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CHARITÉ
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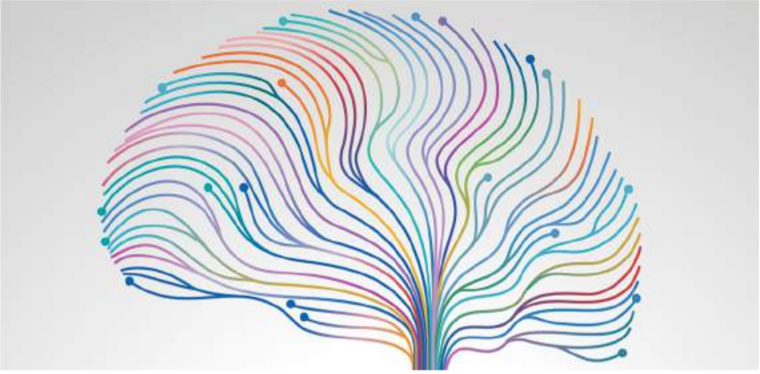
Prediction of Psychiatric Multimorbidity in a Large Pediatric Sample



Prof. Nicolas Langer
University of Zurich
Department of Psychology
Methods of Plasticity Researcch

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Charité
Universitätsmedizin Berlin
Berlin Center for Advanced Neuroimaging (BCAN)

AI for Health
An ITU Focus Group
In collaboration with WHO

3rd meeting of FG-AI4H
EPFL SwissTech Convention Center,
Ecublens (Lausanne), Switzerland , 22-25
Jan. 2019

Outline

- Relevance
- Existing Work
- Current Challenges - Solutions
- Data availability
    - Sample
    - Data (neurophysiology (EEG), cognitive and behavior)
- Data Quality
    - Technical Validation
    - Test-retest preliminary results
- Benchmarking
- Organizers

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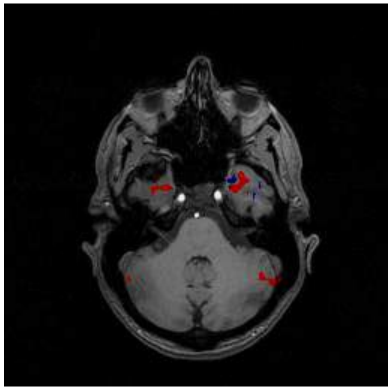
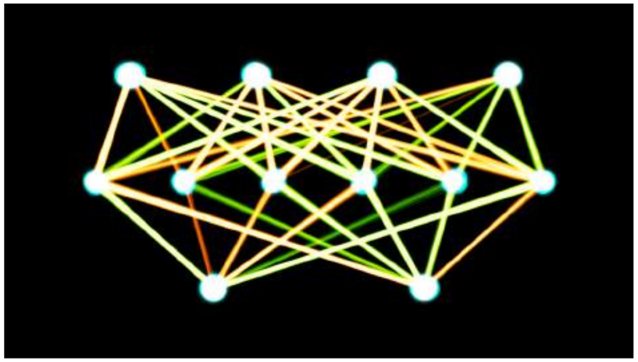
The Final Goal: Biological Tests for Psychiatry

previous approaches with
structural and functional MRI






SKID-I UND SKID-II

Strukturiertes Klinisches Interview für DSM-IV

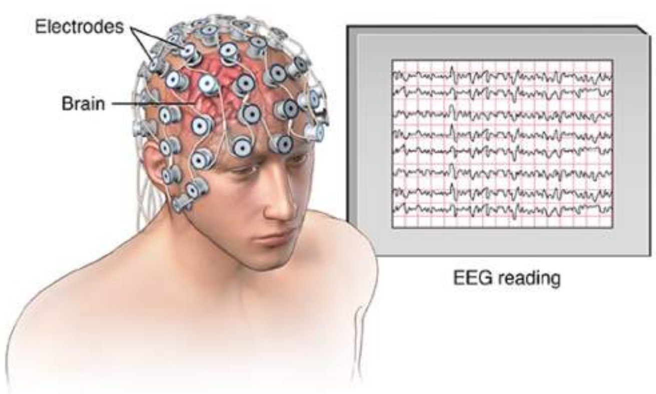
DIPS

DIPS – Diagnostisches Interview bei psychischen Störungen

Psychiatric Diagnosis

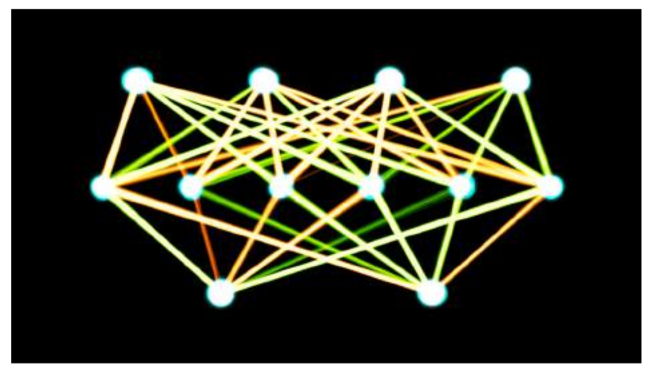
The Final Goal: Biological Tests for Psychiatry

Electroencephalography (EEG)



Why EEG:

- Low cost
- direct measurement of electrical brain activity
- good psychometric properties
- mobility (wide spread availability)



SKID-I UND SKID-II

Strukturiertes Klinisches Interview für DSM-IV

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Psychiatric Diagnosis

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Relevance of the proposal

- **Psychiatric disorders** are among the most common and debilitating illnesses across the lifespan.
- Epidemiologic studies indicate that 70% of all diagnosable psychiatric disorders **begin prior to age 24** (Kessler et al., 2005).
- **Diagnosing** psychiatric developmental disorders:
  - needs multiple prolonged interviews conducted by a psychiatrist with the child and its close relatives.
  - procedure is relatively costly.
  - remains highly subjective (low inter-rater reliability).
- **AI algorithms** promise to overcome the subjectivity of the manual diagnosis.
- An AI based/supported diagnosis would offer a **reliable, objective and cost-worthy** diagnostic method and finally potentially also **shorten the diagnosing time.**

