

**Welcome!**

1. course overview & resources
2. facility, informed consent, accidents, security training, artifacts
3. Structural MRI, volume, surface, cortical thickness
4. Neuro-Query, big data, Pilot studies, Individual subjects
5. Pipelines, transparency, Open Science



**KLINIKUM**  
DER UNIVERSITÄT MÜNCHEN

CAMPUS GROSSHADERN  
CAMPUS INNENSTADT  
Klinik für Psychiatrie und Psychotherapie



# From Scans to Brain: MRI Basics and Safety Issues

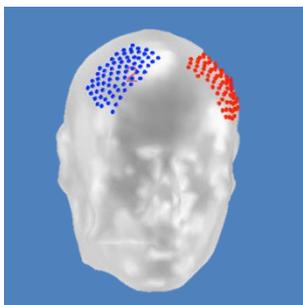


**Daniel Keeser**

**Research group “Neuromodulation and Multimodal NeuroImaging”**

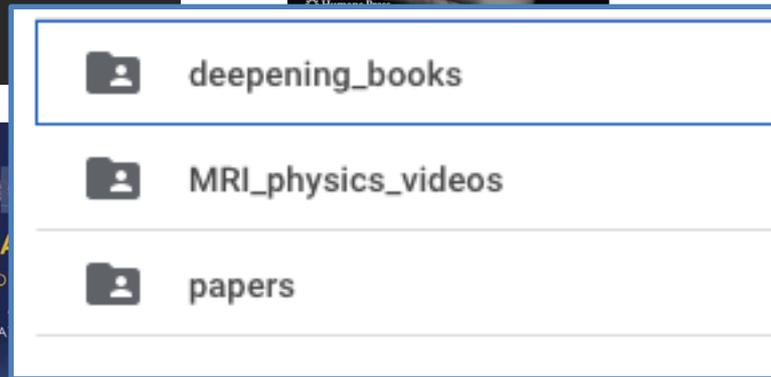
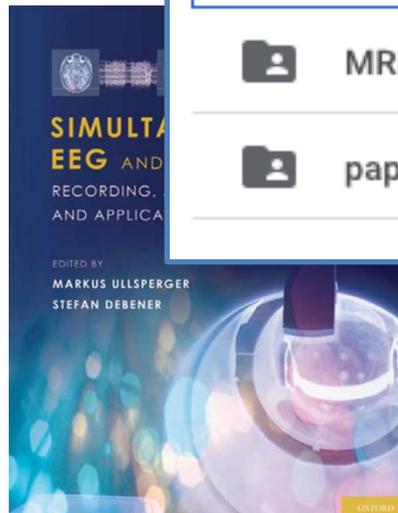
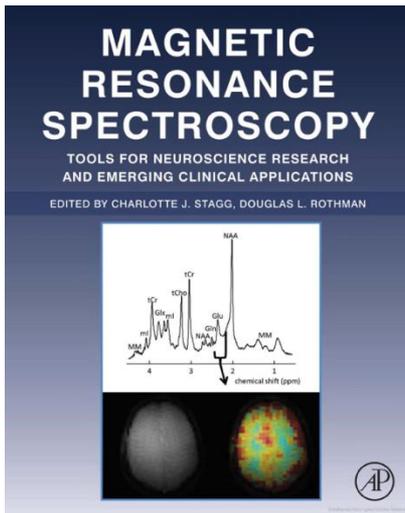
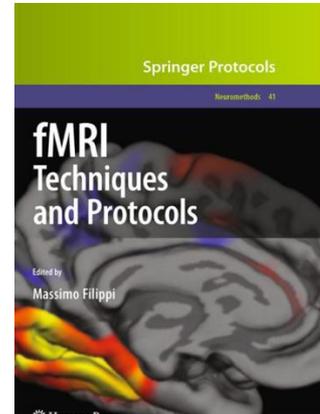
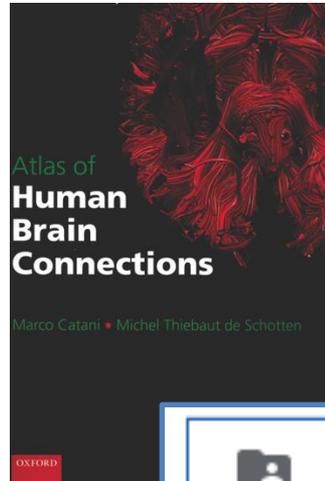
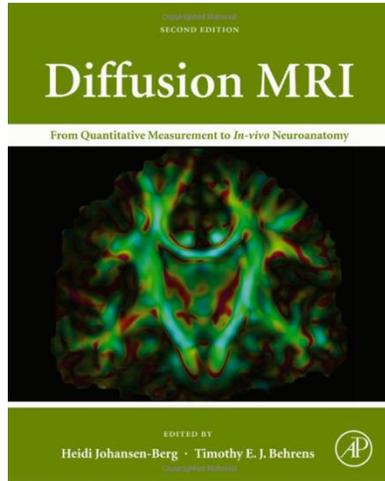
**Dept. of Psychiatry and Psychotherapy, University Hospital (LMU), Munich, Germany**

**NeuroImaging Core Unit Munich (NICUM), University LMU, Munich, Germany**



# Resources provided (subsequent deepening)

[https://drive.google.com/drive/folders/1uSG6F7pJ6EFNODxoUtUSgzsfY\\_IHwd9q?usp=drive\\_link](https://drive.google.com/drive/folders/1uSG6F7pJ6EFNODxoUtUSgzsfY_IHwd9q?usp=drive_link)

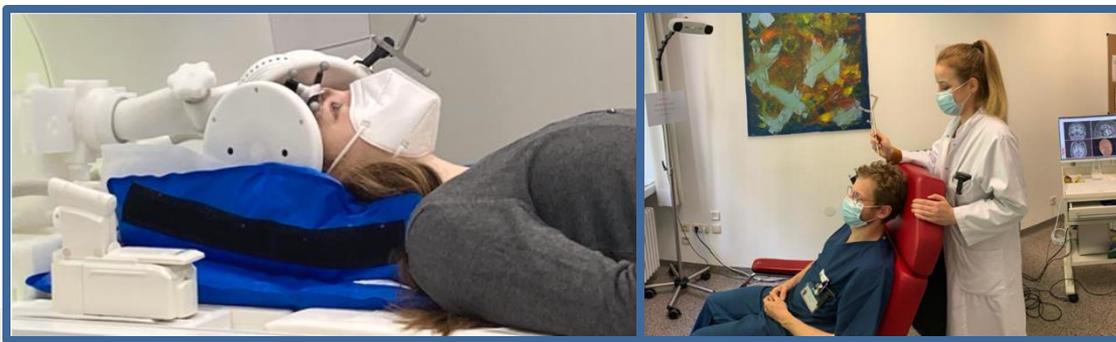
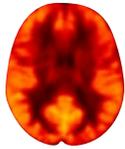


Online version downloaded from  
<http://www.practicereproducibleresearch.org>

Cite as

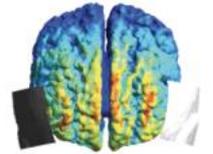
Kitzes, J., Turek, D., & Deniz, F. (Eds.). (2018). *The Practice of Reproducible Research: Case Studies and Lessons from the Data-Intensive Sciences*. Oakland, CA: University of California Press.

ASL

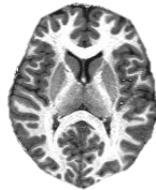


Simulation

1



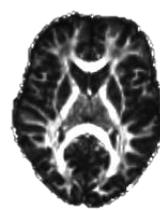
T1



EPI



FA



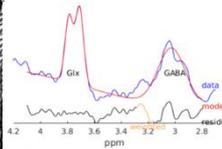
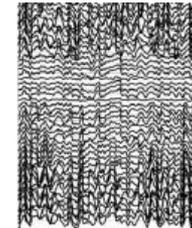
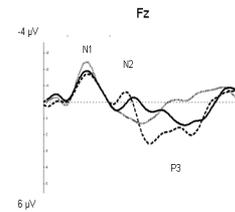
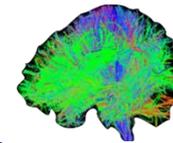
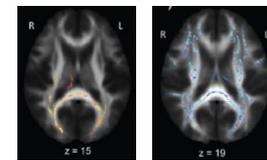
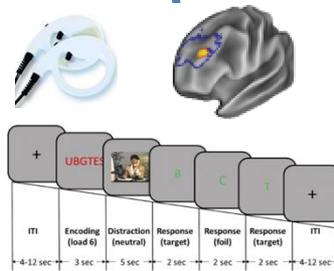
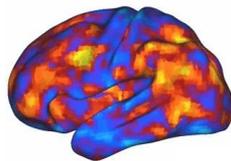
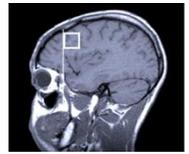
MD



EEG



MRS



GM volumes

GM surfaces

rsfMRI

task-fMRI

Tractography

ERP, Phase

Keeser et al., *J Neuroscience* 2011

Keeser et al., *NeuroImage* 2011

Palm\*, Keeser\* et al., *Schizophrenia Bulletin* 2016

Chang et al., *NeuroImage* 2024

Wörsching et al., *NeuroImage* 2017

Wörsching et al., *Brain Stimulation* 2018

Bulubas et al., *Brain Stimulation* 2019, 2022

Mizutani-Tiebel et al., *NeuroImage Clinical* 2022

# Physics of MRI

---

 1\_Intro\_to\_MR\_physics.mp4 

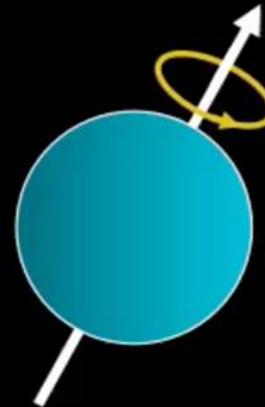
 2\_ImageFormation.mp4 

 2a\_Basic\_Maths\_Week2Lecture2.mp4 

 3\_Pulse\_Sequences.mp4 

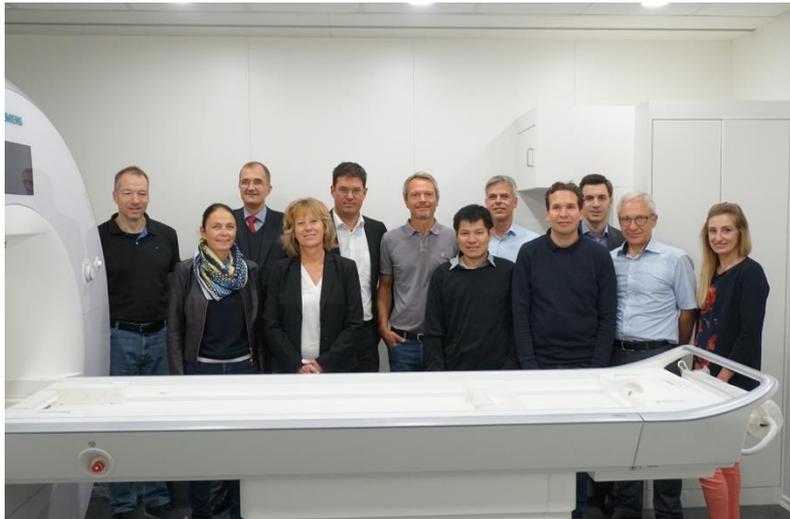
 4\_Contrast\_Manipulation\_2014.mp4 

## Introduction to MRI Physics



Karla Miller ([karla@fmrib.ox.ac.uk](mailto:karla@fmrib.ox.ac.uk))

# MRI facility – arrival of the scanner 2019



## HISTORY



2015

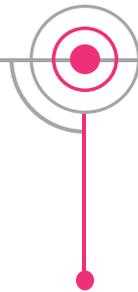


- Proposal for research scanner submitted to DFG
- grant awarded by DFG/Bavarian state (2,45 Mio. €)

2016



2017

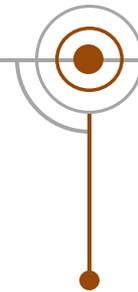


- 2018: Construction planning and construction work
- end of 2019: scanner transferred to KUM/LMU

2018/  
2019



2020



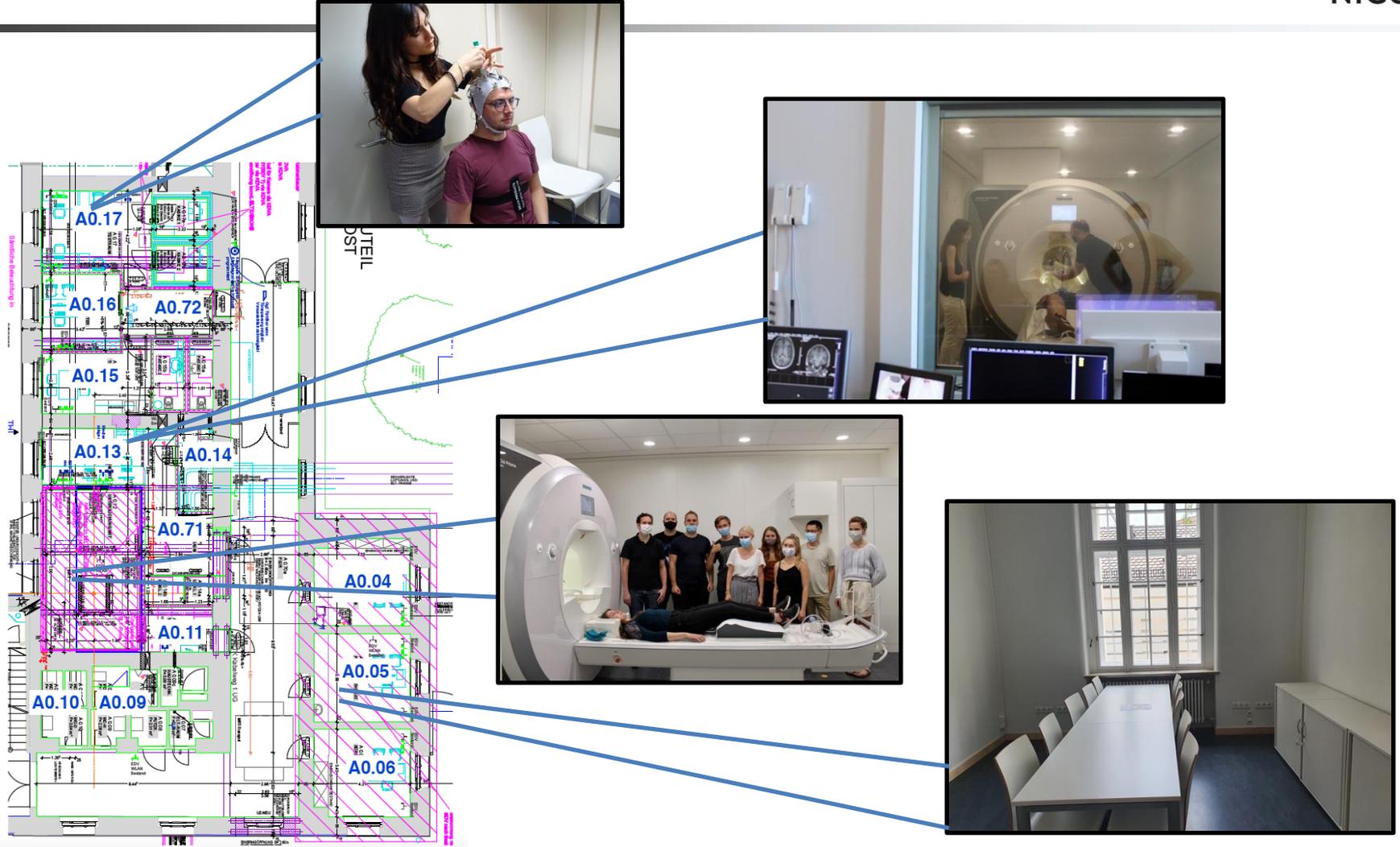
### Roadmap NIMG Research at LMU:

- 2 x 3T scanners (2017)
- Animal MRI (2018)
- 7T scanner (2022)

- Sharing responsibilities LMU/KUM
- construction costs: 660,000€ KUM, 1 Mio. € LMU

8/2020: Release of the NICUM research scanner  
Real start 1/2021

# MRI facility – rooms/location



# Current Research Topics

Biological Psychiatry  
Available online 27 April 2024  
In Press, Journal Pre-proof

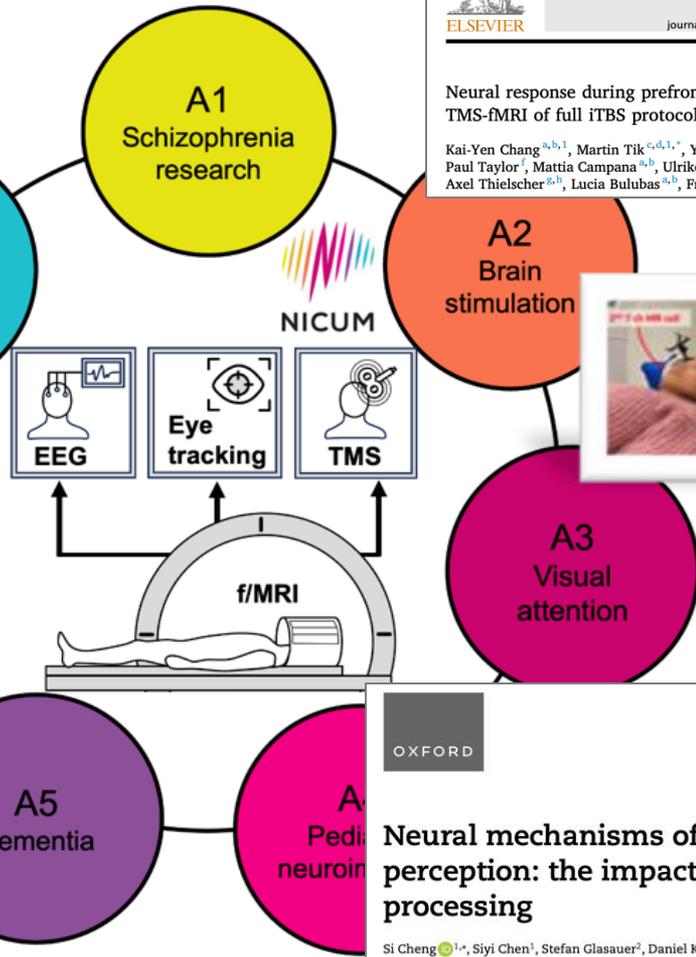
**Signature of altered retinal microstructures and electrophysiology in schizophrenia spectrum disorders is associated with disease severity and polygenic risk**

Emanuel Boudriot<sup>1,2\*</sup>, Vanessa Gabriel<sup>1\*</sup>, David Popovic<sup>1,2</sup>, Pauline Pinget<sup>1</sup>, Vladislav Yakimov<sup>1,3</sup>, Sergi Papiol<sup>2,4</sup>, Lukas Roell<sup>1,5</sup>, Genc Hasanaj<sup>1,6</sup>, Simiao Xu<sup>1</sup>, Joanna Moussiopoulou<sup>1</sup>, Siegfried Priglinger<sup>7</sup>, Christoph Kern<sup>7</sup>, Eva C. Schulte<sup>4,8,9</sup>, Alkomiet Hasan<sup>10,11</sup>, Oliver Pogarell<sup>1</sup>, Peter Falkai<sup>1,2,11</sup>, Andrea Schmitt<sup>1,2,11</sup>, Benedikt Schworm<sup>7</sup>  
CDP Working Group<sup>12,610</sup>

