PRISM: Psychiatric Ratings using Intermediate Stratified Markers

Project Coordinator: Prof. dr. Martien Kas (University of Groningen, NL)

Project Leader: Dr. Hugh Marston (Lilly, UK)

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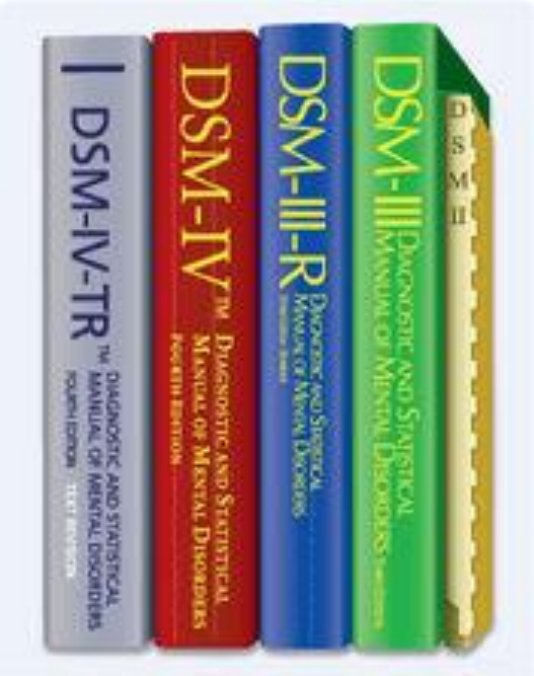
From diagnose to biology



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Disease diversity

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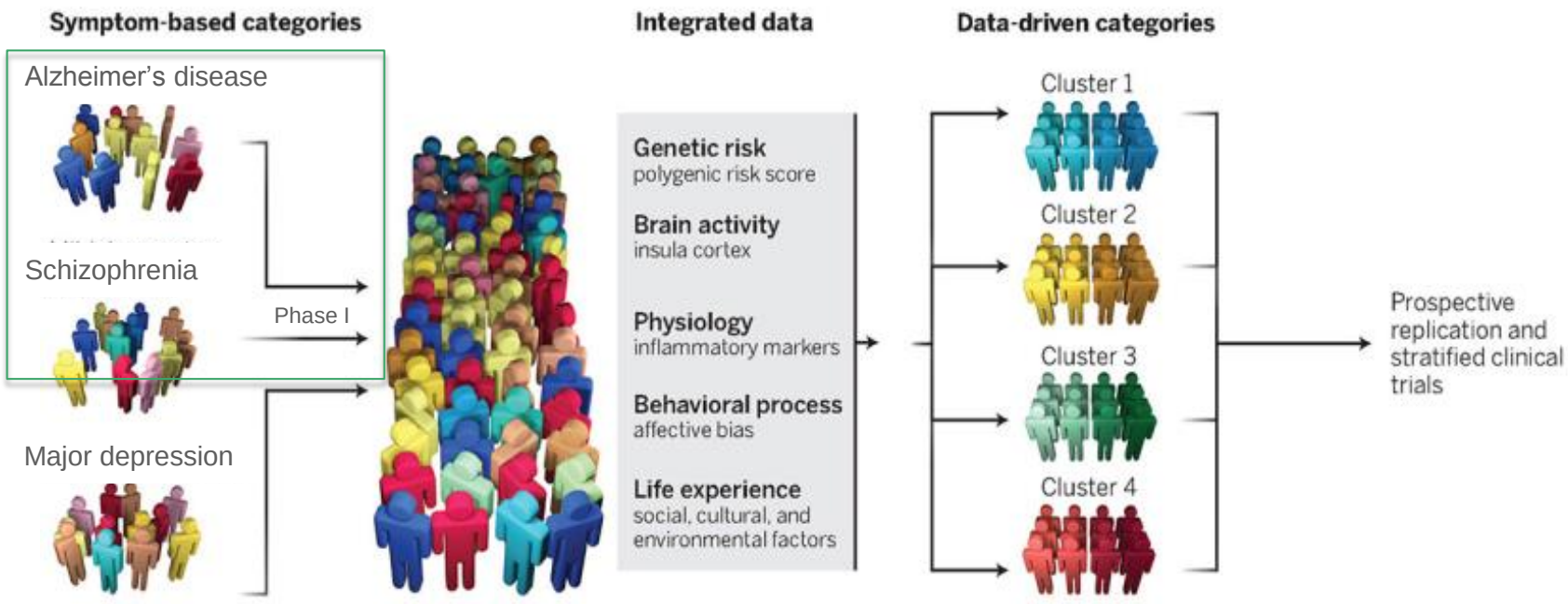
PRISM's general concept:

"Providing quantitative biological measures to facilitate the discovery and development of new treatments for social and cognitive deficits in Alzheimer's disease, schizophrenia and depression"