Existing Work

- **Neurophysiological (EEG) biomarkers:**
  - Theta-beta ratio (TBR) in attention deficit hyperactivity disorder (e.g., Magee et al., 2005, Lenartowicz and Loo., 2014).
  - Frontal alpha asymmetry for depression (e.g. van der Vinne et al., 2017, Olbrich and Arns, 2013)

- The majority of existing studies have focused on differentiating between children with an **isolated psychiatric disorder** and typically developing children.
  - However, this line of research **does not reflect the real-life situation:**
    - over 75% of children with a clinical diagnosis have multiple psychiatric disorders = multimorbidities.
- Furthermore, most of the previous studies employ traditional univariate statistics. **Multivariate machine learning/AI approaches** have a great potential to overcome the limitations of univariate approaches.

Current Challenges

- Focus on **one diagnosis vs. healthy controls**
  - in real life 70% multimorbidity
- Univariate vs. multivariate statistics
- **Small sample size** (not enough data)
- **No objective and standardized preprocessing** for EEG data
- Unknown **reliability** of EEG measures
- Not **enough computing power**
- Too many variables for human mind/eye
  - multi dimensional data space

nature neuroscience

Building better biomarkers: brain models in translational neuroimaging

Choong-Wan Woo[1–4], Luke J Chang[5], Martin A Lindquist[6] & Tor D Wager[3,4]

npg Molecular Psychiatry (2012) 17, 1174–1179
© 2012 Macmillan Publishers Limited All rights reserved 1359-4184/12
www.nature.com/mp

PERSPECTIVE

Why has it taken so long for biological psychiatry to develop clinical tests and what to do about it?

S Kapur[1], AG Phillips[2] and TR Insel[3]

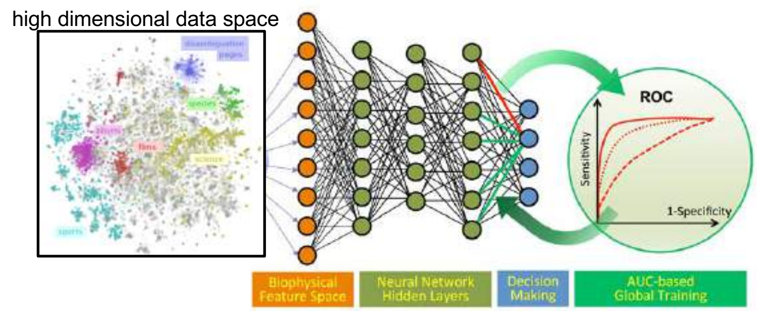
Solution: AI & large representative samples

Availability of Big Data

CHILD MIND® INSTITUTE
healthy brain network

Dr. Michael Milham

Advanced AI Algorithms



Growth in Computing Power

=

2018 2006

Data availability: Sample

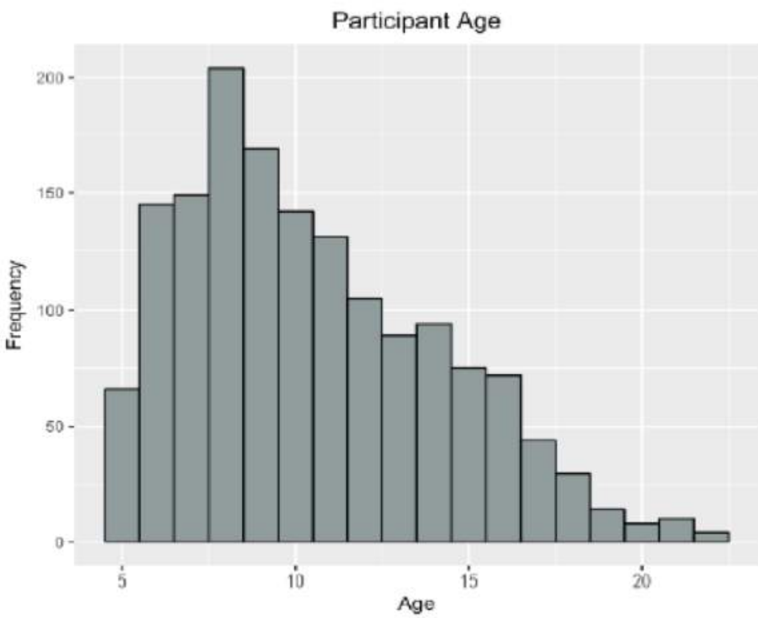
Healthy Brain Network (HBN) sample

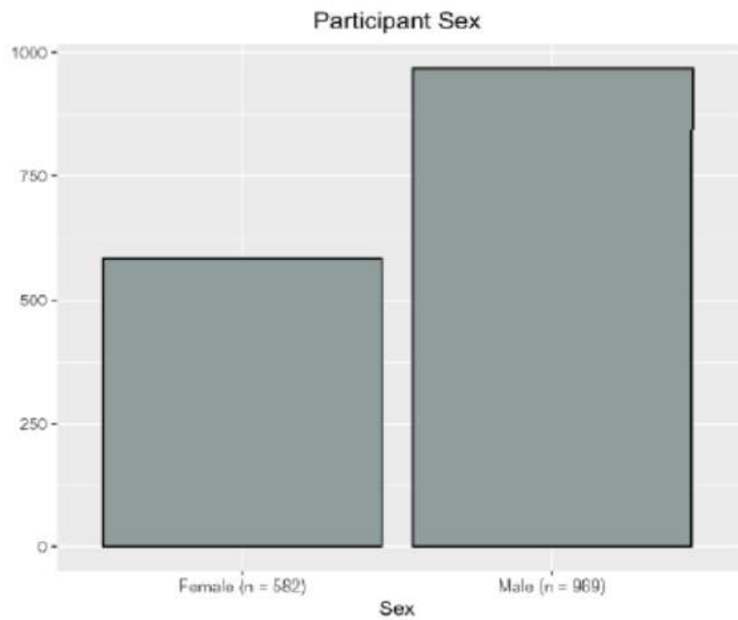
Training Data:

- current release: 1602 subjects
- Age 5-21 years
- Population: typical developing children and children with psychiatric developmental disorders (~70/ multimorbidities)

Test Data:

- Subsample of training data
- Future release: approx. 500 subjects / year





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Child Mind Institute
healthy brain network

Data availability: Sample

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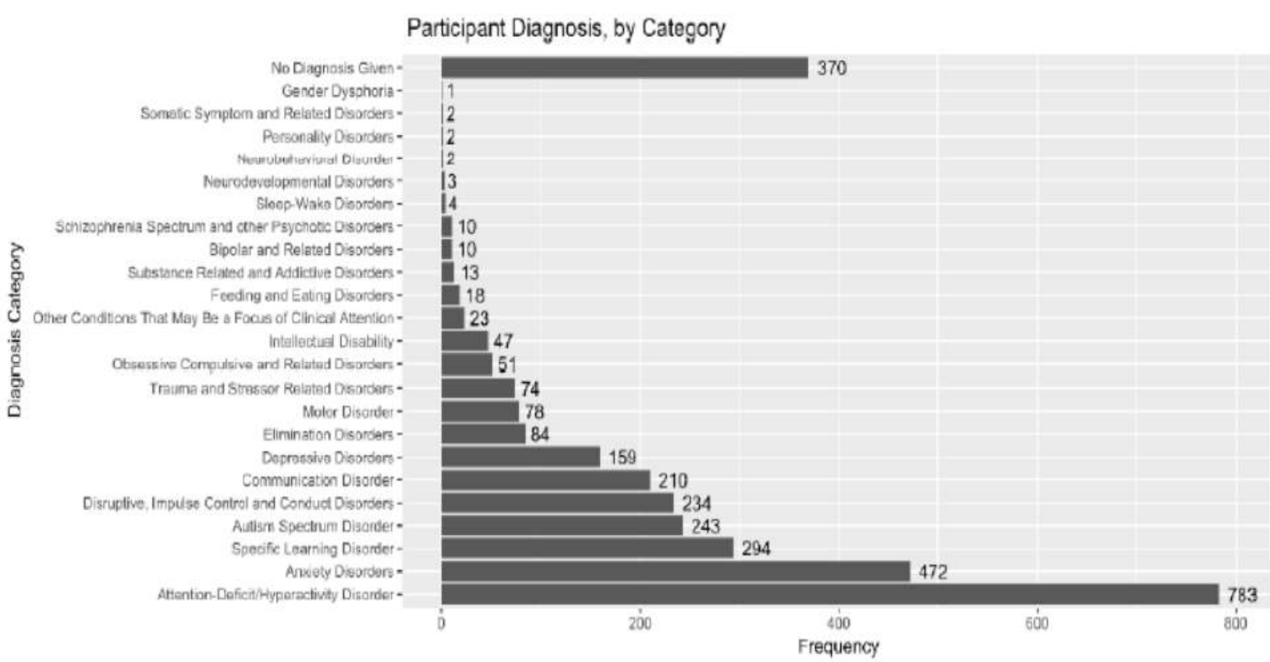
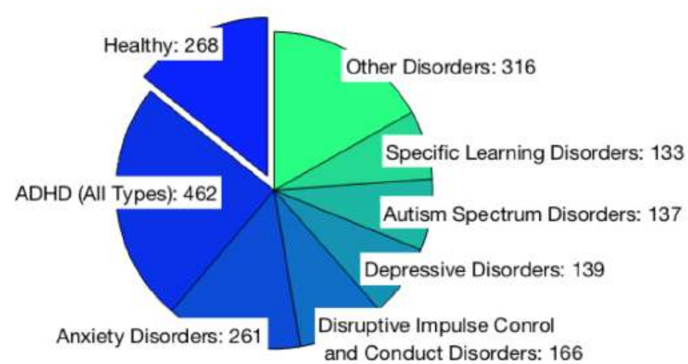
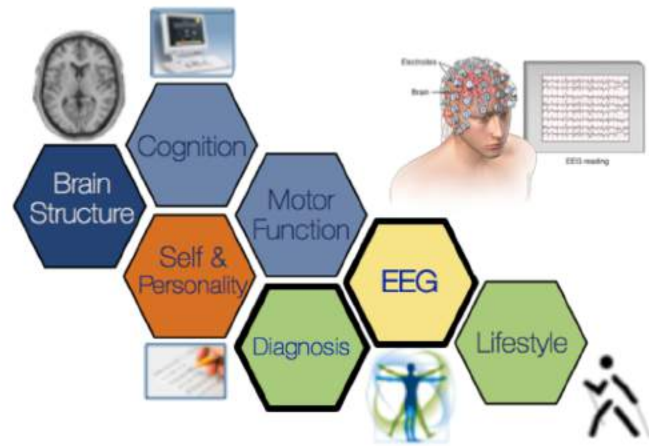




Data availability: Data

- Demographics
  - Age, gender
- Cognitive Data
  - e.g. WISC
- Behavioral Data
  - Questionnaires (SWAN)
- resting EEG
  - Raw data
  - Preprocessed data
  - EEG features
    - e.g. theta-beta ratio, alpha asymmetry
- Possibly T1-weighted MRI images
  - Source reconstruction
  - Cortical thickness



