The eyes are the window to ~~the soul~~ *brain excitability*

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Project StimulEYE was made possible through the *Mary Elizabeth Horney Fellowship in Rehabilitation* provided by St. Joseph's Health Care Foundation.

Measuring TMS responses

TMS: Transcranial Magnetic Stimulation

Measuring TMS responses

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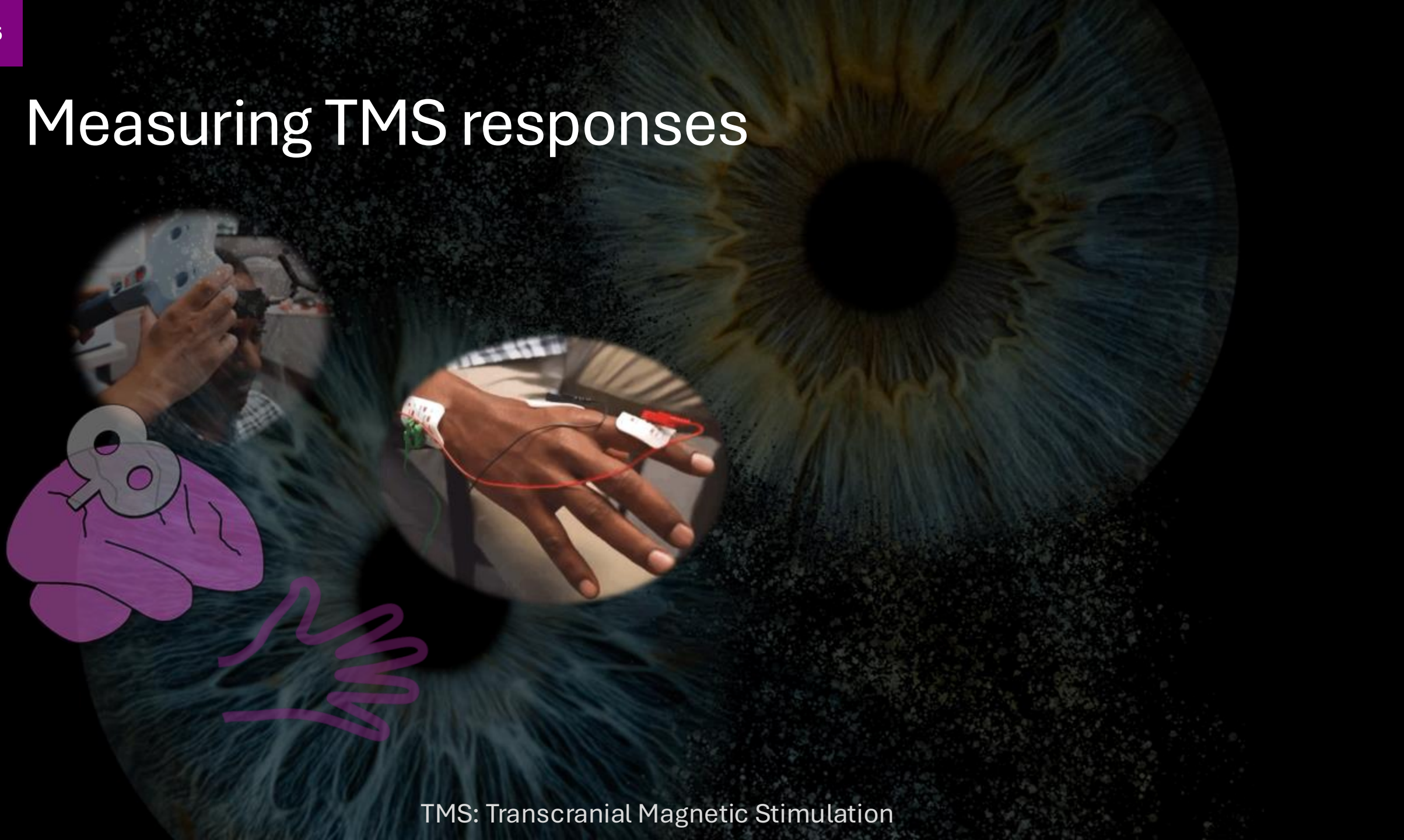
Measuring TMS responses



TMS: Transcranial Magnetic Stimulation

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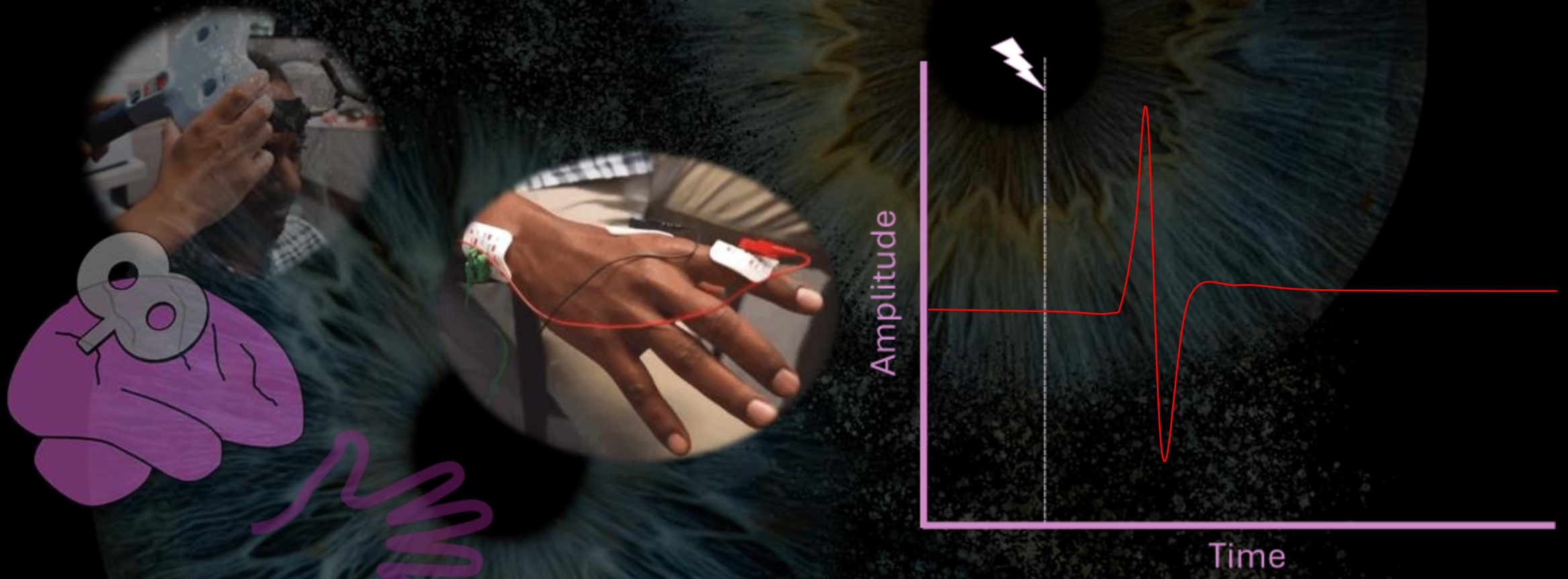
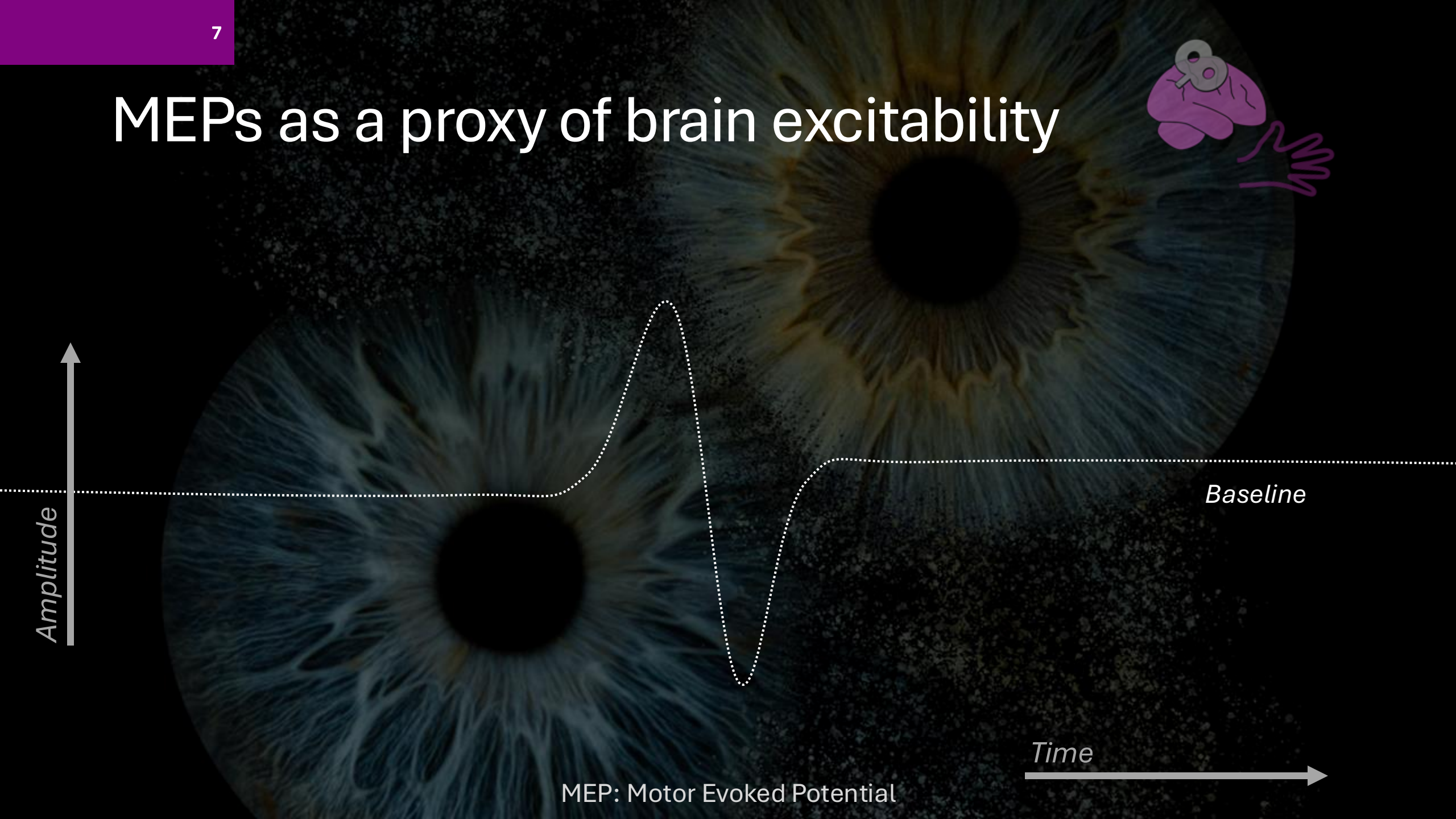


TMS: Transcranial Magnetic Stimulation

MEPs as a proxy of brain excitability



MEP: Motor Evoked Potential

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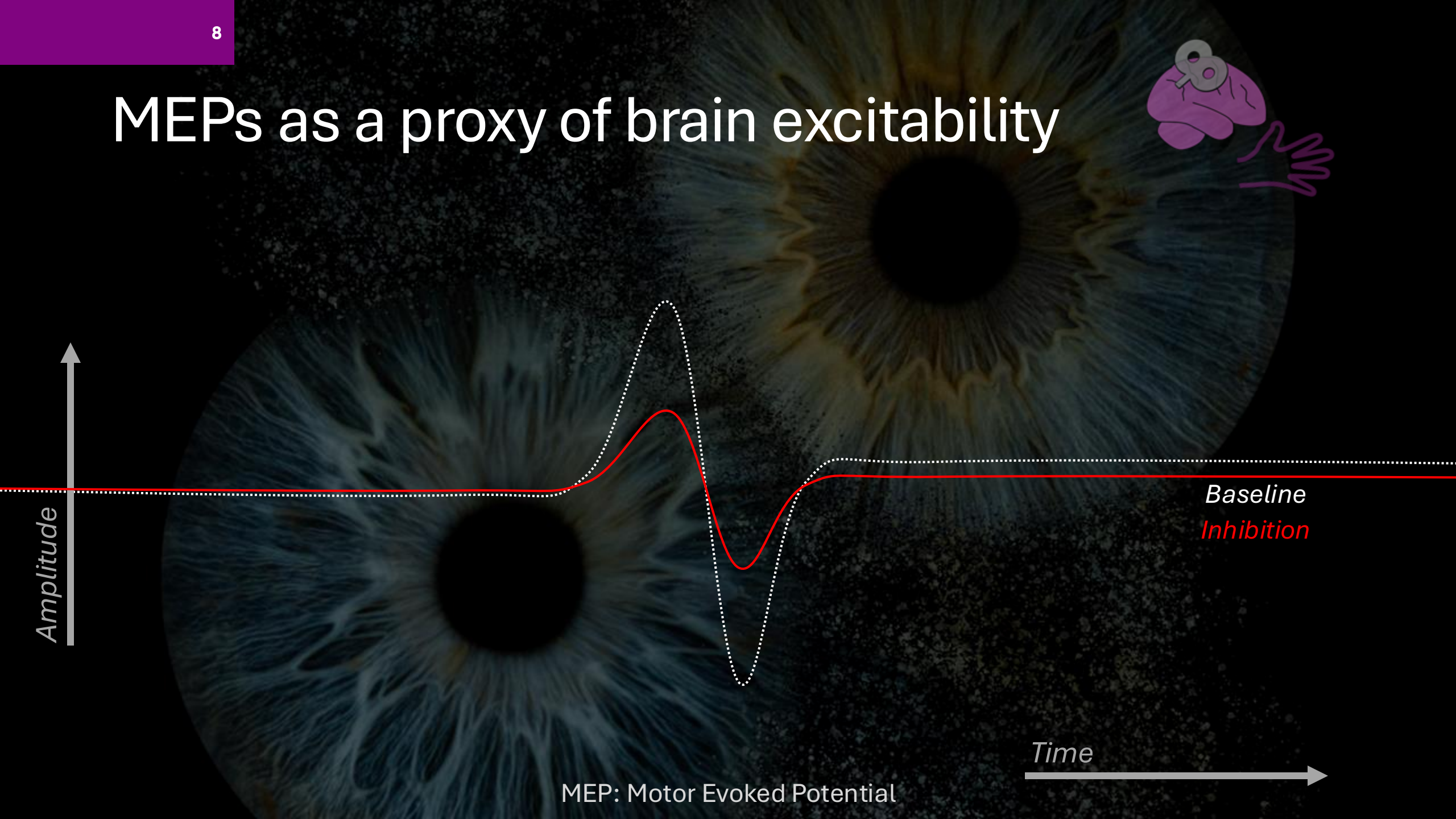

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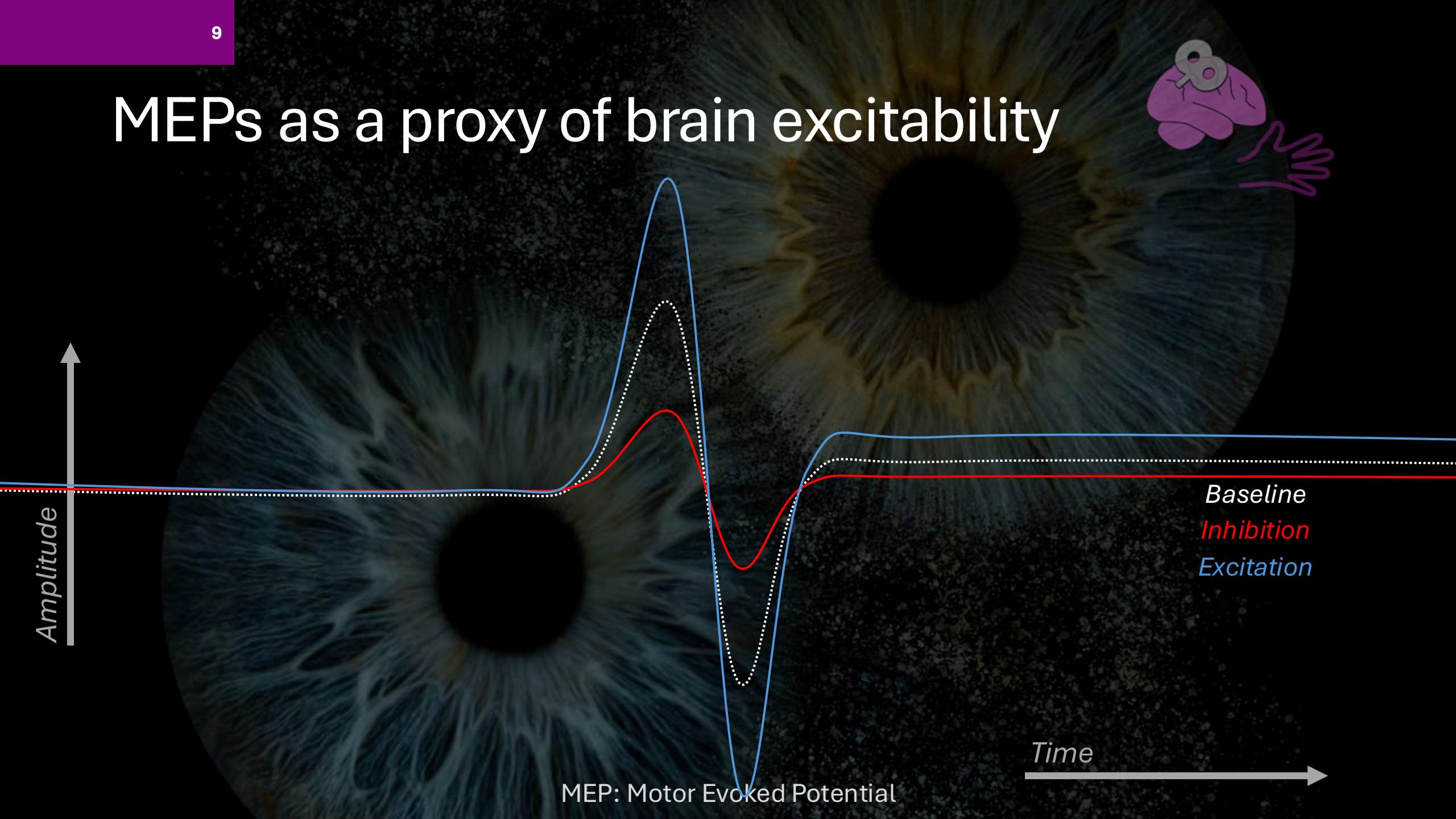


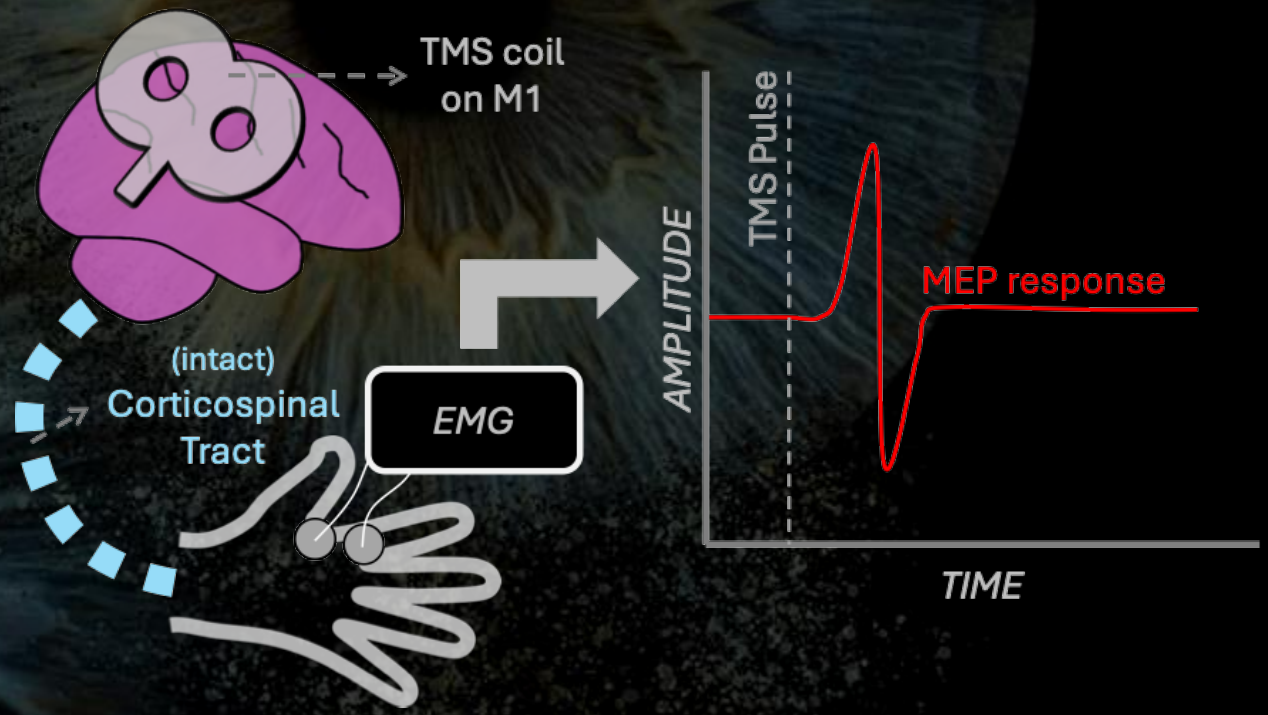
MEP: Motor Evoked Potential

But there’s a problem…

Corticospinal pathway

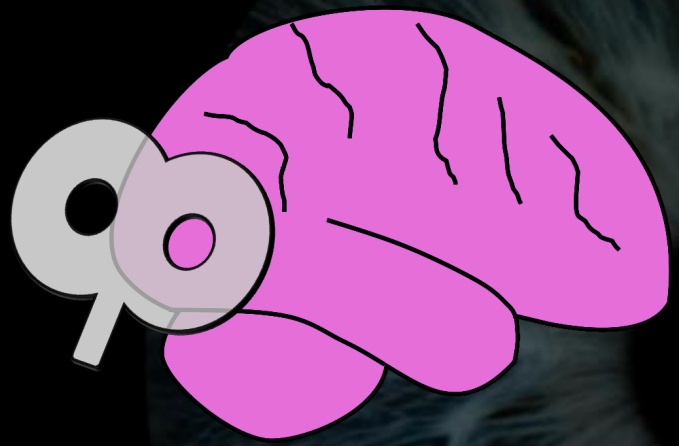
Limitations

- Excludes individuals with damage along the pathway
- Restricted within M1



TMS: Transcranial Magnetic Stimulation; M1: Primary Motor Cortex; EMG: Electromyography; MEP: Motor Evoked Potential