Adapted from: **Thomas R. Insel** *and* **Bruce N. Cuthbert, Science, May 2015**

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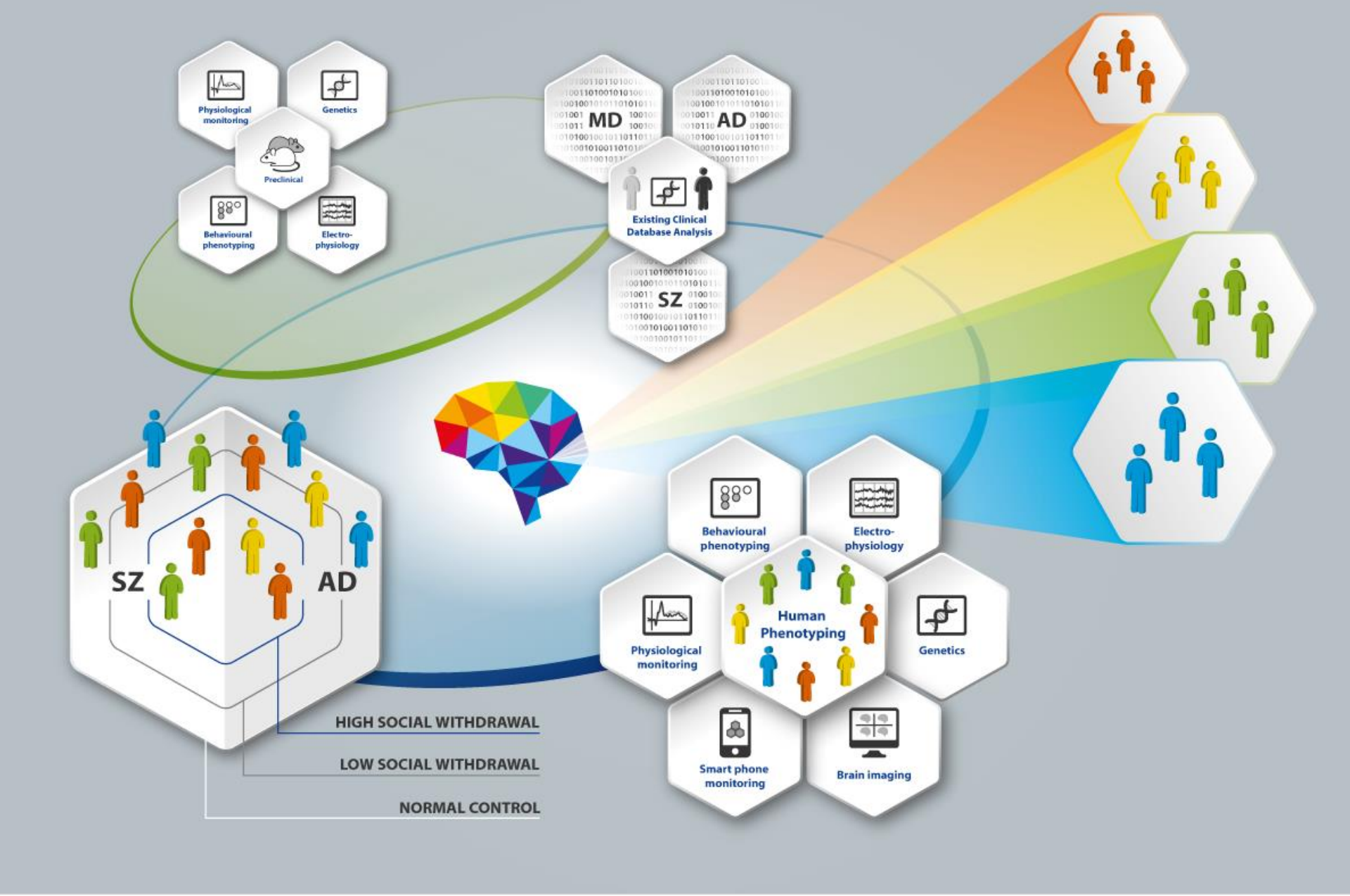
Physiological monitoring
Genetics
Preclinical
Behavioural phenotyping
Electro-physiology
MD
AD
Existing Clinical Database Analysis
SZ
SZ
AD
HIGH SOCIAL WITHDRAWAL
LOW SOCIAL WITHDRAWAL
NORMAL CONTROL
Behavioural phenotyping
Electro-physiology
Physiological monitoring
Human Phenotyping
Genetics
Smart phone monitoring
Brain imaging

PRISM

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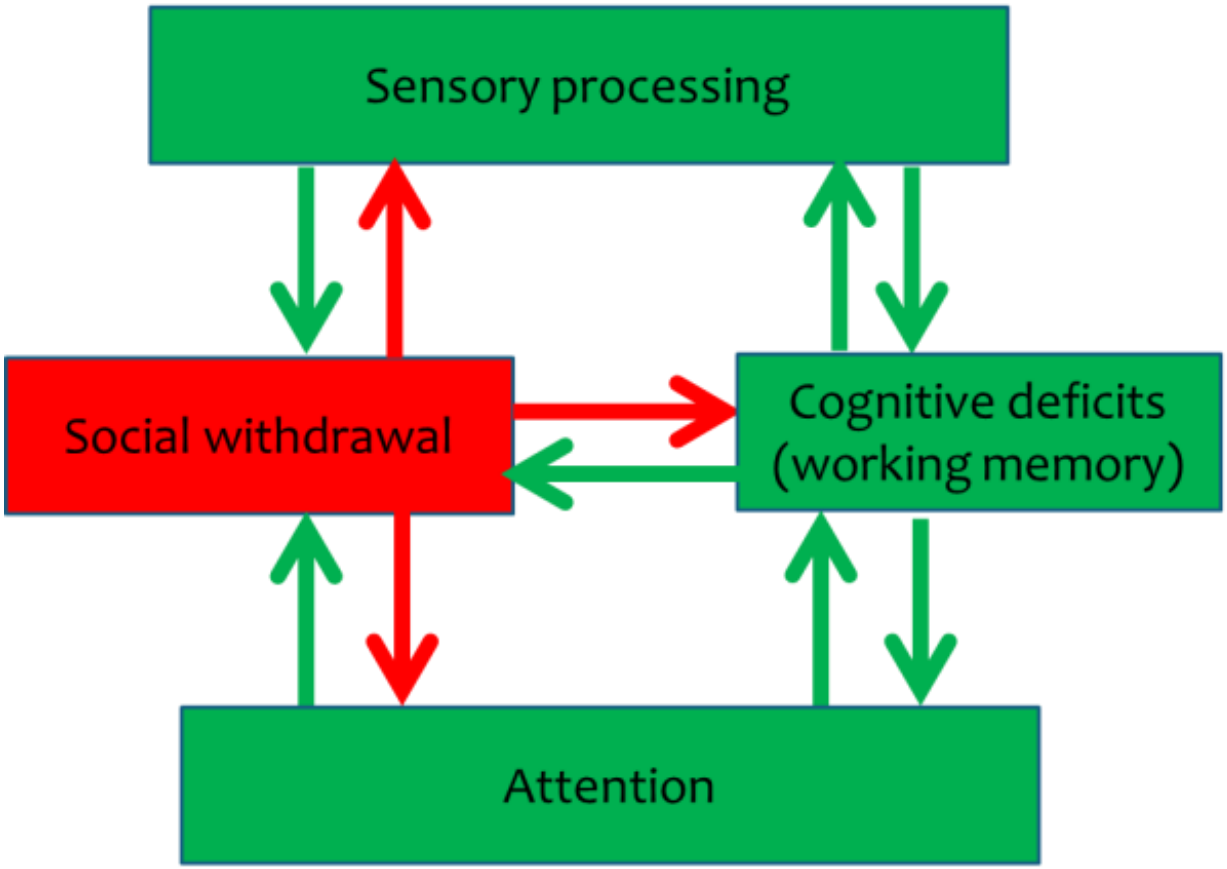
Human and rodent homologies