NeuroImage 291 (2024) 120596  
Contents lists available at ScienceDirect  
**NeuroImage**  
journal homepage: [www.elsevier.com/locate/ynimg](http://www.elsevier.com/locate/ynimg)

**Neural response during prefrontal theta burst stimulation: Interleaved TMS-fMRI of full iTBS protocols**

Kai-Yen Chang<sup>a,b,1</sup>, Martin Tik<sup>c,d,1,\*</sup>, Yuki Mizutani-Tiebel<sup>a,b</sup>, Anna-Lisa Schuler<sup>c</sup>, Paul Taylor<sup>f</sup>, Mattia Campana<sup>a,b</sup>, Ulrike Vogelmann<sup>a</sup>, Barbara Huber<sup>a</sup>, Esther Dechantsreiter<sup>a</sup>, Axel Thielscher<sup>a,h</sup>, Lucia Bulubas<sup>a,b</sup>, Frank Padberg<sup>a,b,1</sup>, Daniel Keiser<sup>a,b,1,\*</sup>



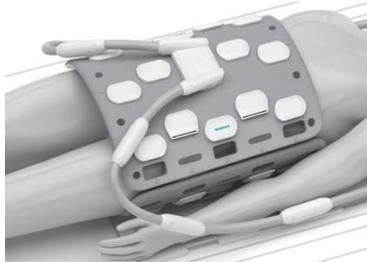
Cerebral Cortex, 2023, 1-14  
<https://doi.org/10.1093/cercor/bhad453>  
Original Article

**Neural mechanisms of sequential dependence in time perception: the impact of prior task and memory processing**

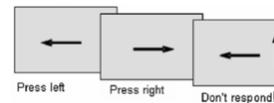
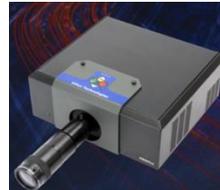
Si Cheng<sup>1,\*</sup>, Siyi Chen<sup>1</sup>, Stefan Glasauer<sup>2</sup>, Daniel Keiser<sup>3</sup>, Zhuanghua Shi<sup>1,3</sup>

# MRI facility - Equipment

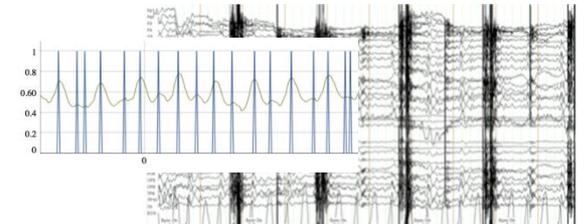
## Head and body coils



## Video projector fMRI

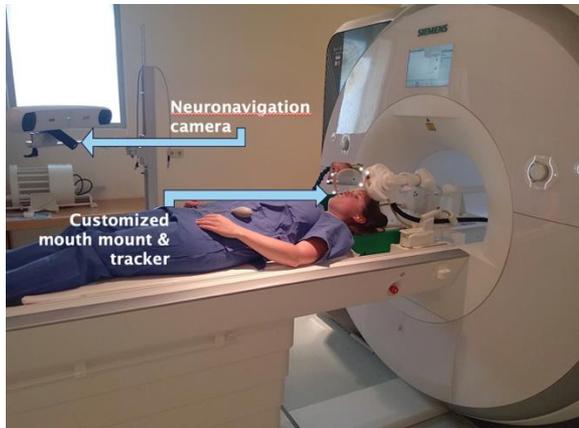
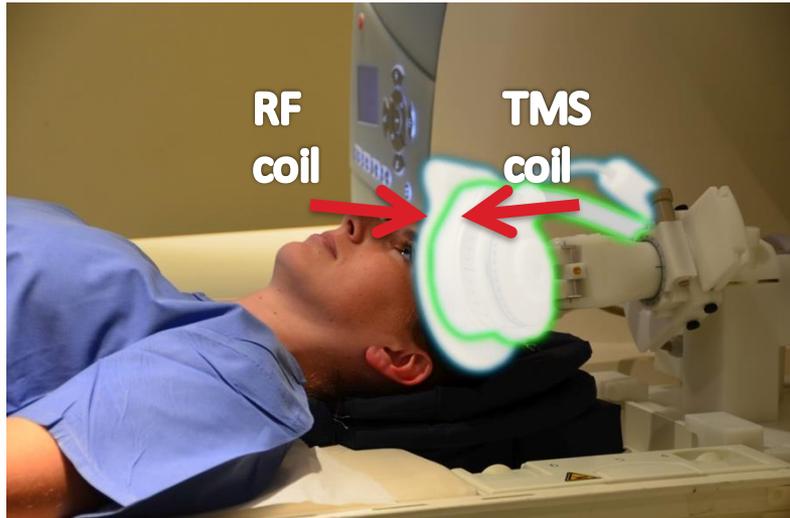


## Simultaneous EEG/ECG/respiration



# MRI facility - Equipment

Neuronavigated  
TMS inside MRI



Eye Tracking



TMS



Contrast agent  
pump



# MR safety

---

1. Do you have an electronic implant or device (e.g. cardiac pacemaker, implanted defibrillator, neurostimulator, insulin pump)?

[Redacted response area]

# MR safety – Informed consent

proCompl  
Ort der Beh  
PatientID  
geboten am  
Krankenkas  
Zusätzliche

unbekannt Radiologie

Hospital Data Imprint/Stamp



Patient identification sticker

Page 3/6

R 20/GB Magnetic Resonance Imaging (MRI/MRS/MRA)

ble administration of a contrast medium containing gadolinium in any case and bring the result with you to the examination.

A magnetic resonance examination of the mammary gland (MRM) must be performed between the 7th and 12th day of the menstrual cycle (1st day of the menstrual cycle = 1st day of monthly bleeding) for women of childbearing age in order to avoid incorrect examination results if possible.

If an examination of the small intestine is planned in your case, your doctor will provide you with further instructions if applicable.

Please follow the doctor's instructions carefully, in particular with regard to taking medication and hormones (e.g. hormone substitutes in the menopause).

If general anaesthesia is planned for you, you will be informed about preparation for this, how it is performed and the associated risks during a separate patient-doctor discussion.

Please be sure to inform the doctor or the medical staff if you have permanent make-up, tattoos or a transdermal plaster or have a magnetically fixed dental prosthesis or other metal or magnetic implants.

### For the examination

Injury can occur if metal objects enter the magnetic field, and this may also lead to image distortion (artefacts)! Therefore, please remove all metal or magnetic items before entering the examination room:

- Watches, eyeglasses, keys, piercings/jewellery, hairpins/hairclips, ballpoint pens, purses, loose coins, wallet including bank or credit cards (magnetic strips will be erased!), etc.
- Clothing with metal parts (e.g. belt buckles), clothing with zippers (zips), functional underwear, metal buttons or similar items (metal catches or fasteners on bras) but also make-up may not be worn.
- Removable dental prostheses, braces.
- Acupuncture needles, hearing aids; cochlea implants in the inner ear could be damaged during magnetic resonance imaging.

### After the examination

If you have received a sedative, please note that your reactions will be slowed temporarily. Therefore, you have to be picked up by an adult. Due to the lingering effects of the medication, you may not actively participate in road traffic, may not perform any dangerous activities, may neither drink any alcohol nor smoke within the first 24 hours or the length of time stipulated by your doctor. You should also refrain from making any important decisions.

If you received Buscopan®, your vision can be temporarily impaired. Therefore, you have to be picked up by an adult, or you are monitored for some time after the examination. The doctor will inform you about how long your ability to participate in road traffic and operate machines will be impaired.

The safety of MRI examination for patients having medical implants or metallic foreign bodies in place is the higher, the lower the field strength of the scanner. For modern MRI scanners with higher field strengths, some implants, e.g. IUD ("coil", contraceptive copper T), are not approved by the manufacturer in general. The doctor will discuss with you whether the IUD could dislocate (slip) as a consequence of the MRI, impairing the contraceptive effect and necessitating a check of the IUD's correct positioning; if necessary, ask him/her about it.

A shunt in the head (ventricular shunt) does not cause any issues for the MRI examination. However, we recommend

having its correct function checked after the examination, if applicable.

### Important questions

In order for the doctor to do this examination for you, we ask you questions carefully and

Age: \_\_\_\_\_ years • Height: \_\_\_\_\_

Gender: \_\_\_\_\_

1. Do you have any implants (e.g. cardiac valve, stent, aneurysm clip, dental prosthesis, cochlear implant, hearing aid, etc.)?

If yes, please indicate! \_\_\_\_\_

2. Please be aware: an MRI there are certain types of to inform your doctor if will decide whether you

Are there any additional parts/implants in the your surgical clips, vessel prosthesis, skin chips, dental prostheses, metal fragments, coil (intracranial), puncture needles, insulin pump, neurostimulator, hearing aid, etc.

If yes, please indicate! \_\_\_\_\_

3. Do you have tattoos?

If yes, please indicate! \_\_\_\_\_

4. Do you have a plaster or cast on any part of your body?

If yes, please indicate! \_\_\_\_\_

5. Do you have any metal objects on your person (e.g. keys, coins, pens, etc.)?

If yes, please indicate! \_\_\_\_\_

6. Do you have any tattoos?

If yes, please indicate! \_\_\_\_\_

7. Do you have any allergies (e.g. to contrast medium, antibiotics, etc.)?

If yes, please indicate! \_\_\_\_\_

8. Do you have any chronic diseases (e.g. diabetes, hypertension, etc.)?

If yes, please indicate! \_\_\_\_\_

9. Do you have any chronic diseases (e.g. diabetes, hypertension, etc.)?

If yes, please indicate! \_\_\_\_\_

10. Do you have any chronic diseases (e.g. diabetes, hypertension, etc.)?

If yes, please indicate! \_\_\_\_\_

11. Do you have any chronic diseases (e.g. diabetes, hypertension, etc.)?

If yes, please indicate! \_\_\_\_\_

12. Do you have any chronic diseases (e.g. diabetes, hypertension, etc.)?

If yes, please indicate! \_\_\_\_\_

13. Do you have any chronic diseases (e.g. diabetes, hypertension, etc.)?

If yes, please indicate! \_\_\_\_\_

R 20/GB Magnetic Resonance Imaging (MRI/MRS/MRA)

Page 4/6

9. Do you have or have you ever had atrial fibrillation?  Yes  No

10. Have you ever had an operation of the heart, the head or of the body region to be examined?  Yes  No

If yes, please indicate! \_\_\_\_\_

11. Did you have any diseases of the upper abdominal organs (e.g. liver inflammation/hepatitis, fatty liver, cirrhosis, biliary colic/bile stones, jaundice, pancreatitis)?  Yes  No

If yes, please indicate! \_\_\_\_\_

12. Do you have or have you ever had any diseases or malformation of the kidneys/urinary organs (e.g. dysfunction of the kidneys, kidney stones, chronic urinary tract infection, nephritis/inflammation of the kidneys, congenital malformation [e.g. duplex kidney], bladder emptying disorder/delayed bladder emptying)?  Yes  No

If yes, please indicate! \_\_\_\_\_

13. Have you had a kidney or liver transplant?  Yes  No

If yes, please indicate! \_\_\_\_\_

14. Do you suffer from noises in the ears (tinnitus)?  Yes  No

If yes, please indicate! \_\_\_\_\_

15. Do you have any eye diseases (e.g. cataract, glaucoma)?  Yes  No

If yes, please indicate! \_\_\_\_\_

16. Do you have a tendency to have claustrophobia (fear of narrow or enclosed spaces) or panic attacks?  Yes  No

If yes, please indicate! \_\_\_\_\_

The following examination is proposed: Magnetic resonance imaging

With contrast medium

Without contrast medium

Body region to be examined: \_\_\_\_\_

Additional questions for women

1. Could you possibly be pregnant?  Yes  No

2. Are you breastfeeding?  Yes  No

Additional questions for men

1. Do you have or have you ever had any diseases of the prostate (e.g. prostatic enlargement, prostatitis [inflammation of the prostate], prostate cancer)?  Yes  No

If yes, please indicate! \_\_\_\_\_

Doctor's notes on the patient-doctor discussion

(e.g. the type and importance of the examination; alternative examination methods; risk and possible complications; instructions for before and after the examination; individual risks and possible associated complications; specific side-effects of the contrast medium; explanations on questions of the patient; possible consequences if the patient/parents refuse(s) to participate(s) in the examination; restrictions to the consent, e.g. with regard to the contrast medium; patient's reasons for refusal; determination of a minor's ability to comprehend; patient has a legal surrogate decision-maker/a legal guardian; patient has appointed a legal representative/provided a medical power of attorney; duration of the discussion)

\_\_\_\_\_

\_\_\_\_\_

\_\_\_\_\_

\_\_\_\_\_

## Nur im Falle einer Ablehnung der Untersuchung

R 20/GB Magnetic Resonance Imaging (MRI/MRS/MRA)

Page 4/6

I/we do not consent to the proposed examination. I/we have read the informed consent form, and I/we understand it. I/we have been explicitly informed of the possible consequences involved in my/our refusal (e.g. failure to detect diseases and determine their level of severity and progression, no exact localisation of the focus of a disease).

\_\_\_\_\_

\_\_\_\_\_

\_\_\_\_\_

\_\_\_\_\_

\_\_\_\_\_

\_\_\_\_\_

\_\_\_\_\_

\_\_\_\_\_

\_\_\_\_\_

\_\_\_\_\_

\_\_\_\_\_

\_\_\_\_\_

\_\_\_\_\_

\_\_\_\_\_

\_\_\_\_\_

\_\_\_\_\_

\_\_\_\_\_

\_\_\_\_\_

\_\_\_\_\_

\_\_\_\_\_

\_\_\_\_\_

\_\_\_\_\_

\_\_\_\_\_

\_\_\_\_\_

\_\_\_\_\_

\_\_\_\_\_

\_\_\_\_\_

\_\_\_\_\_

\_\_\_\_\_

\_\_\_\_\_

notwendige  
wurde nach  
sich daraus  
kennen von  
keine exakte  
niert.

m/des Arztes

\_\_\_\_\_

niert. Dabei  
den Fragen,  
hung, über  
über Neben-  
auch über

1. fühle(n)  
(n) himmelt  
geplante  
stmittelgabe

übertragung  
(g) keine

ersuchungs-  
wir hierzu

\_\_\_\_\_

\_\_\_\_\_

\_\_\_\_\_

\_\_\_\_\_

\_\_\_\_\_

\_\_\_\_\_

\_\_\_\_\_

\_\_\_\_\_

\_\_\_\_\_

\_\_\_\_\_

\_\_\_\_\_

\_\_\_\_\_

\_\_\_\_\_

\_\_\_\_\_

### Sehr

Ihre Ä  
genauer die  
und Folgen  
Aufklärung

### Was

Bei de  
Hilfe eine  
bestimmte  
Echogigale  
Querschnitt  
können kr  
scheibenvo  
exakt nach  
benutzen.  
Gewebent  
eine Verk  
Strahlenbeh

### Wie

Die M  
licht die U  
Spektrosko  
lysieren un  
sungen  
die MRT, s  
Darstellung  
Spektrosko  
aufgenomm  
von Zacke  
wiederspieg  
Ihr Arzt wi  
Innen gepl

### Wie

Je nach  
in der Reg

Dokumentier  
Juristische Be  
verboten.  
Bestell-Adres

### Dear Patient, Dear Parents,

The purpose of this informed consent form is to prepare for the patient-doctor discussion carefully before the discussion and to read it carefully and completely. For your treatment it will always address you directly, treatment is to be performed on your

### Which examination is proposed

Magnetic resonance imaging (MRI) is a non-invasive examination of the body. In this imaging examination probe body regions to be examined are taken with waves and magnetic fields. This way, (e.g. a prolapsed disc, a breast tumour, vascular diseases, diseases in the spine) can be accurately identified or excluded without the need to use X-rays.

Additional measurement technologies provide important information. Magnetic resonance spectroscopy (MRS) facilitates a non-invasive measurement of metabolic processes in the tissue. Diffusion-weighted imaging (DWI) or a specific examination of the nervous system (diffusion-weighted imaging, DWI/DTI) are possible with magnetic resonance imaging.

Your doctor will inform you which examination is proposed for your particular case.

### How is the examination performed

Generally, you will be lying on a table in a cylindrical opening in a cylindrical scanner. Please follow the position instructed, breathe regularly and relax. Otherwise, local

Informed Consent Documentation | Publisher: Thieme  
Autoren: Prof. Dr. med. V. Rahn, Prof. Dr. med. M. Weichselbaum  
© 2020 Thieme Compliance GmbH, Am Weichselgarten 3  
www.thieme-compliance.de

# Neuroradiolog

## Kurzbefund für Studien-MRT

Bitte an [sek.neurorad@med.lmu.de](mailto:sek.neurorad@med.lmu.de) schicken.

Von verantwortlichem\*r Mitarbeiter\*in auszufüllen:

Probanden ID/Name Studienpatient\*in: NIMG\_course\_20

MRT vom (Datum der Untersuchung):

Studie: multimodal Neuroimaging Course 2021

Verantwortliche\*r Wissenschaftler\*in: Daniel Keiser

E-Mail verantwortliche\*r Wissenschaftler\*in:



e\_2021\_004

beser@med.uni-muenchen.de

Vom\*n N

Vorliegen

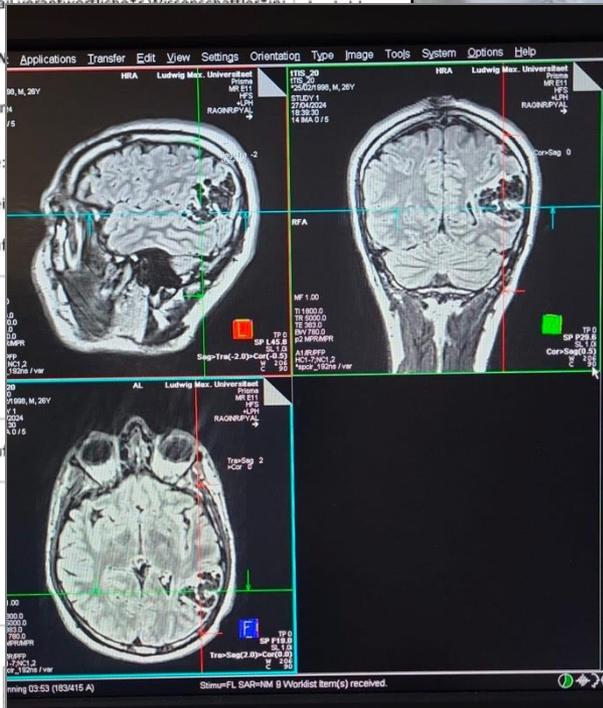
Befunde:

Keine Pathologien oder Auffälligkeiten nachweisbar.

Zufallsbefund ohne medizinische Relevanz.

Zufallsbefund, weitere diagnostische Abklärung wird empfohlen.