Alternatively…

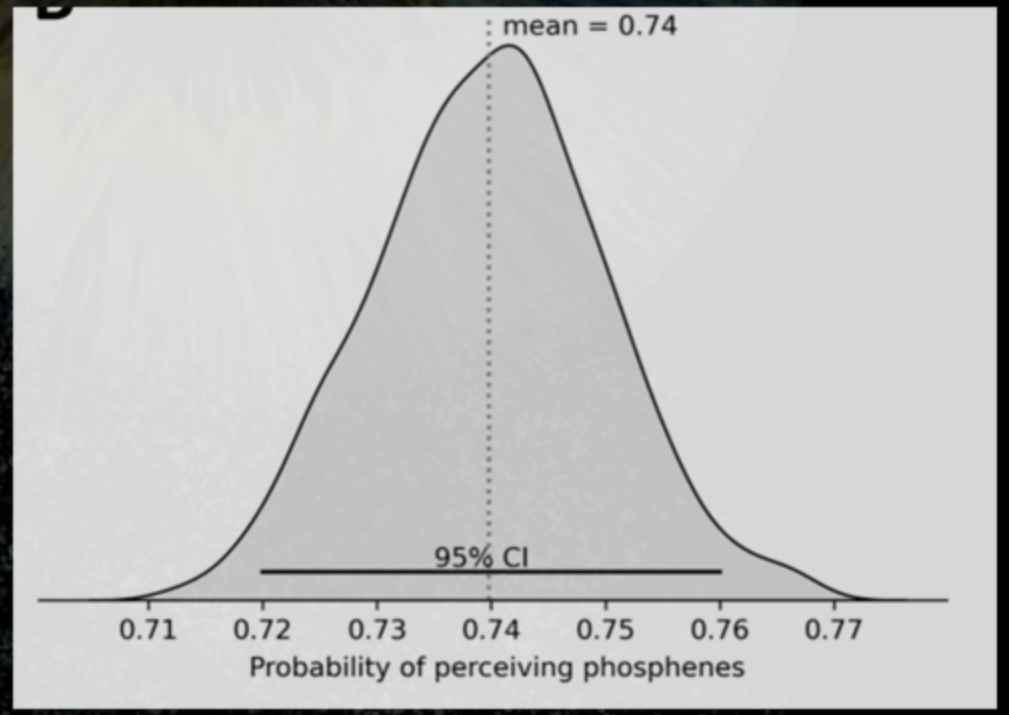


CORRESPONDENCE · Volume 16, Issue 1, P23-24, January-February, 2023
Open Access

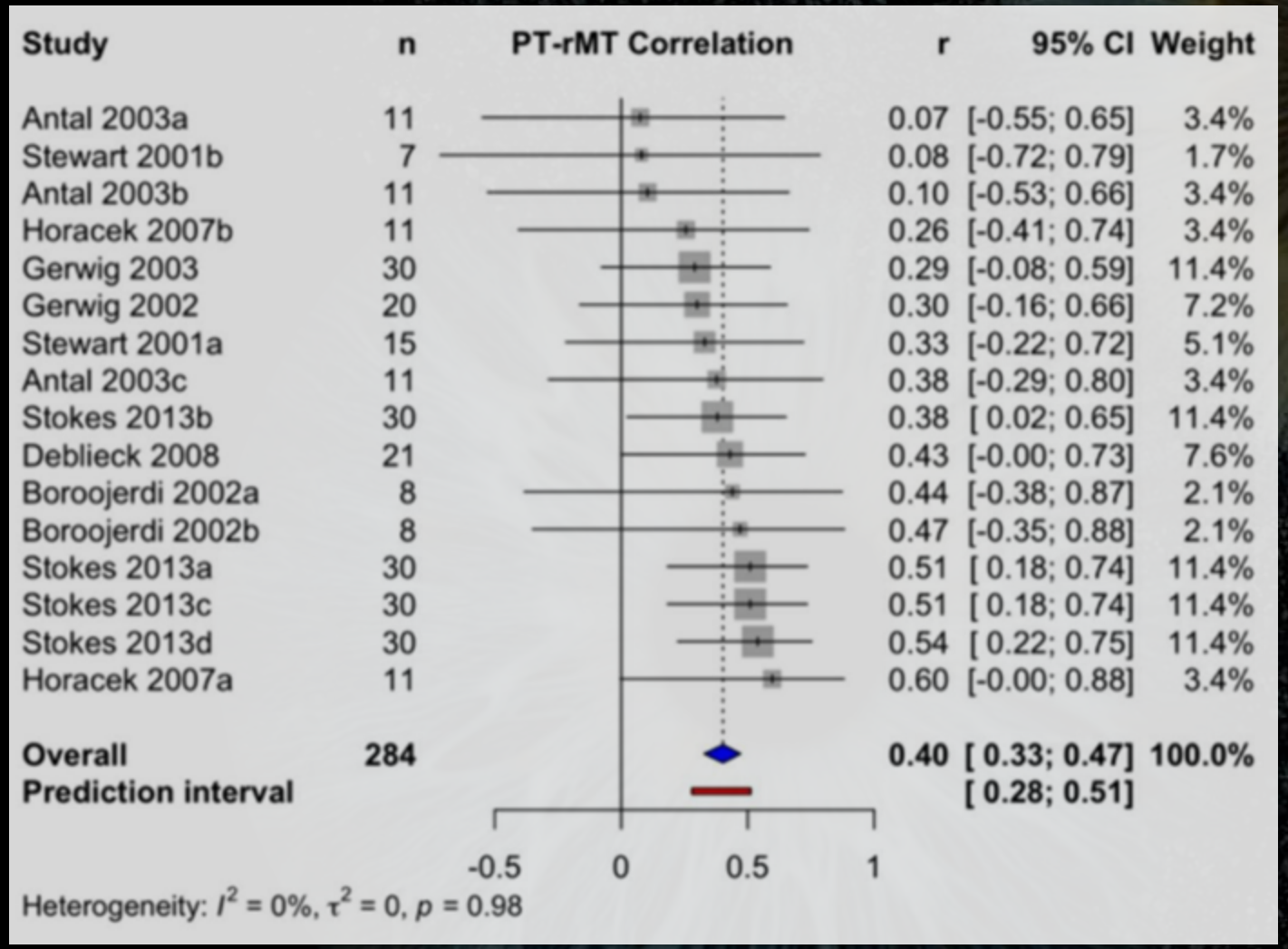
One in four people fail to perceive phosphenes during early visual cortex transcranial magnetic stimulation

Phivos Phylactou · Artemis Traikapi · Nikos Konstantinou

BRAIN STIMULATION



Brain excitability proxies...



ELSEVIER
Progress in Neuro-Psychopharmacology and Biological Psychiatry
Volume 133, 13 July 2024, 111020

Phosphene and motor transcranial magnetic stimulation thresholds are correlated: A meta-analytic investigation

P. Phylactou [a b], T.N.M. Pham [b], N. Narskhani [b], N. Diya [b], D.A. Seminowicz [c], S.M. Schabrun [a b]

Brain excitability proxies...

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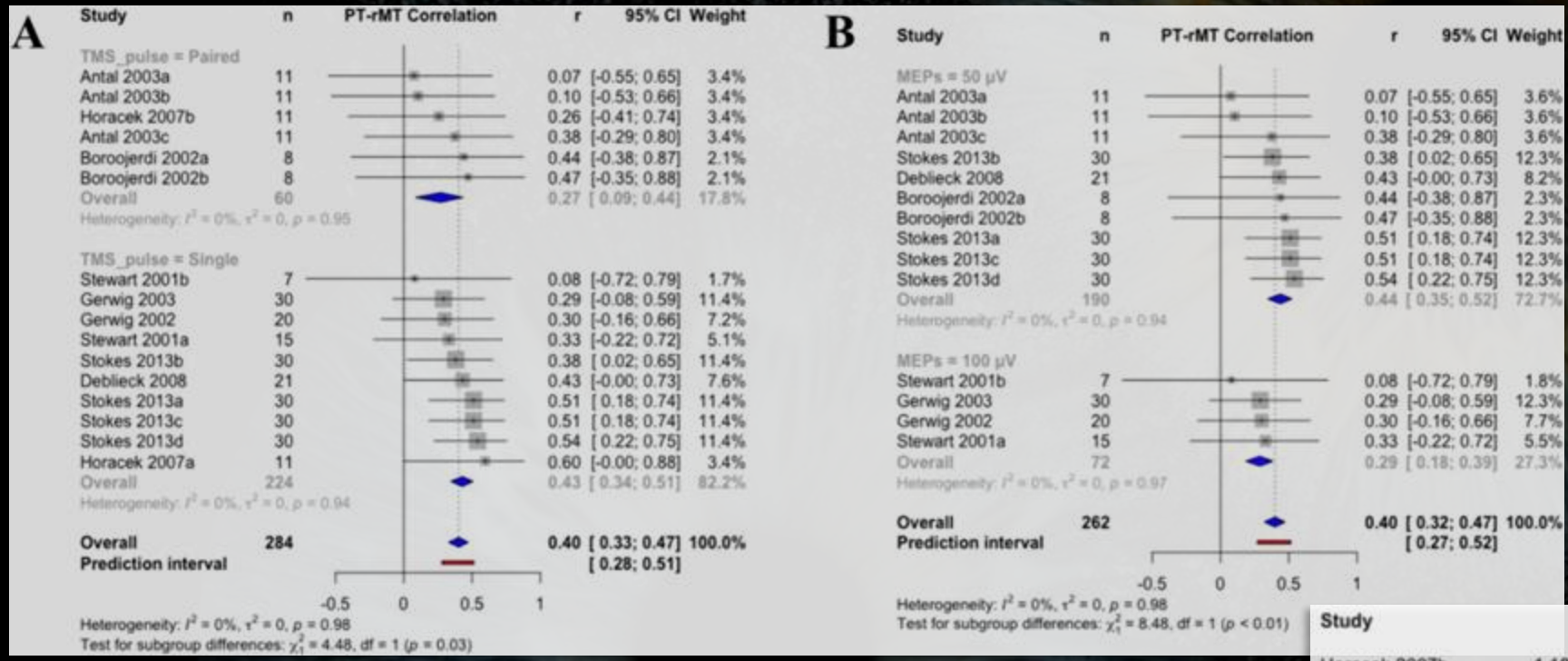
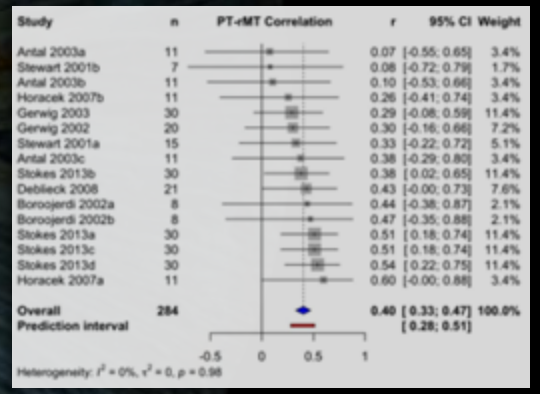
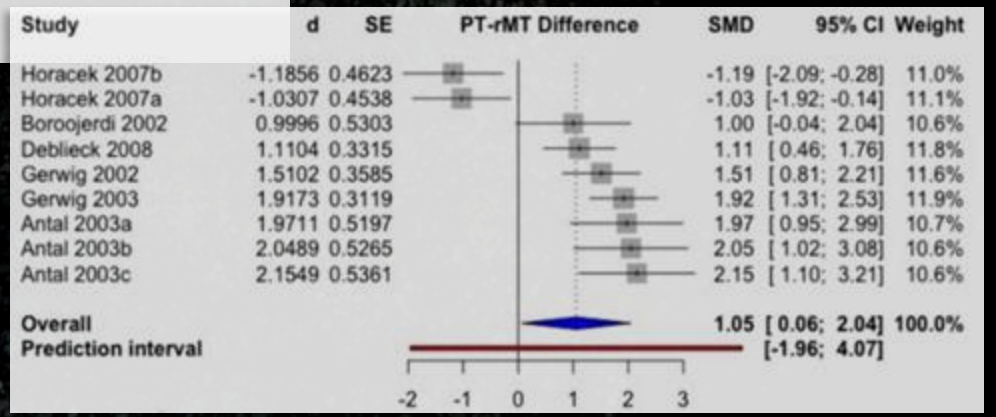
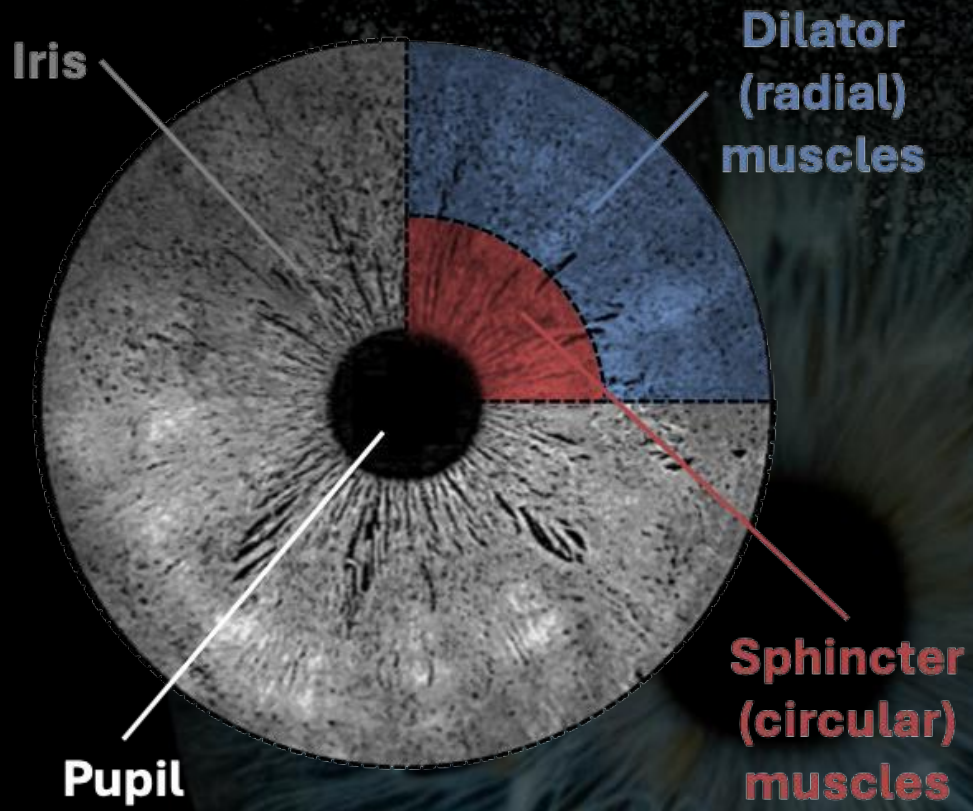







A new measure?

Pupil response and cortical plasticity



Cognitive Neurodynamics (2025)19:29
https://doi.org/10.1007/s11571-024-10208-8

REVIEW PAPER

Unraveling the functional complexity of the locus coeruleus-norepinephrine system: insights from molecular anatomy to neurodynamic modeling

Chun-Wang Su[1,2] · Fan Yang[1,2] · Runchen Lai[1,2] · Yanhai Li[1] · Hadia Naeem[1,2] · Nan Yao[3] · Si-Ping Zhang[1,2] · Haiqing Zhang[4] · Youjun Li[1,2] · Zi-Gang Huang[1,2]

HUMAN BRAIN MAPPING

Pupil diameter covaries with BOLD activity in human locus coeruleus

ARTICLE · Volume 89, Issue 1, P221-234, January 06, 2016 · Open Archive · Download Full Issue

Relationships between Pupil Diameter and Neuronal Activity in the Locus Coeruleus, Colliculi, and Cingulate Cortex

Siddhartha Joshi[1,2,*], Yin Li[1,*], Rishi M. Kalwani[1], Joshua I. Gold[1]

Affiliations & Notes · Article Info

Neuron

Volume 28, Issue 11, P574-632, November 2005 · Download Full Issue

Network reset: a simplified overarching theory of locus coeruleus noradrenaline function

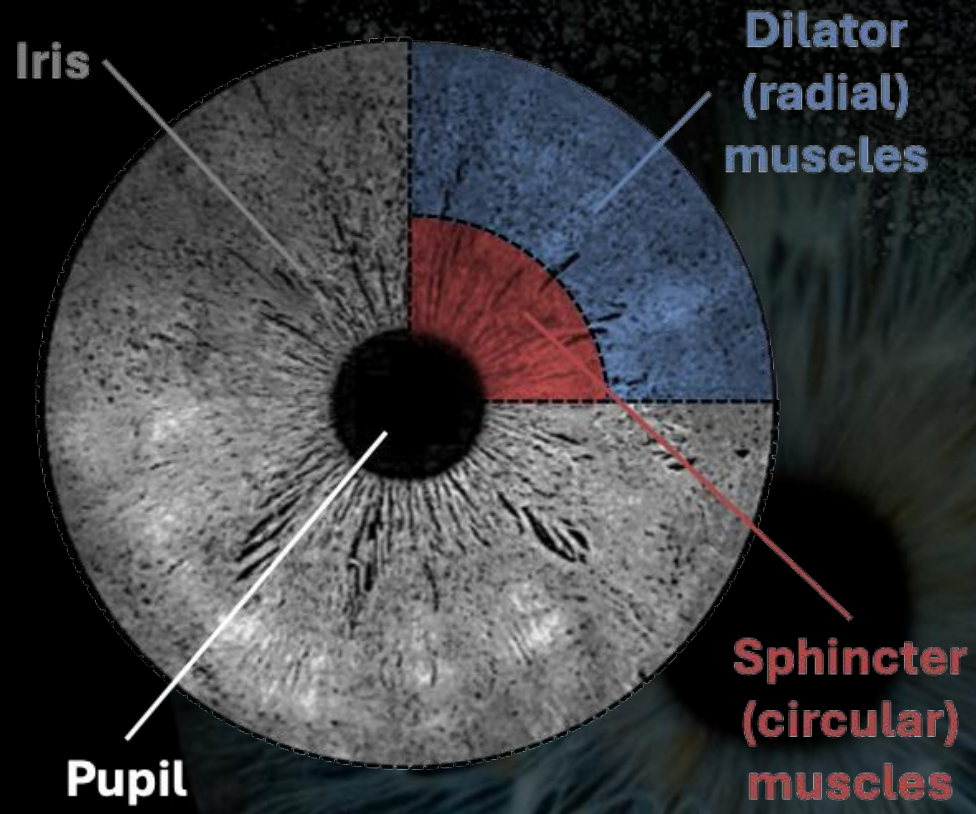
Sebastien Bouret · Susan J. Sara

frontiers | Frontiers in Neural Circuits

From pupil to the brain: New insights for studying cortical plasticity through pupillometry

Aurelia Viglione[1*], Raffaele Mazziotti[2,3], Tommaso Pizzorusso[2,3]

Pupil response and cortical plasticity



Unraveling the functional complexity of the locus coeruleus-norepinephrine system: insights from molecular anatomy to neurodynamic modeling

HUMAN BRAIN MAPPING

Research Article · Free to Read

Pupil diameter covaries with BOLD activity in human locus coeruleus

Peter R. Murphy · Redmond G. O'Connell, Michael O'Sullivan, Ian H. Robertson, Joshua H. Balsters

First published: 07 February 2014 | https://doi.org/10.1002/hbm.22466 | Citations: 583

ARTICLE · Volume 89, Issue 1, P221-234, January 06, 2016 · Open Archive · Download Full Issue

