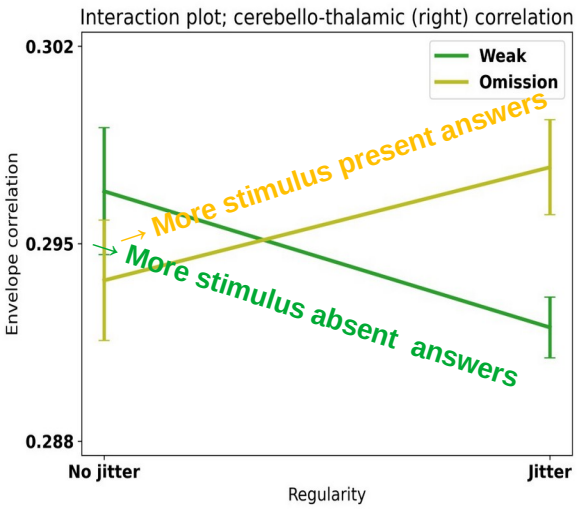
$F_{1,100} = 4.42$, $p = 0.0376$

Andersen & Dalal, 2024

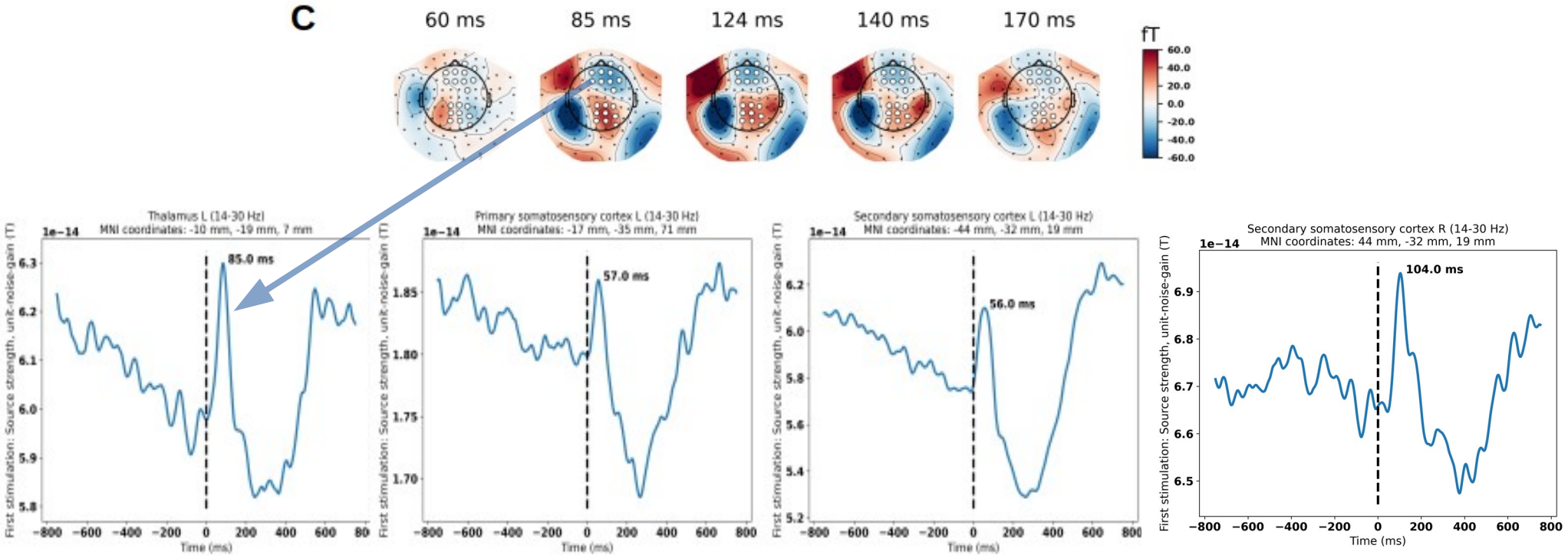
RIGHT THALAMUS

- Subjects were to deliver their answers with their **left** hand (connected to right thalamus)
- This fits with an interpretation of cerebello-thalamic correlation increasing when subjects answer “stimulus present”





IS IT REALLY THE THALAMUS?