Datum:



Befunde:

Keine Pathologien oder Auffälligkeiten nachweisbar.

Zufallsbefund ohne medizinische Relevanz.

*Befund: Vaskuläre - Zysten - keine*

Zufallsbefund, weitere diagnostische Abklärung wird empfohlen.

Datum:

*14.11.21*

Name/Unterschrift Neuroradiologe\*in:

*[Handwritten Signature]*

# MR safety – dangers

---



## Risk through magnetic fields:

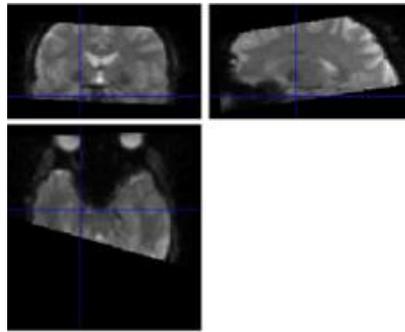
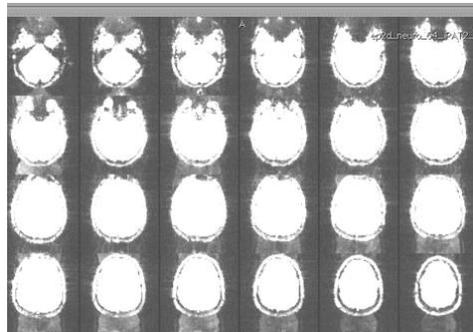
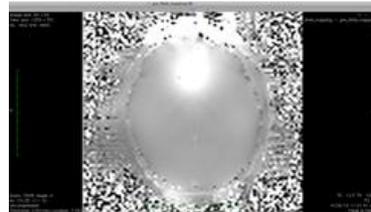
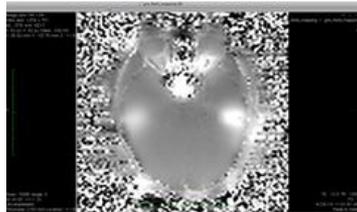
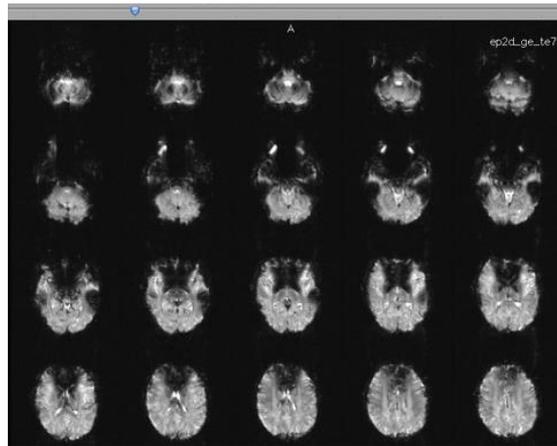
- Static magnetic fields (metal objects pulled)
- Moving objects in static field (induction, heat)
- HF-fields, gradients (heat, induction, nerve stim)



## MRI safety training

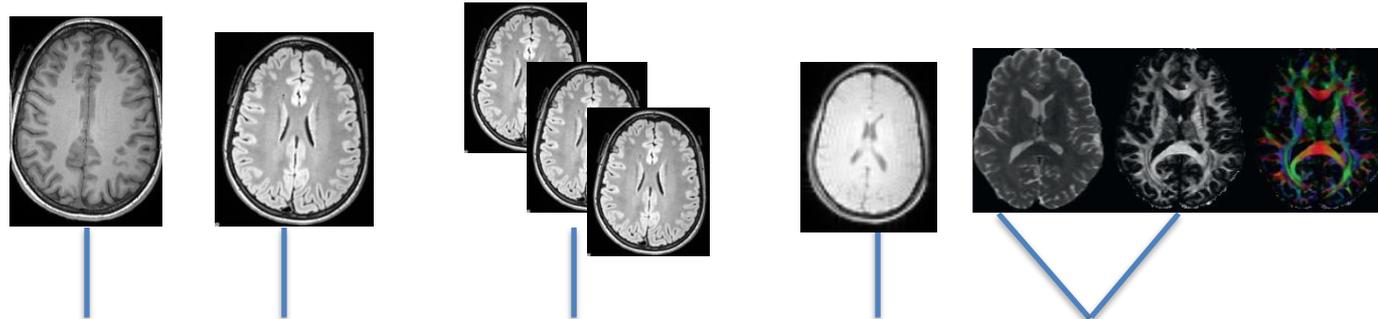
This lecture must be attended at least once a year (signature required).

# MR artifacts



Artifacts:	Variables:
<b>Type of Artifact:</b>	
No Artifacts	0
CSF Pulsation Artifacts	1
Wrapping/Aliasing Artifacts	2
Shading Artifact	3
Zebra Stripes	4
Motion Artifacts	5
Magnetic Susceptibility Artifacts	6
Insufficient FOV	7
Failed Image Transfer	8
Zippering Artifact	9
<b>Severity:</b>	
No Artifacts	0
Minimal (non-significant)	1
Significant (but probably usable for most research questions)	2
Severe (probably non-usable)	3
<b>Location:</b>	
No Artifacts	0
Whole Brain	1
Frontobasal	2
Frontal	3
Temporomesial	4
Occipital	5
Diencephalon	6
Mesencephalon	7
Pons	8
Cerebellum	9
Frontal and Occipital	25

# MR Sequences

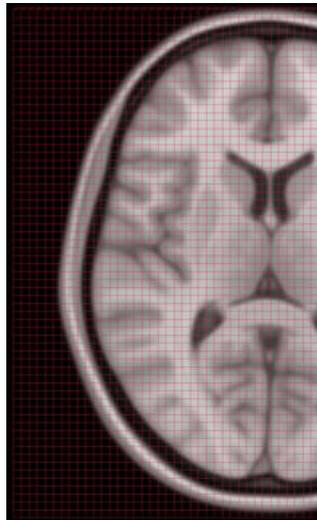
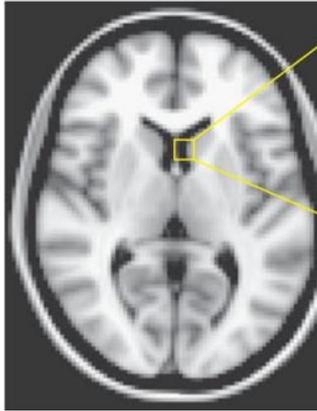


	T1-weighted	T2-weighted	EPI 1 (Resting State)	EPI 2 (Resting State)	Field maps	Diffusion weighted
Sequence	MP-RAGE	T1 / T2 weighted 'structural' scans			• <i>Motion</i>	
TR (ms)	1900	EchoPlanar SpinEcho Images			• <i>Motion (less so)</i>	
TE (ms)	2.22					
flip angle	9	T2* weighted images sensitive to BOLD			• <i>Motion</i> • <i>Breathing</i> • <i>Cardiac pulsation</i> • <i>Fatigue</i> • <i>Performance</i> • <i>Other</i>	
B value (s/mm <sup>2</sup> )	-	EPI Diffusion Weighted Images (DWI)			• <i>Motion</i>	
Diffusion directions	-					
Resolution (mm <sup>3</sup> )	0.7 x 0.7 x 0.7					
Thickness	0.7					
Accelerator/Multiband factor	2/-					
Field of View	225 x 225					
Number of slices	176					
Imaging direction	Sagittal					

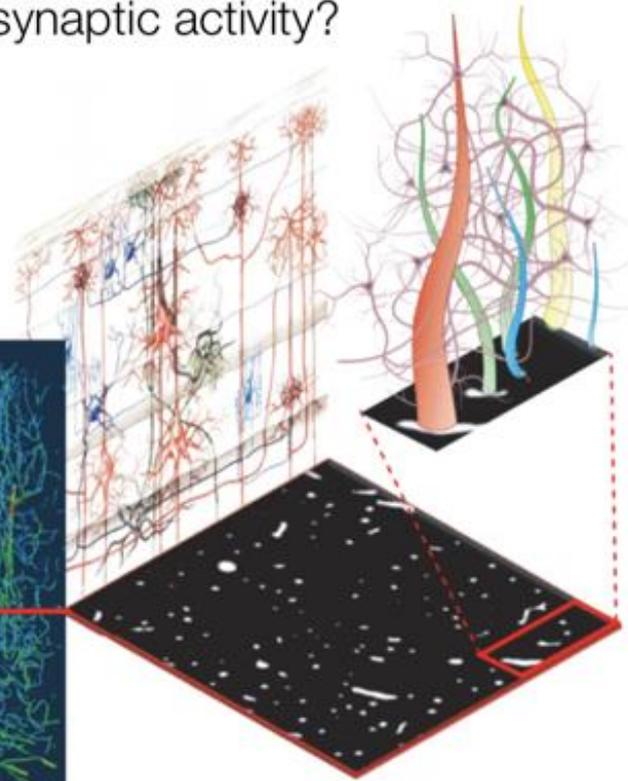
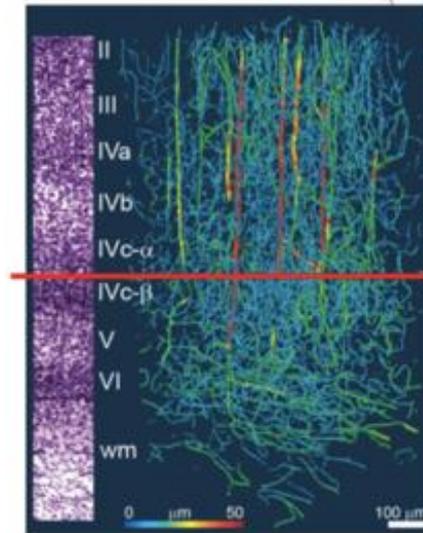
MP-RAGE = magnetization prepared-rapid gradient echo  
 mm=milimeter; . <https://www.cmrr.umn.edu>

# Volumetr

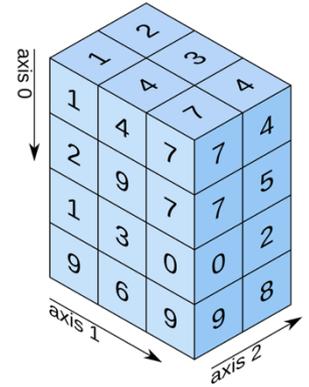
Aggregate measure  
of total synaptic activity?



Logotheitis (2008). Nature.



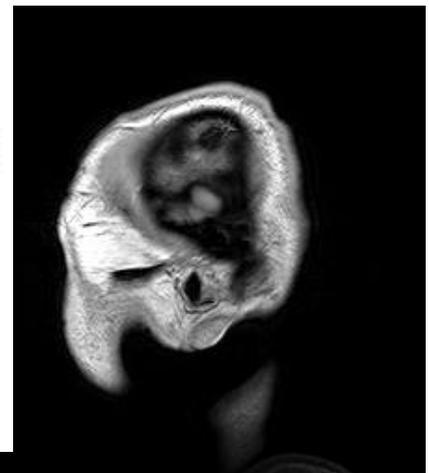
3D array



shape: (4, 3, 2)

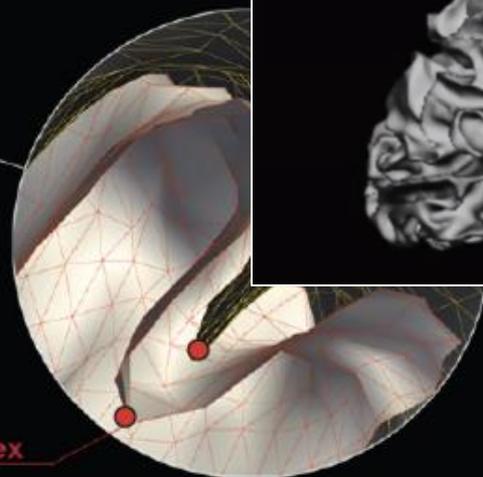
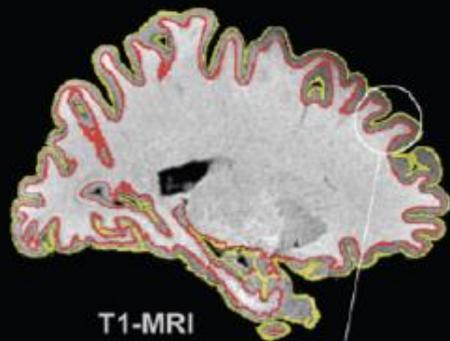
A typical fMRI voxel of 55 ml in size contains:

- 5.5 million neurons
- $2.2-5.5 \times 10^{10}$  synapses
- 22 km of dendrites
- 220 km of axons



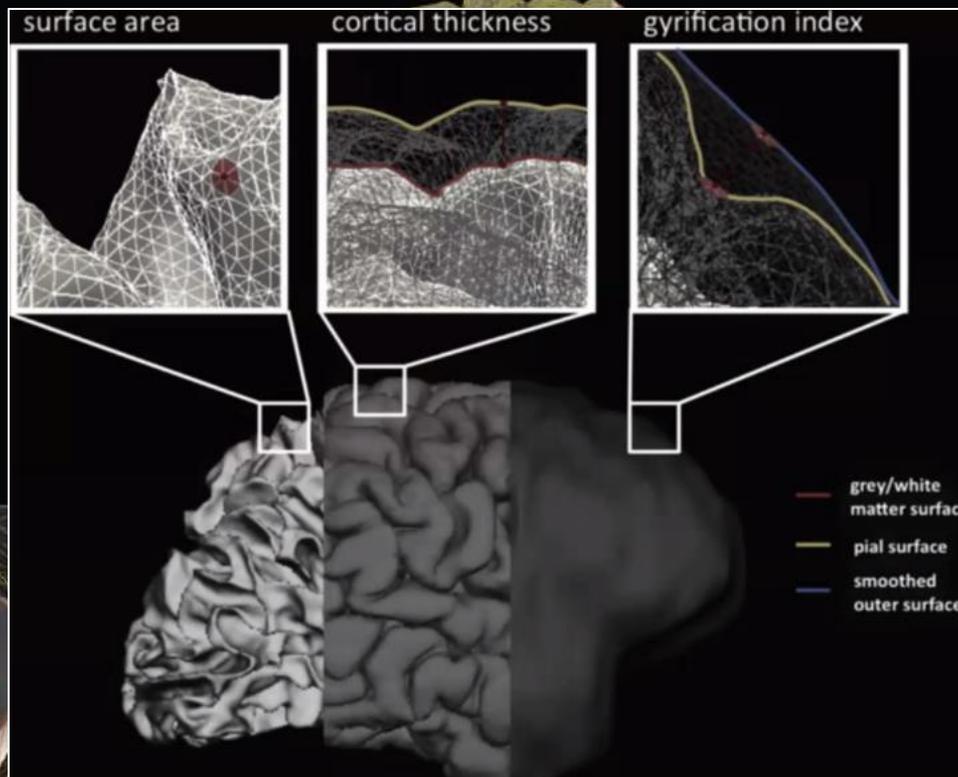
# Structural MRI

## CORTICAL THICKNESS MEASUREMENT



vertex

cortical thickness measurement



Source: Bernhardt & Misic

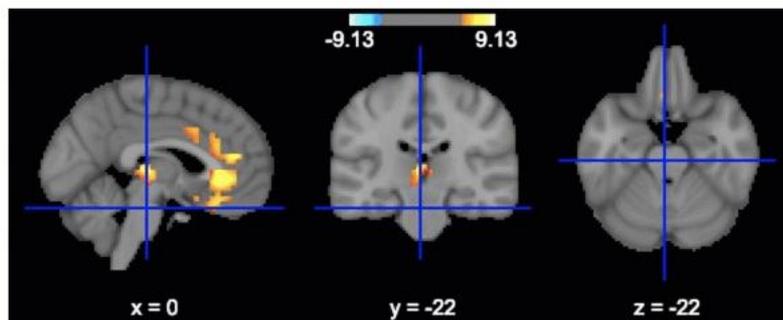
# MDD meta-analysis using Neuroquery

## 11/2019: Encode major depression into a statistical map of the brain

```
[1] from neuroquery import fetch_neuroquery_model, NeuroQueryModel
    from nilearn.plotting import view_img

encoder = NeuroQueryModel.from_data_dir(fetch_neuroquery_model())
```

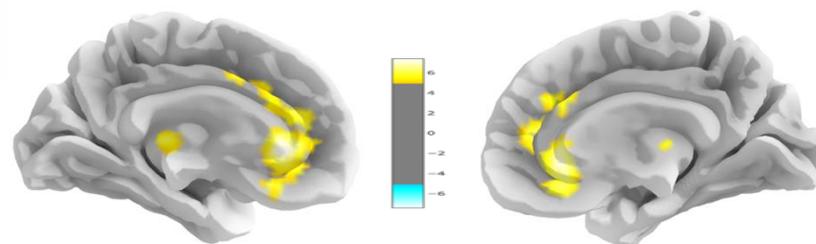
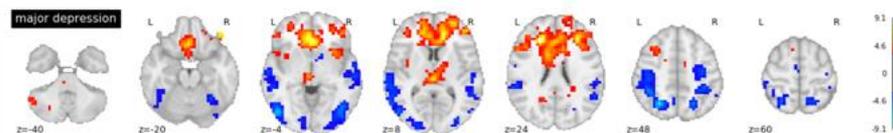
```
[8] query = """major depression"""
    result = encoder(query)
    view_img(result["z_map"], threshold=5.1)
```



```
[16] print("\nTerms recognized in the query:\n")
    print(
        response["similar_words"]
        .query("weight_in_query != 0")
        .sort_values(by="weight_in_query", ascending=False)
        .head()
    )
```

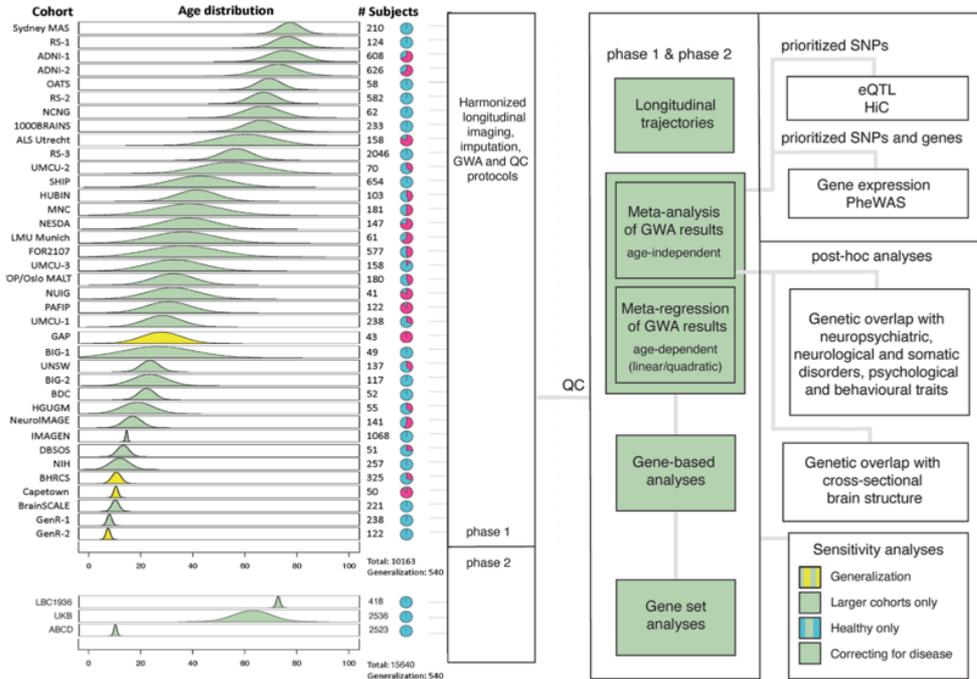
Terms recognized in the query:

	similarity	weight_in_brain_map	weight_in_query	\
major depression	0.994231	0.0	1.0	
major depression		n_documents	896	