- Prediction of Diagnosis
  - DSM-V consensus diagnosis
- Annotation Quality:
  - based on the decision of a clinical team
  - all interviews and materials conducted as basis for the DSM-5 consensus diagnosis
  - conducted by licensed clinicians

Data availability: Data

- Demographics
  - Age, gender
- Cognitive Data
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Cognitive & Behavioral Data:

- Demographics
- Cognition / Intelligence (e.g. WIAT, WISC-V, NIH-Toolbox)
- Medical History (e.g. addiction family history)
- Family Structure, Stress and Trauma (negative life events, parenting)
- Personality Traits (Big 5, self-esteem)
- Coping Strategies (communication skills, interpersonal factors)
- Physical Measures (e.g. bio-electric impedance analysis, BMI, Metabolic rate, heart rate, blood pressure, height, weight, handedness,…)
- Social Status (SES, parents education, family structure)

Nr. of features: ~270 (self-/ parent-/ teacher-report)

Data availability: Data

- Demographics
  - Age, gender
- Cognitive Data
  - e.g. WISC
- Behavioral Data
  - Questionnaires (SWAN)
- resting EEG
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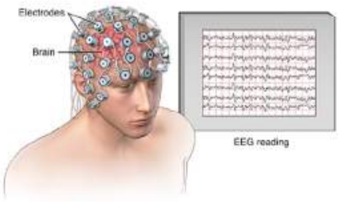

Raw EEG:

- 5 min.
- Eyes closed (40 s) & eye open (20 s)
- 128 electrodes (Geodesic EGI system)
- sampling rate 500 Hz
- Nr. of features: ~ 150’000

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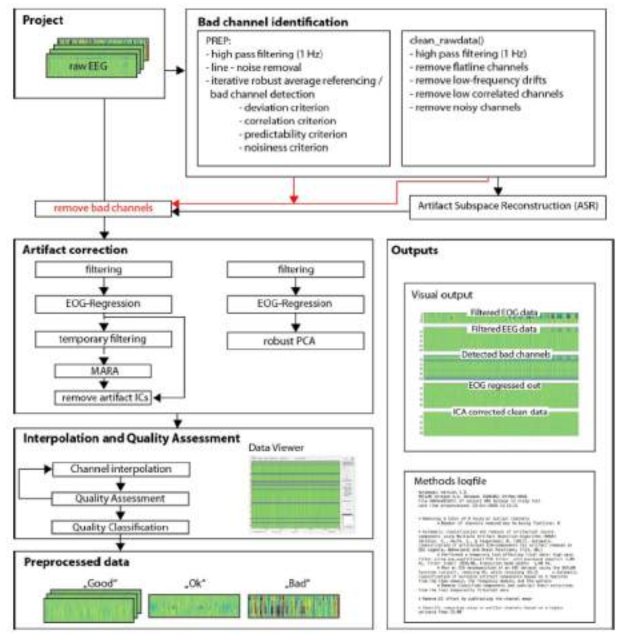
Prerequisite for Biomarker Research: Reliability of measures

Prerequisite for Reliability: Standardized Preprocessing

- Demographics
  - Age, gender
- Cognitive Data
  - e.g. WISC
- Behavioral Data
  - Questionnaires (SWAN)
- resting EEG
  - Raw data
  - Preprocessed data
  - EEG features
    - e.g. theta-beta ratio, alpha asymmetry