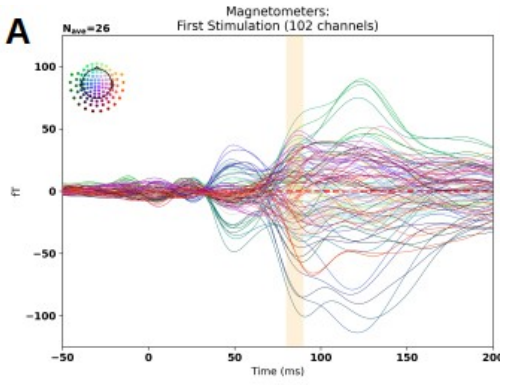


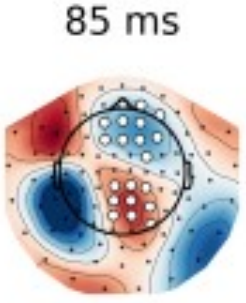
Andersen & Dalal, 2024

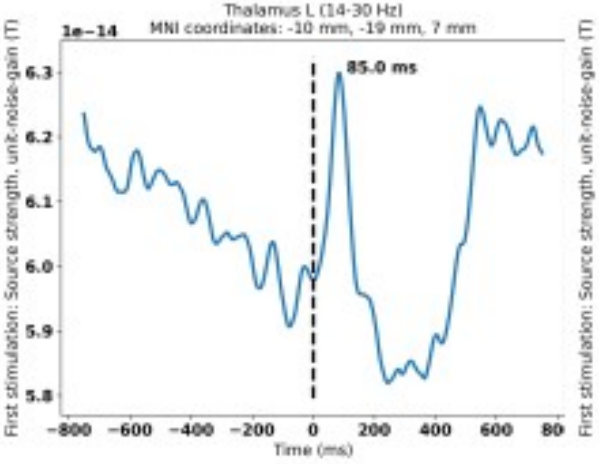
MAIN ARGUMENTS FOR DEEP ACTIVITY

1) the thalamic peak response at 85 ms for the beta band (14-30 Hz) coincides with an evoked response at 85 ms visible in sensor space

2) the topographical pattern at 85 ms for the magnetometers is compatible with a central, deep source





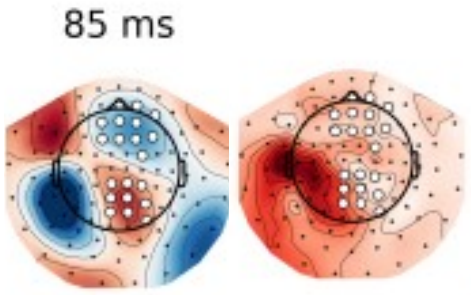


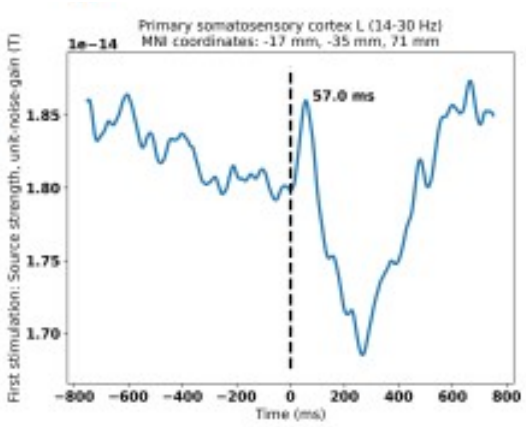
Andersen & Dalal, 2024

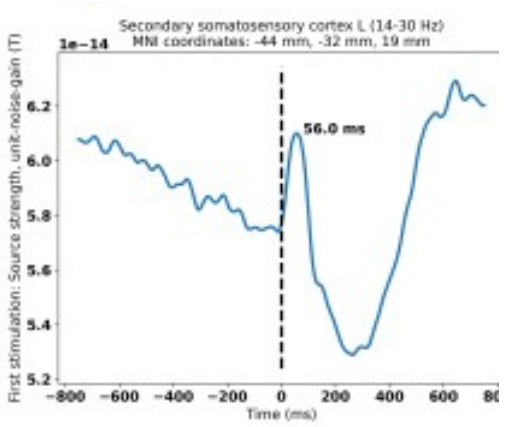
MAIN ARGUMENTS FOR DEEP ACTIVITY

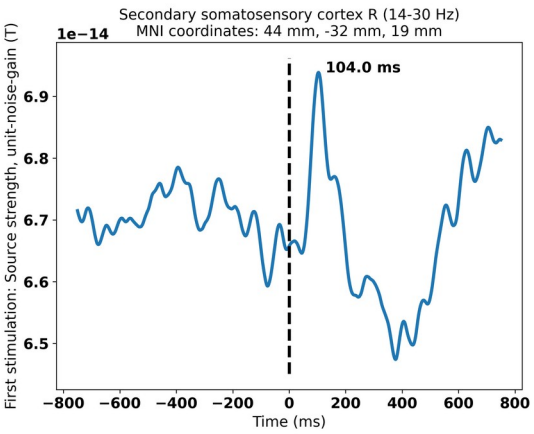
3) the topographical pattern at 85 ms (or later) for the planar gradiometers does not include a similar, central activation, but only a lateral one

4) neither the primary somatosensory cortex nor the secondary somatosensory cortex peaked at a similar time (~55 ms & 104 ms) for the beta band







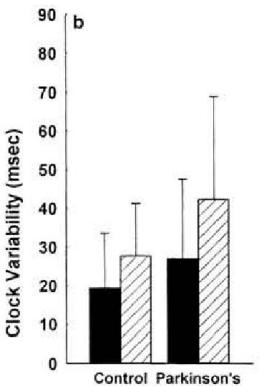


Andersen & Dalal, 2024

INTERPRETATION

Cerebellar expectations are functionally relevant to behaviour, possibly getting translated into informed action by the thalamus