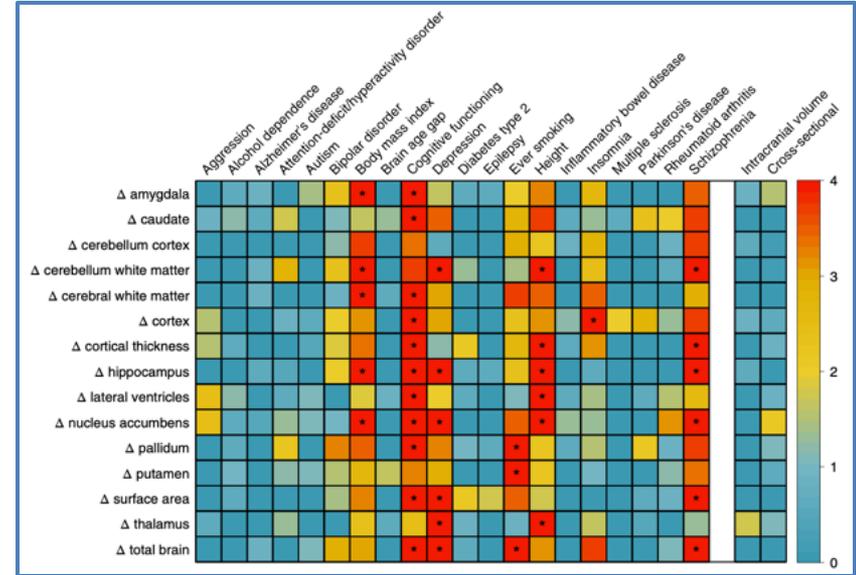


N=15640

# Genetic variants associated with longitudinal changes in brain structure across the lifespan



## GPR139, DACH1 und APOE

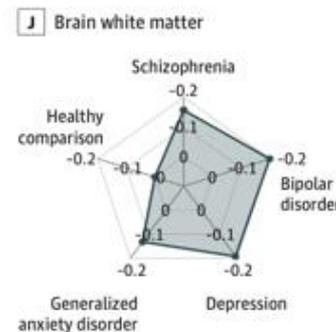
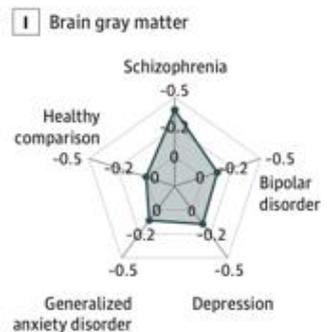
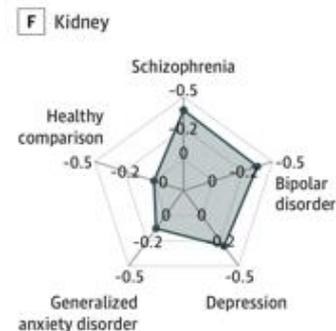
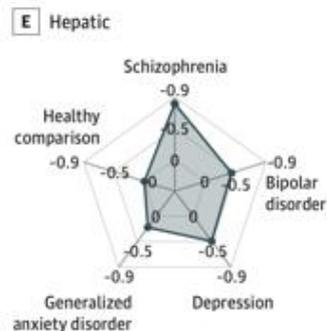
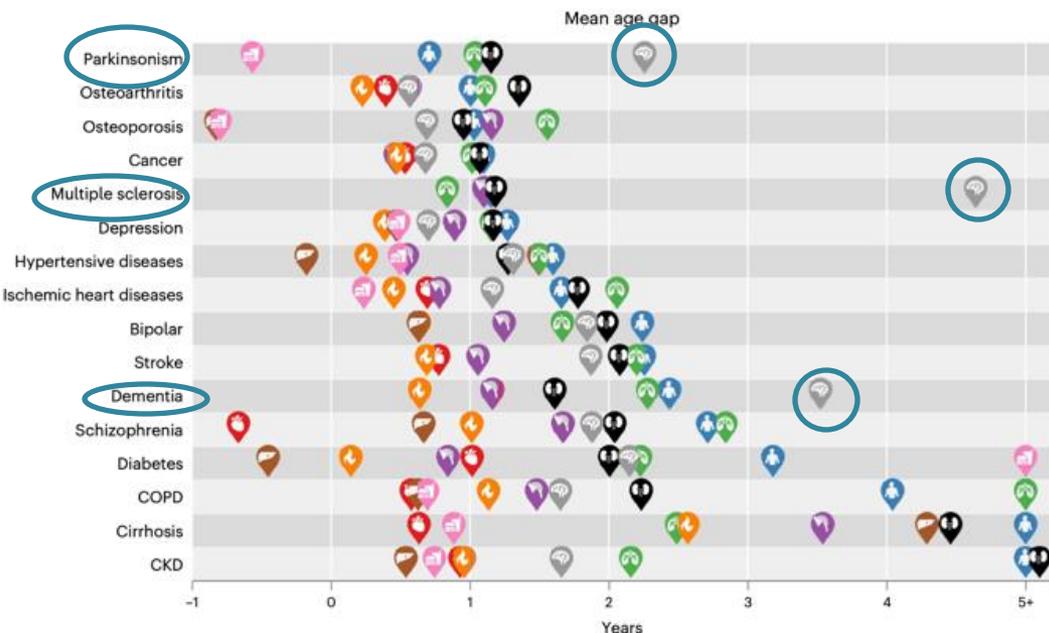
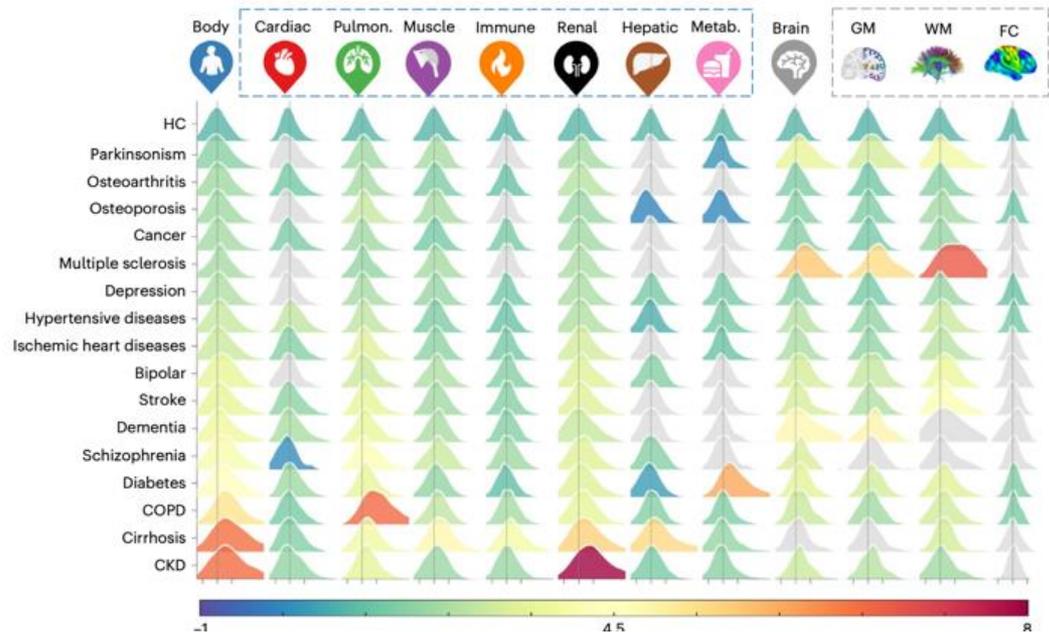


The ENIGMA Plasticity working group presents



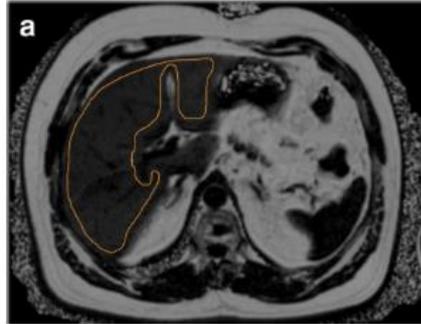
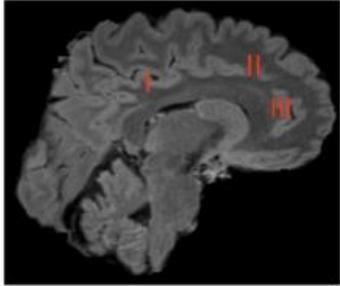
**Genetic overlap**  
 global genetic overlap with depression, schizophrenia, cognitive functioning, #insomnia, height, BMI, and smoking

# Brain Age gap across organs



# Hepatic fat is superior to BMI, visceral and pancreatic fat as a potential risk biomarker for neurodegenerative disease

Ebba Beller<sup>1,2</sup>  • Roberto Lorbeer<sup>2</sup> • Daniel Keeser<sup>2</sup> • Franziska Schoeppe<sup>2</sup> • Sabine Sellner<sup>2</sup> • Holger Hetterich<sup>2</sup> • Fabian Bamberg<sup>3,4</sup> • Christopher L. Schlett<sup>3,4</sup> • Annette Peters<sup>5</sup> • Birgit Ertl-Wagner<sup>2,6</sup> • Sophia Stoecklein<sup>2</sup>



MRI-based Hepatic fat

**R=-0.34, p<0.01**

*Corrected for:*

- age
- sex
- hypertension
- smoking
- BMI
- LDL
- total cholesterol
- alcohol

• n=361  
(152 women, 199 men)

• ICV-corrected GM  
brain volume

# Reproducible brain-wide association studies require thousands of individuals

<https://doi.org/10.1038/s41586-022-04492-9>

Received: 19 May 2021

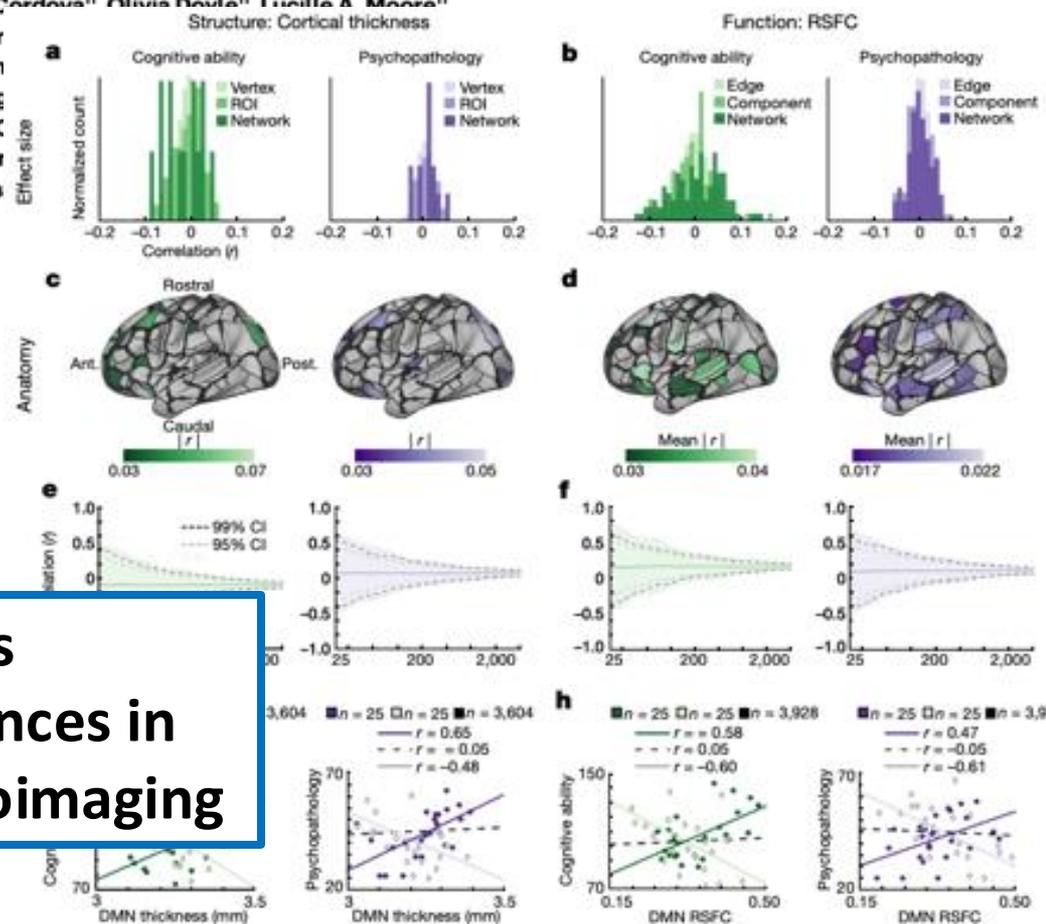
Accepted: 31 January 2022

Published online: 16 March 2022

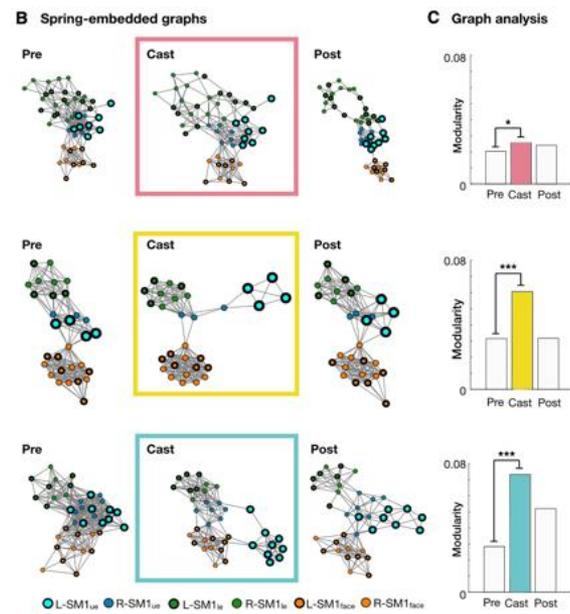
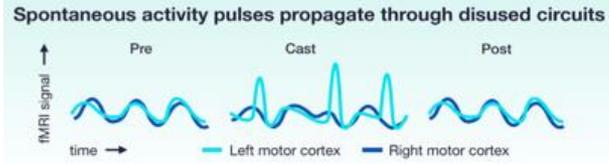
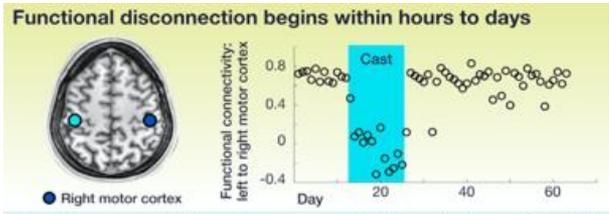
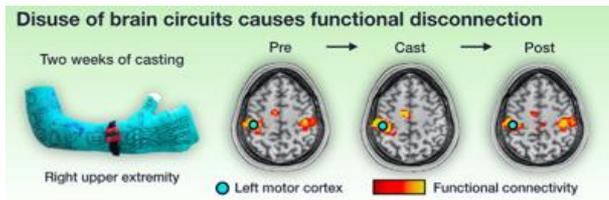
Open access

 Check for updates

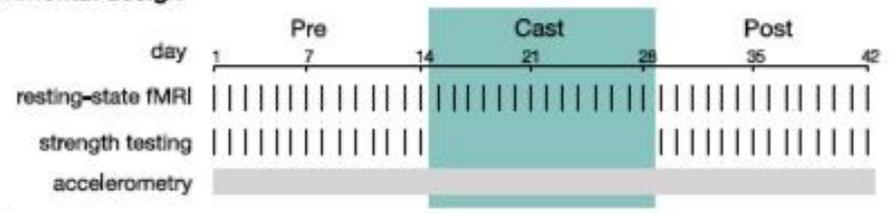
Scott Marek<sup>1,30</sup>, Brenden Tervo-Clemmens<sup>2,3,30</sup>, Finnegan J. Calabro<sup>4,5</sup>, David F. Montez<sup>6</sup>, Benjamin P. Kay<sup>6</sup>, Alexander S. Hatoum<sup>1</sup>, Meghan Rose Donohue<sup>1</sup>, William Foran<sup>4</sup>, Ryland L. Miller<sup>1,6</sup>, Timothy J. Hendrickson<sup>7</sup>, Stephen M. Malone<sup>8</sup>, Sridhar Kandala<sup>1</sup>, Eric Feczko<sup>9,10</sup>, Oscar Miranda-Dominguez<sup>9,10</sup>, Alice M. Graham<sup>11</sup>, Eric A. Earl<sup>9,11</sup>, Anders J. Perrone<sup>9,11</sup>, Michaela Cordova<sup>11</sup>, Olivia Doula<sup>11</sup>, Lucille A. Moore<sup>11</sup>, Gregory M. Conan<sup>9,11</sup>, Johnny Ur James C. Wilgenbusch<sup>9,12</sup>, Thom Dillan J. Newbold<sup>6</sup>, Annie Zheng Roselyne J. Chauvin<sup>6</sup>, Timothy C Hugh Garavan<sup>2,2</sup>, Wesley K. Thor Deanna M. Barch<sup>1,21</sup>, Beatriz Lun



cross-sectional correlations  
between individual differences in  
functional/structural neuroimaging



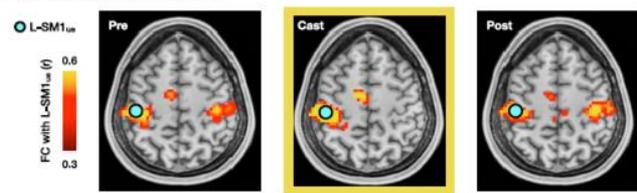
**A Experimental design**



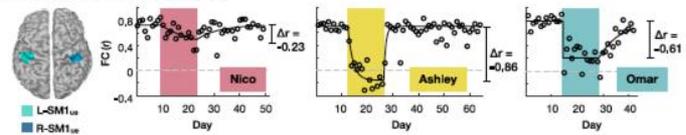
**B Casts**



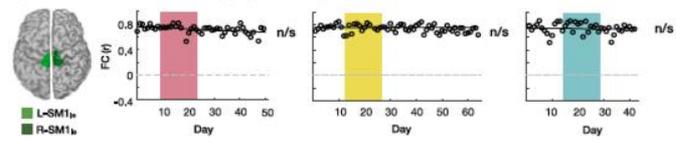
**A Functional connectivity (FC) seed maps**



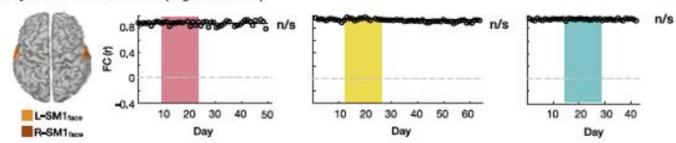
**B Daily time course of FC: upper extremity**