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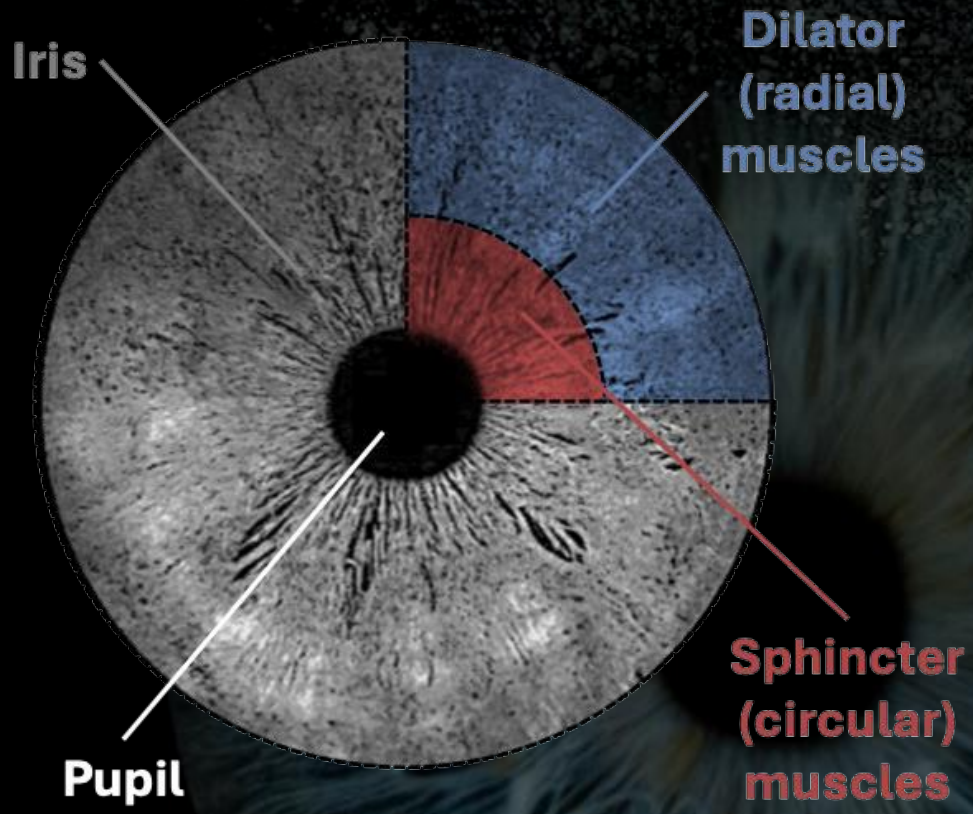

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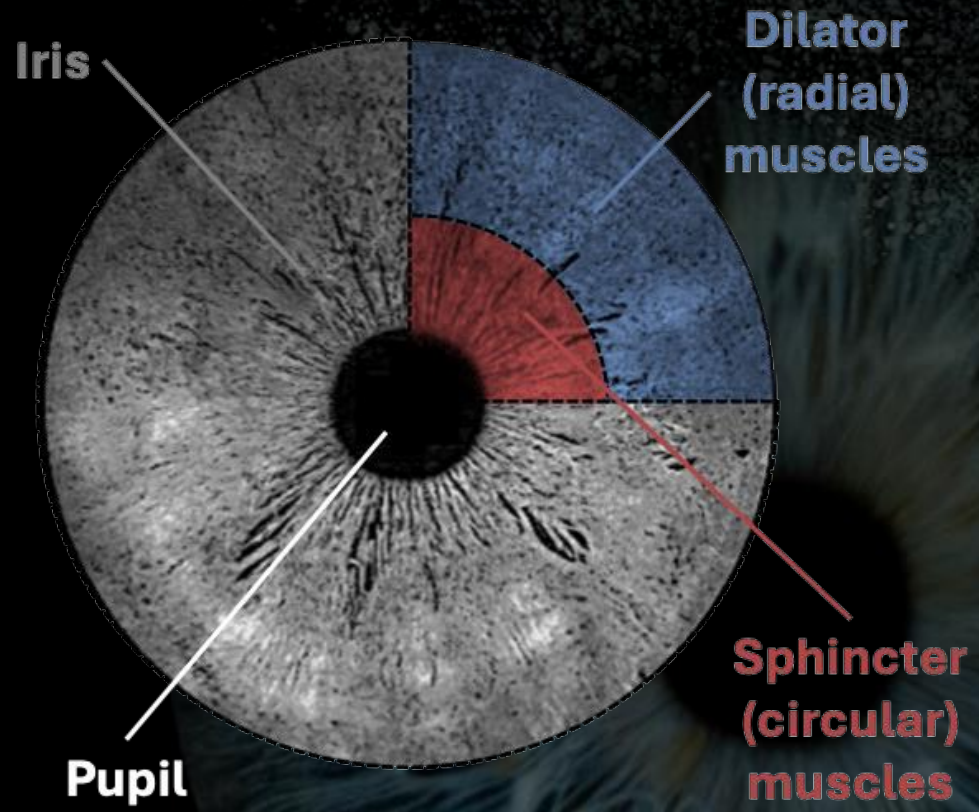

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Locus Coeruleus & TMS

Clinical Neurophysiology
Volume 114, Issue 10, October 2003, Pages 1834-1840

The α2-adrenergic agonist guanfacine reduces excitability of human motor cortex through disfacilitation and increase of inhibition

Alexei Korchounov, Tihomir V Ilić, Ulf Ziemann

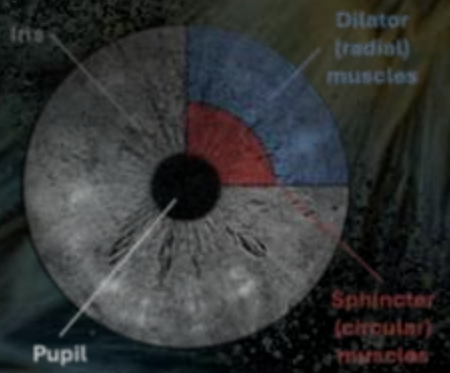
Acute and Chronic Noradrenergic Effects on Cortical Excitability in Healthy Humans

Hsiao-I Kuo, PhD, Walter Paulus, MD, Giorgi Batsikadze, PhD, Asif Jamil, PhD, Min-Fang Kuo, PhD, Michael A Nitsche, MD Author Notes

International Journal of Neuropsychopharmacology, Volume 20, Issue 8, August 2017, Pages 634–643, https://doi.org/10.1093/ijnp/pyx026
Published: 19 April 2017 **Article history**

Intracortical excitability is modulated by a norepinephrine-reuptake inhibitor as measured with paired-pulse transcranial magnetic stimulation

Psychopharmacology



Pupil & TMS

Influence of transcranial magnetic stimulation on pupil size

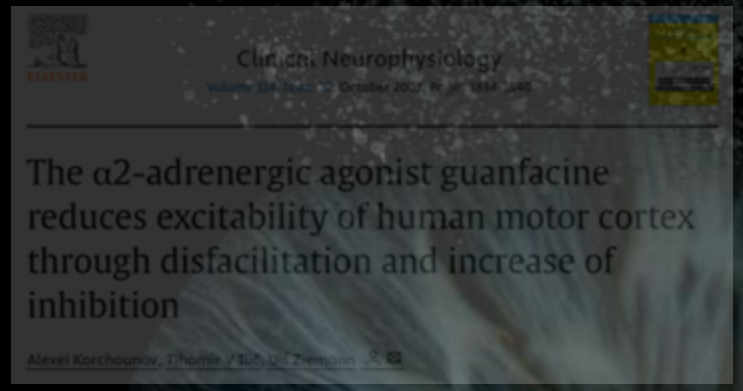
Ludwig Niehaus, Barbara Guldin, Bernd-Ulrich Meyer

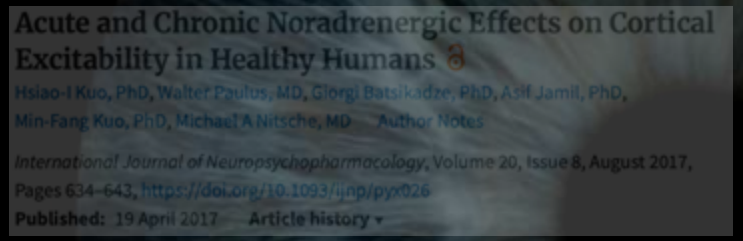
Pupillary reactions during transcranial magnetic stimulation

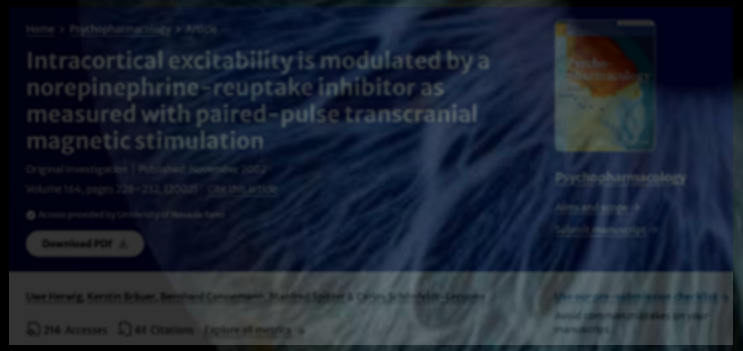
nature communications

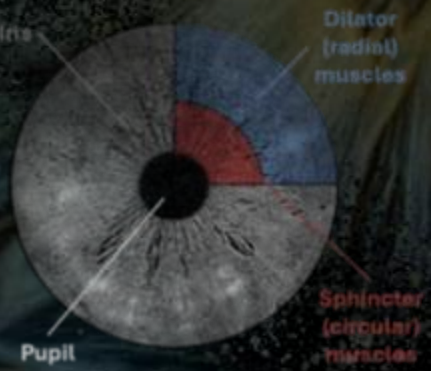
Modulating cortical excitability and cortical arousal by pupil self-regulation

Locus Coeruleus & TMS

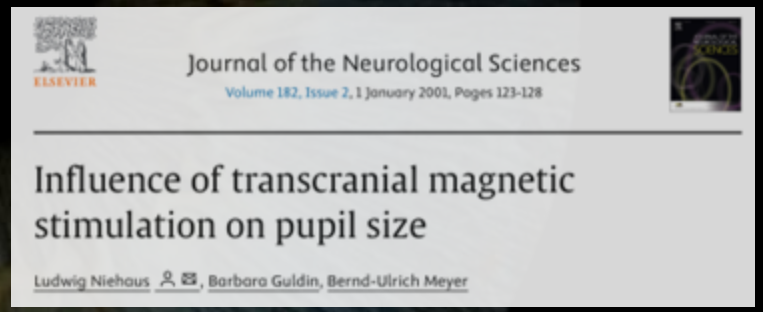


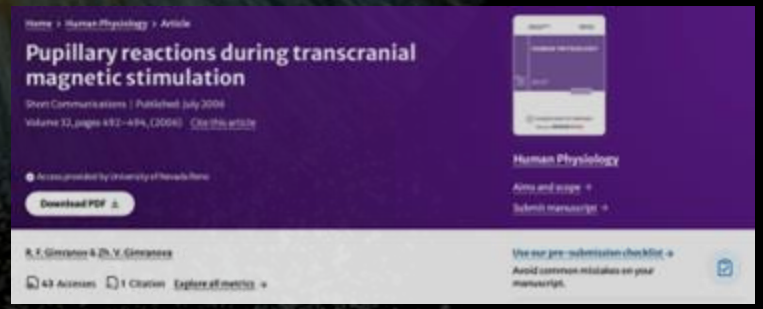






Pupil & TMS





Locus Coeru & TMS

Pupil & TMS

ON DILATATION OF THE PUPIL FROM STIMULATION OF THE CORTEX CEREBRI.

By J. HERBERT PARSONS, B.Sc., F.R.C.S., *Research Scholar of the British Medical Association.* (Two Figures in Text.)

(*From the Physiological Laboratory, University College, London.*)

CONTENTS.

I. History.

Several previous observers have noticed dilatation of the pupil following excitation of various parts of the cerebral cortex.

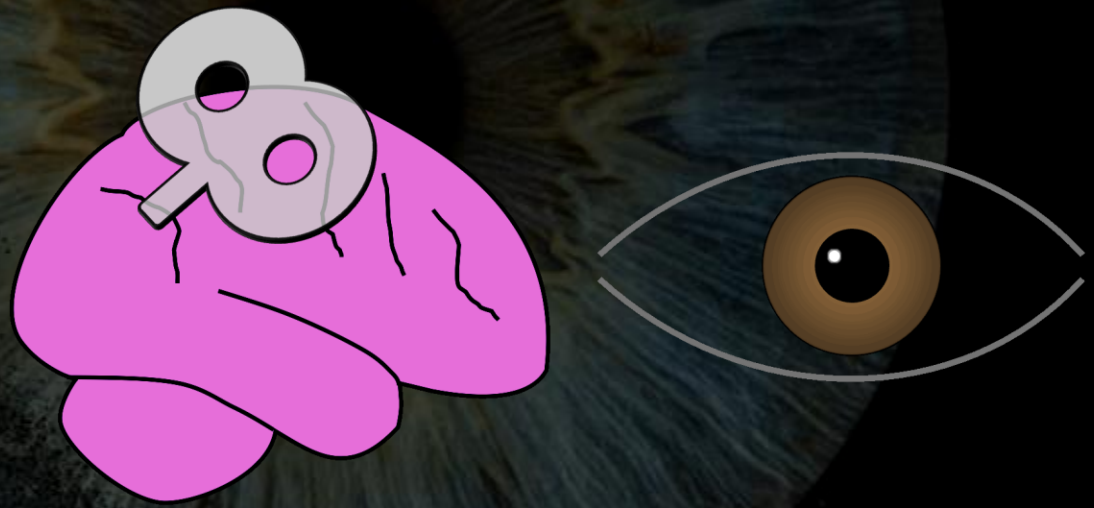
Bochefontaine[1] (1875) was the first to record the fact as the result of experiments upon dogs. He showed that it might occur when the animals were curarised.

Luciani and Tamburini[2] observed both dilatation and constriction in some of their experiments.

Ferrier[3] confirmed these results, and added further details; thus, indicating the spots stimulated by numbers, he makes the following statements:—In monkeys, "(12) Including the posterior half or two-thirds of the superior and middle frontal convolutions, the eyes widely open, the pupils dilate, and head and eyes turn to the opposite side." "(13) and (13*a*) On the anterior and posterior limb of the angular gyrus respectively the eyes move to the opposite side.....usually also the pupils become contracted." "(14) On the superior temporo-

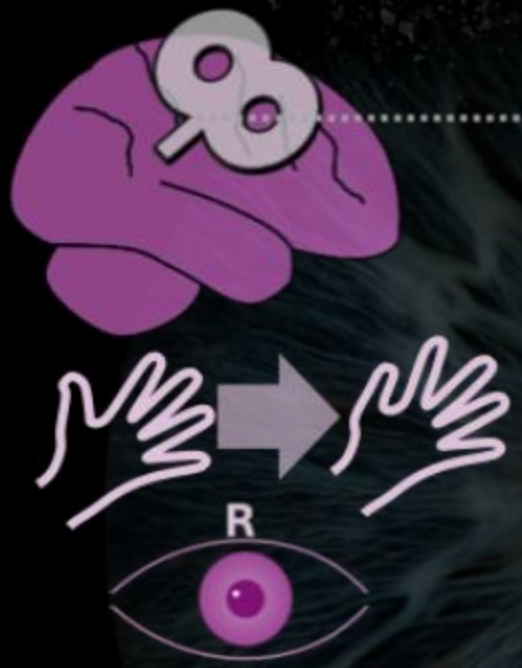
Overarching aim

Can the pupil serve as an objective measure of brain excitability?



StimulEYE

Proof-of-concept



counterbalanced

100 TMS active pulses & 100 sham pulses

80% or rMT
90% of rMT
100% of rMT
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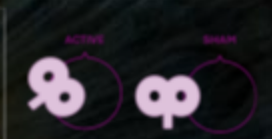
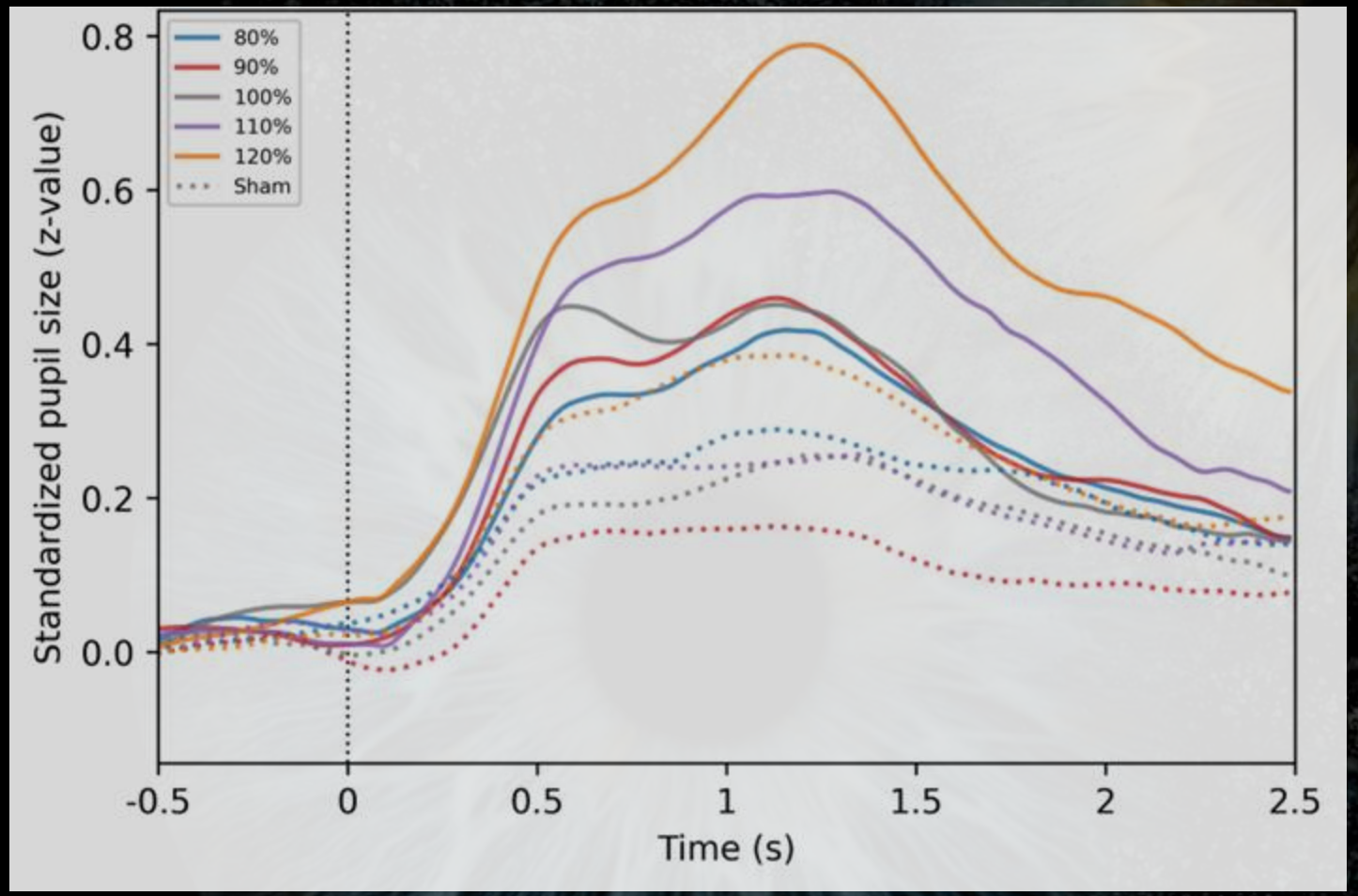
random order

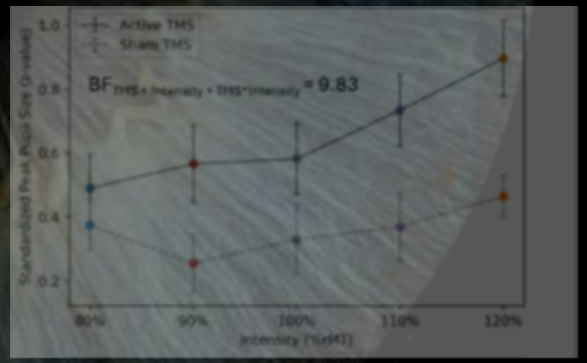
20 pulses each intensity
for each TMS condition (active vs sham)
200 pulses in total.