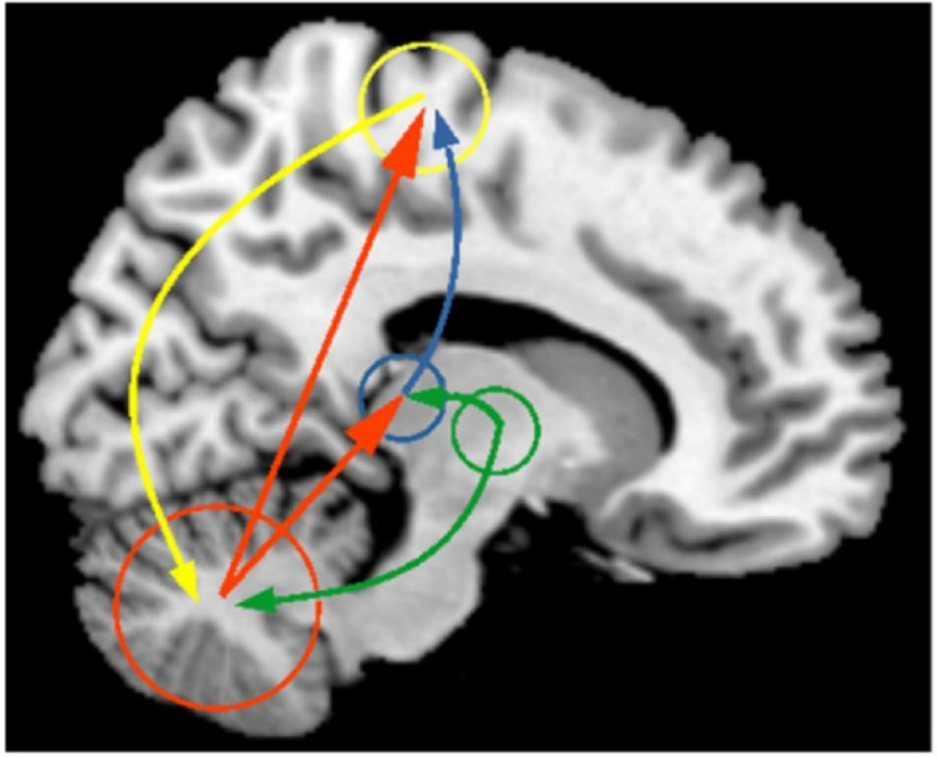
How can we learn more?
Patient groups?



Harrington DL, Haaland KY, Hermanowitz N (1998) Temporal processing in the basal ganglia. Neuropsychology 12:3–12. https://doi.org/10.1037/0894-4105.12.1.3

Proposed network of timing

OBJECTIVES



Current Opinion in Behavioral Sciences

(Andersen and Dalal, 2024a)

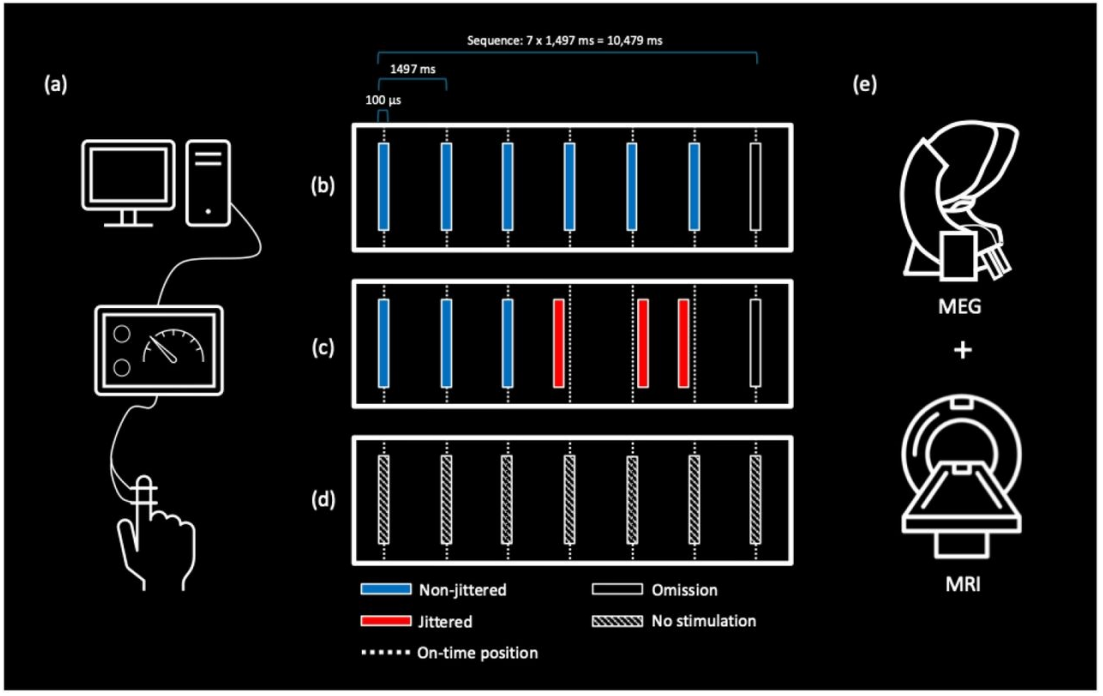
Proposed model for the cerebellum's involvement in timing action:

- *Basal ganglia passes timing information on to cerebellum*
- *Sensory expectations in the cerebellum then inform thalamus that inform primary motor cortex*
- *At the same time sensory predictions and feedback are sent back and forth between cerebellum and primary motor cortex*

CHALLENGES FROM AN MEG PERSPECTIVE

Thalamus and basal ganglia are deeply located with a less-than-optimal field structure