**C Daily time course of FC: lower extremity (negative control)**



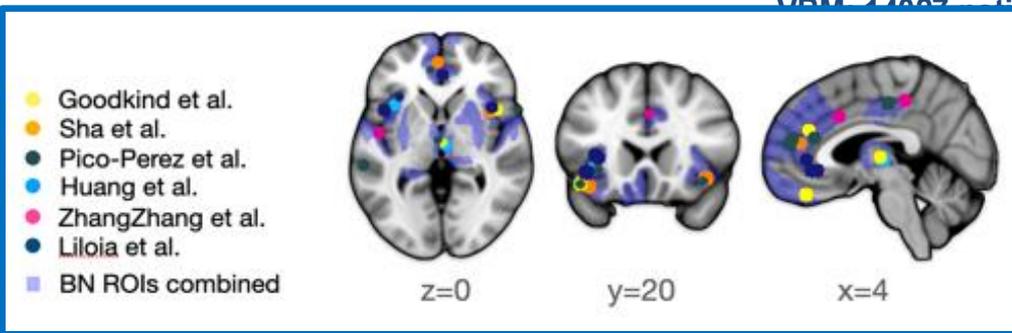
**D Daily time course of FC: face (negative control)**



# Transdiagnostic network changes in psychiatric diseases 3

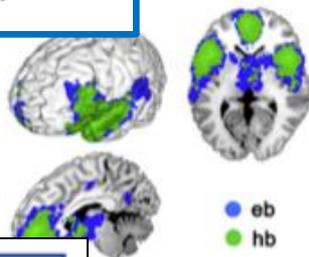
- 7381 patients, 8511 m
- SCZ, BPD, MDD, ANX

Overlap of struct  
(based on meta-analy

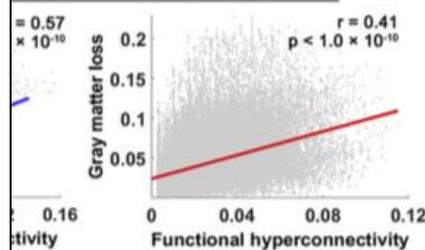


VBM, 14997 patients, 14504 HC  
analysis of 363 VBM studies)  
MRI: 8298 patients, 8165 HC  
analysis of 242 rsfMRI studies)  
orders

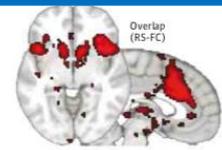
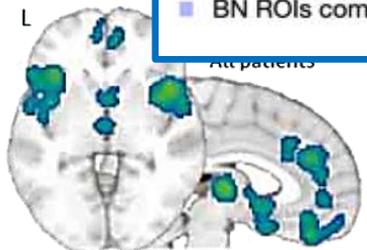
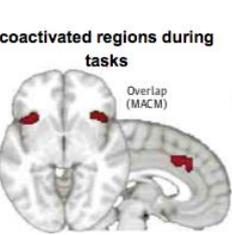
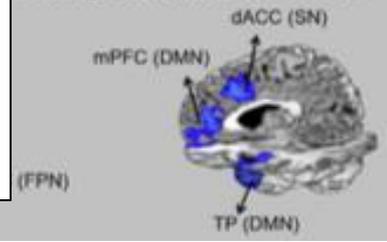
gray matter loss  
psychiatric disorders



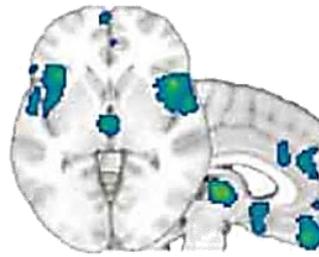
red network connectivity and gray matter loss



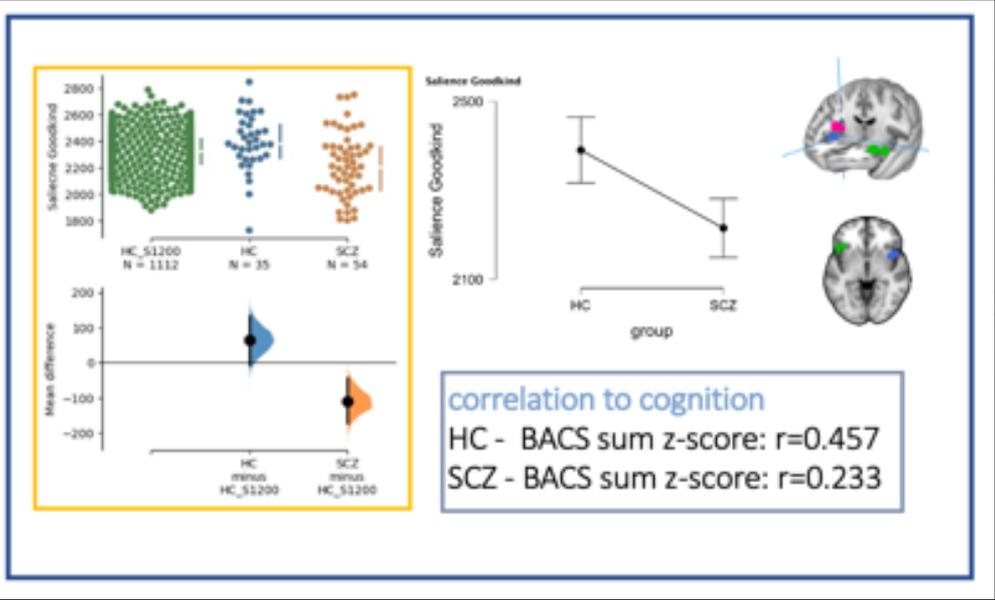
activity with the SN seeds



Psychotic only



Insul



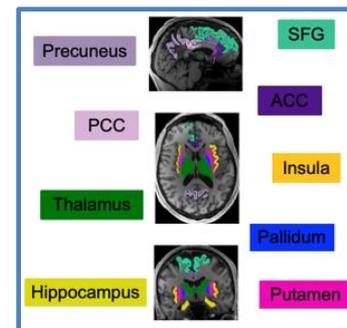
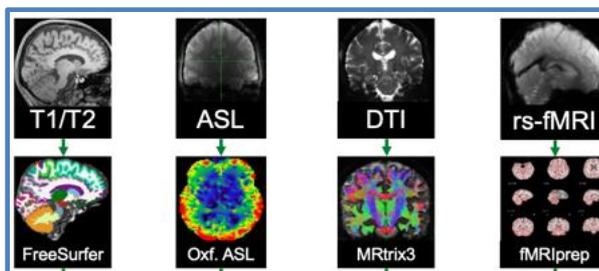
# Neuroimaging modalities

## Sample characteristics

Data set	N	Age range	Sex
HCP-Ageing	725	36 – 100 years	406 ♀, 319 ♂
MPI Leipzig:	227	20 – 85 years	82 ♀, 145 ♂

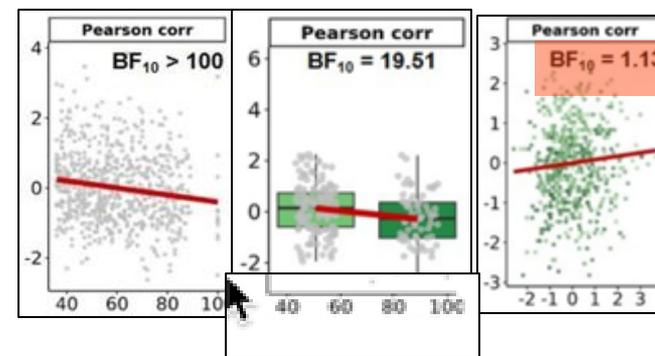
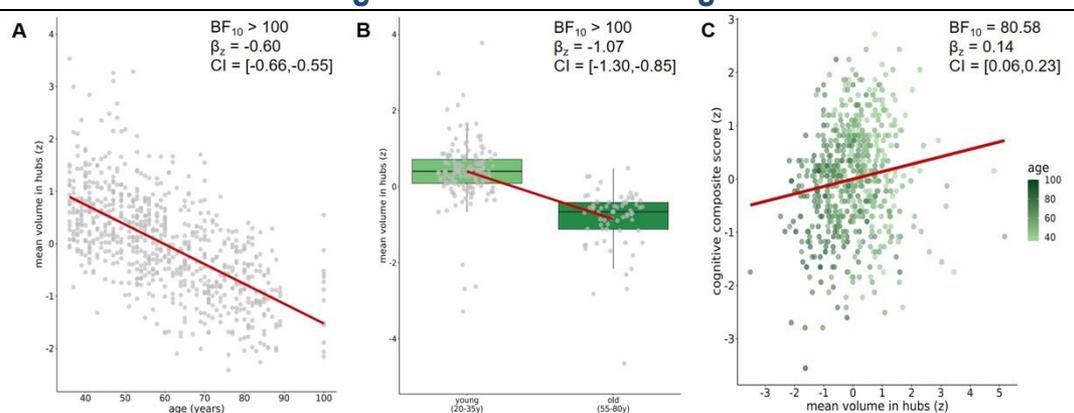


N=952



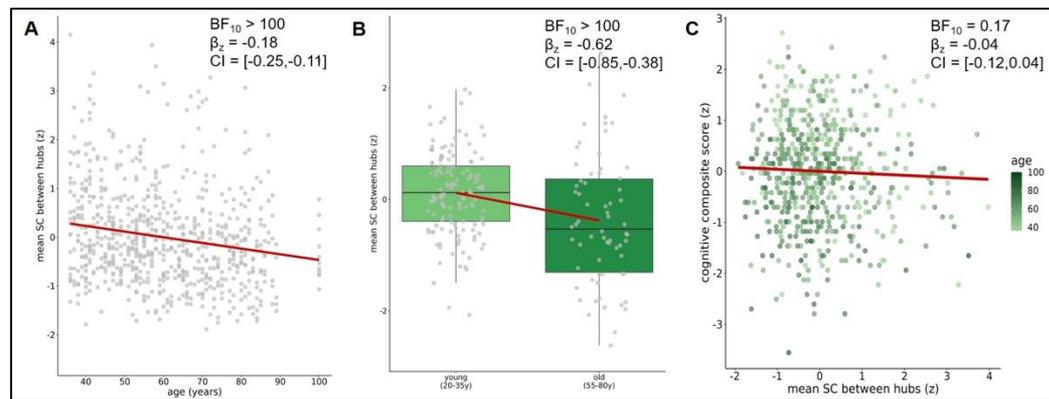
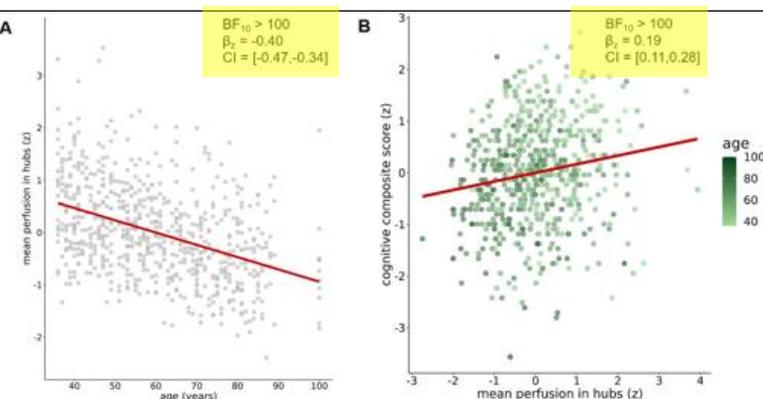
## Structural MRI: Age - Brain Volumes - Cognition

## rs-fMRI: Age – Functional Connectivity – Cognition

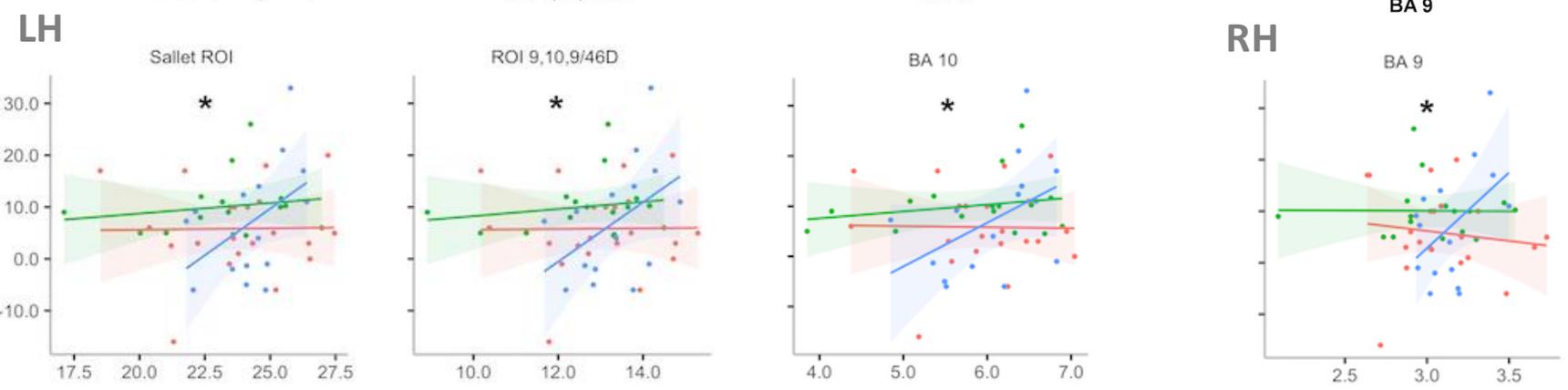
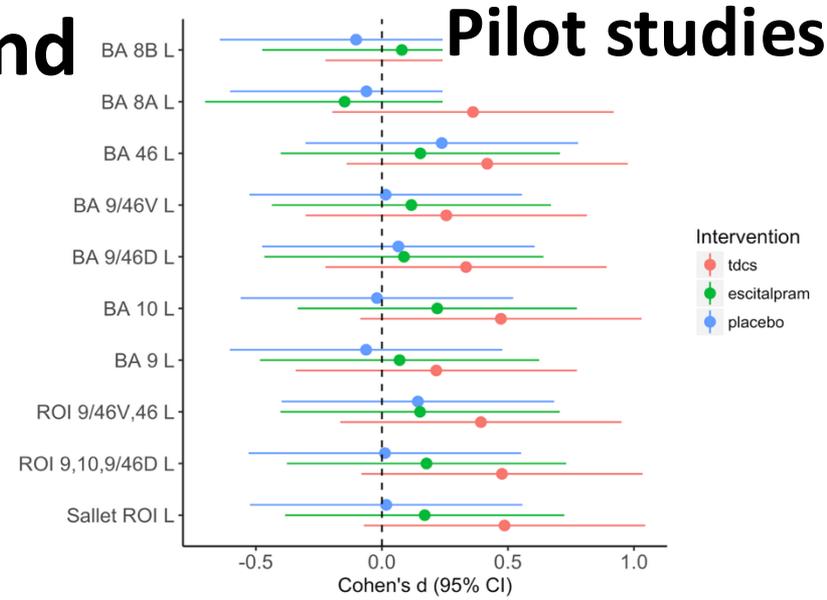
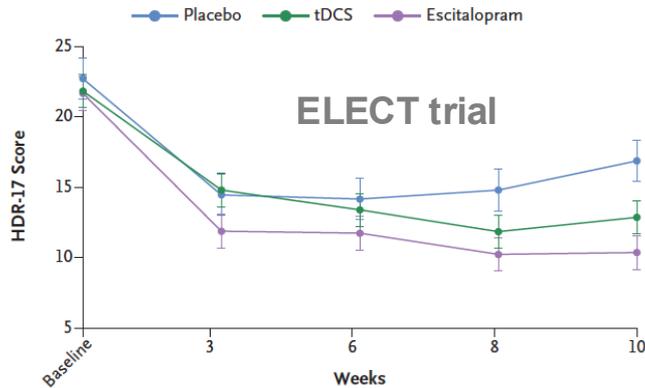


## ASL: Age – Brain Perfusion – Cognition

## DTI: Age – Structural Connectivity – Cognition



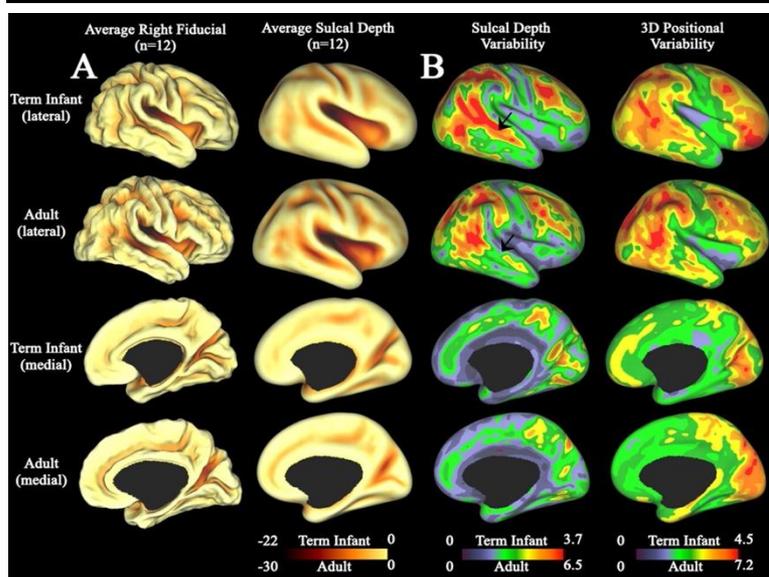
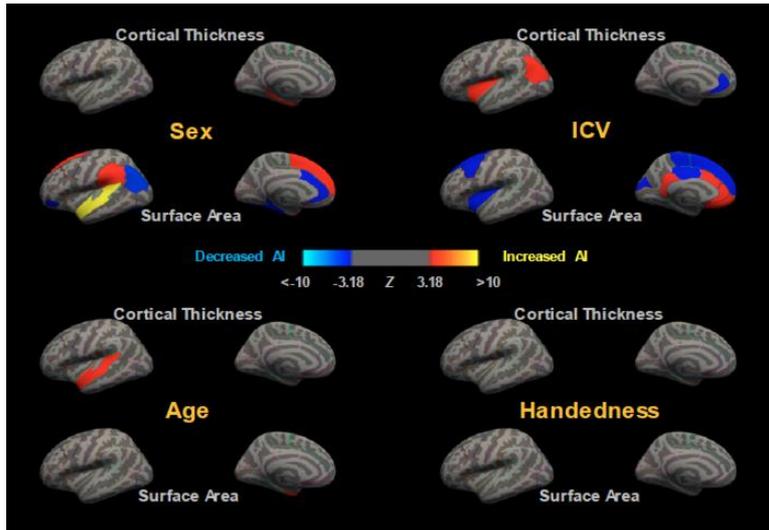
# Association of GM volume and antidepressive response