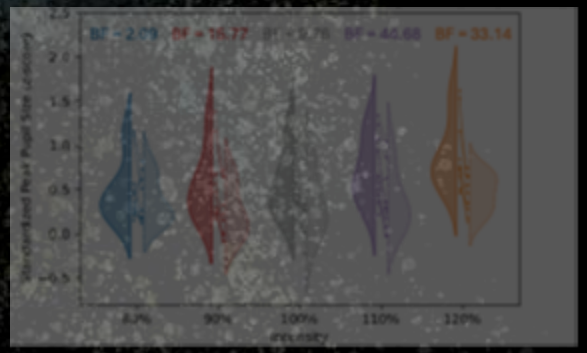
8F, 3M
age 26.73±3.35

Proof-of-concept









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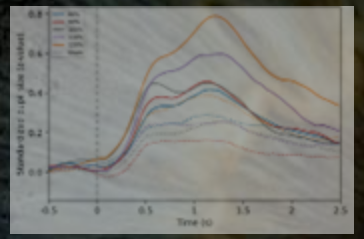
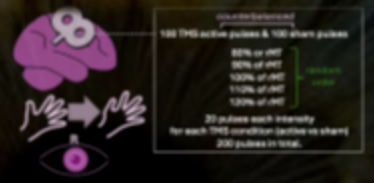
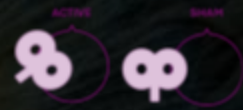
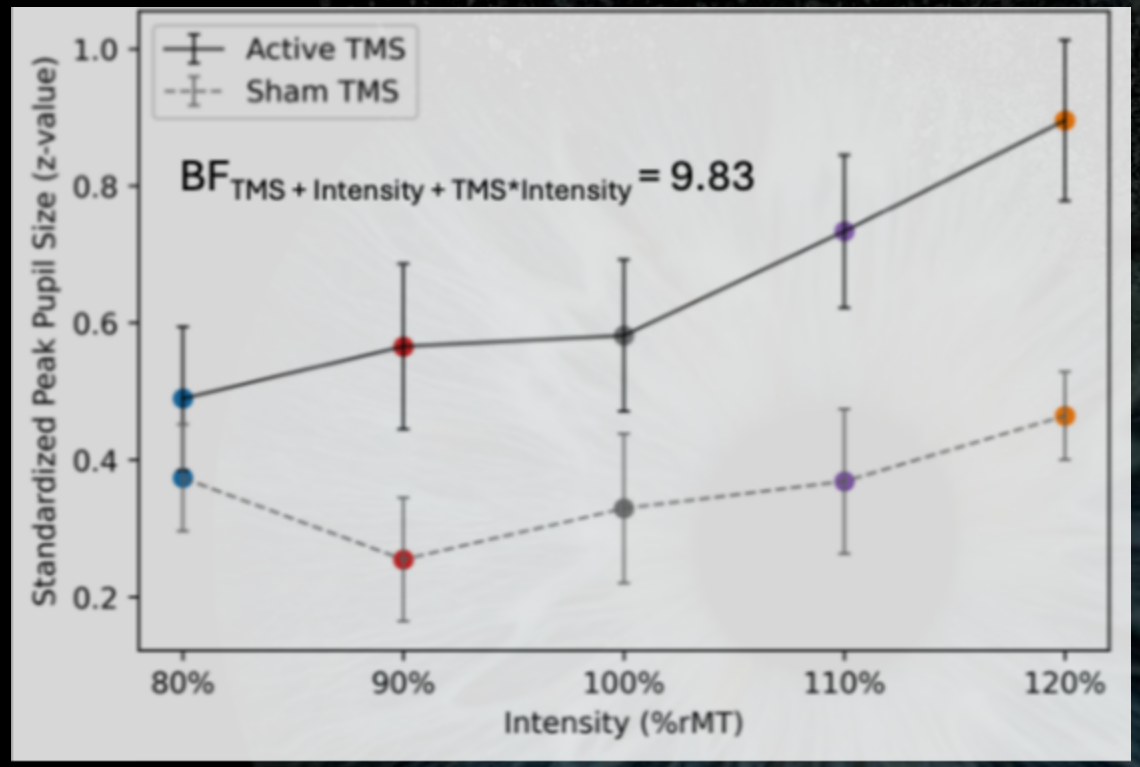
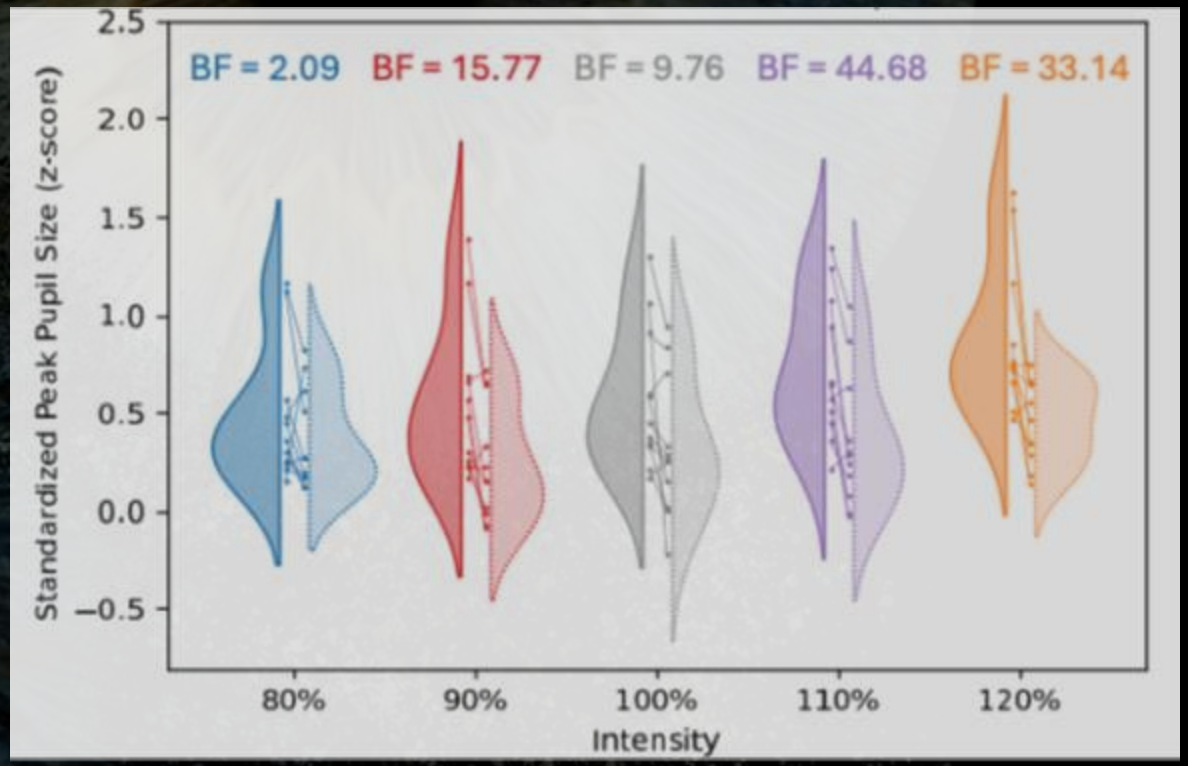


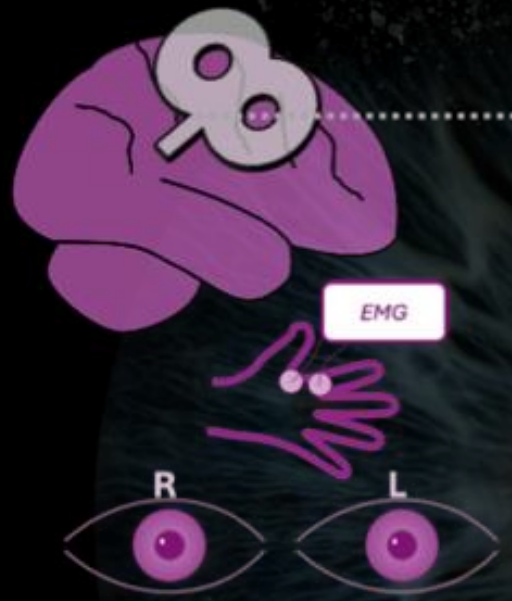








Replication



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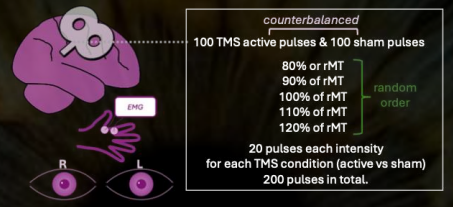

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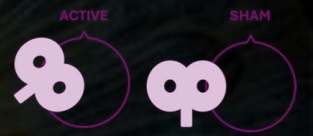

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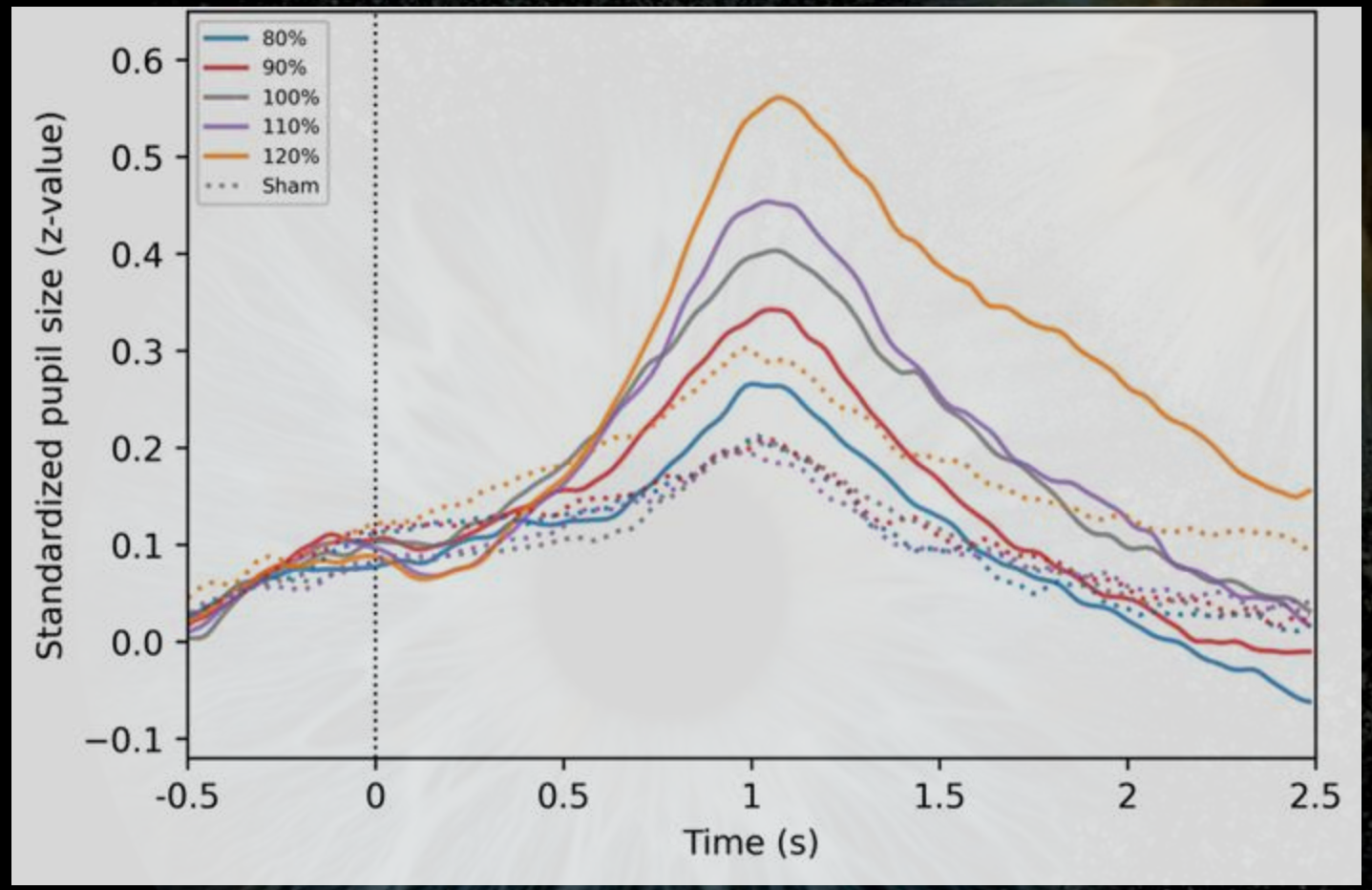

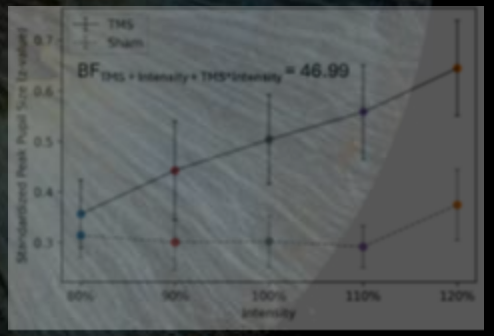

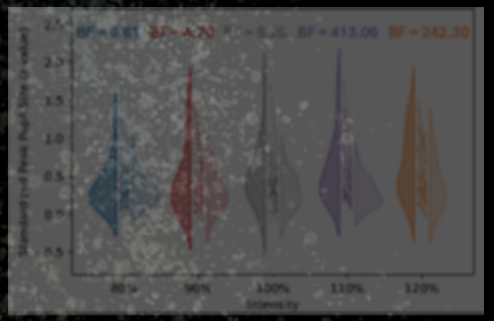

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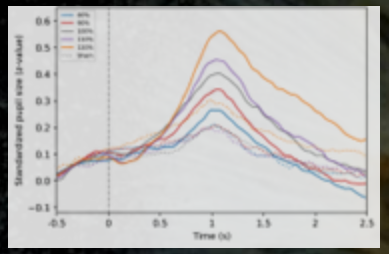
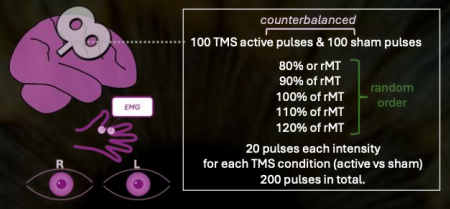
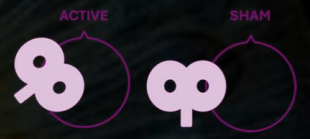
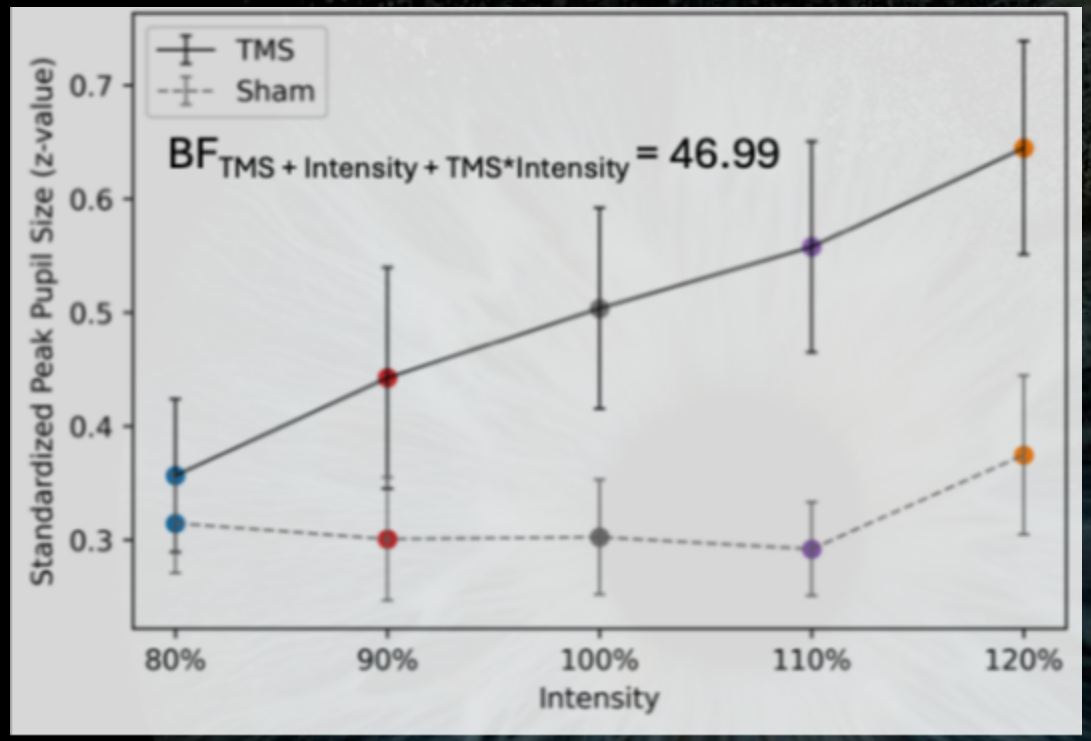
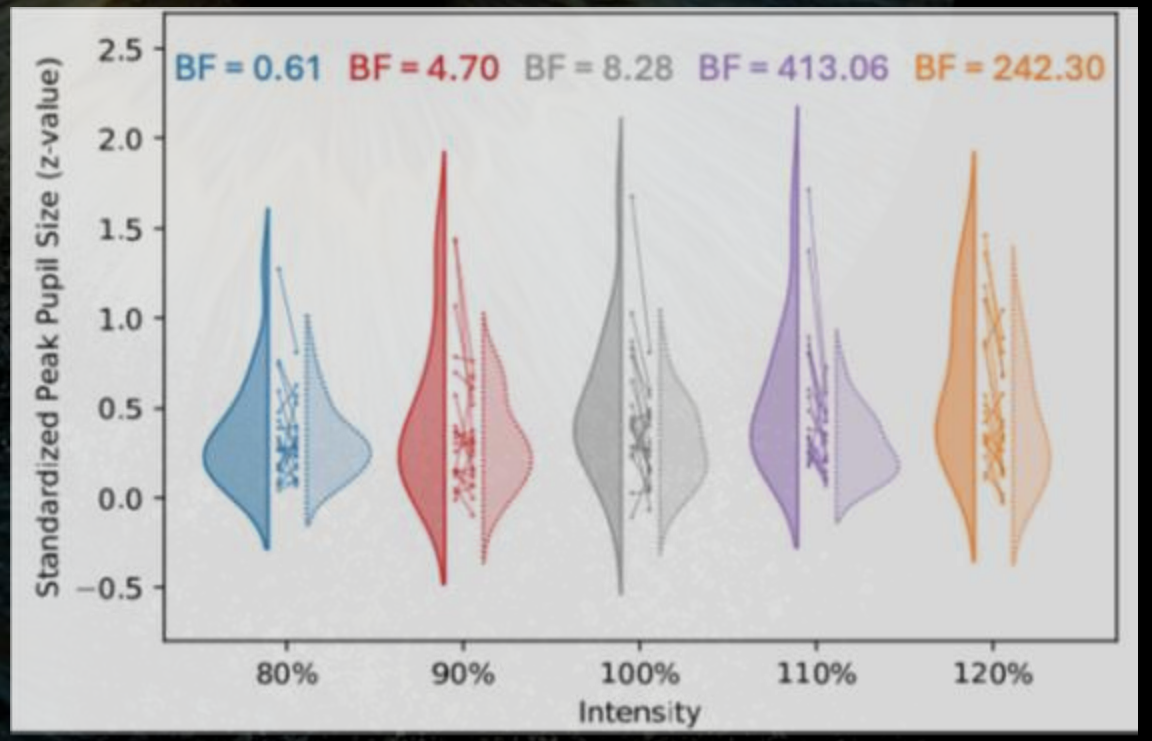




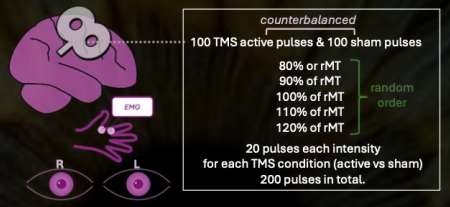


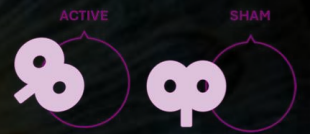
20
11F, 9M
age 24.65±5.39





What if it's due to eye-muscle stimulation?