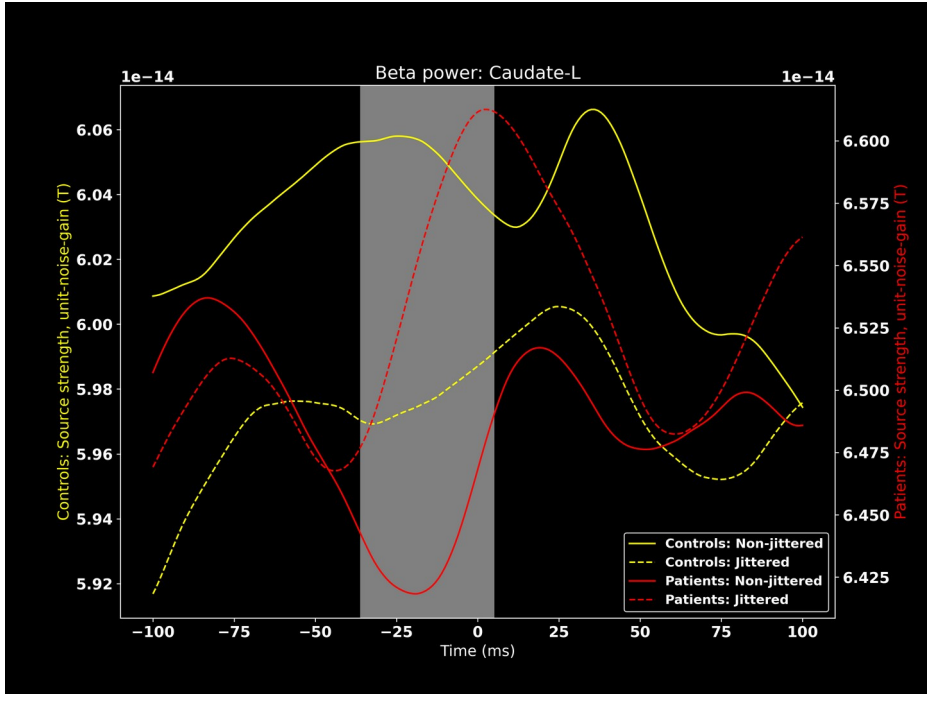
Parkinson’s disease

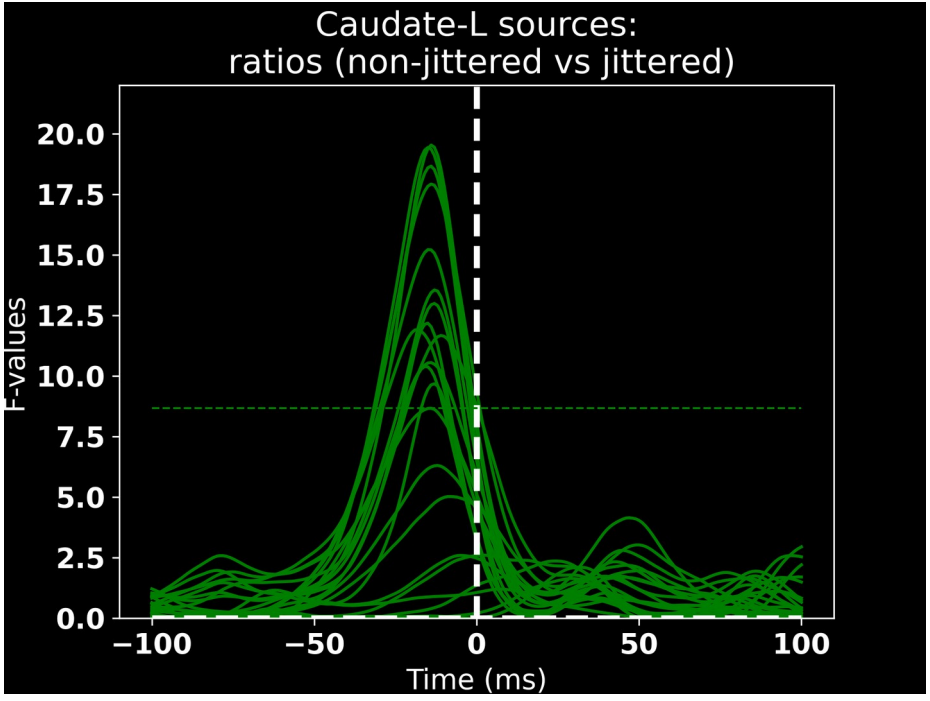


(Pando-Naude and Andersen 2025)

Parkinson’s disease

CAUDATE (BASAL GANGLIA)