Automagic

Pedroni, Bahreini Langer, (2018), biorXiv



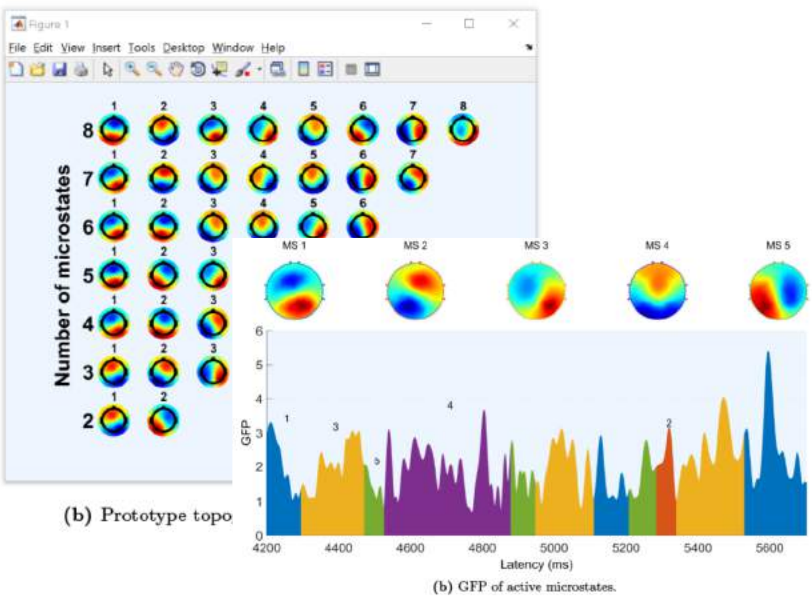
https://github.com/methlabUZH/automagic

<u>Preprocessed EEG:</u>

- Number of features: ~ 150'000

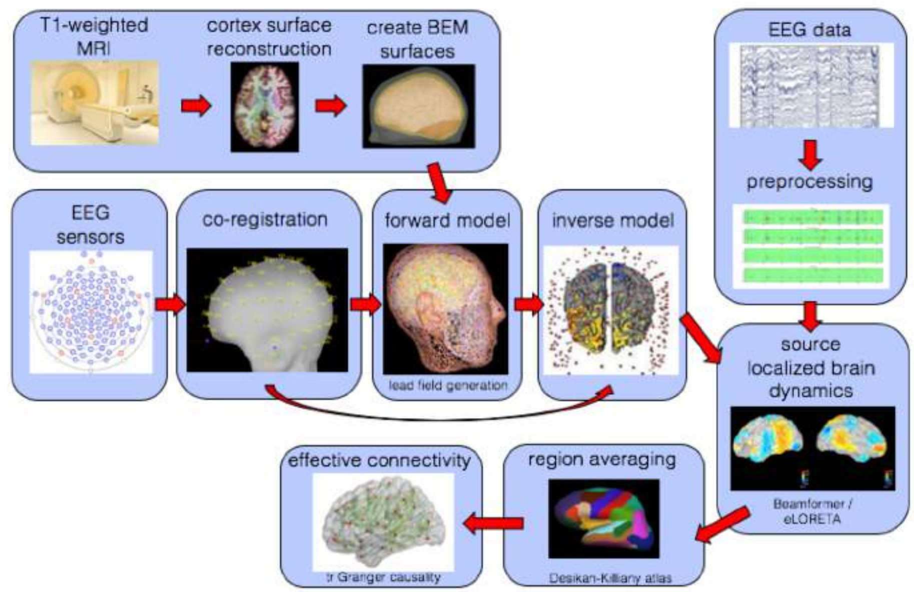
Developing Methods for EEG analysis

EEG Microstates Toolbox



Poulsen, Pedroni, Langer, Hansen (2018)

EEG Connectivity Analysis



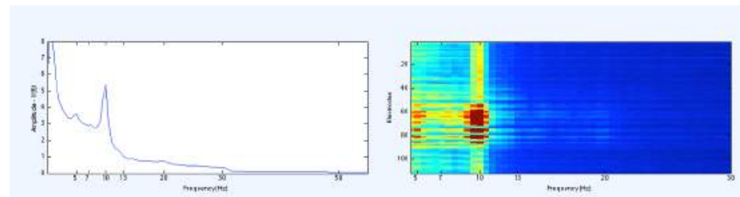
Haufe & Langer in prep.

EEG features

- Demographics
  - Age, gender
- Cognitive Data
  - e.g. WISC
- Behavioral Data
  - Questionnaires (SWAN)
- resting EEG
  - Raw data
  - Preprocessed data
  - EEG features
    - e.g. theta-beta ratio, alpha asymmetry

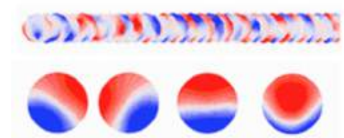
<u>Frequency Domain:</u>

- Frequency Power analysis
  - (e.g. theta/beta ratio; alpha assymetry; 1/f noise, alpha peak)
- Number of features: ~ 122



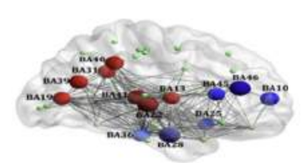
<u>Time Domain:</u>

- Microstates:
  - „MS are stable spatial configurations of the electric field. These spatially stationary microstates might be the basic building blocks of information processing.“ (Lehmann, 1978)
- Number of features: ~ 40



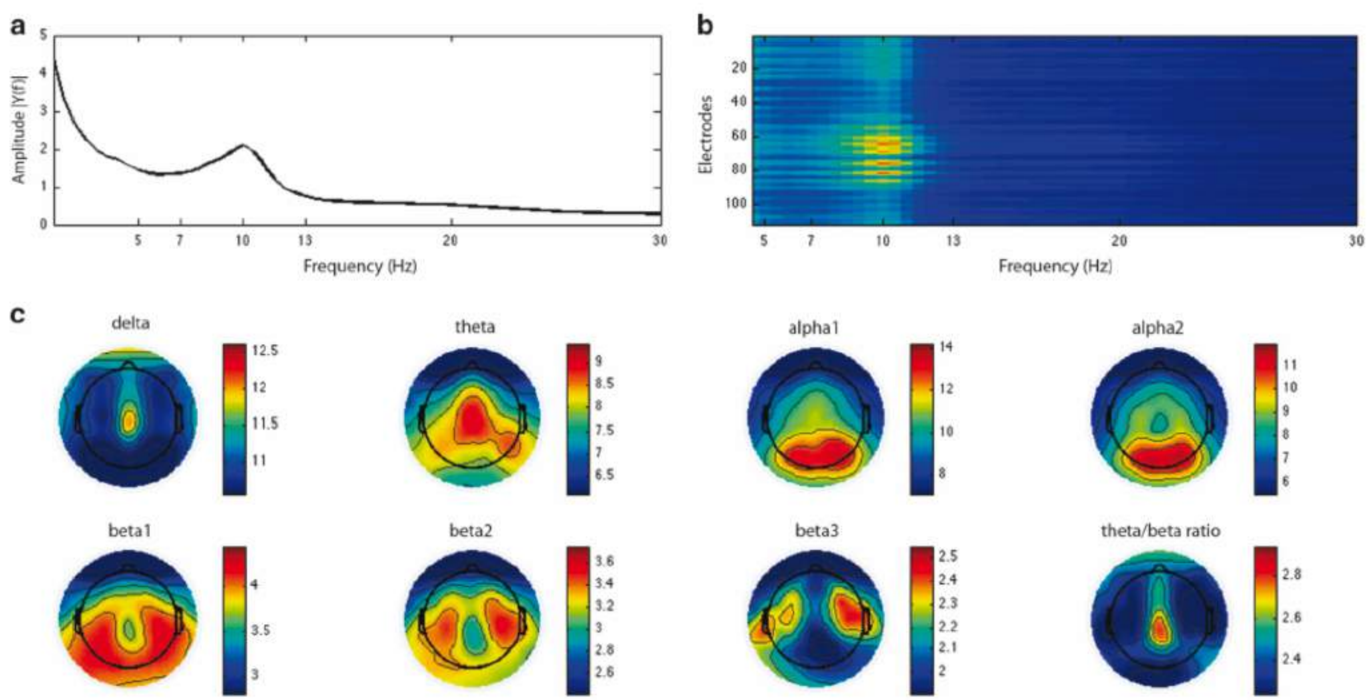
<u>Functional Connectivity:</u>

- Imaginary part of coherency
- Time-reversed Granger causality
- Number of features: ~ 9216