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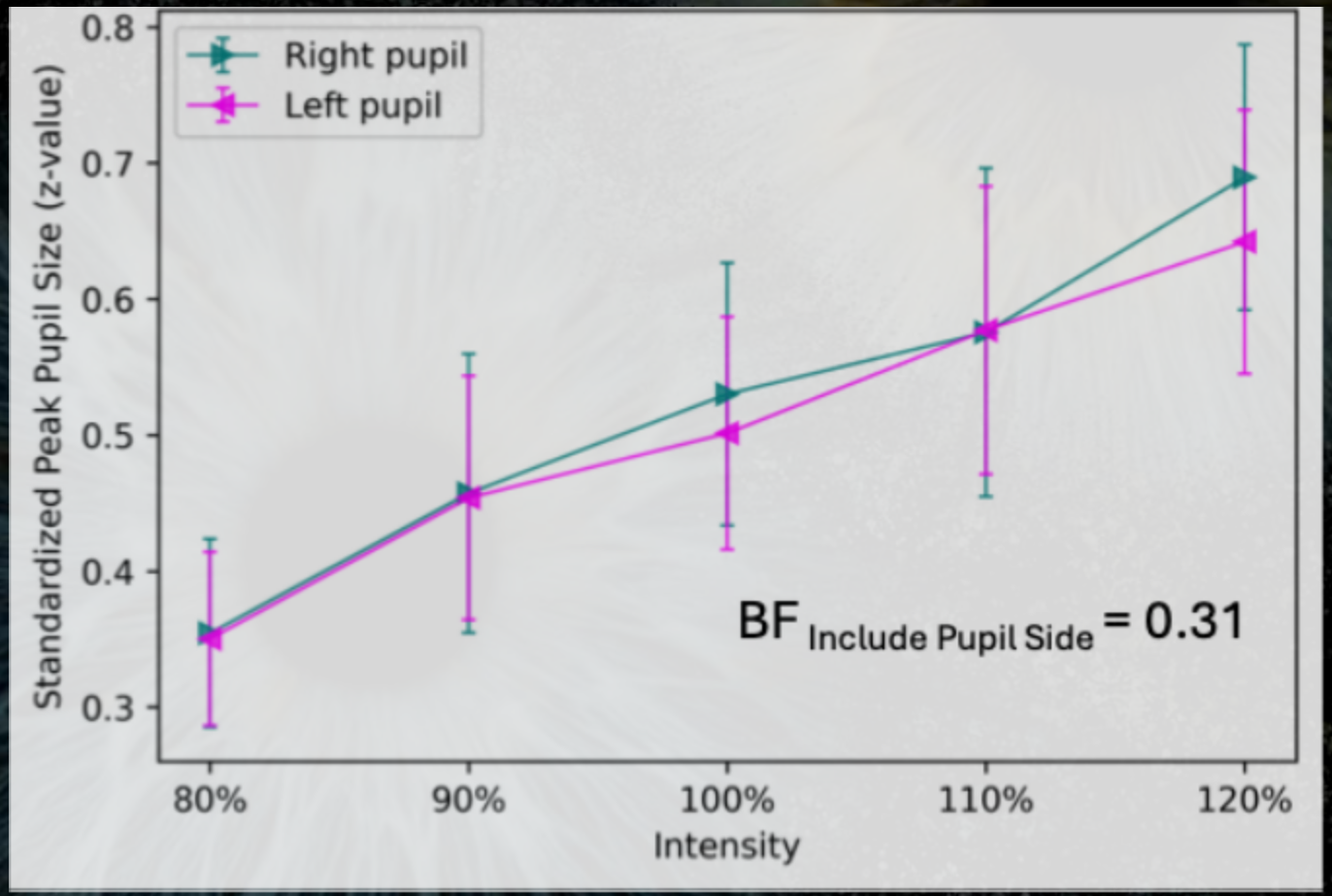
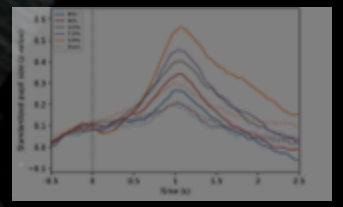
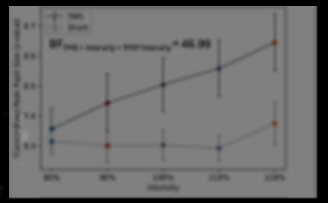
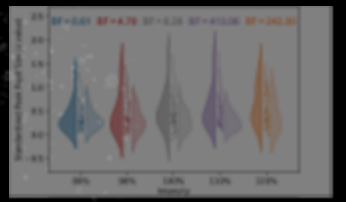
11F, 9M
age 24.65±5.39

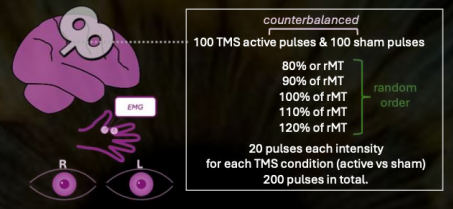




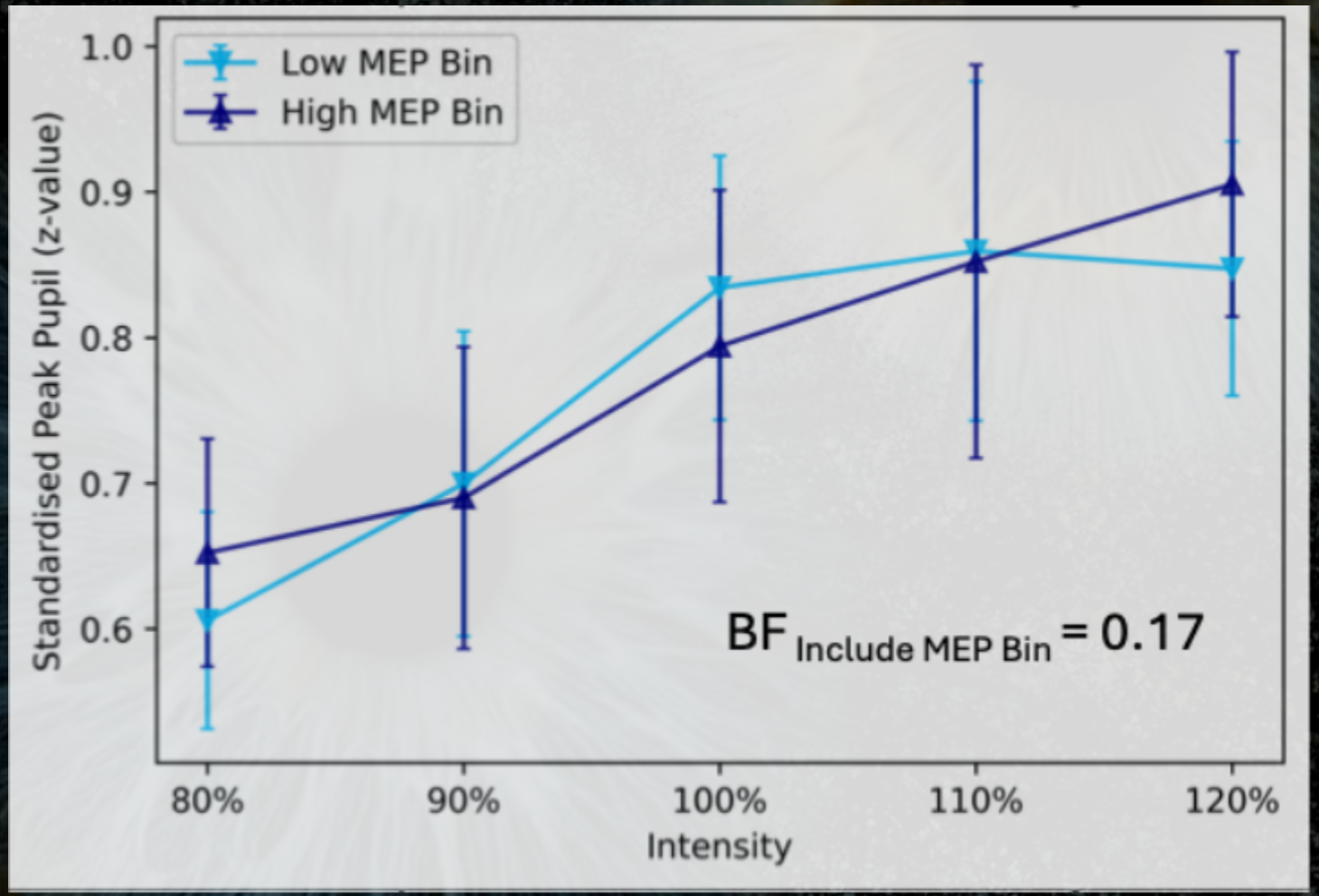


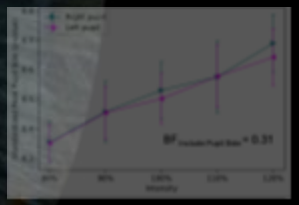


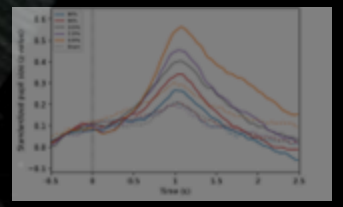
What if it's due to hand-muscle artifacts?

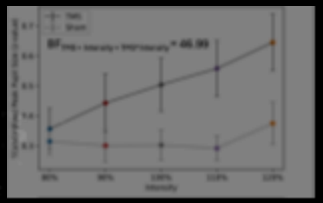


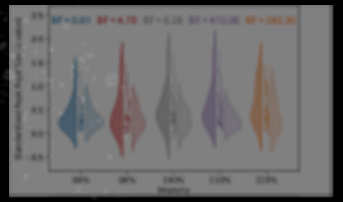
20
11F, 9M
age 24.65±5.39



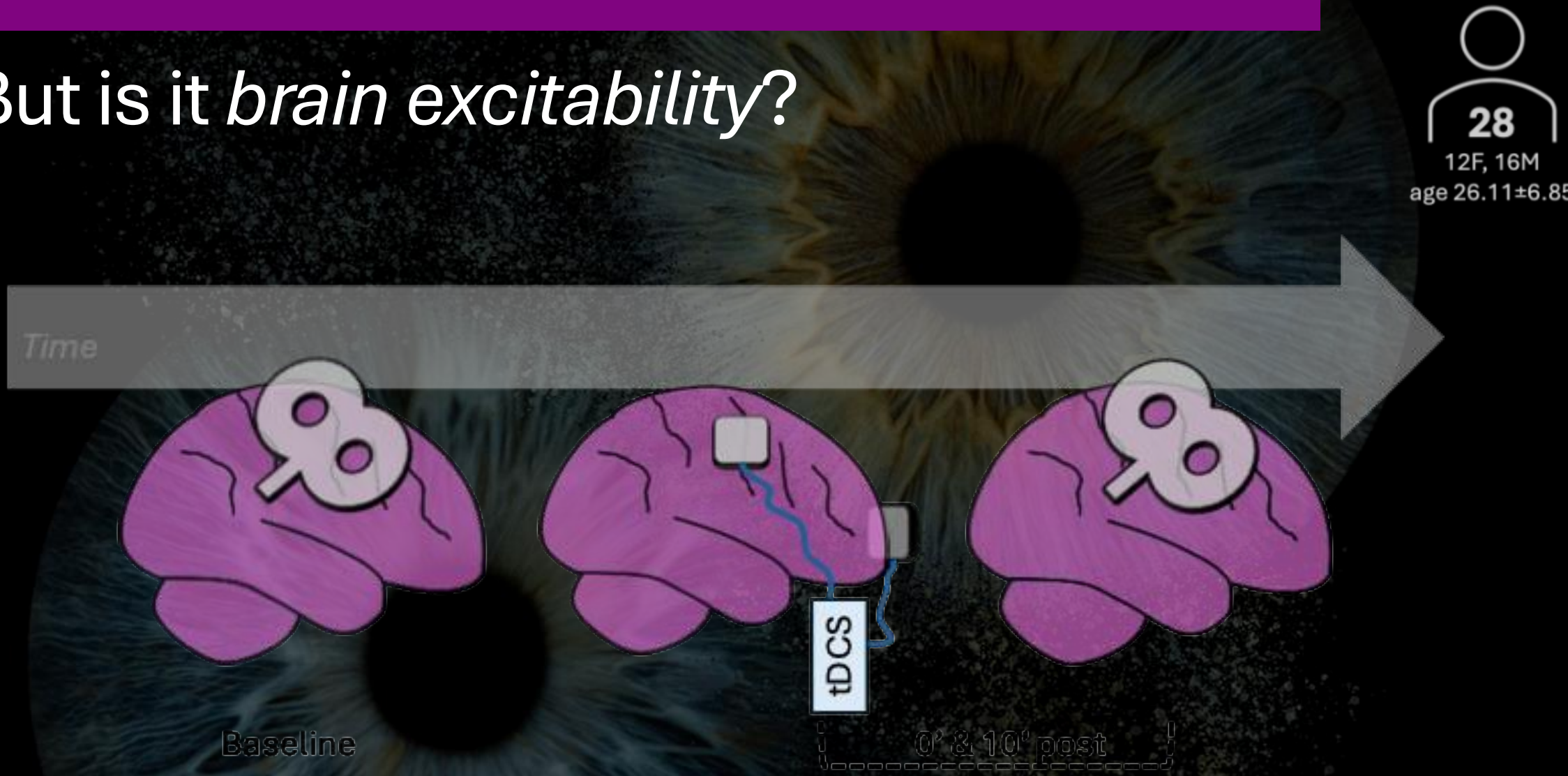






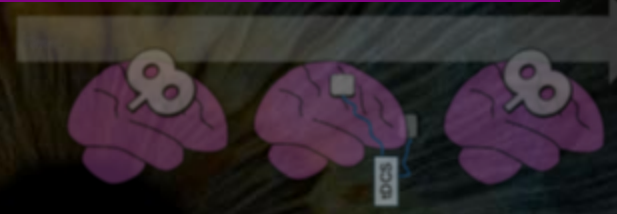


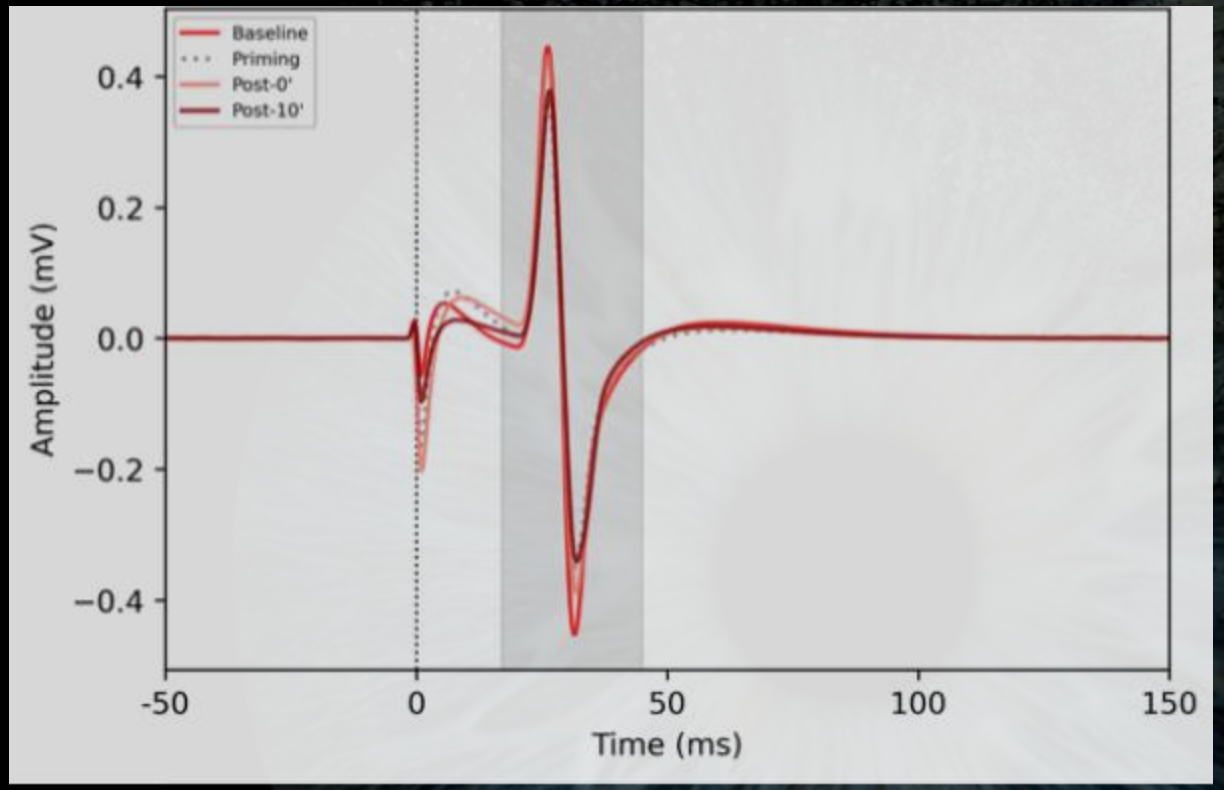
But is it *brain excitability*?

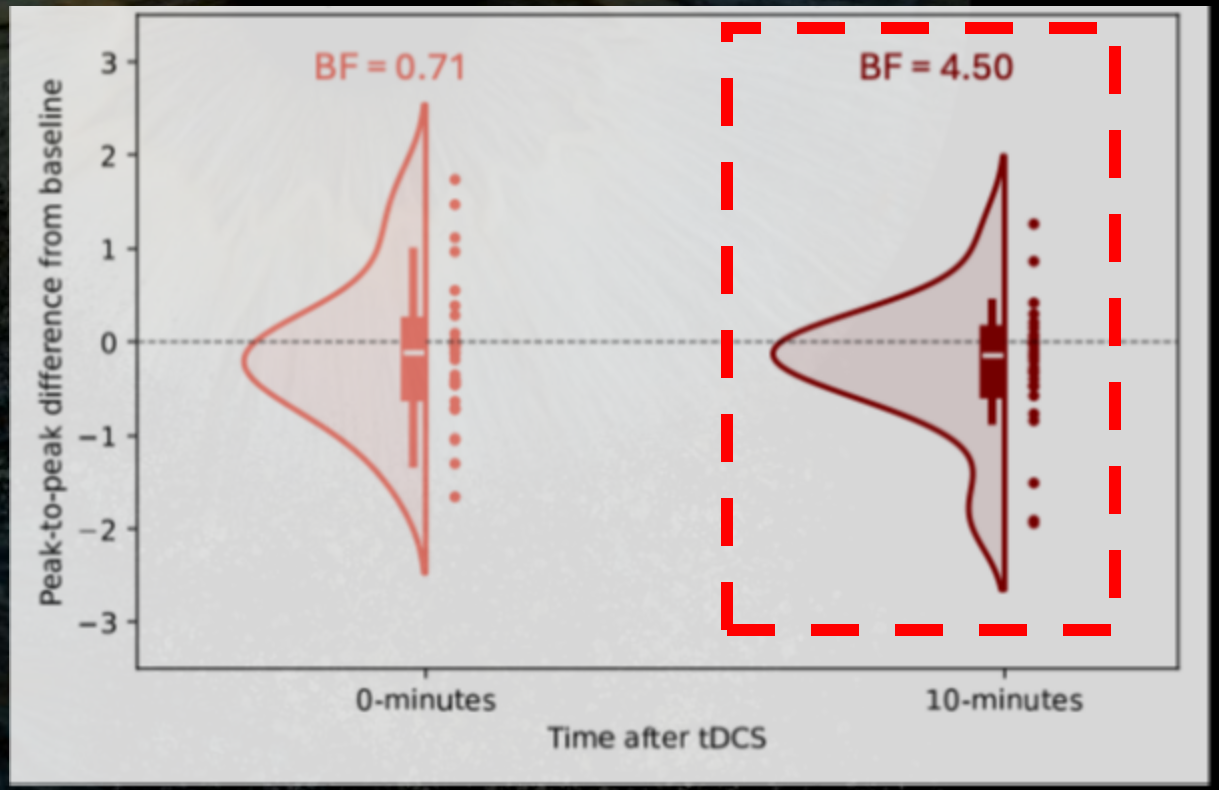


tDCS: Transcranial Direct Current Stimulation

But is it *brain excitability*?