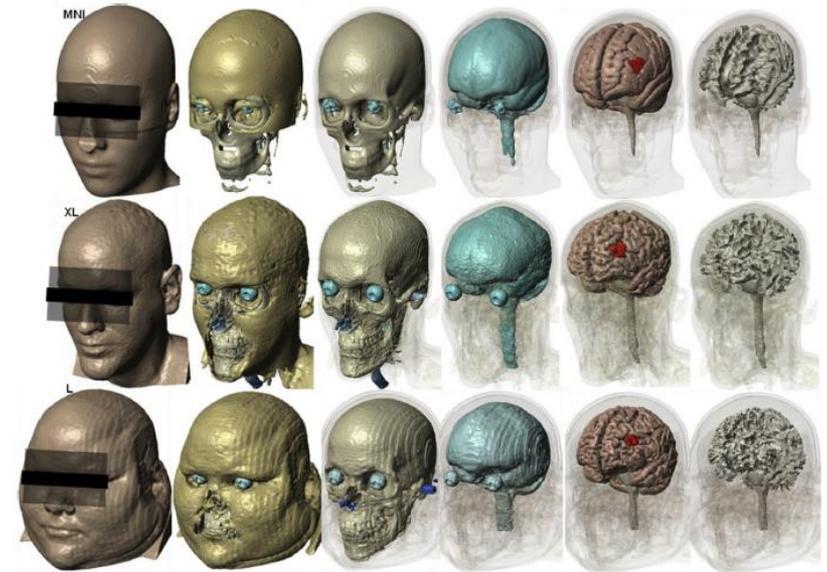
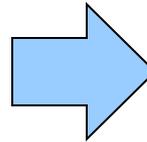
Brunoni et al., New England Journal of Medicine 2017

Bulubas et al., Brain Stimulation 2019

+ 17141 subjects  
99 datasets worldwide



# Anatomical variability



Seibt, *Brain Stimulation*, 2015

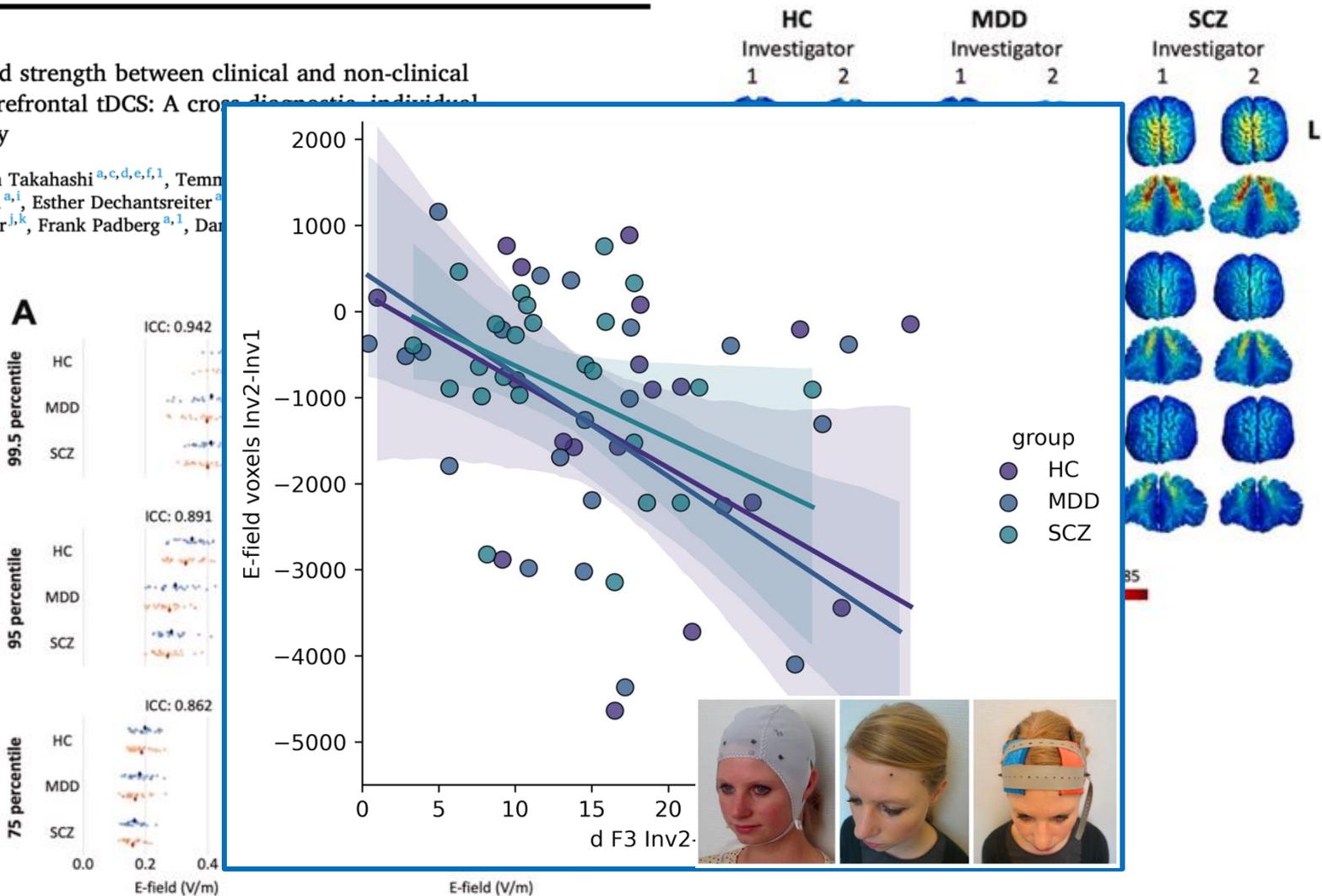
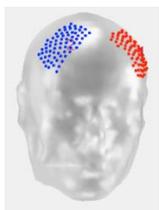
Kong et al., *PNAS* 2018

J. Hill, *Journal of Neuroscience*, 2010

Differences in electric field strength between clinical and non-clinical populations induced by prefrontal tDCS: A cross-diagnostic, individual MRI-based modeling study

Yuki Mizutani-Tiebel<sup>a,b,1,\*</sup>, Shun Takahashi<sup>a,c,d,e,f,1</sup>, Temu Lucia Bulubas<sup>a,h</sup>, Irina Papazova<sup>a,i</sup>, Esther Dechantsreiter<sup>a</sup>, Boris Papazov<sup>b,g</sup>, Axel Thielscher<sup>j,k</sup>, Frank Padberg<sup>a,1</sup>, Dan

HC, n=25  
MDD, n=25  
SCZ, n=24

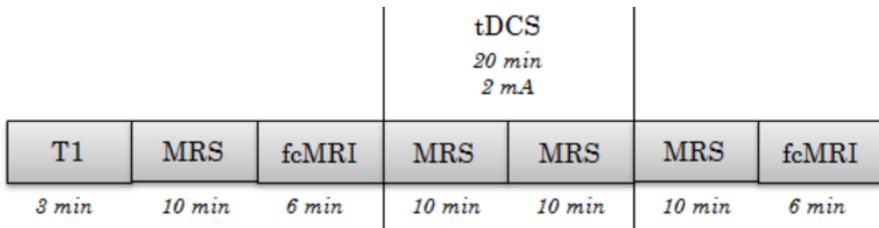
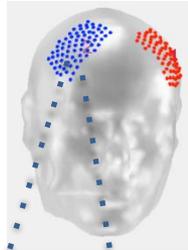
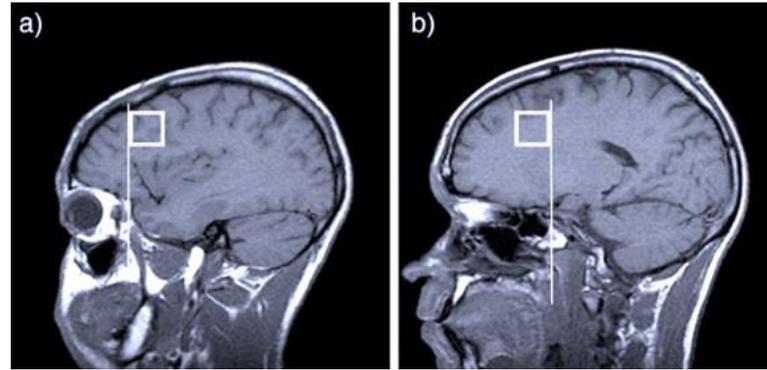
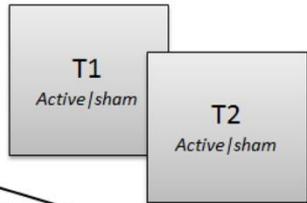


# Magnetic Resonance Spectroscopy – MRSDC0

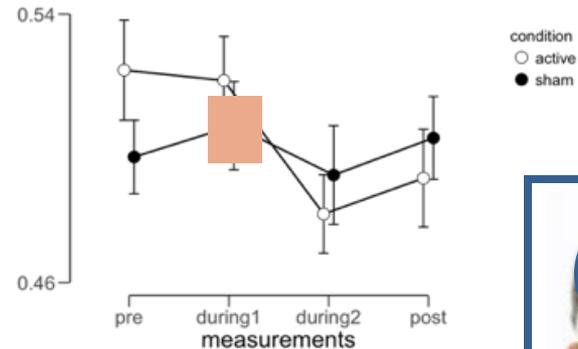
MRSDC0



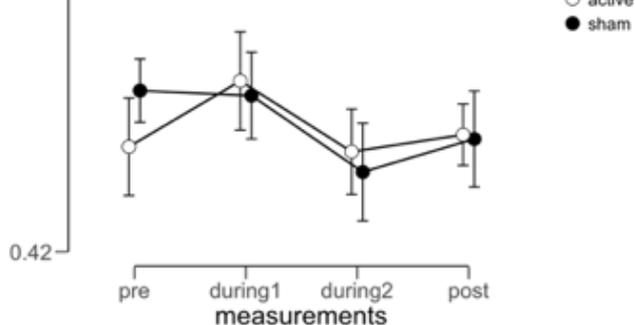
- cross-over design, healthy subjects, gender-mixed sample, n=19, MRSDC0
- **translational**: study on major depressive patients and schizophrenic patients (MRSDC1)



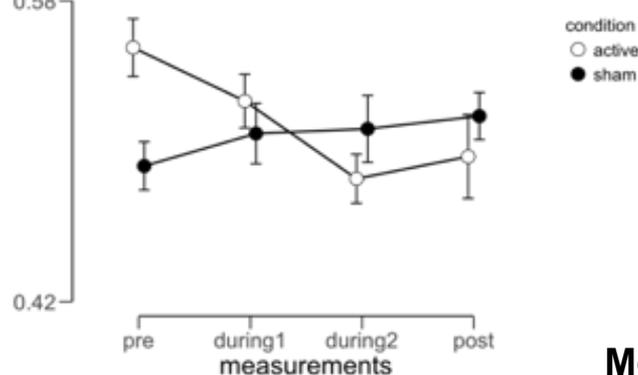
men & women



men



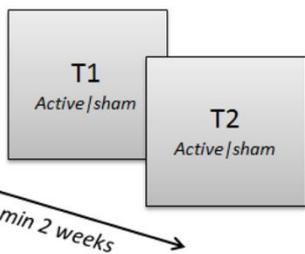
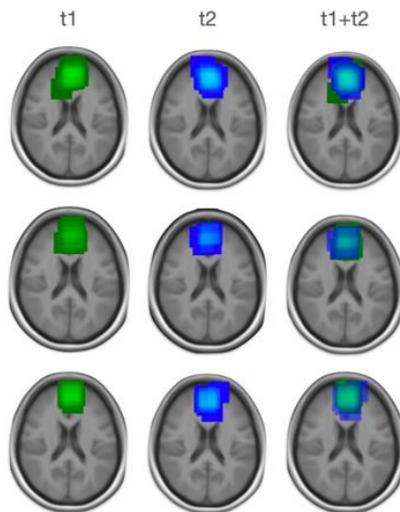
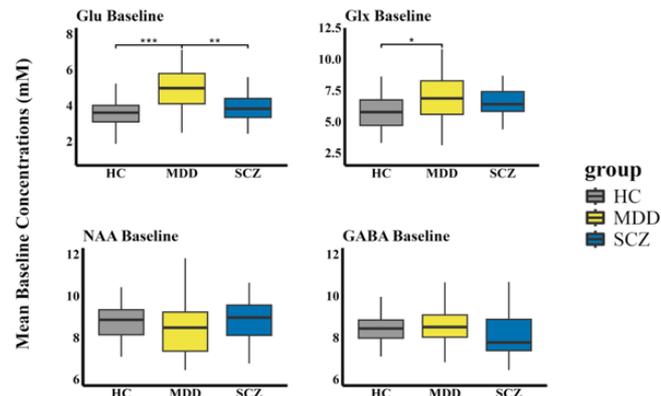
women



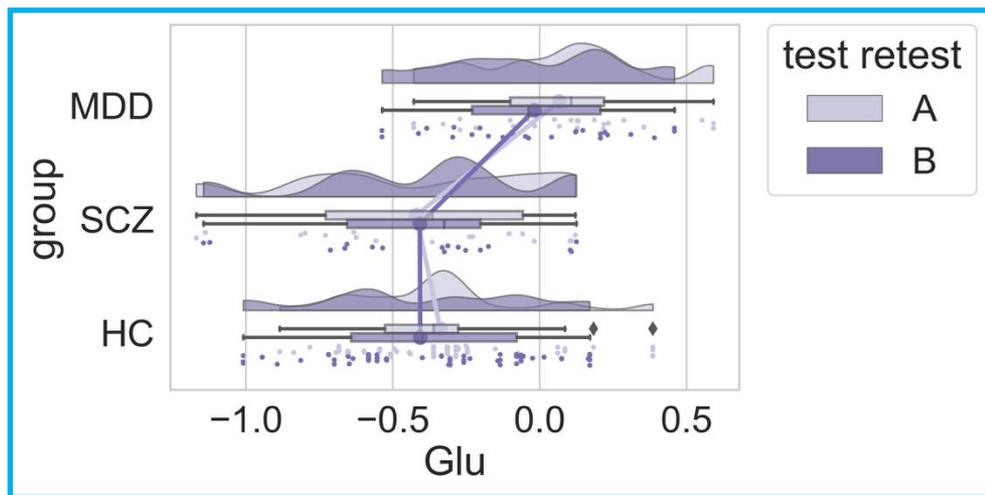
# Magnetic Resonance Spectroscopy – MRSDC1



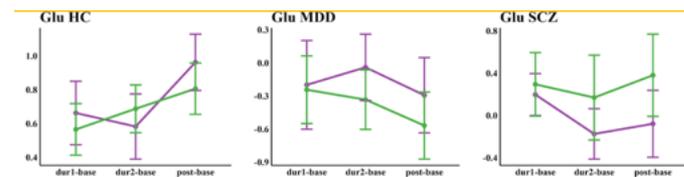
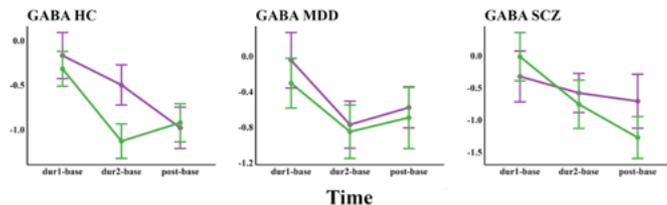
HC, N=38  
 MDD, N=24 (un-medicated)  
 SCZ, N=17  
**Total N=79**



tDCS  
 20 min  
 2 mA



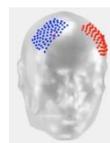
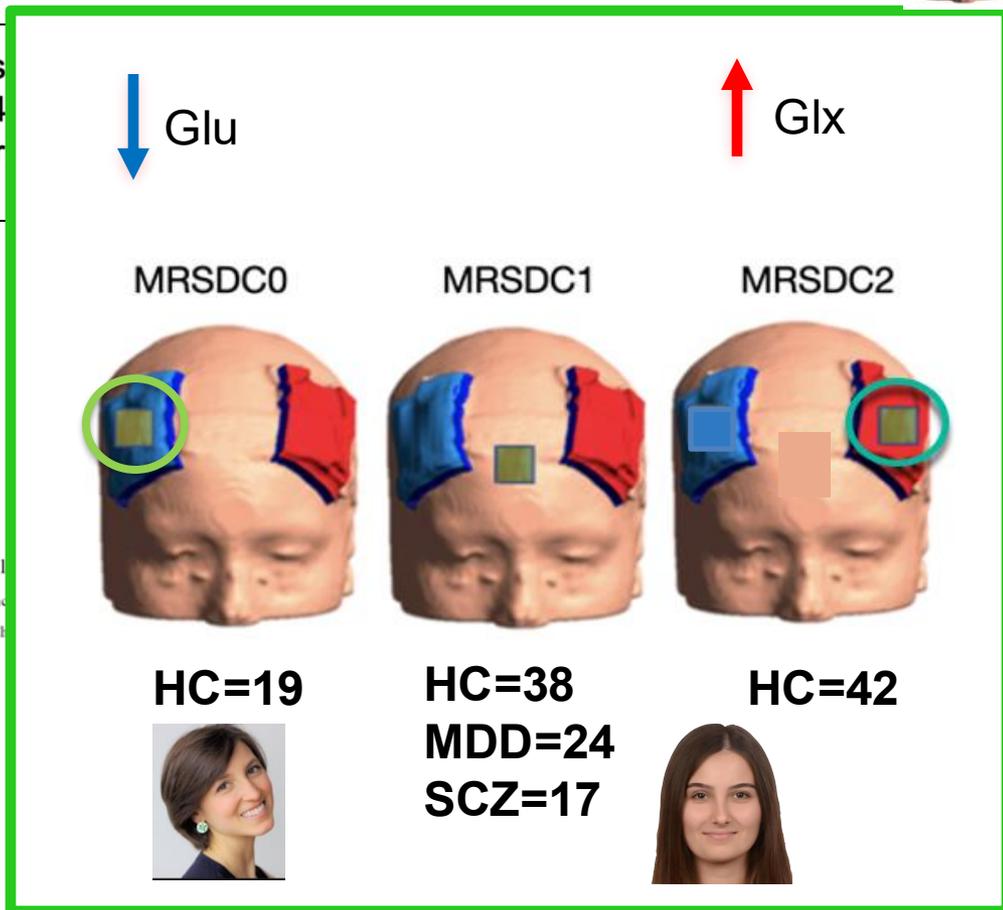
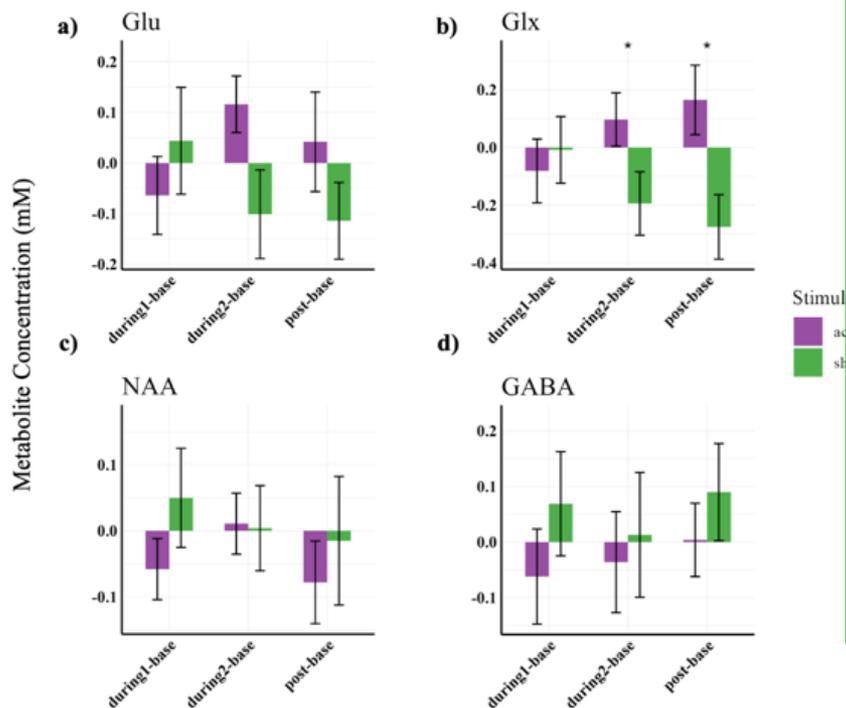
T1	MRS	fcMRI	MRS	MRS	MRS	fcMRI
3 min	10 min	6 min	10 min	10 min	10 min	6 min