Biological substrate

EEG

Neuro-Imaging

Behaviour

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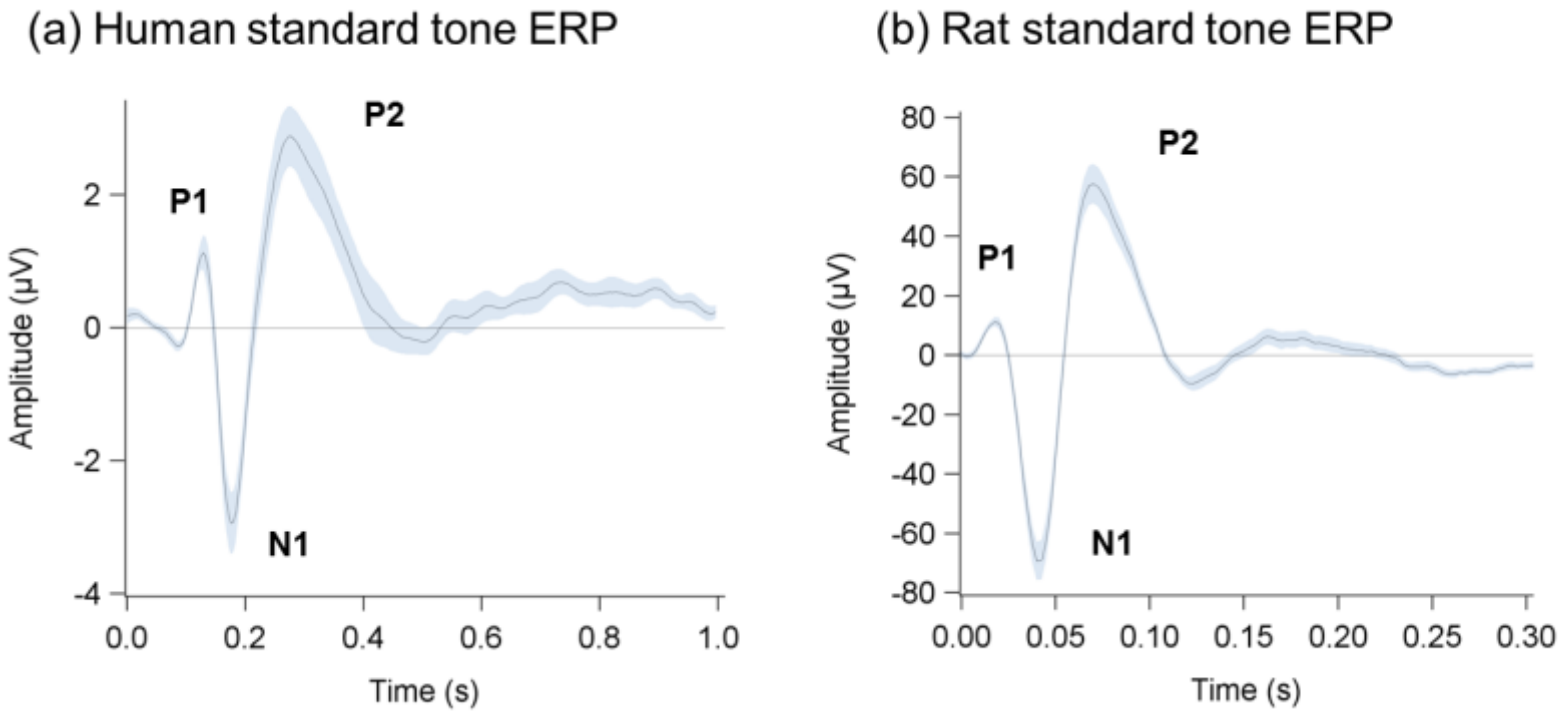
Homologies in evoked related potentials



Kas, Penninx, Sommer, Serretti, Arango, & Marston, Neuroscience & BioBehavioural Reviews, in press

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Neuroscience & Biobehavioral Reviews: Special Issue

Quantitative neurosymptomatics; linking quantitative biology to Neuropsychiatry

Guest Editors:

Martien Kas* (University of Groningen, Groningen, The Netherlands) *Managing editor
Hugh Marston (Eli Lilly & Company, Windlesham, UK)
Alessandro Serretti (University of Bologna, Bologna, Italy)

Manuscripts:

1. **A quantitative approach to neurosymptomatics: the why and the how** M Kas et al – **in press**
2. **Neurobiology of Social withdrawal** S Porcelli et al - **in press**
3. **Commentary: Operationalization of RDoCs as an approach to the study of social withdrawal in schizophrenia and Alzheimer's disease** B Cuthbert (NIMH) – **in press**
4. **Defining and objective assessments of social withdrawal in schizophrenia and Alzheimer's dementia patient populations** N van der Wee et al – **in press**
5. **Quantitative and translational measures of attention in schizophrenia, Alzheimer's disease, and major depressive disorder**A Serretti et al – **in press**
6. **Electrophysiological assessments of sensory processing dysfunction in schizophrenia and Alzheimer's dementia** P Danjou et al **in press**
7. **Commentary: The challenges of quantitative biology in the study of social withdrawal in schizophrenia and Alzheimer's disease** W T Carpenter – **in press**
8. **Overview of the clinical implementation of a study exploring social withdrawal in schizophrenia and Alzheimer's disease** Amy Bilderbeck et al – **in press**
9. **Commentary: PRISM project viewed from the regulatory perspective** Maria Tome et - **in press**
10. **The reverse translation of a quantitative neuropsychiatric framework into pre-clinical studies** B Hengerer et al – **in press**
11. **Sleep disturbances and (other) neuropsychiatric symptoms in neurodegeneration** Winsky-Sommerer et al - **in press**
12. **Multisensory cortical processing and dysfunction across the neuropsychiatric spectrum** Hornix et al – **in press**

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Clinical deep phenotyping study