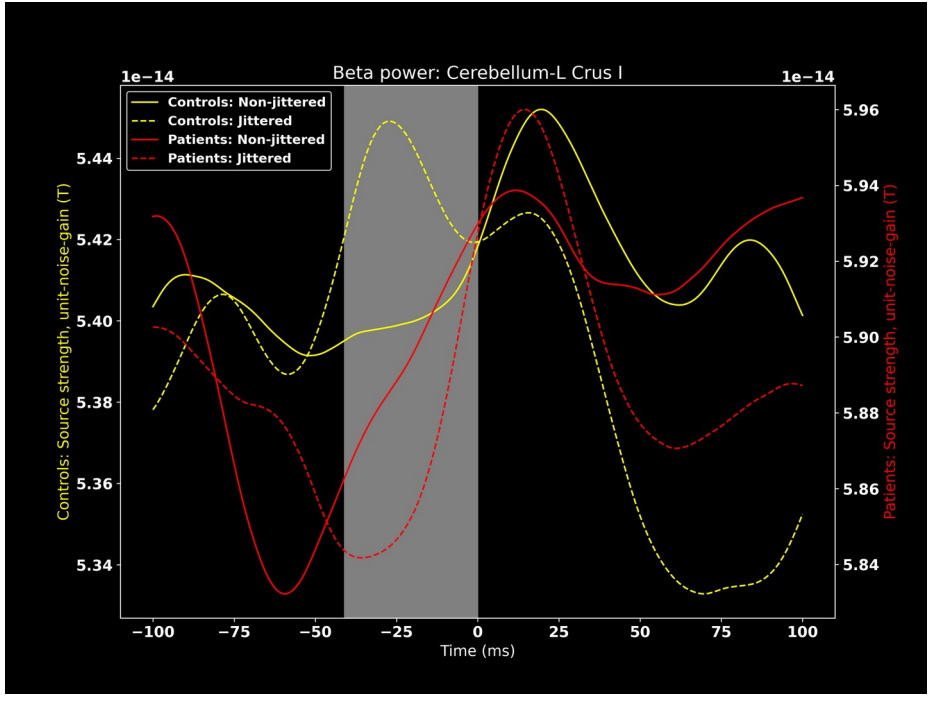


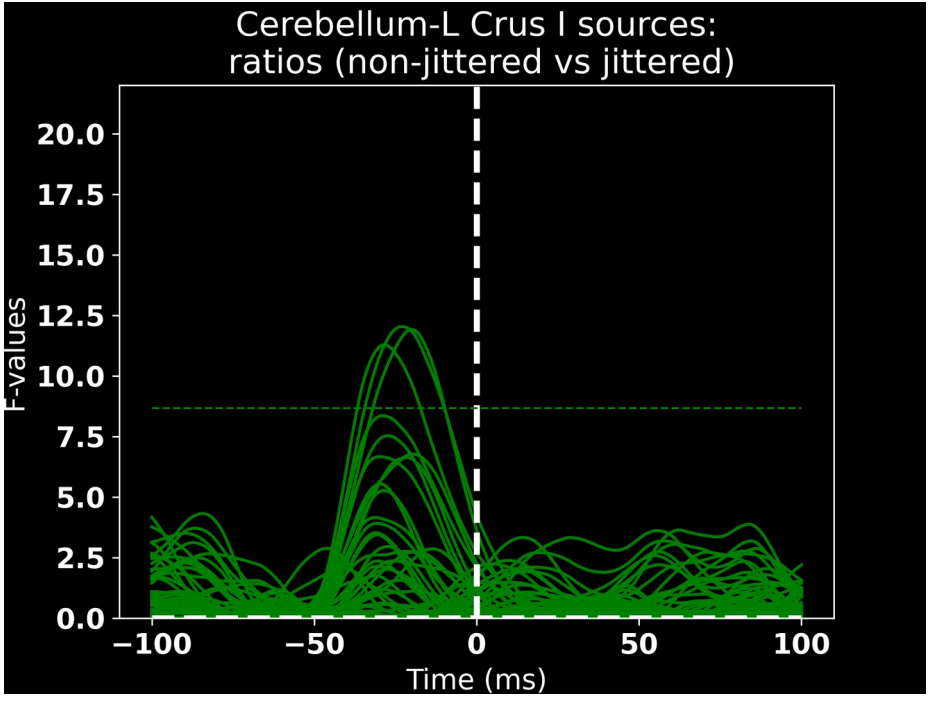


(Pando-Naude and Andersen 2025)