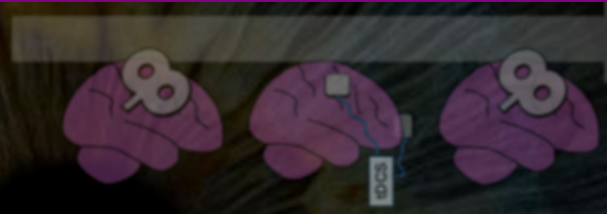


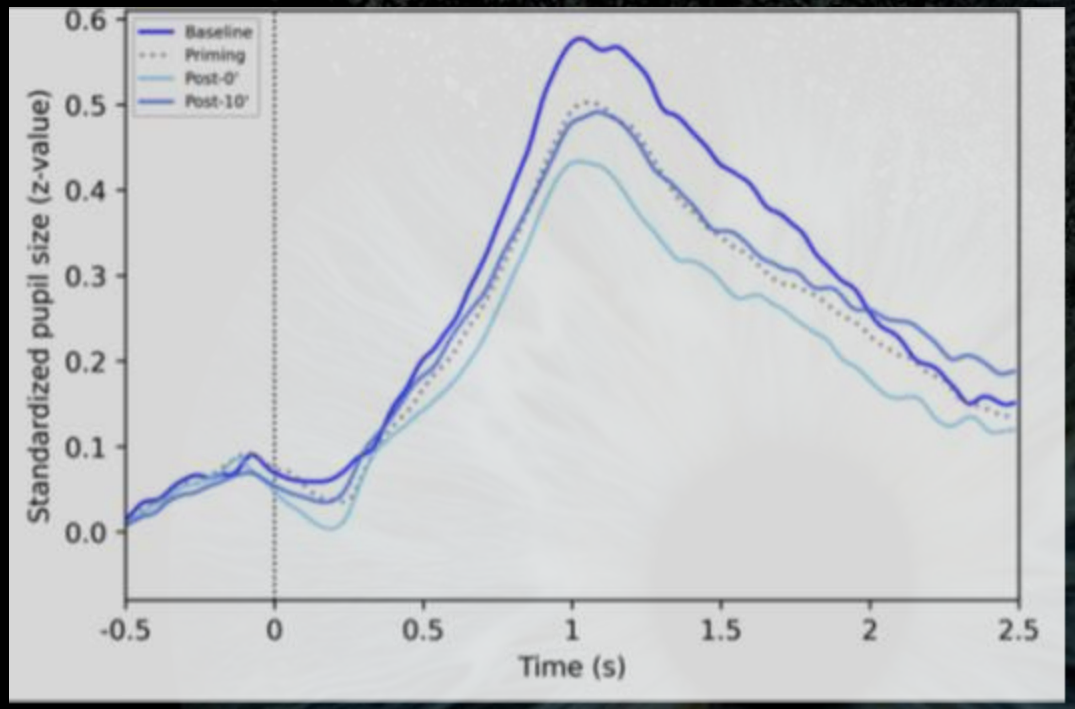


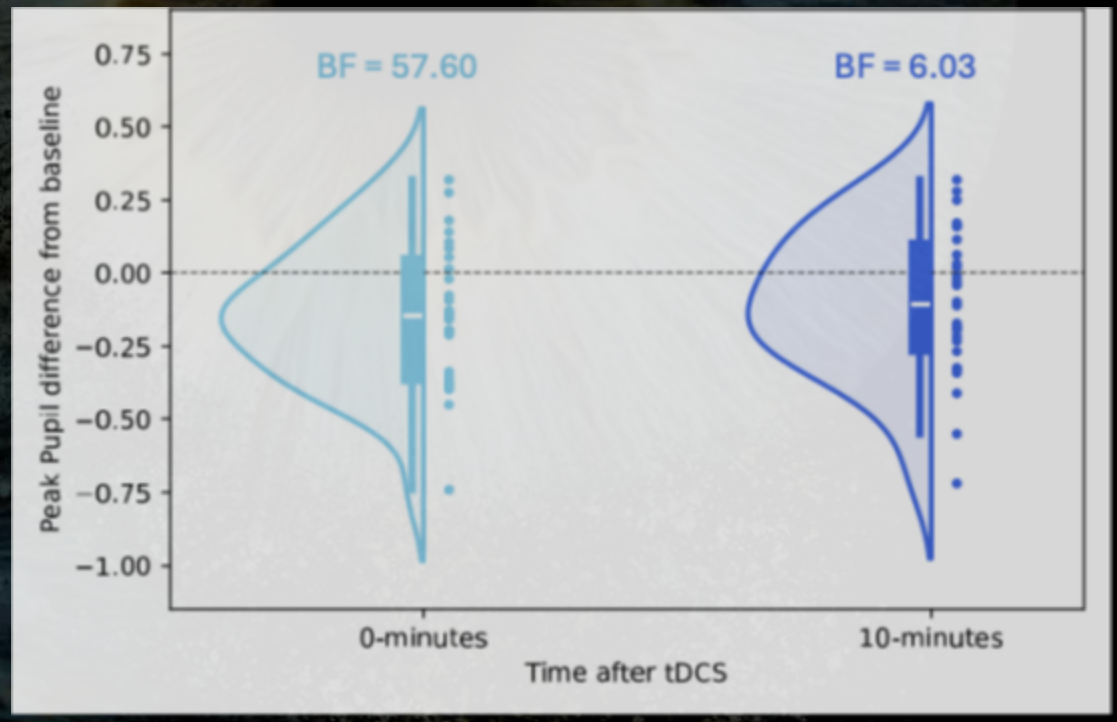


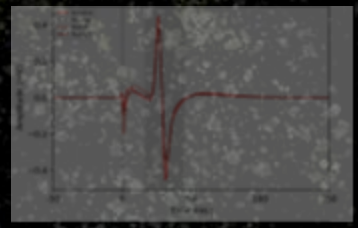
tDCS: Transcranial Direct Current Stimulation

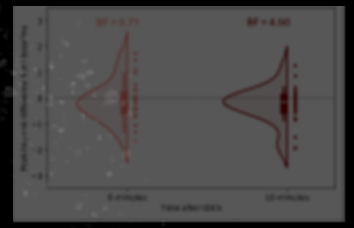
But is it *brain excitability*?





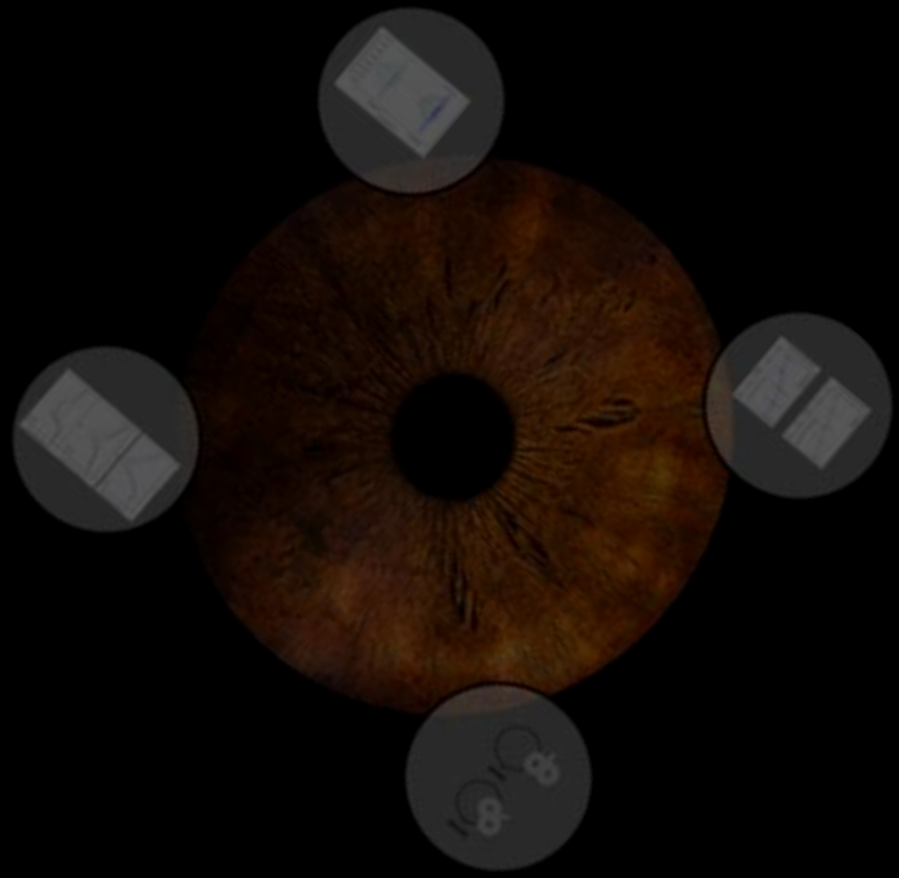






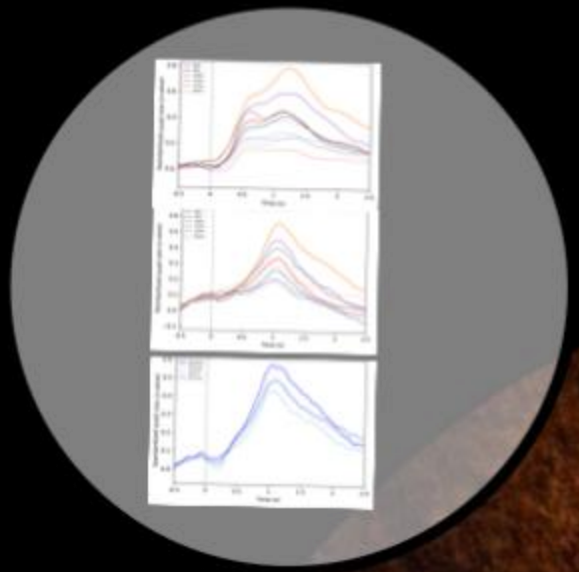
tDCS: Transcranial Direct Current Stimulation

The pupil can serve as a brain excitability measure



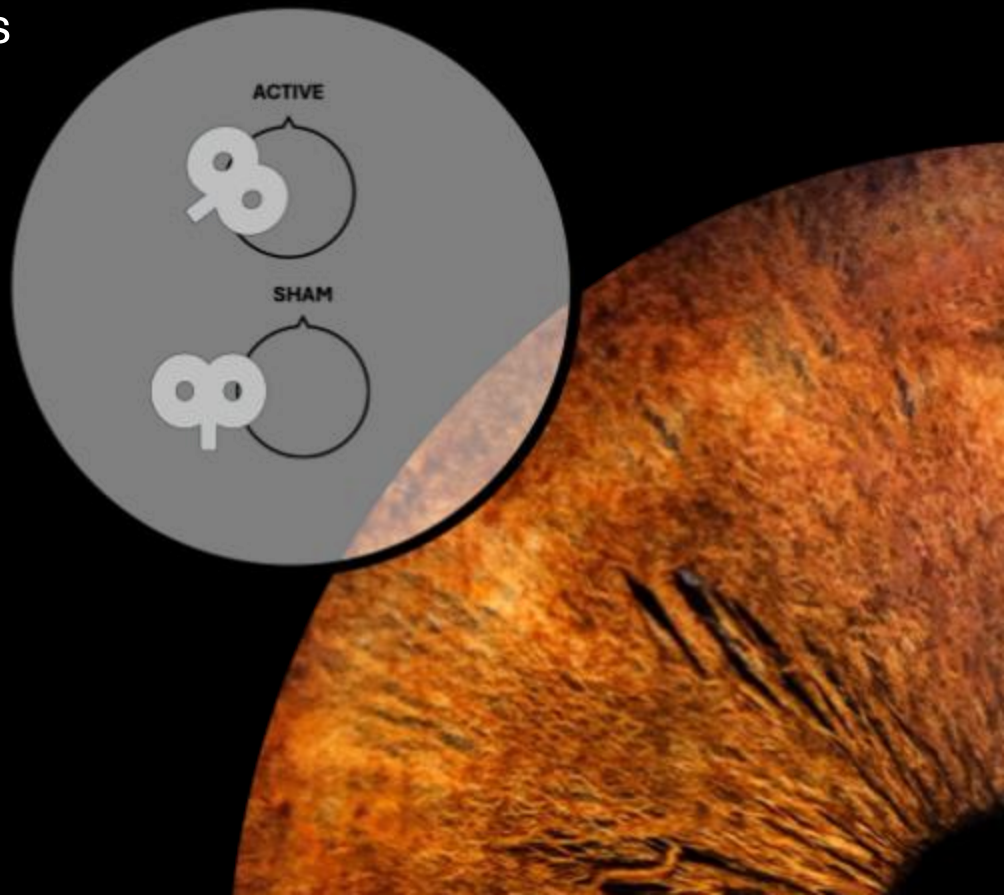
The pupil can serve as a brain excitability measure

Consistent &
dissociable
pupil response



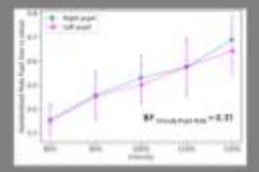
The pupil can serve as a brain excitability measure

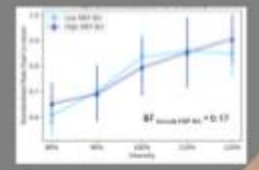
Not due to auditory artifacts



The pupil can serve as a brain excitability measure

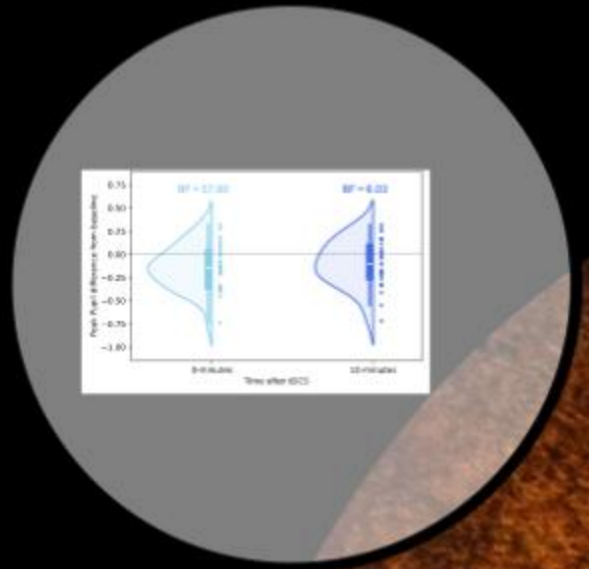
Not due to muscle artifacts





The pupil can serve as a brain excitability measure

Reflects brain excitability changes

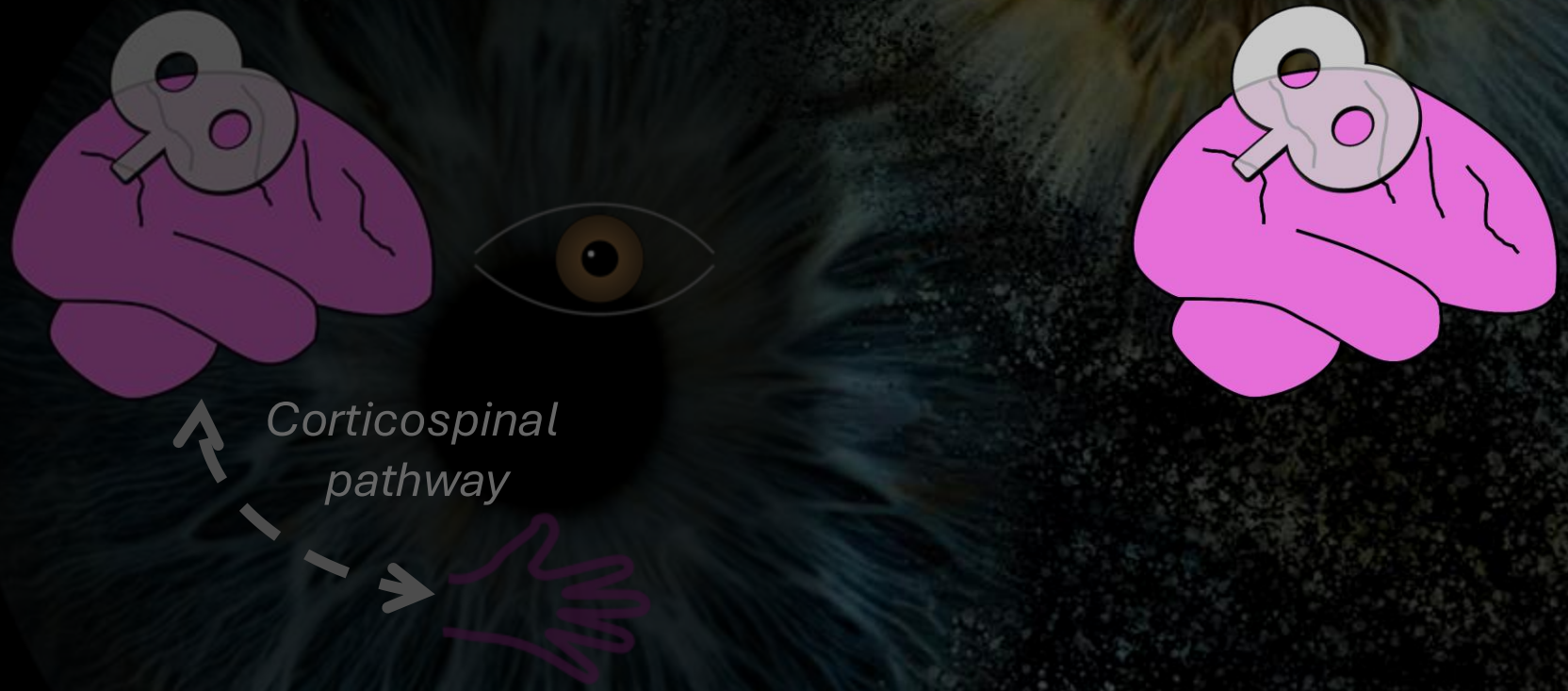


Alright, so what?

TMS can be become more:

Inclusive

Effectual



Alright, so what?

TMS can be become more:

For example...

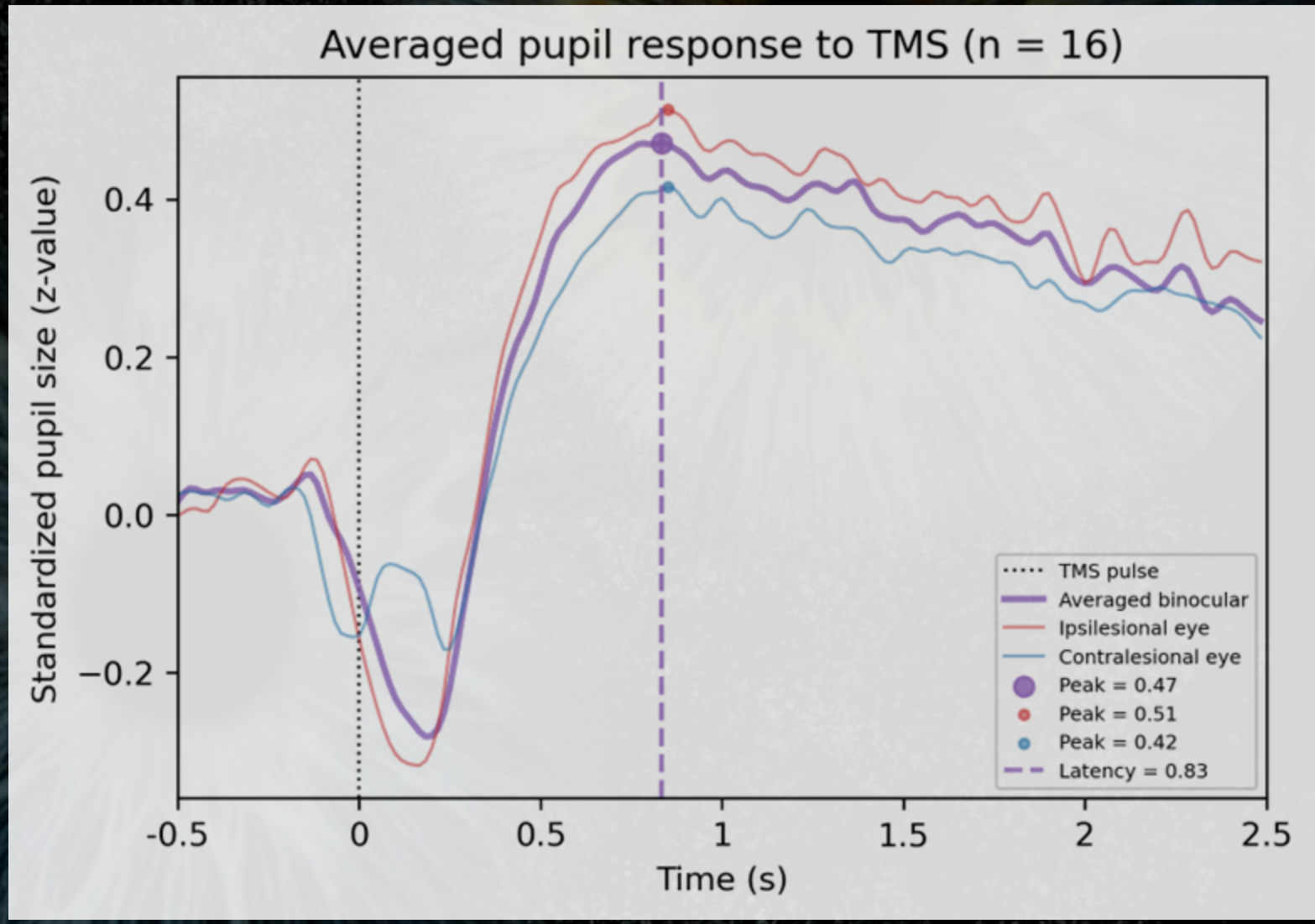
Fraser MacRae

Lexie Delisle

Sue Peters, Ph.D.
www.suepeters.ca

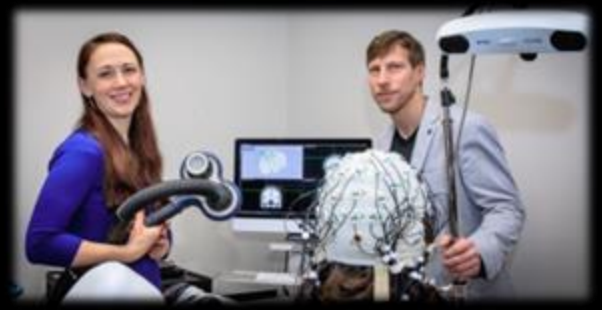
Western HealthSciences

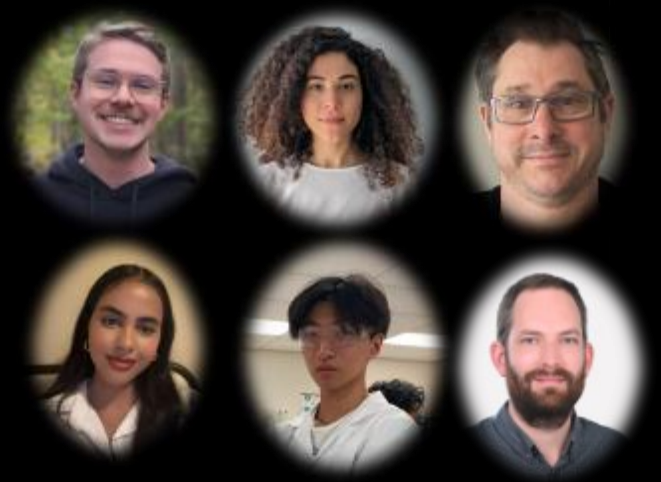
LAWSON Research Institute
ST. JOSEPH'S HEALTH CARE LONDON



Thank you!

Phivos Phylactou, Ph.D.