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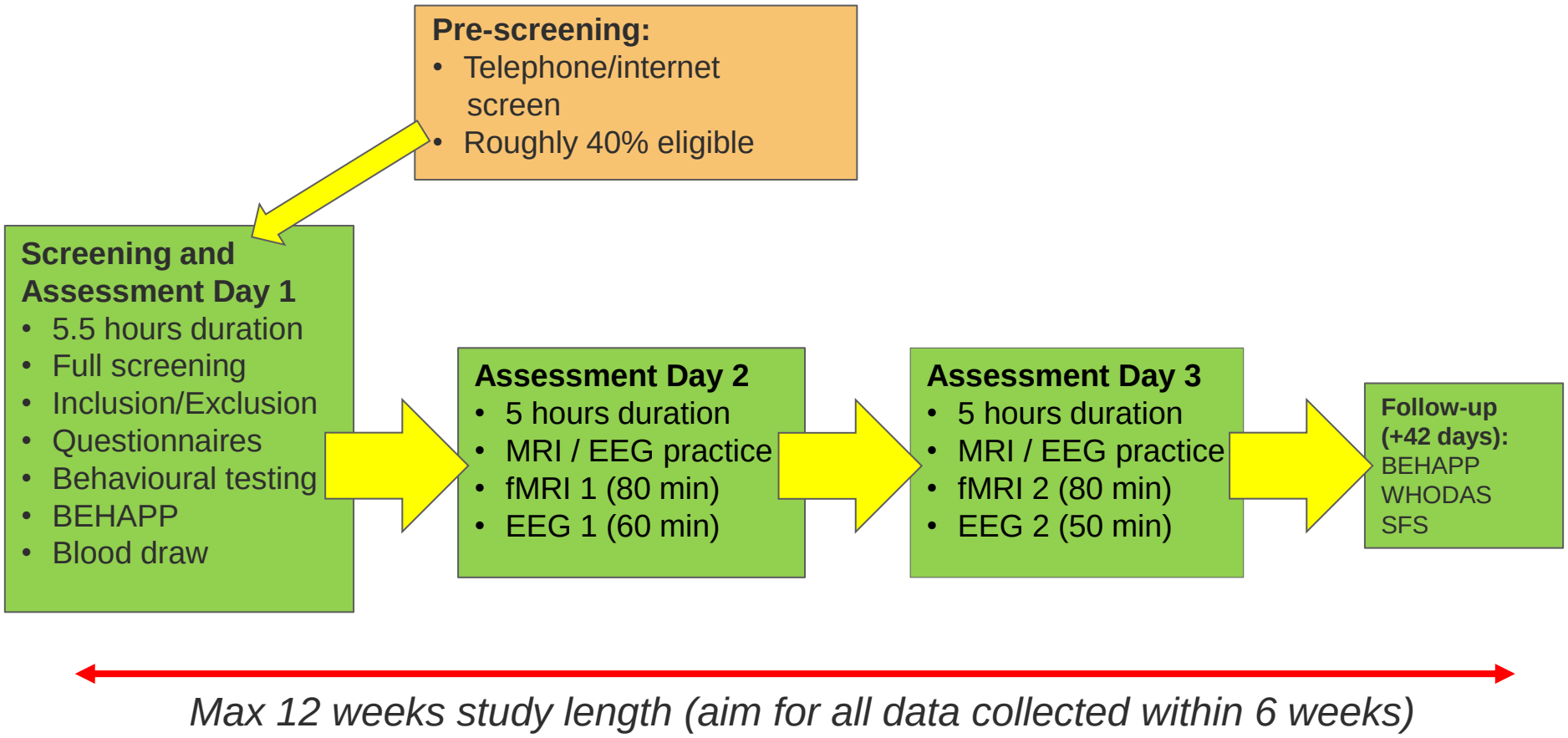
Study design



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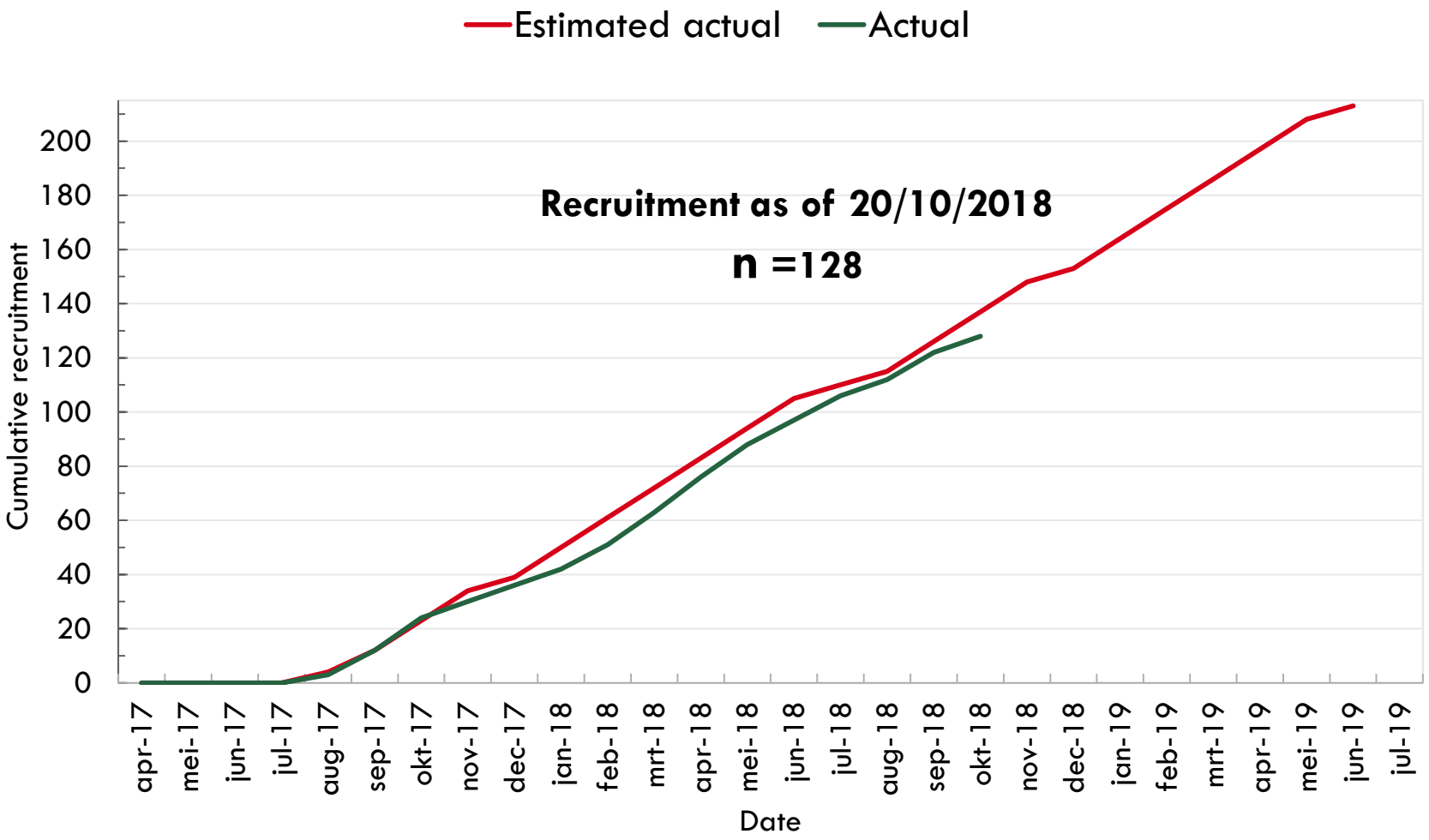
Recruitment Estimated vs. Actual