Parkinson’s disease

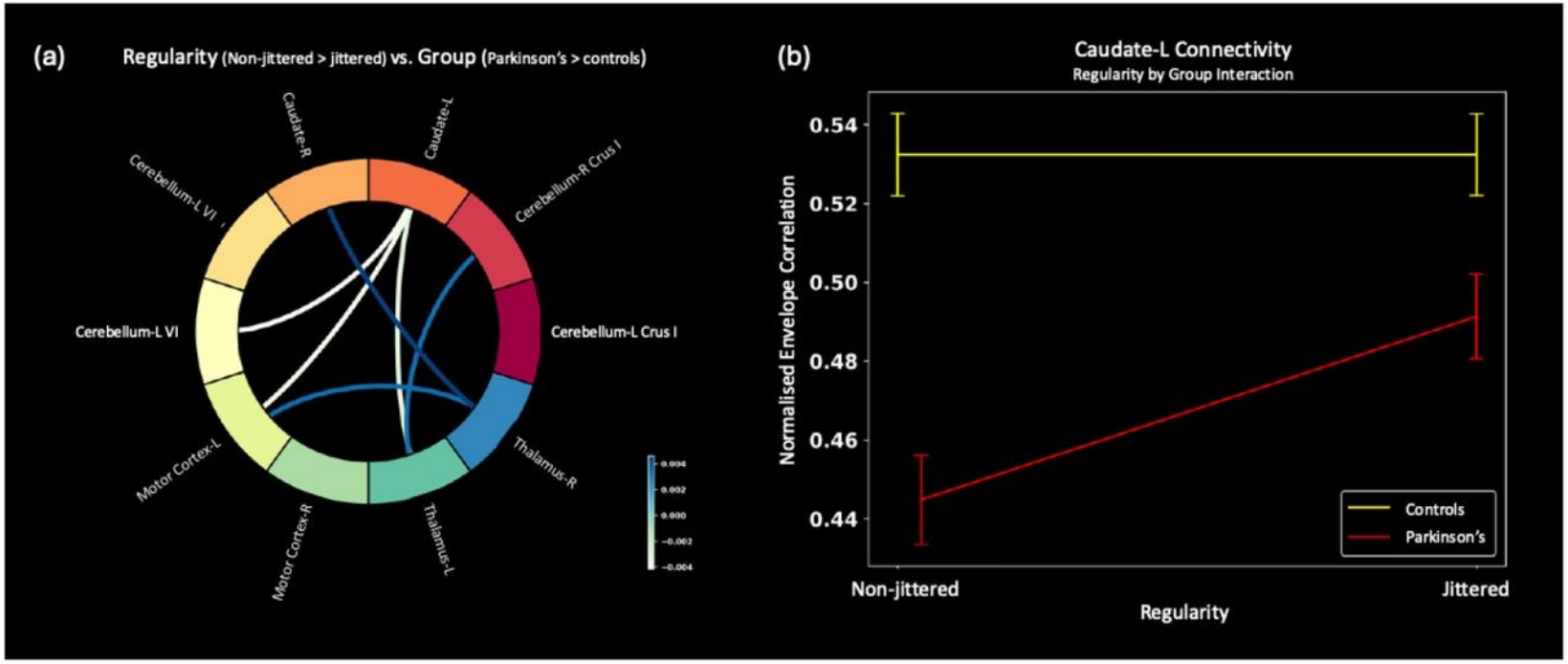
CEREBELLUM





(Pando-Naude and Andersen 2025)

Parkinson’s disease



(Pando-Naude and Andersen 2025)

INTERPRETATION

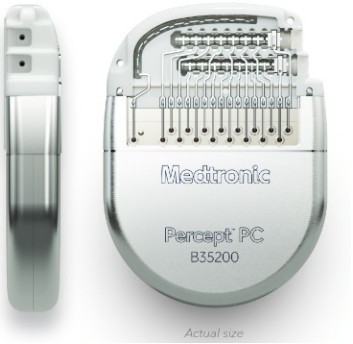
Basal ganglia involved in timing. When dysfunctional, cerebellum may compensate.

Can we acquire causal evidence?

Final summary

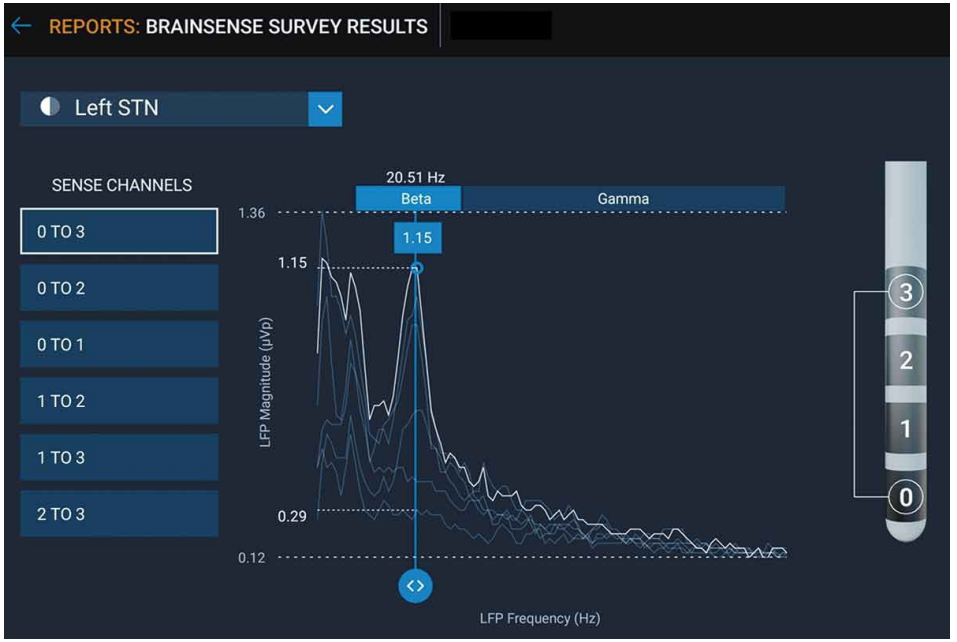
- We can measure the cerebellum using MEG and EEG
- The cerebellum builds sensory and temporal expectations
- These expectations are functionally relevant, making informed behaviour possible (through thalamus)
- Timing responses in basala ganglia and cerebellum, are different in Parkinson’s disease
- Cerebellar-basal-ganglia-thalamic disruptions in connectivity underlie differences in Parkinson’s disease patients?
- Further questions for the future:
  - Do optically pumped magnetomers allow for better cerebellar MEG? (Barbara)
  - Does respiration modulate cerebellar timing-related activity? (Laura)
  - Can we causally change my proposed timing network by turning on and off DBS?