# Magnetic Resonance Spectroscopy – MRSDC2



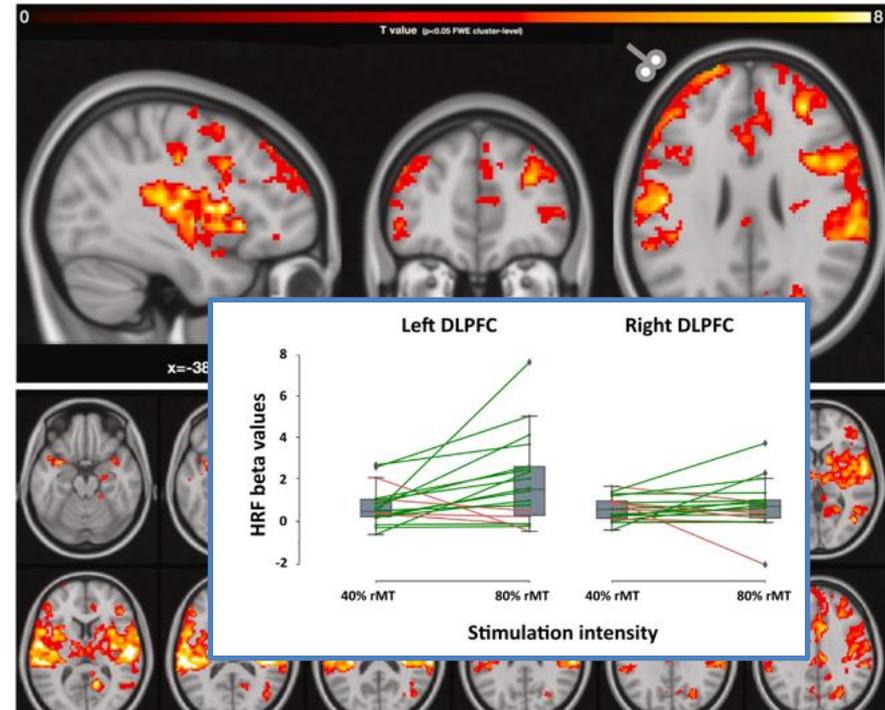
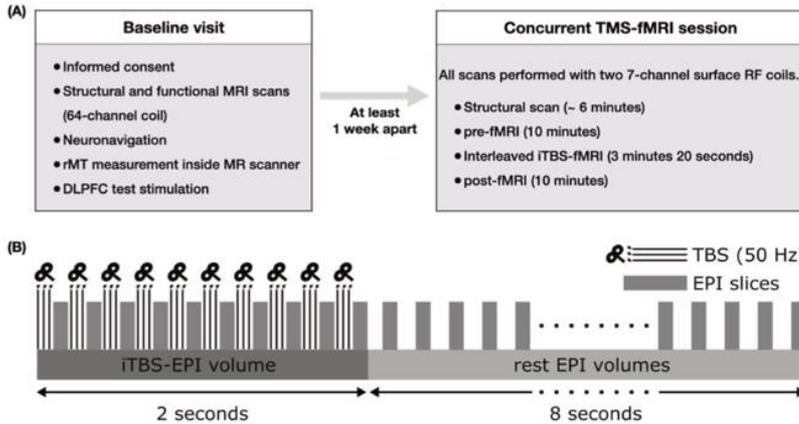
**Design:** Double Blind Placebo-Controlled, cross  
**Sample:** 41 healthy participants (21 males, ± 24  
**Scanner:** Siemens Prisma 3-Tesla MRI scanner  
**tDCS Device:** NeuroConn DC-Stimulator Plus



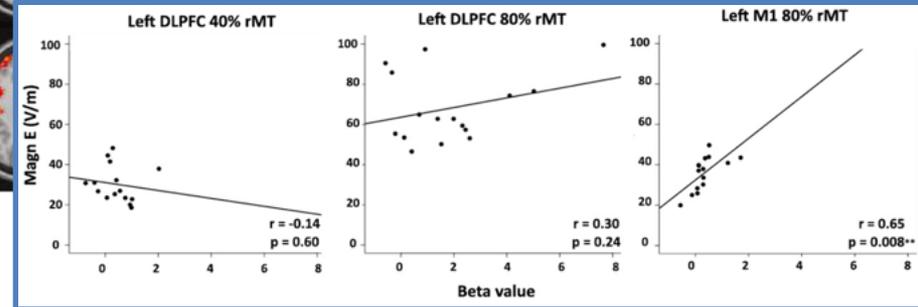
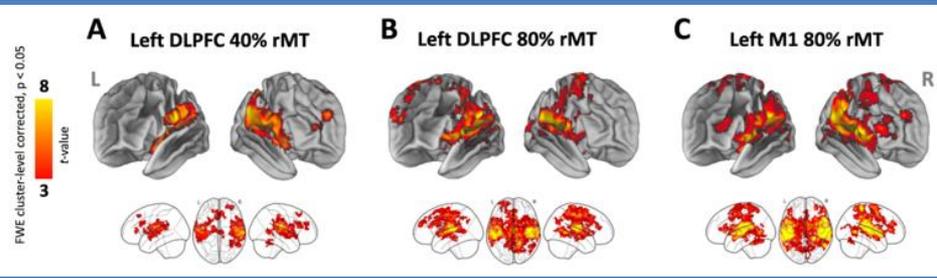
20 Mins



# Online TBS-fMRI



5



Mizutani-Tiebel et al., *Frontiers in Psychiatry* 2022

Chang et al., *NeuroImage* 2024

Chang et., *Biological Psychiatry:CNNI* 2024

# Ongoing CDP research



## Biological Psychiatry

Available online 27 April 2024

In Press, Journal Pre-proof [What's this?](#)



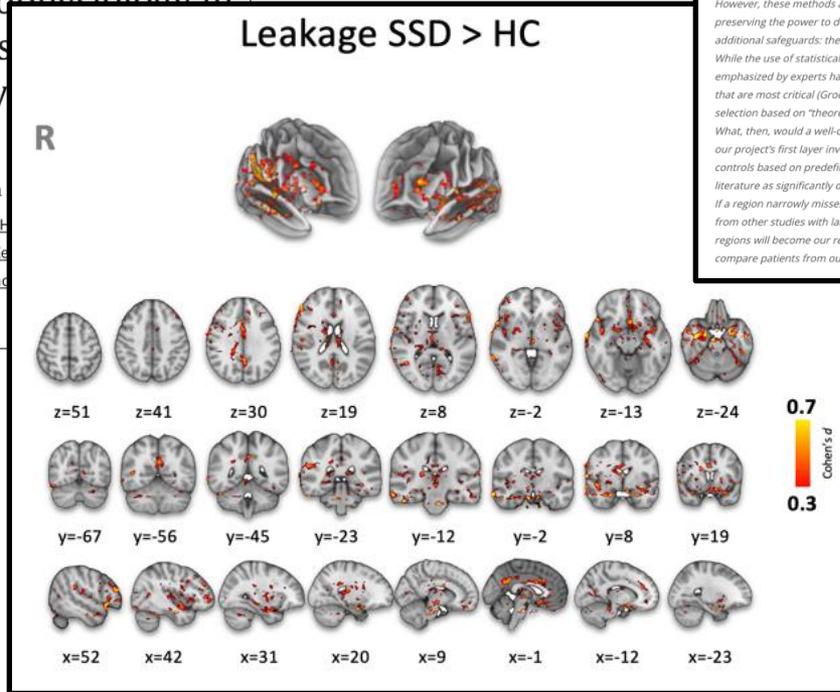
---

Archival Report

## Signature of altered retinal microstructures and electrophysiology in schizophrenia spectrum disorders associated with disease severity and polygenic risk

Emanuel Boudriot<sup>1,2\*</sup>, Vanessa Gabriel<sup>1\*</sup>, David Popovic<sup>1</sup>, Vladislav Yakimov<sup>1,3</sup>, Sergi Papiol<sup>2,4</sup>, Lukas Roell<sup>1,5</sup>, Genc Hasanaj<sup>1</sup>, Joanna Moussiopoulou<sup>1</sup>, Siegfried Priglinger<sup>7</sup>, Christoph Kalkbrenner<sup>1</sup>, Alkomiet Hasan<sup>10,11</sup>, Oliver Pogarell<sup>1</sup>, Peter Falkai<sup>1,2,11</sup>, and Benedikt Schworm<sup>7</sup>

CDP Working Group<sup>12,610</sup>





[Search](#) [Support](#) [Donate](#) [Sign Up](#) [Sign In](#)

Multimodal Clustering Analysis...

[Metadata](#) [Files](#) [Wiki](#) [Analytics](#) [Registrations](#)

## Multimodal Clustering Analysis of meta-analytically derived brain regions in Schizophrenia Spectrum Disorder

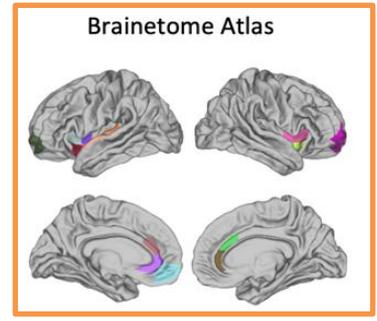
0.0B Public 0 0

Contributors: Maxim Korman, Daniel Keeser

Date created: 2024-03-18 05:29 PM | Last Updated: 2024-06-11 02:51 AM

Category: Analysis

**Description:** Schizophrenia Spectrum Disorders (SSD) represent a broad spectrum of psychotic disorders. Their prevalence and severity highlight the urgent need for a deeper understanding of these heterogeneous diseases, which is crucial for developing tailored treatment strategies. A key determinant of progress in any scientific field is the discovery of associations that, over time, demonstrate replicability. Given our inability to completely eliminate the chance of finding false positives (i.e., to reject the null hypothesis definitively), an error threshold of 5% (p-value of 0.05) has been widely accepted. As we enter the era of big data, and hence an era of being able to test for an almost unlimited number of hypotheses, established thresholding becomes problematic, leading to a significant number of false positives (up to 1 in every 20 tests). To address this, multiple testing correction methods such as the Bonferroni correction and the False Discovery Rate (FDR) have been used. However, these methods are never a perfect solution, but rather represent trade-offs between minimizing the risk of false positives while preserving the power to detect true associations. To further increase the likelihood that the associations we detect are valid, we implement two additional safeguards: the pre-selection of our hypotheses and the pre-registration of our analyses. While the use of statistical corrections for multiple testing has become standard practice, other methodological aspects that are frequently emphasized by experts have received less attention. Groenwold et al. suggest reducing the number of hypotheses tested by prioritizing those that are most critical (Groenwold et al., 2021). Similarly, a recent article on replicability in brain imaging supports this by recommending a pre-selection based on "theoretical considerations" (Kelly et al., 2022). What, then, would a well-considered hypothesis in the area of brain imaging be based upon? A variety of methods are conceivable. To this end, our project's first layer involves finding all meta-analyses that address gray matter volume differences between SSD patients and healthy controls based on predefined criteria (see Analysis Plan for the specific criteria). We will then identify brain regions that have been reported in literature as significantly different more than once. We commit to including regions reported in at least half of the meta-analyses in our analysis. If a region narrowly misses this threshold in meta-analyses but is supported by strong theoretical arguments—evidenced by consistent results from other studies with large sample sizes and rigorous methodological designs—we will consider including it in our study. Collectively, these regions will become our regions of interest (ROIs), which we will examine in our cohort for patients vs. healthy controls (HC). Additionally, we will compare patients from our cohort with an age and sex matched group of HC from the Human Connectome Project (HCP).



**medRxiv**  
THE PREPRINT SERVER FOR HEALTH SCIENCES

## Investigation of choroid plexus variability in schizophrenia-spectrum disorders – insights from a multimodal study

- Vladislav Yakimov, Joanna Moussiopoulou, Lukas Roell, Martin Mortazavi, Iris Jäger, Emanuel Boudriot,
- Genc Hasanaj, Mattia Campana, Lenka Krčmář, Marcel S. Kallweit, Sean Halstead, Nicola Warren,
- Dan Siskind, Sergi Papiol, Isabel Maurus, Alkomiet Hasan, Peter Falkai, Andrea Schmitt, Florian Raabe,
- Daniel Keeser, Elias Wagner

**Boudriot et al., *Biological Psychiatry* 2024**  
**Moussiopoulou et al., *under review***  
**Korman et al., *in preparation***  
**Yakimov et al., *under review***

# Lack of group-to-individual generalizability is a threat to human subjects research

Aaron J. Fisher<sup>a,1</sup>, John D. Medaglia<sup>b,c</sup>, and Bertus F. Jeronimus<sup>d</sup>

<sup>a</sup>Department of Psychology, University of California, Berkeley, CA 94720; <sup>b</sup>Department of Psychology, Drexel University, Philadelphia, PA 19104; <sup>c</sup>Department of Neurology, University of Pennsylvania, Philadelphia, PA 19104; and <sup>d</sup>Department of Developmental Psychology, Faculty of Behavioural and Social Sciences, Groningen University, 9712 TS Groningen, The Netherlands



## Feature Review

Building a Science of Individual Differences from fMRI

CellPress

Julien Dubois<sup>1,\*</sup> and Ralph Adolphs<sup>1</sup>

## Trends in Cognitive Sciences



Group average of all sushis

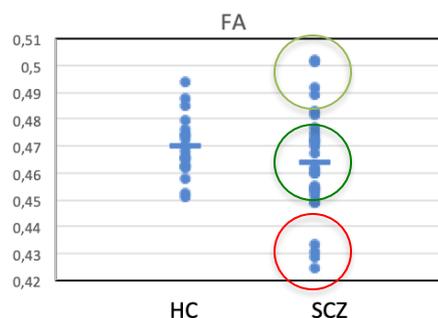
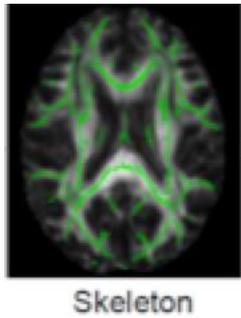
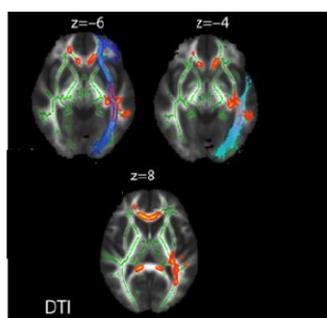
Patients

healthy subjects



Even within group no two subjects are alike

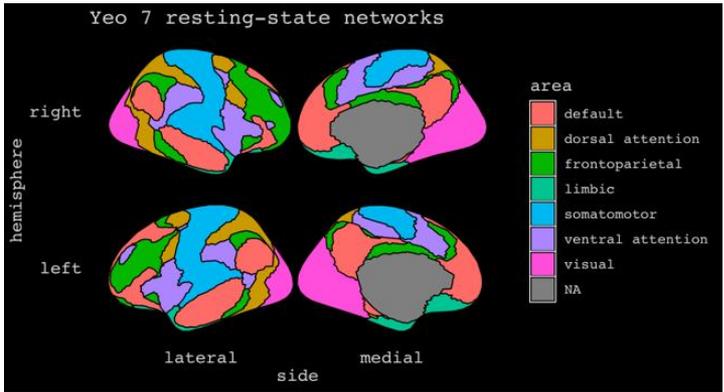
Sushis adapted from *Nora Maria Raschle*  
Takahashi et al., in preparation



# (Individual) Brain parcellation

Brainetome –  
**Multimodal atlas1**  
**Multimodal atlas2**

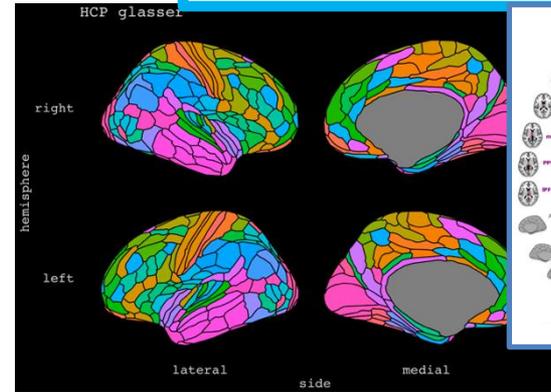
„Classical“ RSN atlas



rsfMRI

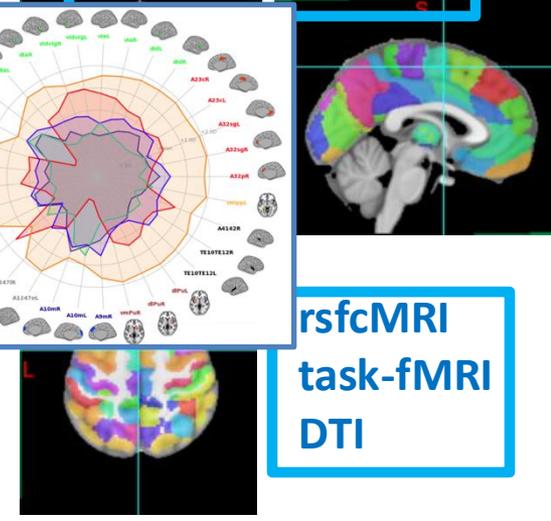
Yeo et al., J Neurophysiol 2011

Glasser – **Multimodal atlas1**

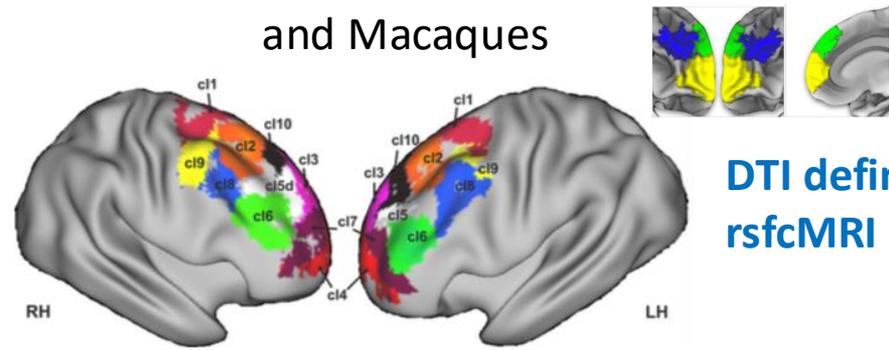


rsfMRI  
task-fMRI  
Myelin maps (T1/T2)