Data Quality: Validation Analysis

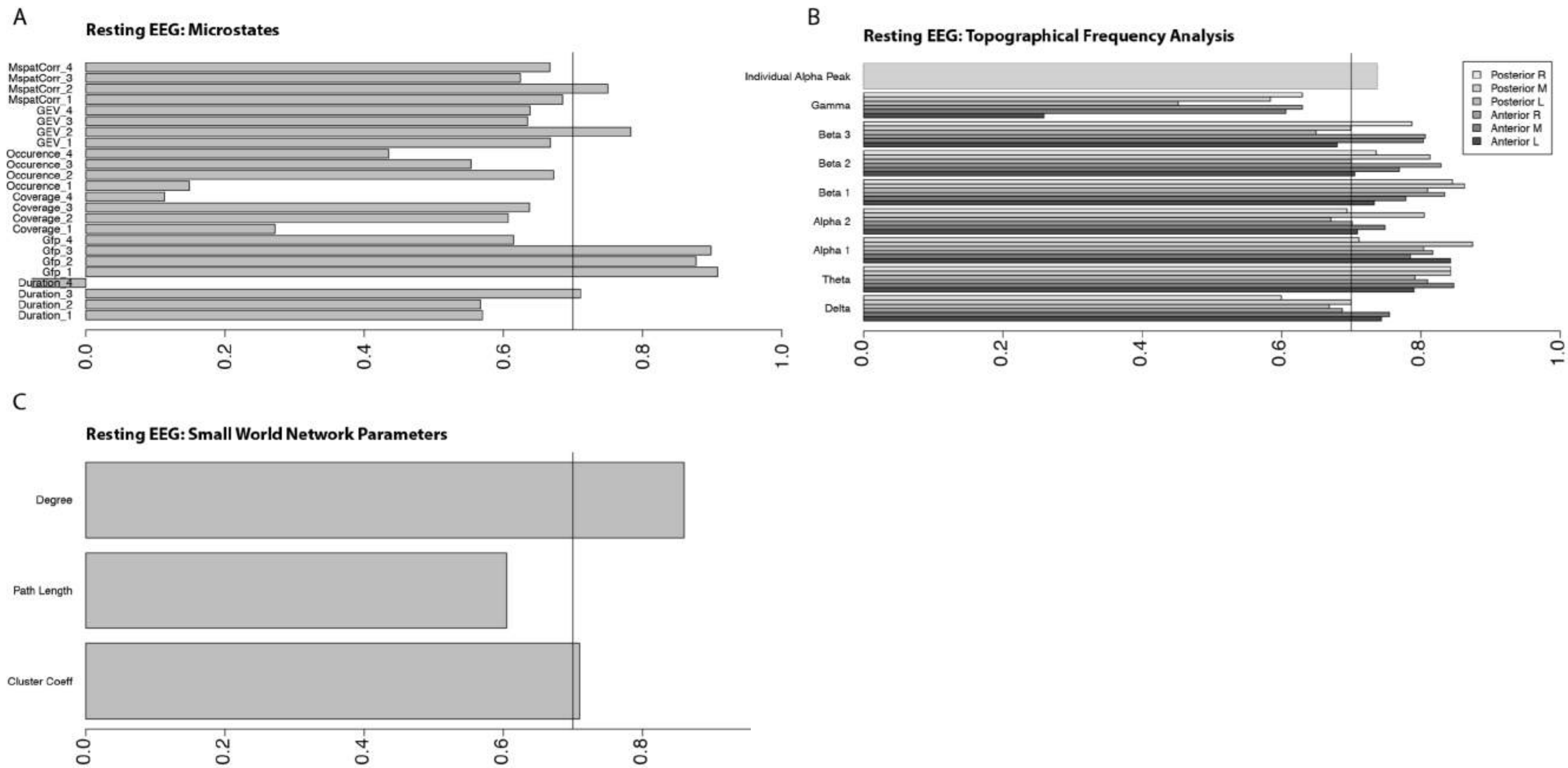
Technical Validation (N = 126)



Langer et al., (2017), Nature Scientific Data

Data Quality: Test-retest Reliability

Preliminary results (N = 30)



Benchmarking

Task: prediction of multiple disorders from demographic, phenotypical (cognitive and behavioral) and EEG data

Training: on public HBN data

Benchmarking: on future releases of HBN data sets (approx. 500 subjects / year)

Implementation: participants submit executable code

- Standardized input (data folder) and output (binary classification matrix)
- Container architecture (docker/kubernetes)
  - Free choice of development tools for participants
  - Safe for organizers
- Cloud computing: GCP/AWS or similar
- Challenge platform: crowdai.org/Kaggle etc.