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Futility analysis

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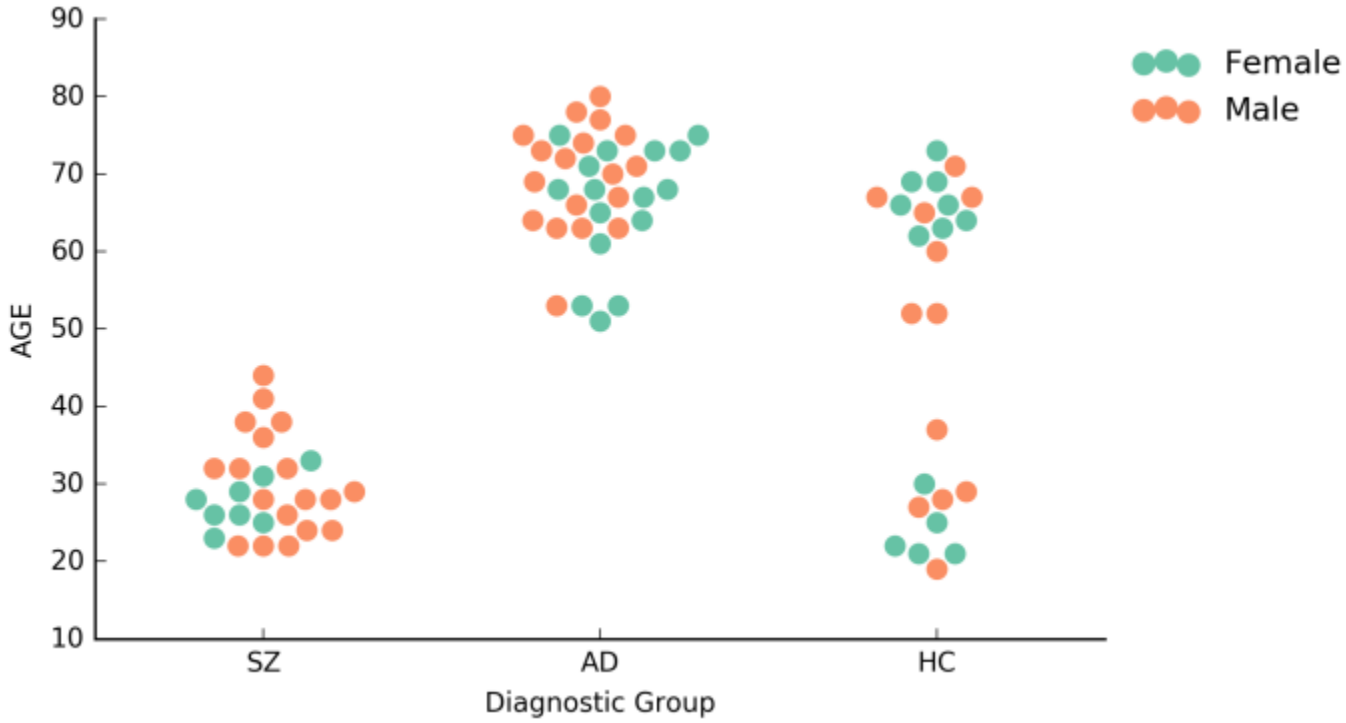
Participants



N=85

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Endpoints

Modality	Endpoint
EEG Visit 2	various
Anatomical MRI	volume
	thickness
	area
BOLD fMRI Resting State	DMN
	seed-maps
BOLD fMRI Facial Expression Processing Task (FEP)	mean z-score in regions of interest
BOLD fMRI Virtual Morris Water Maze (VMWM)	mean z-score in regions of interest

Modality	Endpoint
BOLD fMRI Monetary and Social Incentive Delay task (MSID)	mean z-score in regions of interest
Diffusion Imaging	FA, MD, MO
Facial Expression Recognition Task (FERT; Behaviour)	various
Hinting Task (Behaviour)	
Digit Symbol Substitution Task (DSST; Behaviour)	various
Effort Expenditure for Rewards Task (EEfRT; Behaviour)	various
Continuous Performance Test (CPT; Behaviour)	various

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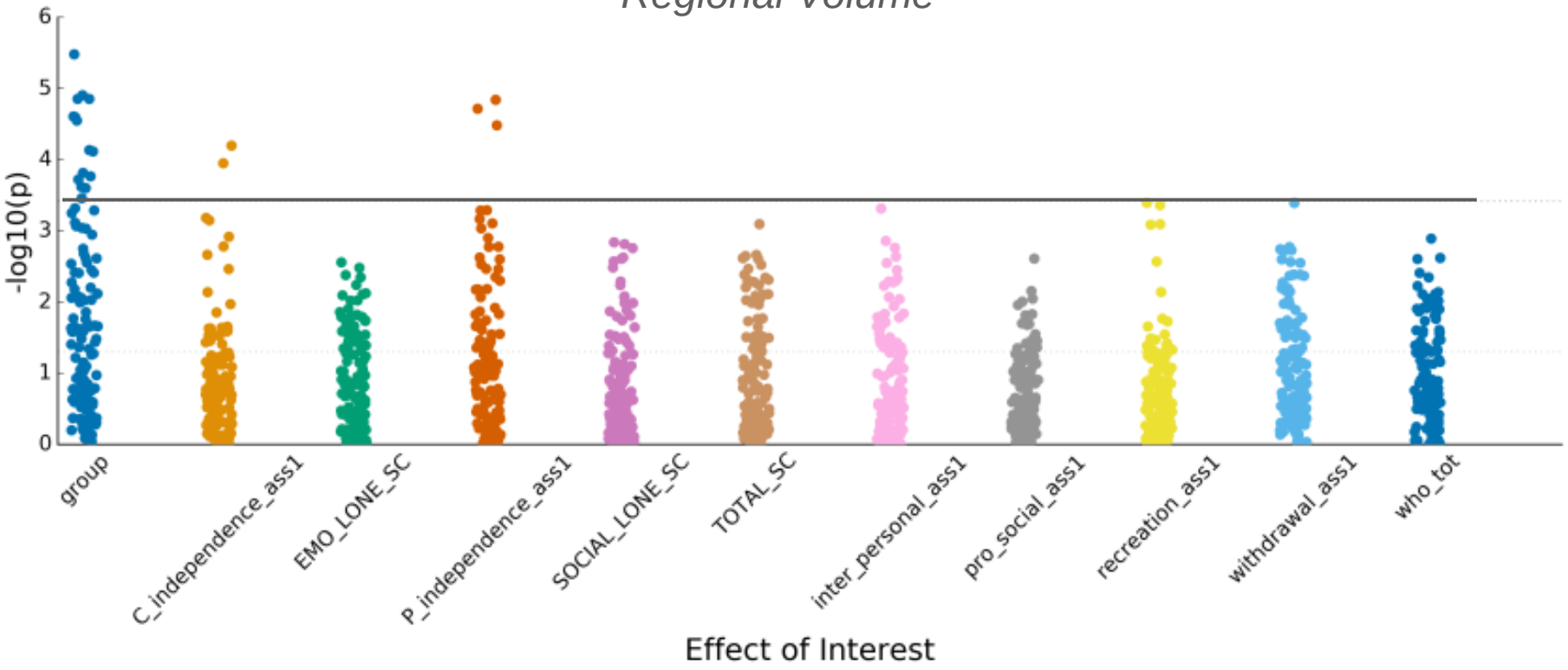
Futility results for individual endpoints