Brief look at the future



Deep brain stimulation

By Svenskbygderna (talk) - Spiral drawing - essential tremor.jpg by Undescribed, CC BY-SA 4.0, https://commons.wikimedia.org/w/index.php?curid=78497463



Deep brain stimulation **and** sensing

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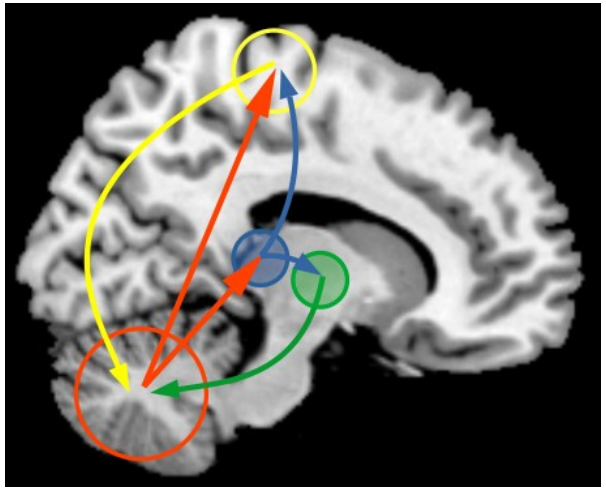
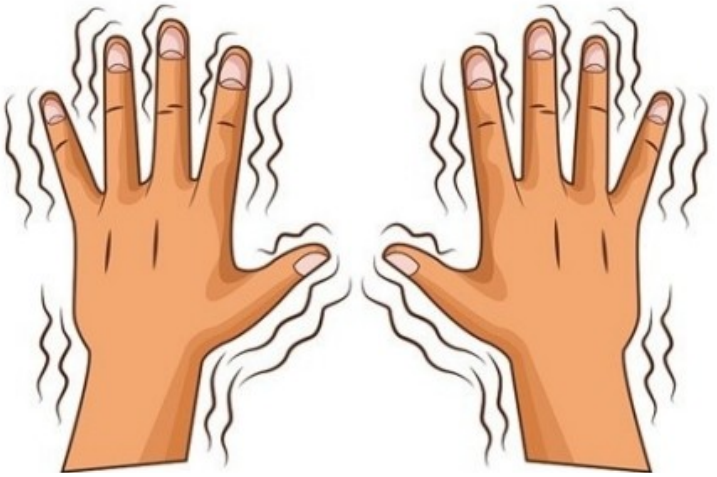
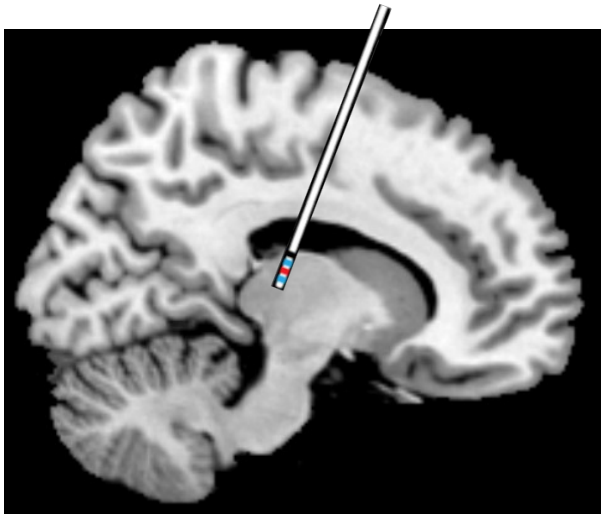
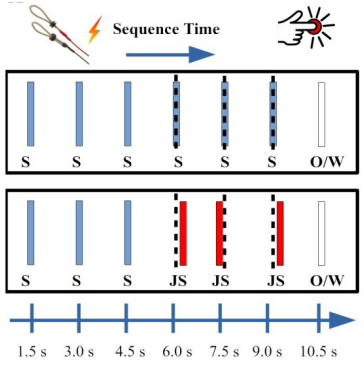
Line Elgaard Kruse Danielsen

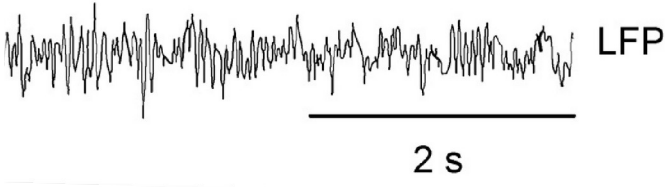


Essential tremor Parkinson's disease









The cerebellum translates sensory expectations into informed action

CFIN www.cfin.au.dk

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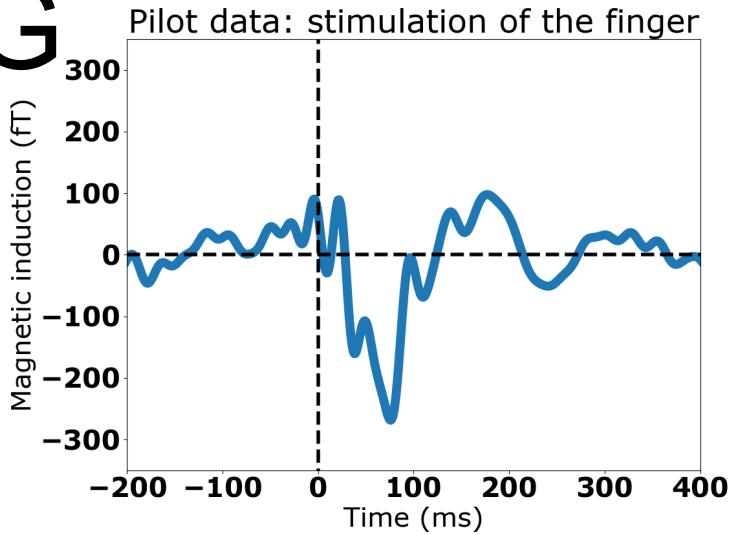
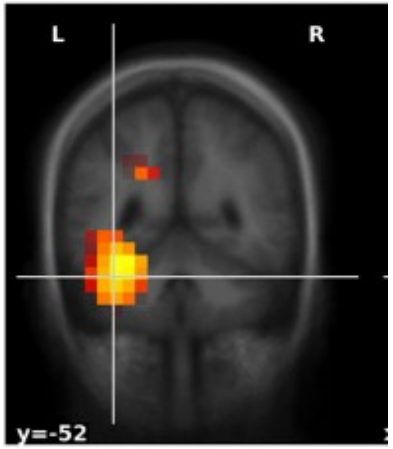
OPM MEG