Performance metrics

Y^{true} : true test labels

D disorders (columns) × N subjects (rows)

1	1	1
1	1	1
0	0	0
0	1	1
1	1	1
1	1	0
1	0	1

Y^{pred} : predicted labels

D disorders (columns) × N subjects (rows)

0	1	1
0	0	1
0	0	0
1	1	1
0	1	0
1	1	0
1	1	1

Main metric (used for ranking): multi-task accuracy

$$\mathrm{ACC} = 1 - \frac{1}{ND} \sum_{n=1}^{N} \sum_{d=1}^{D} |Y_{n,d}^{\mathrm{true}} - Y_{n,d}^{\mathrm{pred}}|$$

Secondary metrics: F1-score, sensitivity, specificity, precision, recall

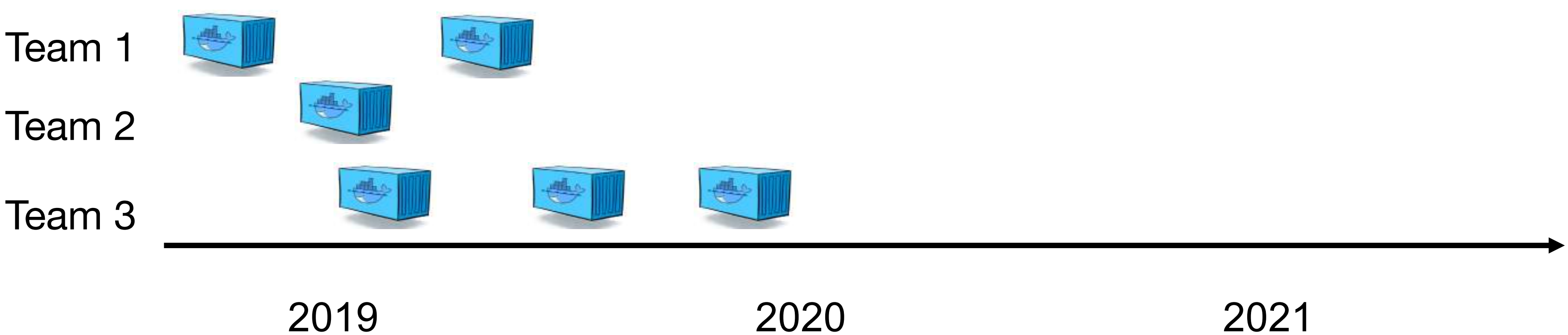
Multi-task metrics for continuous labels (severity scores) available.

Timeline

Idea: continuous prediction challenge

- Participant teams can refine and upload containers any time
- Benchmarking of most recent containers each time new data are released
- Time stamp system allows public release of test set without delay
- Tracking progress over time as new releases become available

Initial training phase



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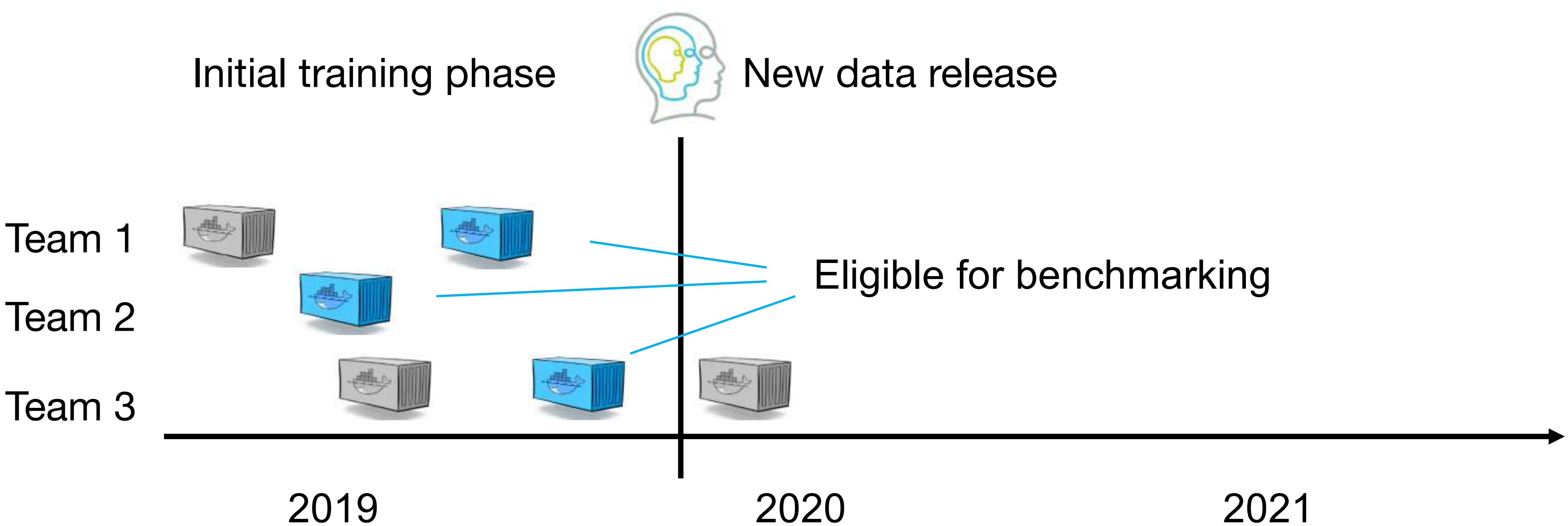