Regional Volume



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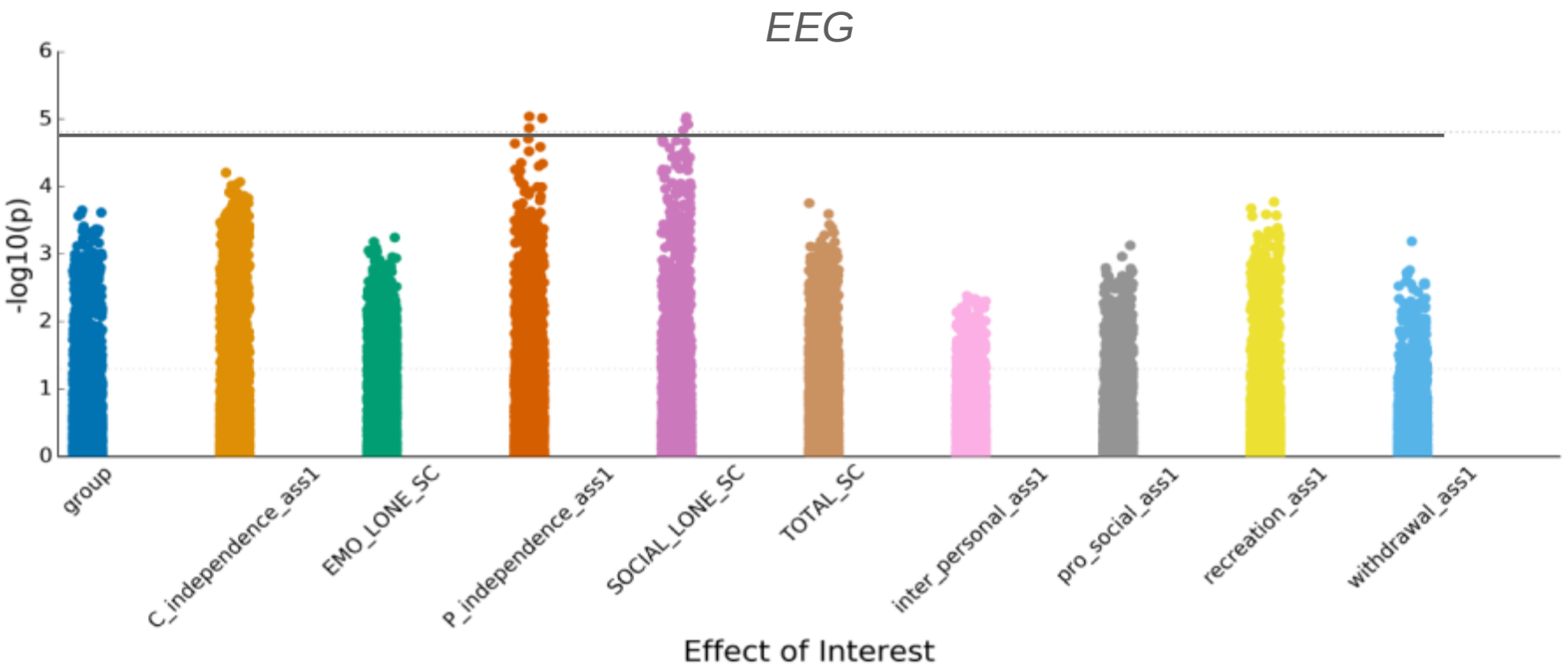
Futility results for individual endpoints



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How to assess longitudinal and objective measures of social withdrawal in a trans-diagnostic manner?

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WHODAS 2.0

WORLD HEALTH ORGANIZATION
DISABILITY ASSESSMENT SCHEDULE 2.0

PRISM

Think back over the past 30 days and answer these questions, thinking about how much difficulty you had doing the following activities. For each question, please circle only one response.

Getting along with people						
D4.1	Dealing with people you do not know?	None	Mild	Moderate	Severe	Extreme or cannot do
D4.2	Maintaining a friendship?	None	Mild	Moderate	Severe	Extreme or cannot do
D4.3	Getting along with people who are close to you?	None	Mild	Moderate	Severe	Extreme or cannot do
D4.4	Making new friends?	None	Mild	Moderate	Severe	Extreme or cannot do

Participation in society						
In the past 30 days:						
D6.1	How much of a problem did you have in joining in community activities (for example, festivities, religious or other activities) in the same way as anyone else can?	None	Mild	Moderate	Severe	Extreme or cannot do