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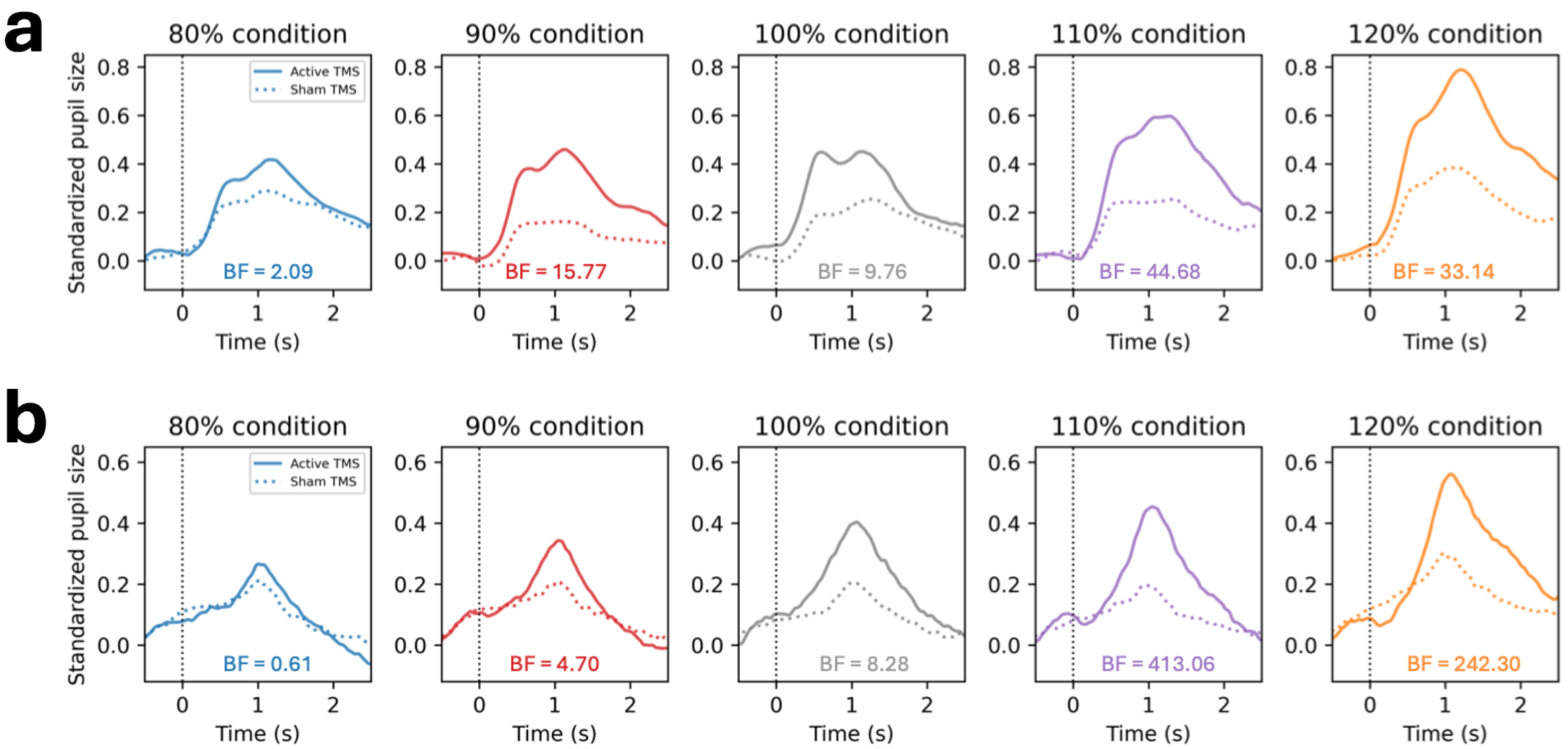
StimulEYE

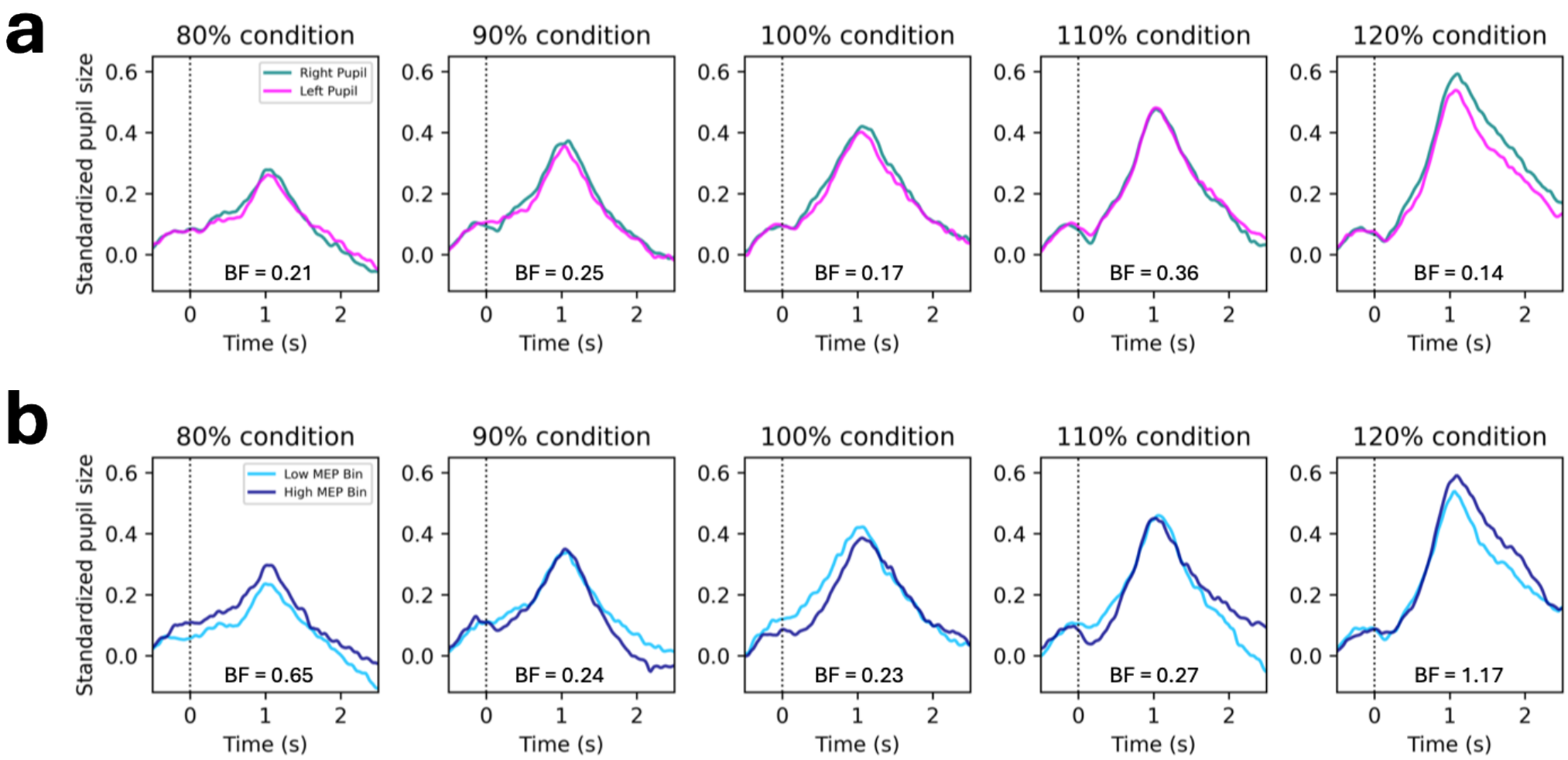
Project StimulEYE was made possible through the *Mary Elizabeth Horney Fellowship in Rehabilitation* provided by St. Joseph's Health Care Foundation.

Supplementary

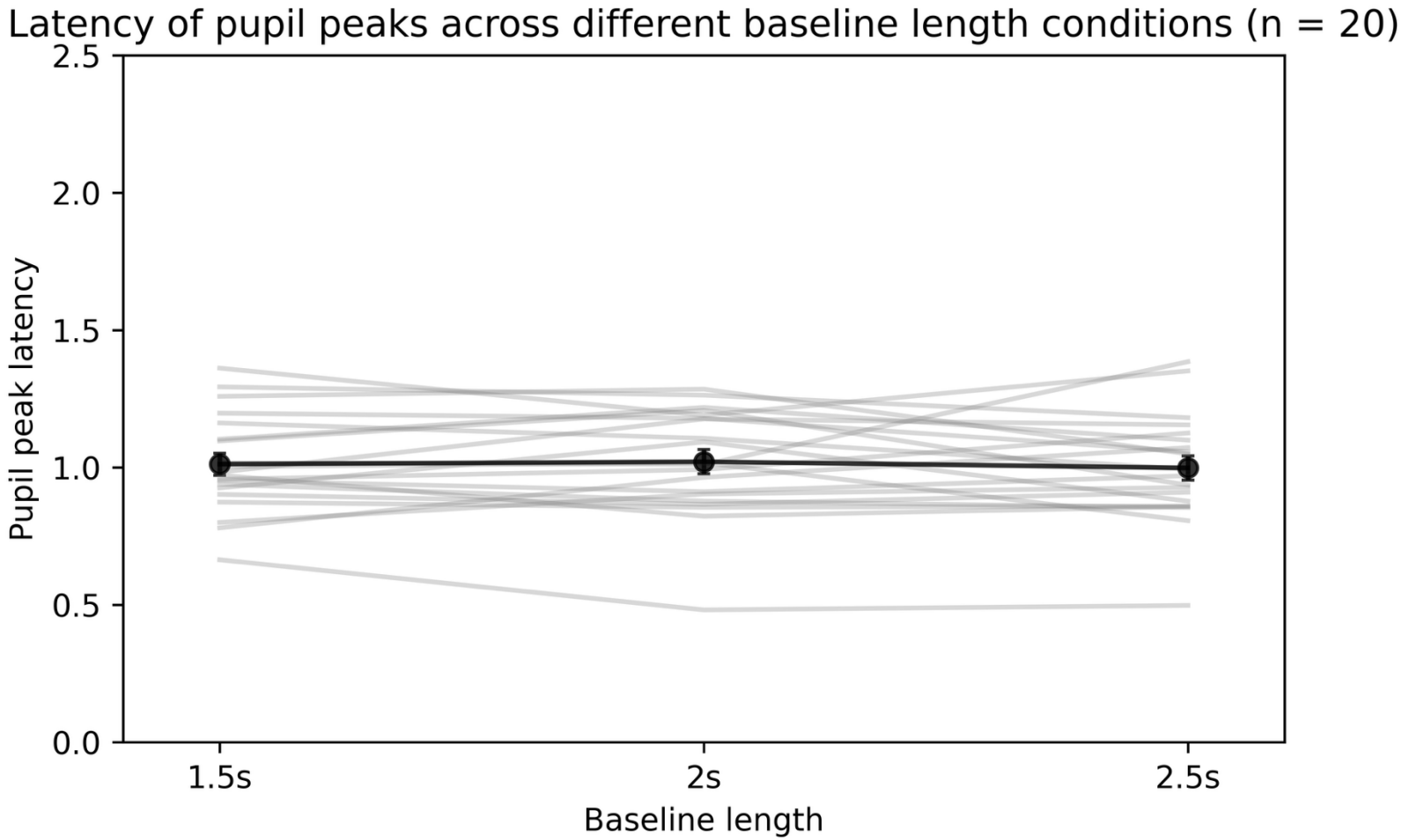
Pupil responses by condition



Control analyses by condition

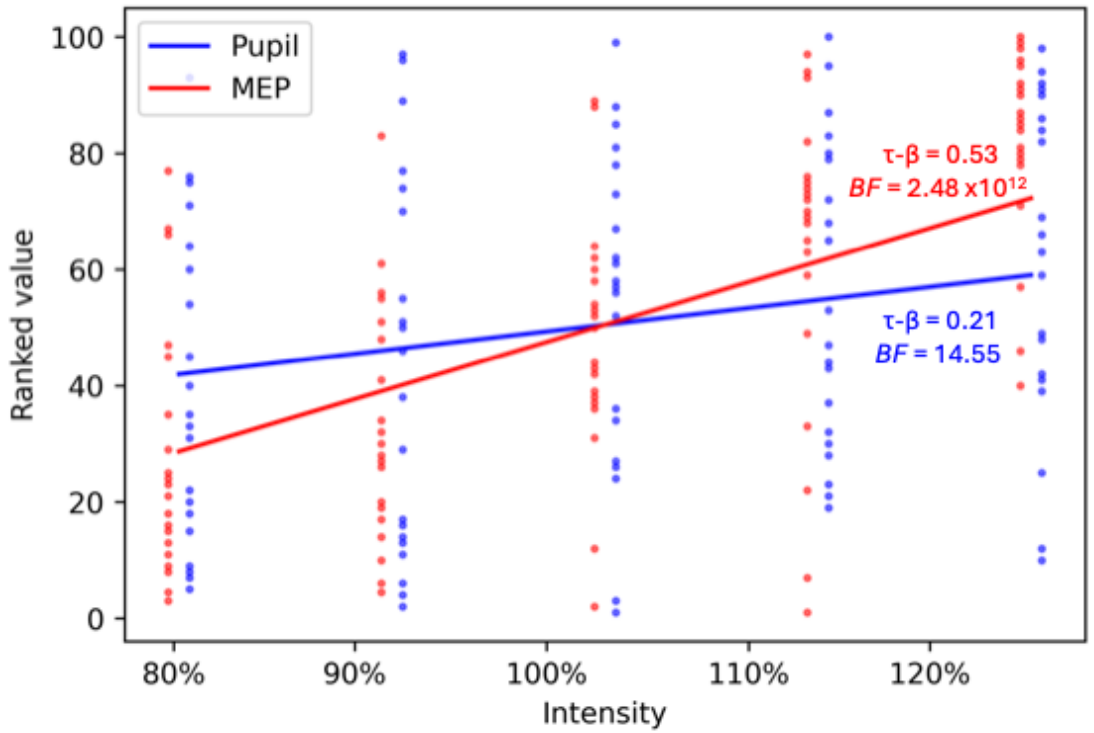


Anticipation effects control



Are MEPs and pupils in a relationship?

20
11F, 9M
age 24.65±5.39



MEP: Motor Evoked Potential

Are MEPs and pupils in a relationship?

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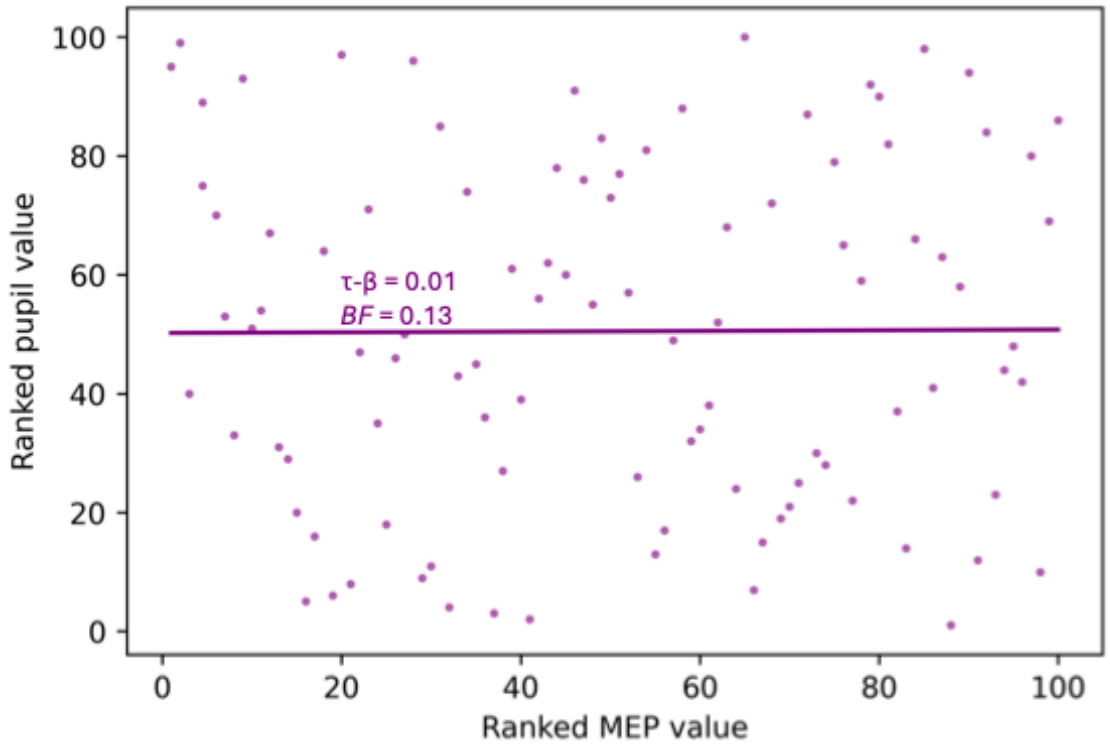
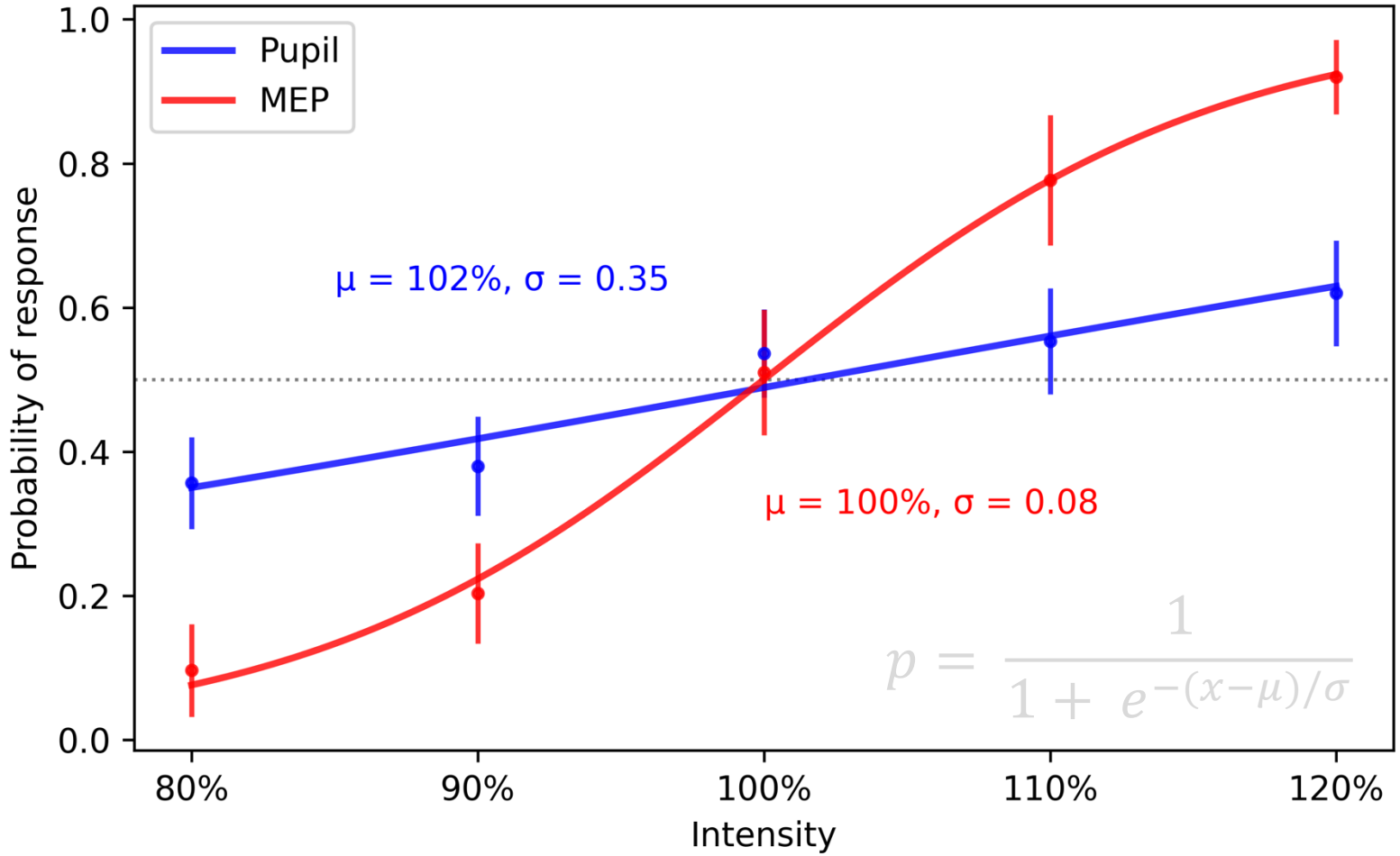


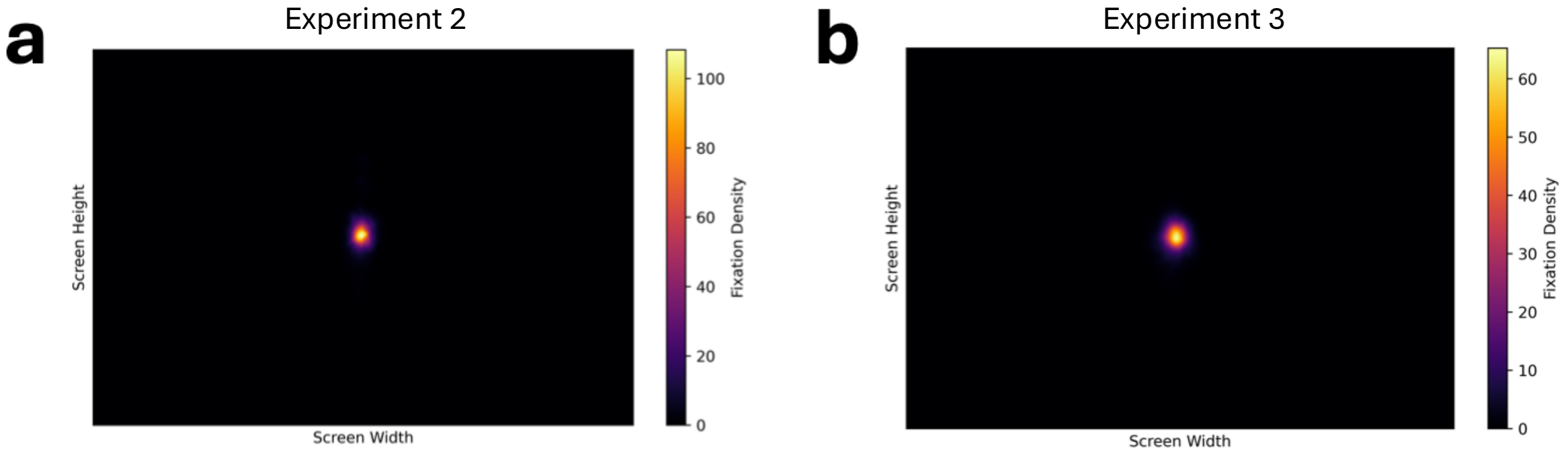
MEP: Motor Evoked Potential

Why did they break up?