Glasser et al., Nature 2015    Fan et al., Cerebral Cortex 2016



Dorsal frontal Cortex Atlas in Humans and Macaques

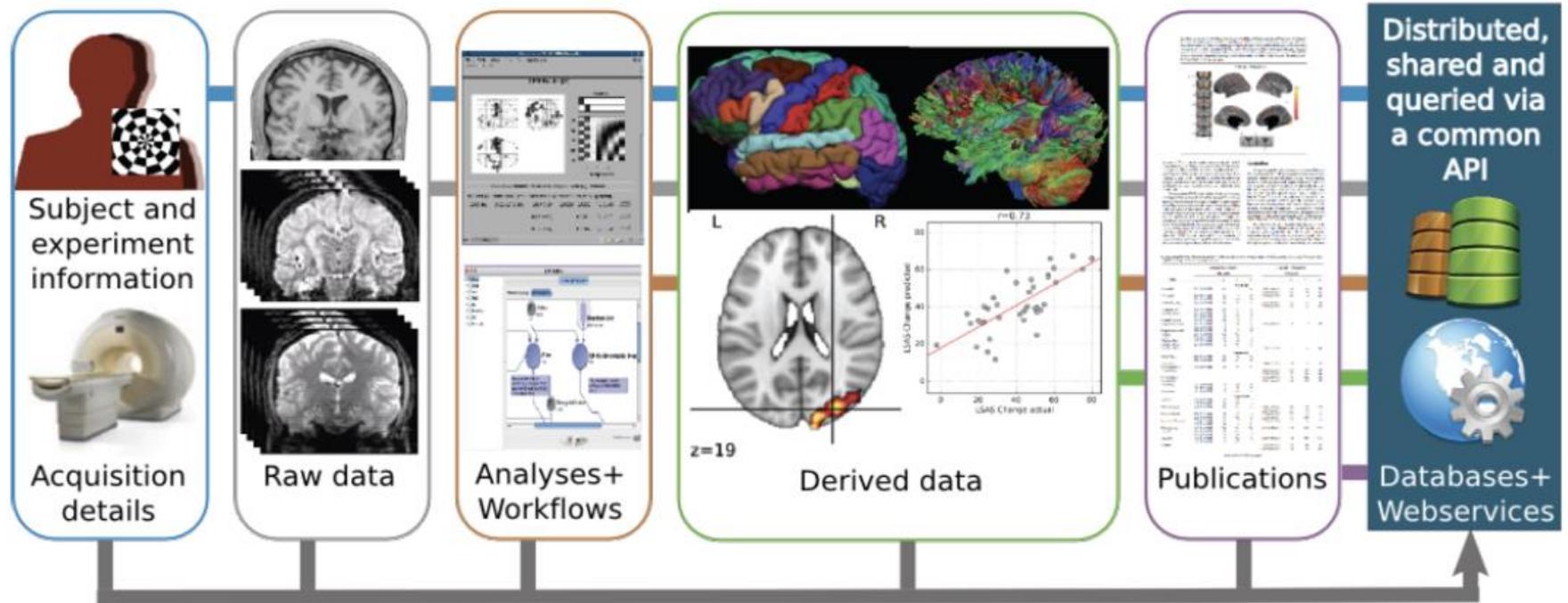


Sallet et al., J Neuroscience 2013

DTI defined  
rsfMRI

Wörsching et al., *NeuroImage* 2017  
 Wörsching et al., *Brain Stimulation* 2018  
 Bulubas et al., *Brain Stimulation* 2019  
 Mizutani et al., *NeuroImage Clinical* 2022  
 Chang et al., *NeuroImage* 2024

# Dataflow in Brain Imaging



Demographics  
Stimuli  
Scanner  
Sequence  
  
Assays  
- Clinical  
- Neuropsych  
- Behavioral

MRI  
- T1  
- T2  
dMRI  
fMRI  
- Task  
- Resting  
EEG, MEG,  
PET, MRS

SPM  
FSL  
FreeSurfer  
AFNI  
...  
Nipype  
LONI  
...  
QA/QC

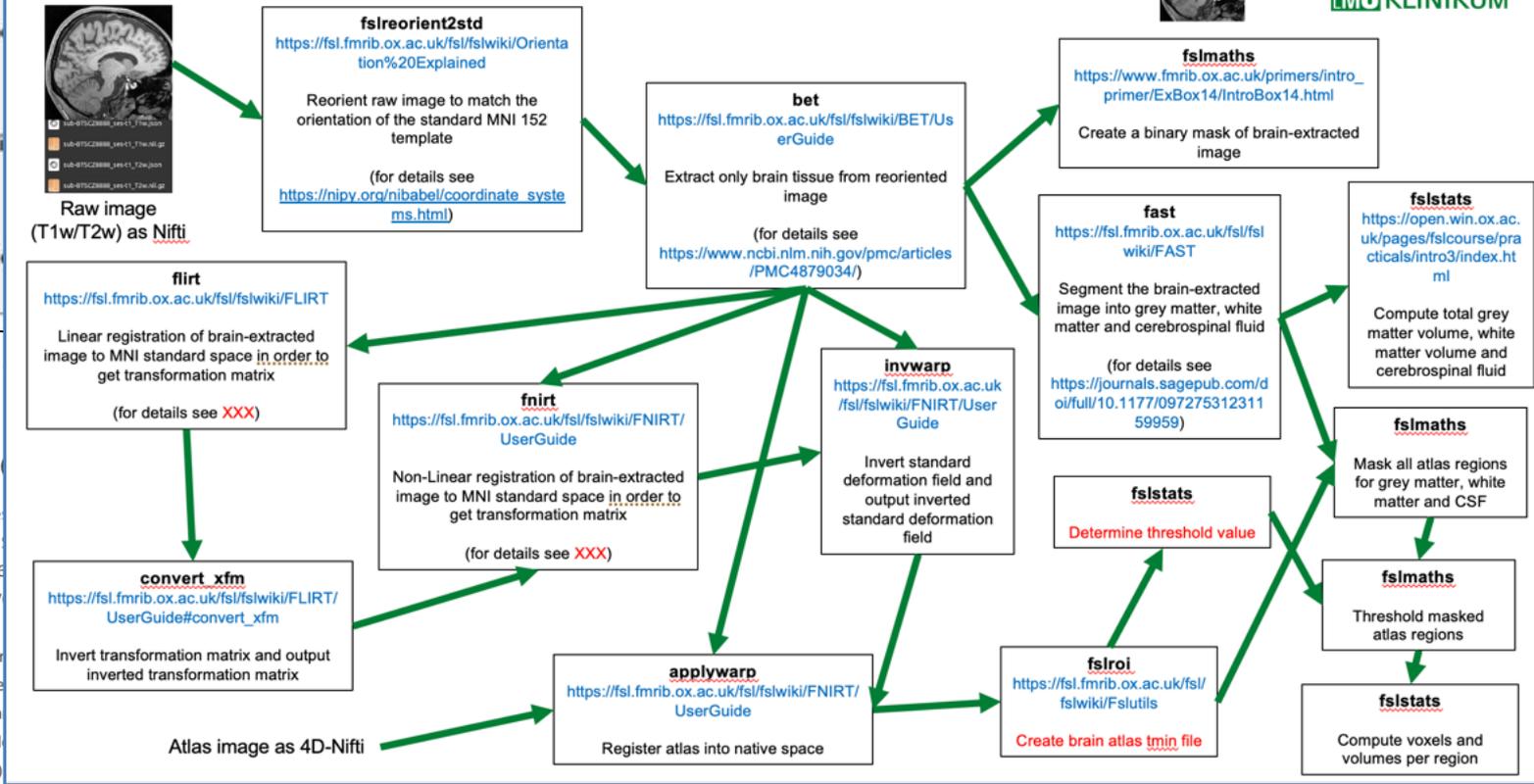
Contrasts  
Correlation  
Prediction

Journals  
Preprint  
archives  
Websites  
Blogs

XNAT  
IDA  
LORIS  
COINS  
Amazon S3  
DropBox  
Globus  
Neurovault  
Neurosynth

# Neuromodulation And Multimodal NeuroImaging scripts

## Structural MRI: Data Processing with NAMNIS



Effect of a cortical thickness in schizophrenia

Contributors: Daniel Kee, Alkomiet Hasan, Andrea Schmitt  
Date created: 2020-02-06  
Identifier: DOI 10.17605/2020-02-06  
Category: Project  
Description: Aerobic exercise in patients with schizophrenia and healthy controls. We investigated the relationship of these characteristics with brain structure in patients who played table soccer and healthy control groups, we found no significant longitudinal correlation of cortical thickness at baseline with clinical measures. Our results suggest that a structure adjacent to the hippocampus. Greater cortical thickness of the right lateral prefrontal cortex was associated with intervention in patients with schizophrenia.

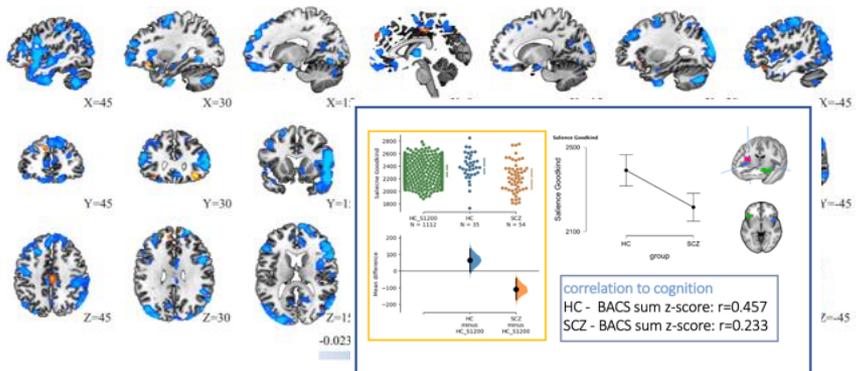
was assessed with FreeSurfer 6.0. The schizophrenia aerobic exercise group showed a significant correlation between the cortical thickness of the right lateral prefrontal cortex and clinical measures. In contrast, in the healthy control group, we found no significant longitudinal correlation of cortical thickness at baseline with clinical measures. Our results suggest that a structure adjacent to the hippocampus. Greater cortical thickness of the right lateral prefrontal cortex was associated with intervention in patients with schizophrenia.

### Effect of aerobic exercise combined with cognitive remediation on cortical thickness and prediction of social adaptation in patients with schizophrenia

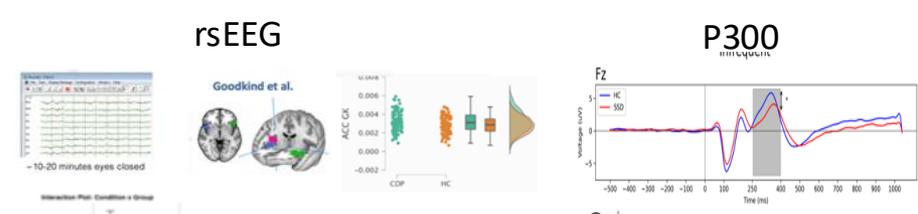
Shun Takahashi<sup>a, b, \* 1</sup>, Daniel Keiser<sup>a, c, 1</sup>, Boris-Stephan Rauchmann<sup>a, c</sup>, Thomas Schneider-Axmann<sup>a</sup>, Katriona Keller-Varady<sup>a</sup>, Isabel Maurus<sup>a</sup>, Peter Dechent<sup>d</sup>, Thomas Wobrock<sup>e, f</sup>, Alkomiet Hasan<sup>a</sup>, Andrea Schmitt<sup>a, g</sup>, Birgit Ertl-Wagner<sup>c, h</sup>, Berend Malchow<sup>a, i, 1</sup>, Peter Falkai<sup>a, 1</sup>

# mMRI reduces variability outcome? CDP study as an example...

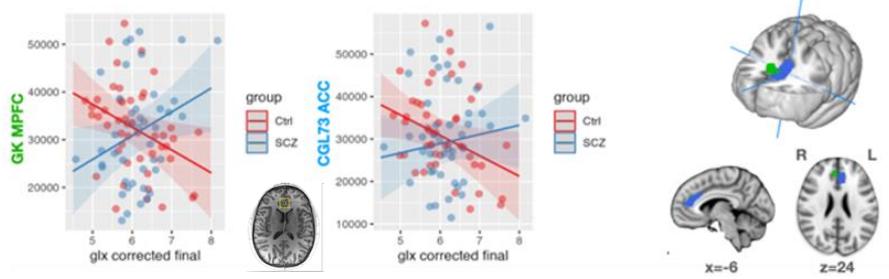
## sMRI



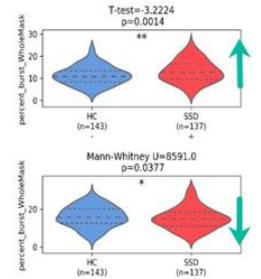
## EEG



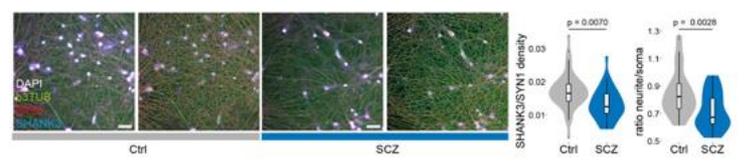
## rsfMRI/MRS (subsample)



## bursts



## iPSC

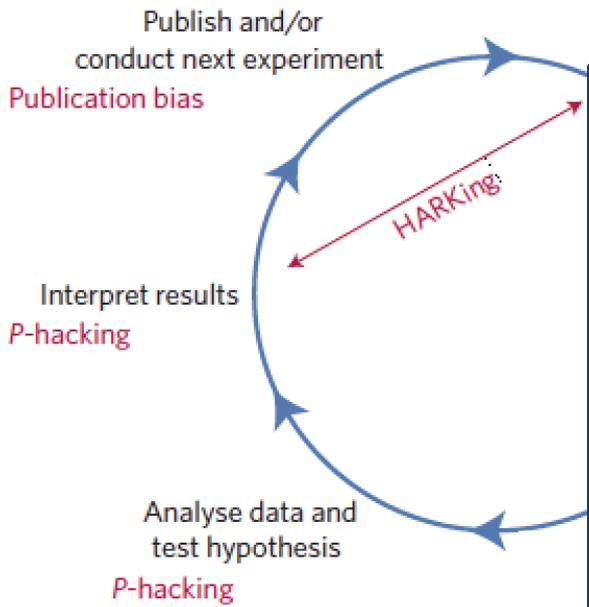


mechanistic insights

HC, N=287  
 SCZ, N=272



CDP: Krmar et al., *Frontiers in Psychiatry* 2023  
 Raabe\*, Hasanaj\*, Karsli\* et al, in Präparation



Generate and specify hypothesis

Prefrontal transcranial direct current stimulation changes connectivity of resting-state networks during fMRI.

ARTICLE IN PRESS

Schizophrenia Research xxx (xxxx) xxx

OSF

Contents lists available at ScienceDirect

Schizophrenia Research

ELSEVIER journal homepage: [www.elsevier.com/locate/schres](http://www.elsevier.com/locate/schres)

Effect of aerobic exercise combined with cognitive remediation on cortical thickness and prediction of social adaptation in patients with schizophrenia

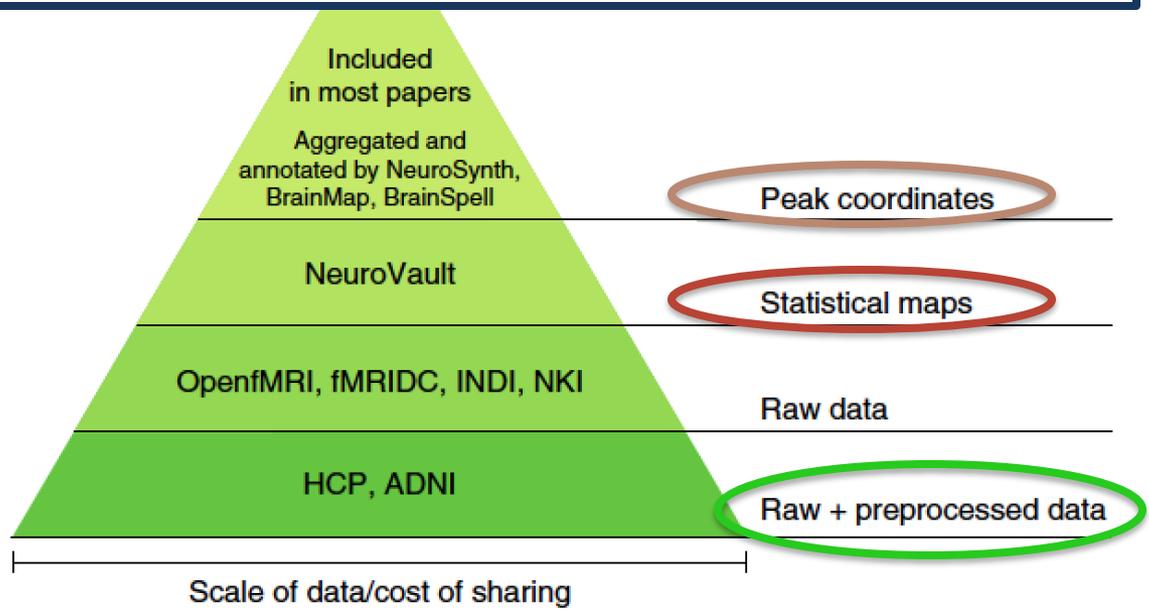
Shun Takahashi <sup>a, b, \*, 1</sup>, Daniel Keeser <sup>a, c, 1</sup>, Boris-Stephan Rauchmann <sup>a, c</sup>, Thomas Schneider-Axmann <sup>a</sup>, Katriona Keller-Varady <sup>a</sup>, Isabel Maurus <sup>a</sup>, Peter Dechent <sup>d</sup>, Thomas Wobrock <sup>e, f</sup>, Alkomiet Hasan <sup>a</sup>, Andrea Schmitt <sup>a, g</sup>, Birgit Ertl-Wagner <sup>c, h</sup>, Berend Malchow <sup>a, i, 1</sup>, Peter Falkai <sup>a, 1</sup>

Munafo et al., Nature Hu



Potential for reuse

More



# NeuroImaging Core Unit Munich





<https://www.en.nicum.uni-muenchen.de/>



LUDWIG-  
MAXIMILIANS-  
UNIVERSITÄT  
MÜNCHEN

NEUROIMAGING LABOR  
AT THE CITY CENTER CAMPUS OF LMU MUNICH



NICUM

[www.en.lmu.de](http://www.en.lmu.de) | [LMU-Portal](#) | [Sitemap](#)

- ABOUT
- PEOPLE
- GUIDELINES
- DOWNLOADS
- EVENTS
- CONTACT
- LINKS

## Welcome to NICUM!





[www.neuroimaging-munich.de](http://www.neuroimaging-munich.de)

Dept. of Psychiatry and Psychotherapy, University Hospital LMU, Head: Prof. Dr. Peter Falkai