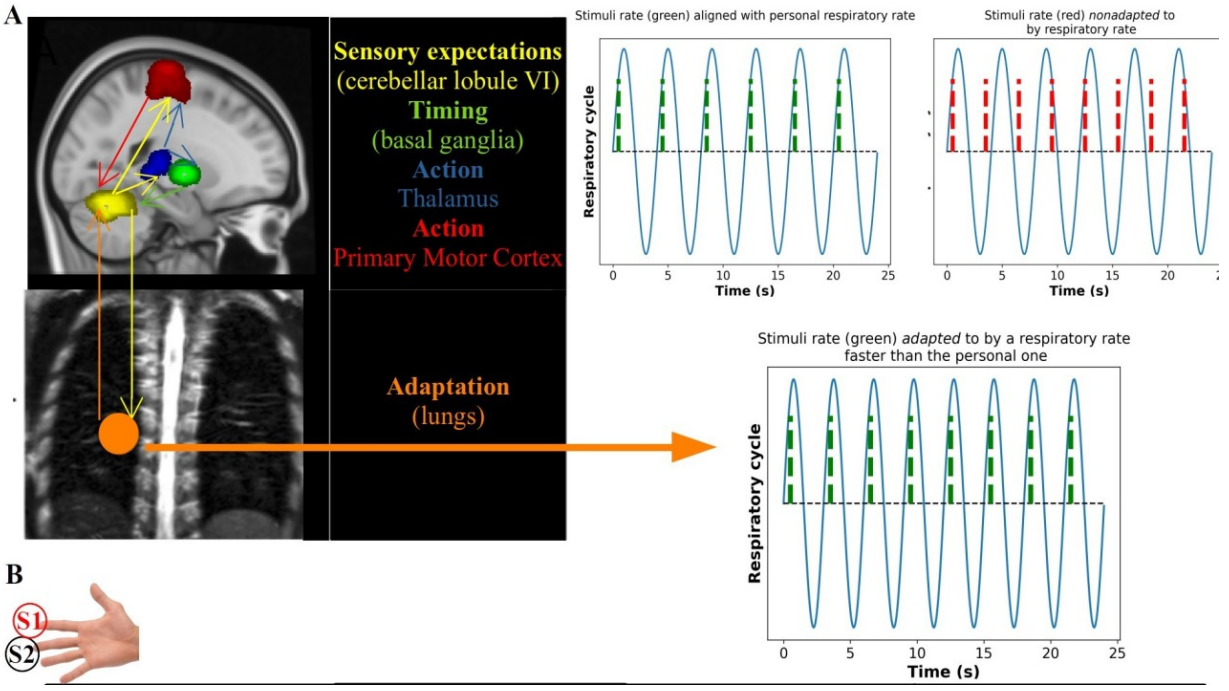
Laura Bock Paulsen
PhD student





Respiration and the cerebellum

Laura Bock Paulsen
PhD student



The course plan

Week 36:
Lesson 0: What is it all about?
Class 0: Setting up UCloud and installing MNE-Python

Week 37:
No Teaching

Week 38:
Lesson 1: Workshop paradigm: Measuring visual subjective experience + MR Recordings
Class 1: Running an MEG analysis of visual responses

Week 39:
MEG workshop: Measuring and predicting visual subjective experience

Week 40:
Lesson 2: Basic physiology and Evoked responses
Class 2: Evoked responses to different levels of subjective experience

Week 41:
Lesson 3: Multivariate statistics
Class 3: Predicting subjective experience in sensor space
Deadline for feedback: Video Explainer

Week 42:
Autumn Break

Week 43:
Lesson 4: Forward modelling and dipole estimation
Class 4: Creating a forward model and fitting dipoles

Week 44:
Lesson 5: Inverse modelling: Minimum-norm estimate
Class 5: Predicting subjective experience in source space

Week 45:
Lesson 6: Inverse modelling: Beamforming
Class 6: Predicting subjective experience in source space, continued

Week 46:
Lesson 7: What about that other cortex? - the cerebellar one
Class 7: Oral presentations (part 1)
Deadline for feedback: Lab report

Week 47:
Lesson 8: Guest lecture: Laura Bock Paulsen: Respiratory analyses
Class 8: Oral presentations (part 2)

Week 48:
Lesson 9: Guest lecture: Barbara Pomiechowska: Using OPM-MEG to study brain and cognitive development in infancy
Class 9: Oral presentations (part 3)

Week 49:
Lesson 0 again: What was it all about?
Class 10: Oral presentations (part 4)

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Reading questions

- None yet (some may come)

Next class – oral presentations (part 1)