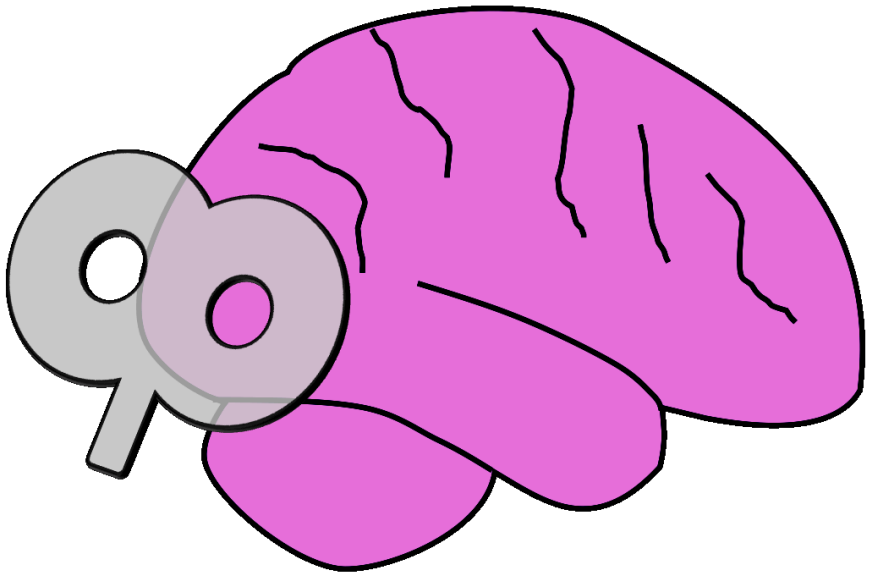
20
11F, 9M
age 24.65±5.39



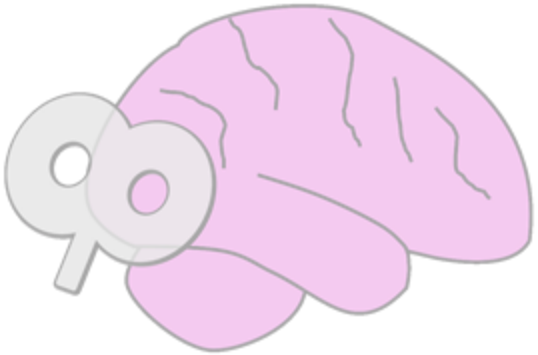
Fixations Exp2 & Exp3



What about alternatives?



What about alternatives?



But there are still problems…

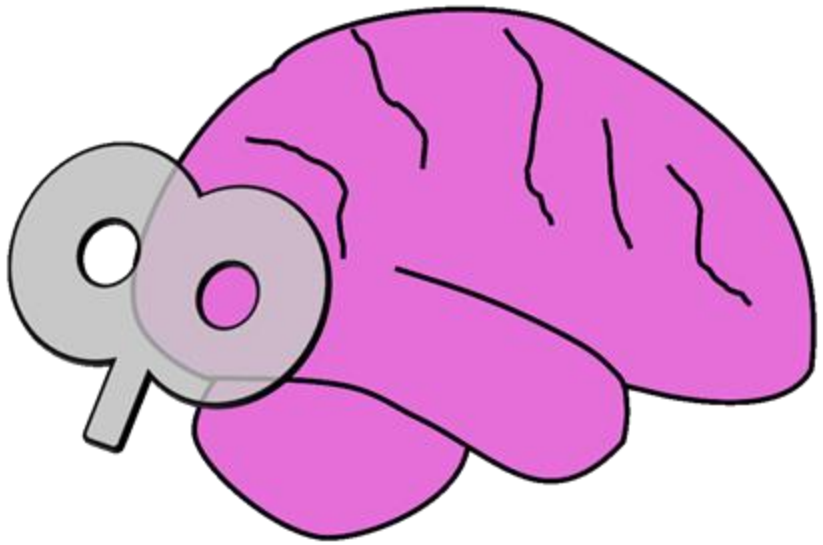
CORRESPONDENCE · Volume 16, Issue 1, P23-24, January-February, 2023

Open Access

One in four people fail to perceive phosphenes during early visual cortex transcranial magnetic stimulation

Phivos Phylactou · Artemis Traikapi · Nikos Konstantinou

BRAIN STIMULATION



?

PT and rMT

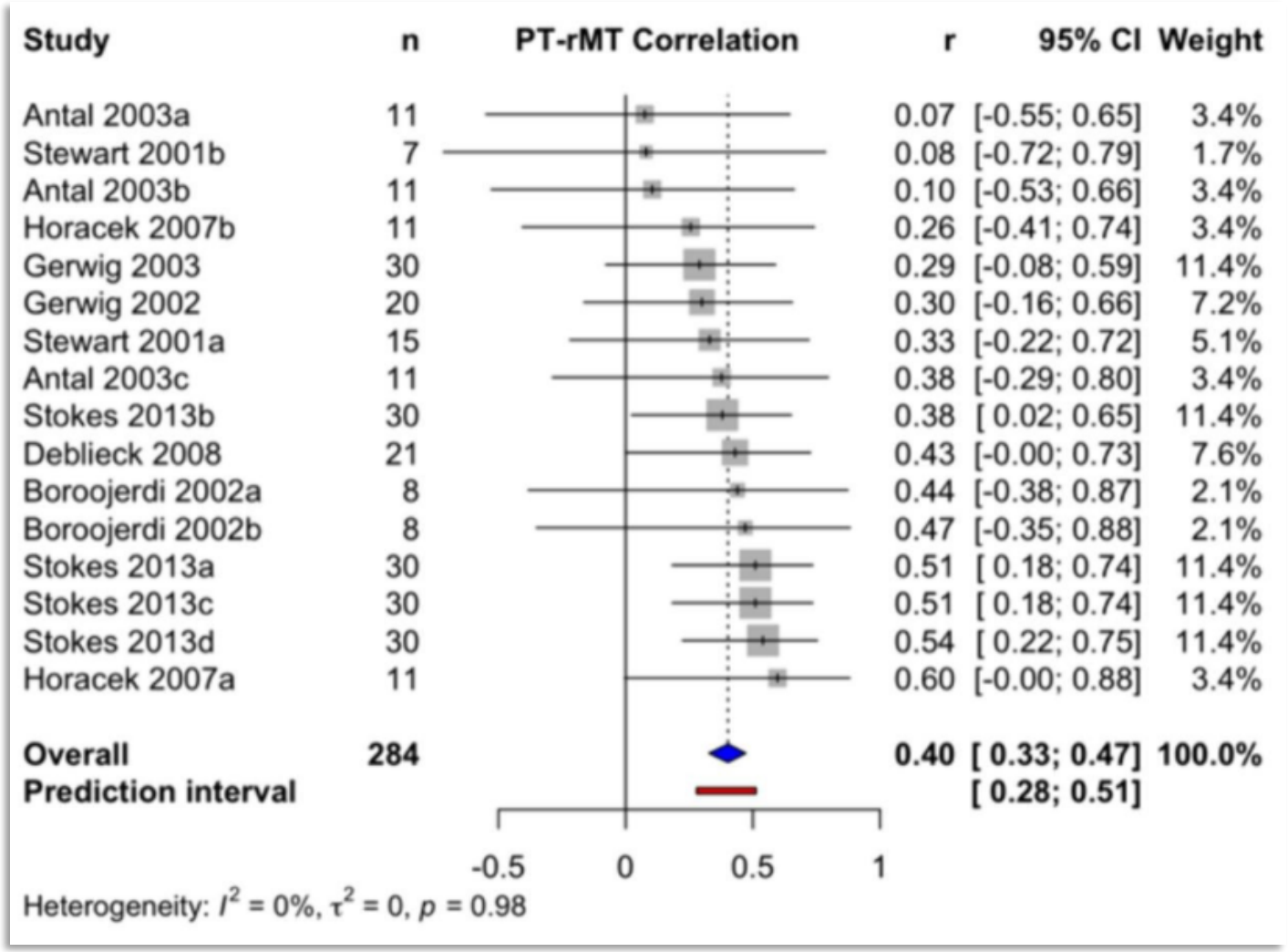
ELSEVIER

Progress in Neuro-Psychopharmacology and Biological Psychiatry

Volume 133, 13 July 2024, 111020

Phosphene and motor transcranial magnetic stimulation thresholds are correlated: A meta-analytic investigation

P. Phylactou [a b], T.N.M. Pham [b], N. Narskhani [b], N. Diya [b], D.A. Seminowicz [c], S.M. Schabrun [a b]



PT: Phosphene Threshold; rMT: Resting Motor Threshold

PT and rMT

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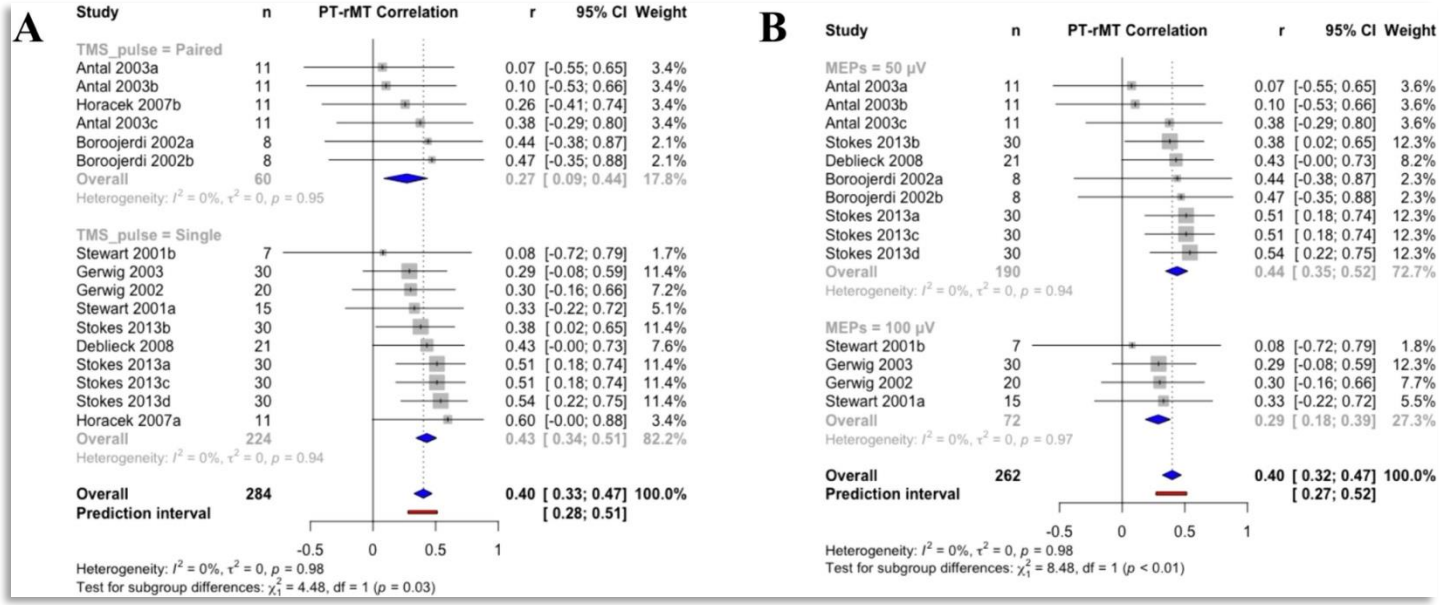
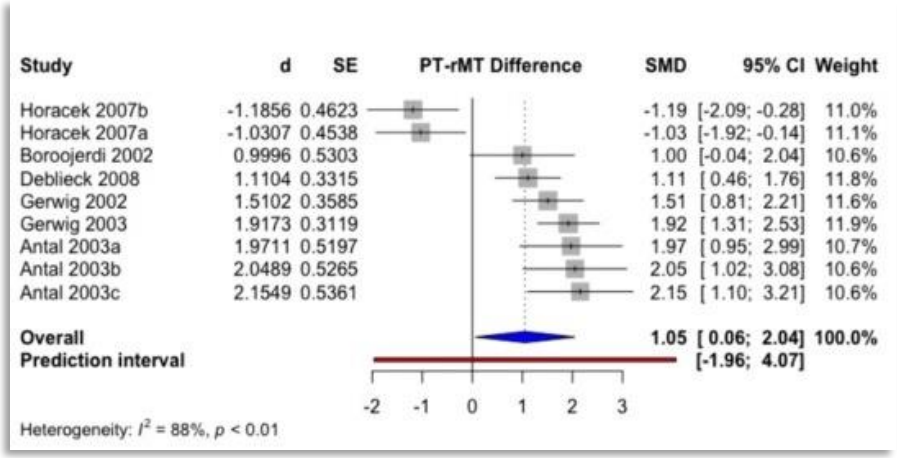
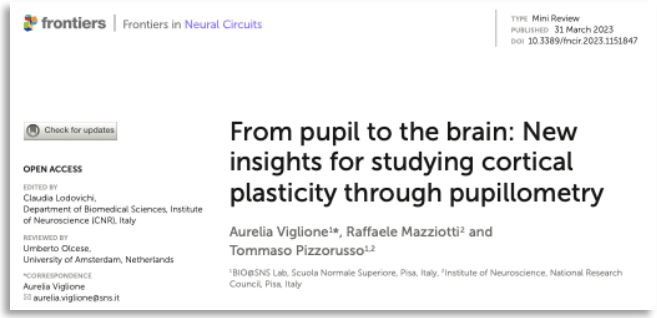




PT: Phosphene Threshold; rMT: Resting Motor Threshold

LC & NE



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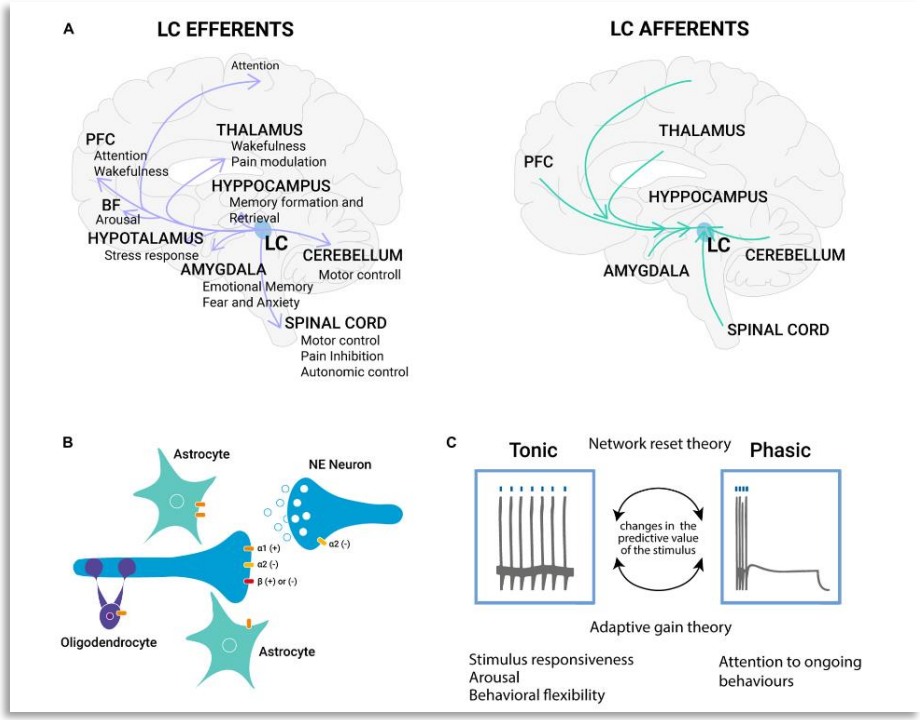
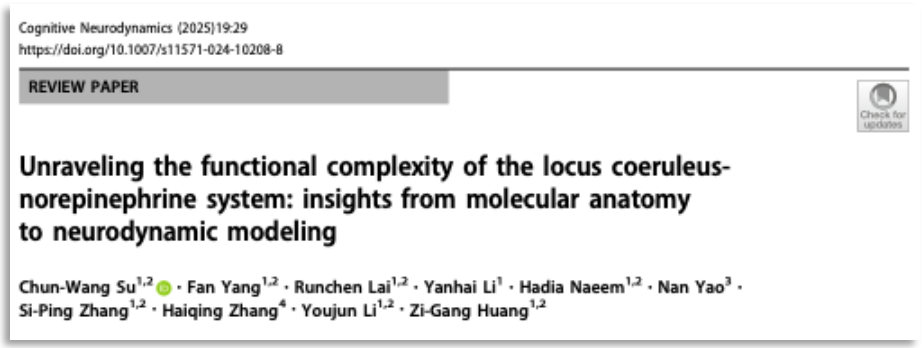
From pupil to the brain: New insights for studying cortical plasticity through pupillometry

Aurelia Viglione[1]*, Raffaele Mazziotti[2] and Tommaso Pizzorusso[1,2]

[1]BIO@SNS Lab, Scuola Normale Superiore, Pisa, Italy, [2]Institute of Neuroscience, National Research Council, Pisa, Italy





Cognitive Neurodynamics (2025)19:29
https://doi.org/10.1007/s11571-024-10208-8

REVIEW PAPER

Check for updates

Unraveling the functional complexity of the locus coeruleus-norepinephrine system: insights from molecular anatomy to neurodynamic modeling

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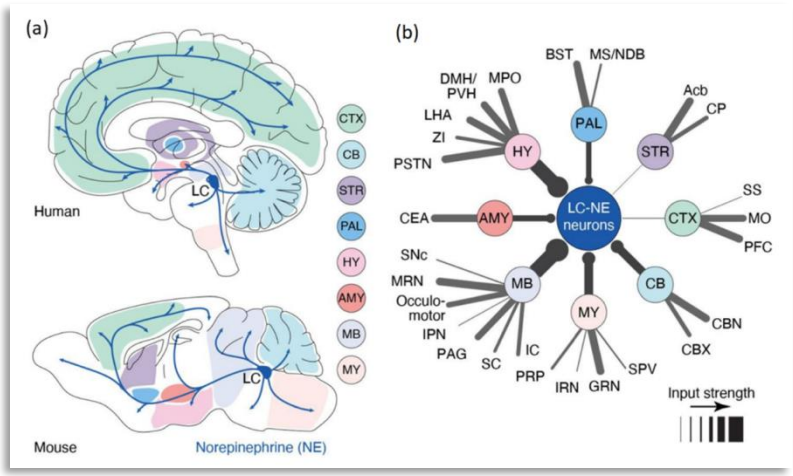

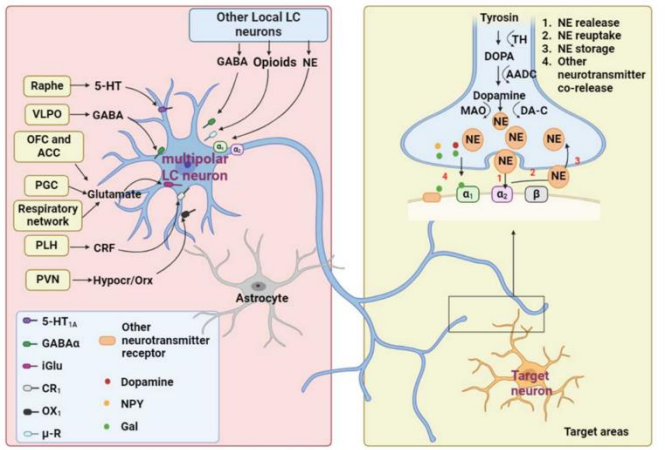

LC: Locus Coeruleus; NE: Norepinephrine