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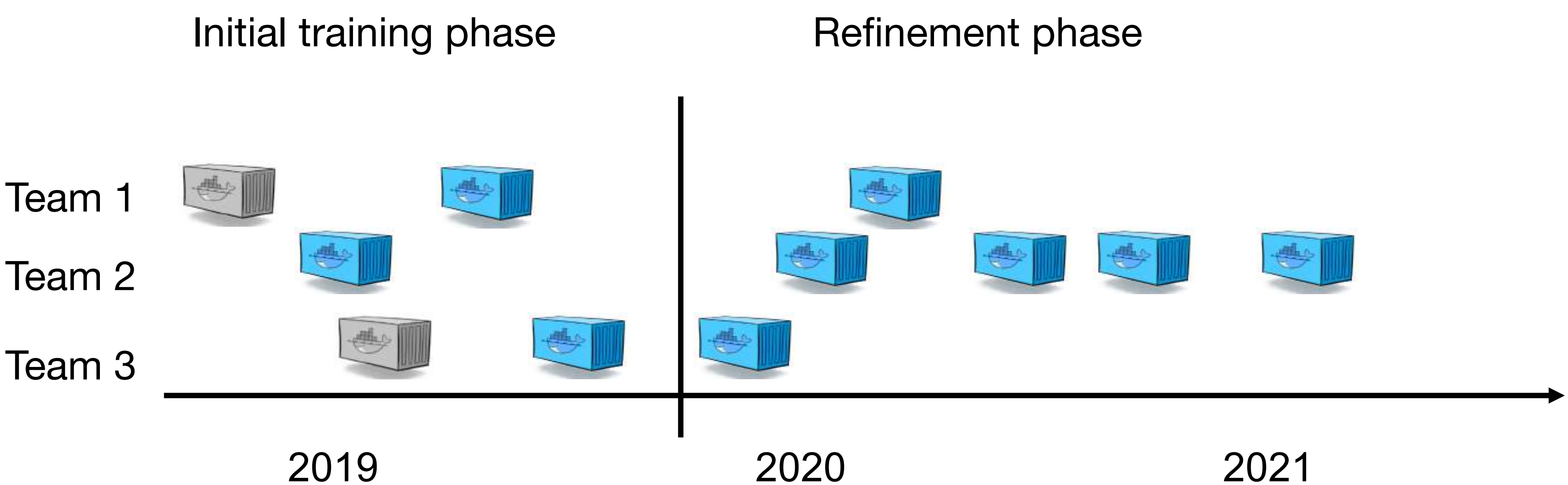

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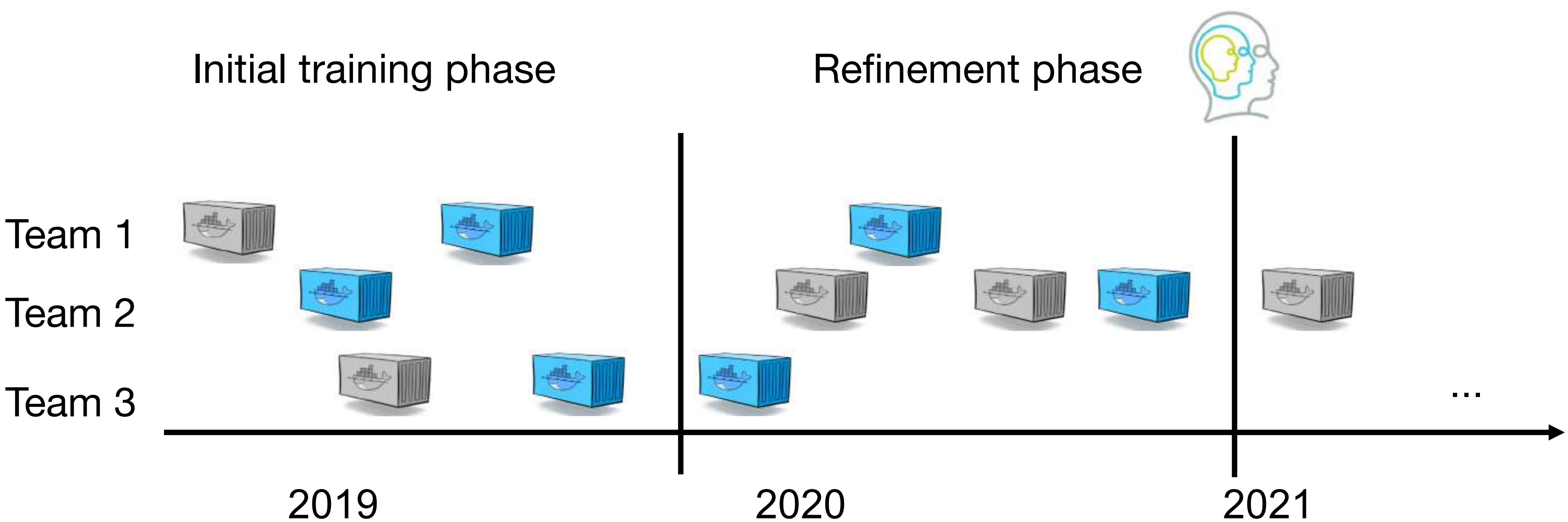

Feasibility

- Close collaboration with the ongoing HBN initiative (support of Dr. Michael Milham)
- Training data already publicly available
- Good data quality
- Expertise regarding signal processing of EEG and statistical analyses
- Previous studies have demonstrated predictive value of EEG data to discriminate between children with an isolated psychiatric developmental disorder and control children

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Organizers

Prof. Nicolas Langer

Bio:

- PhD in Neuroscience & Psychology at University of Zurich
- Postdoctoral Fellow at Harvard Medical School
- Endeavor Scientist at Child Mind Institute
- Now: Assistant Professor with Tenure Track at University of Zurich

Research interest: development of new methods for neuroimaging, EEG, eye-tracking

- design multi-level, multi-modal paradigms to study cognitive performance and perception
- Clinical focus: psychiatric developmental disorders (e.g. ADHD)
- Open Science Advocate (open software, open data)

Interested in solving big data neuro-health problems using AI as part of a collaborative/community driven effort.

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Organizers

Dr. Stefan Haufe

Bio:

- PhD in Computer Science/Machine Learning at TU Berlin
- Marie Curie Postdoctoral Fellow at Columbia University
- Now ERC Research Group Leader at Charité

Research interest: analysis of EEG data using signal processing/AI

- Reconstruction of brain sources and estimation of brain connectivity
- Prediction of mental/clinical states using AI, interpretation of AI models
- Clinical focus: psychiatric and neurological disorders

Interested in solving big data neuro-health problems using AI

as part of a collaborative/community driven effort.

THANK YOU FOR YOUR ATTENTION

Prof. Nicolas Langer and Dr. Stefan Haufe have no conflict of interest