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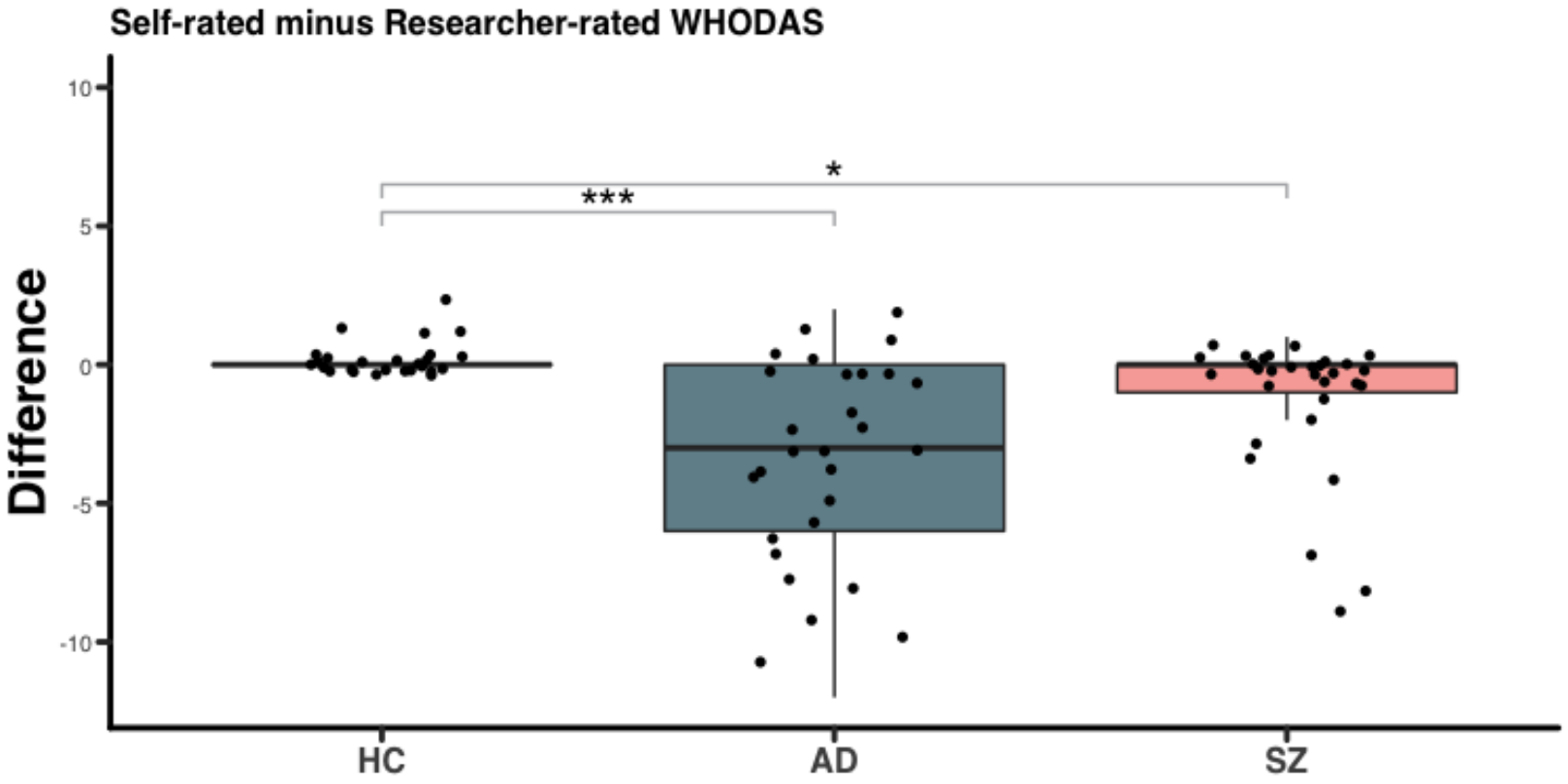
Participant versus researcher rating

preliminary results



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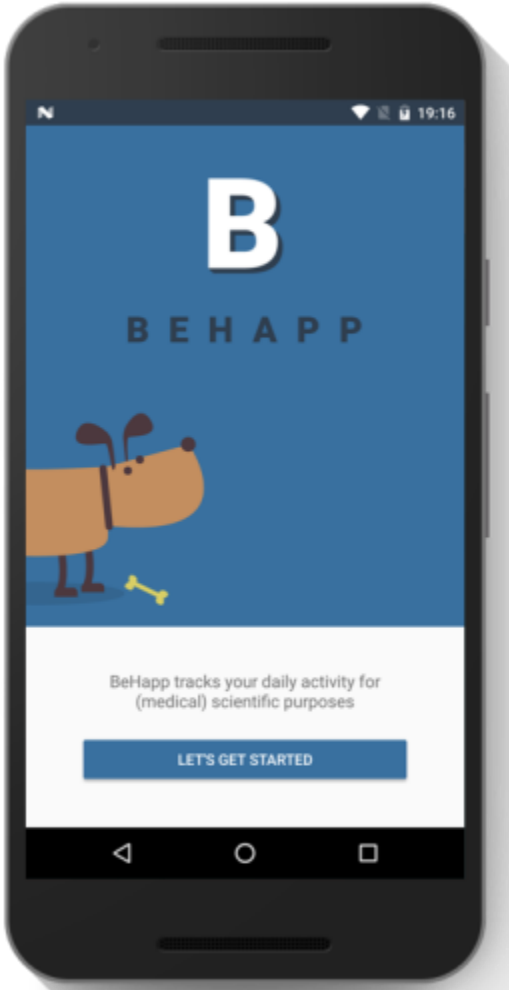
BEHAPP – passive remote behavioural monitoring



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BEHAPP features

Current features:

- Call History
- SMS Messaging History
- Interval based WiFi Scans
- Interval based Bluetooth Device Scans
- Location Data
- App Usage

Upcoming features:

- Accelerometer
- Ambient noise
- Ambient light

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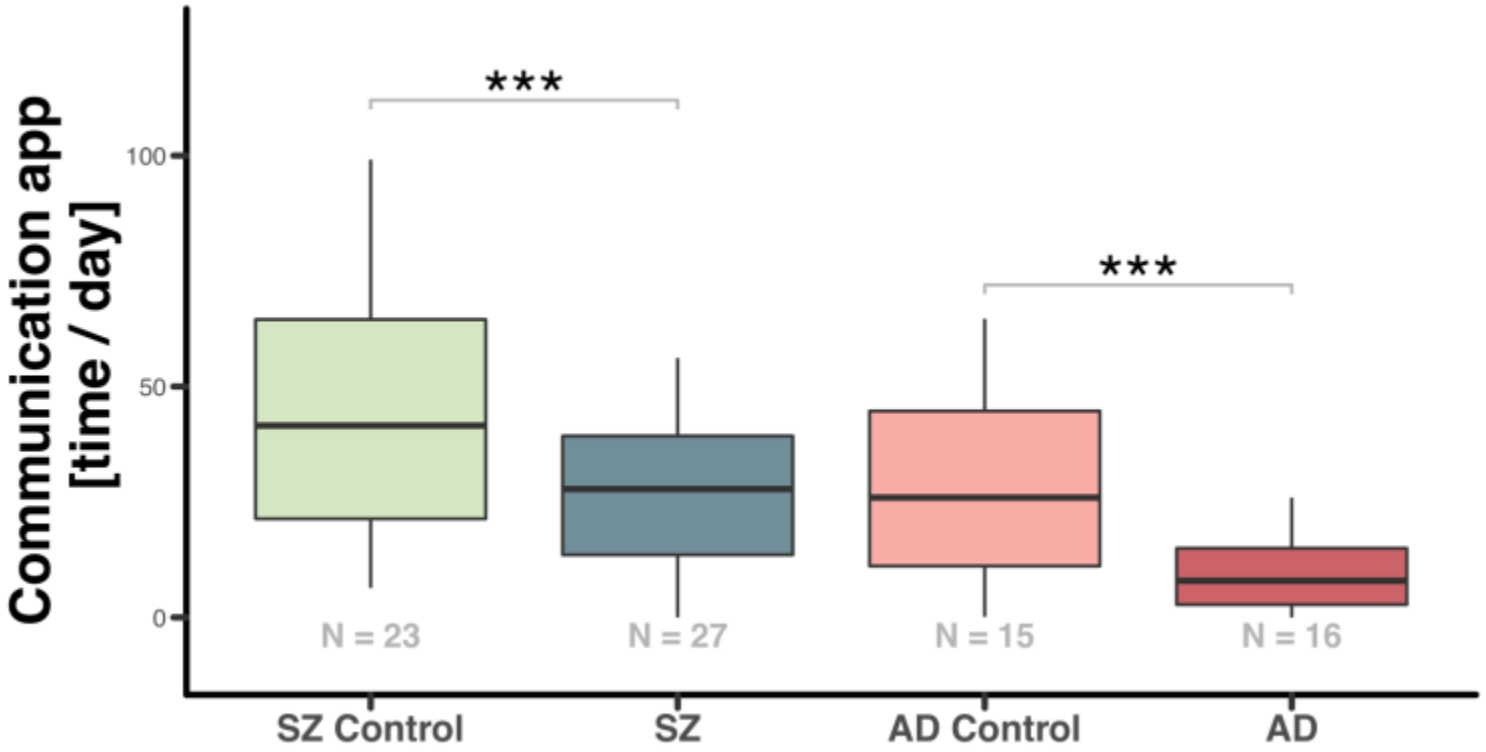
BEHAPP: communication app usage

preliminary results



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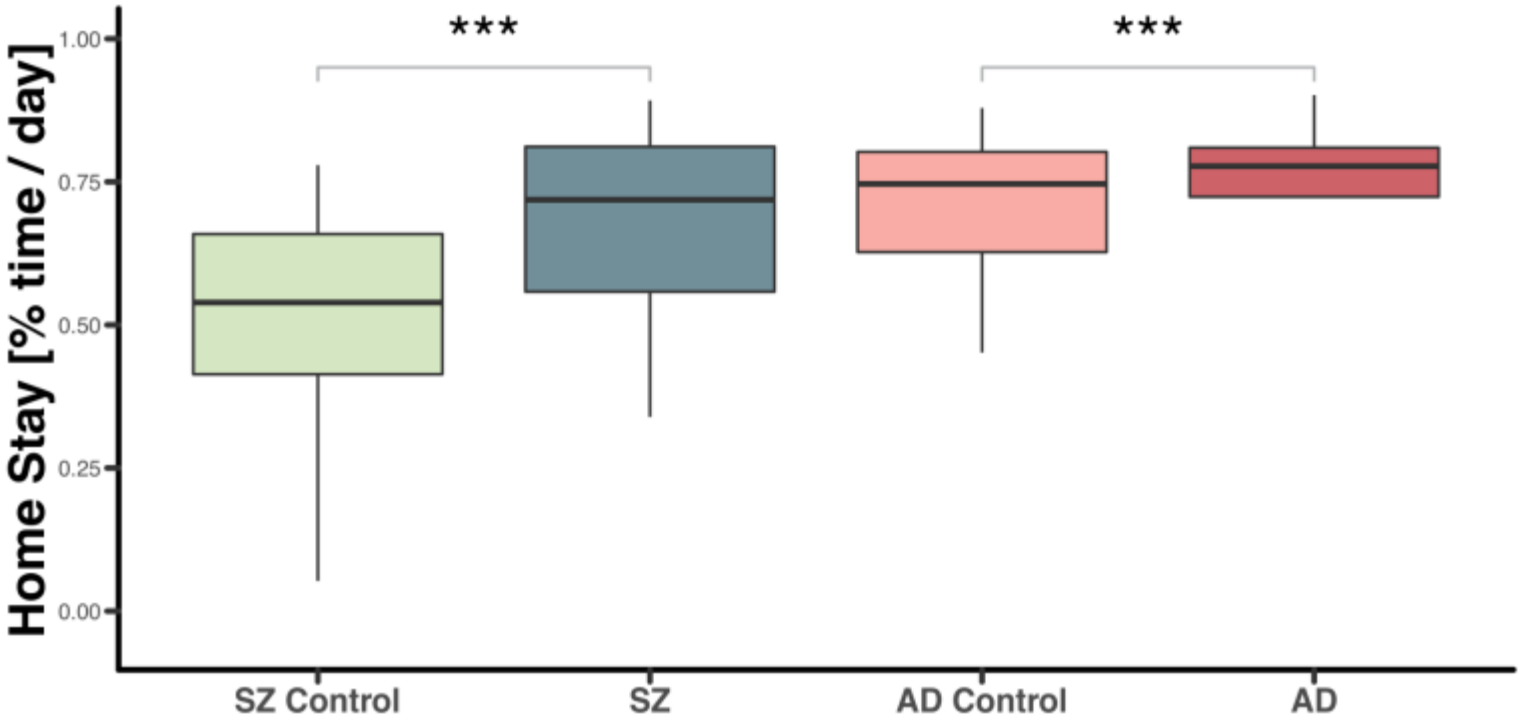
BEHAPP: Home stay scores

preliminary results



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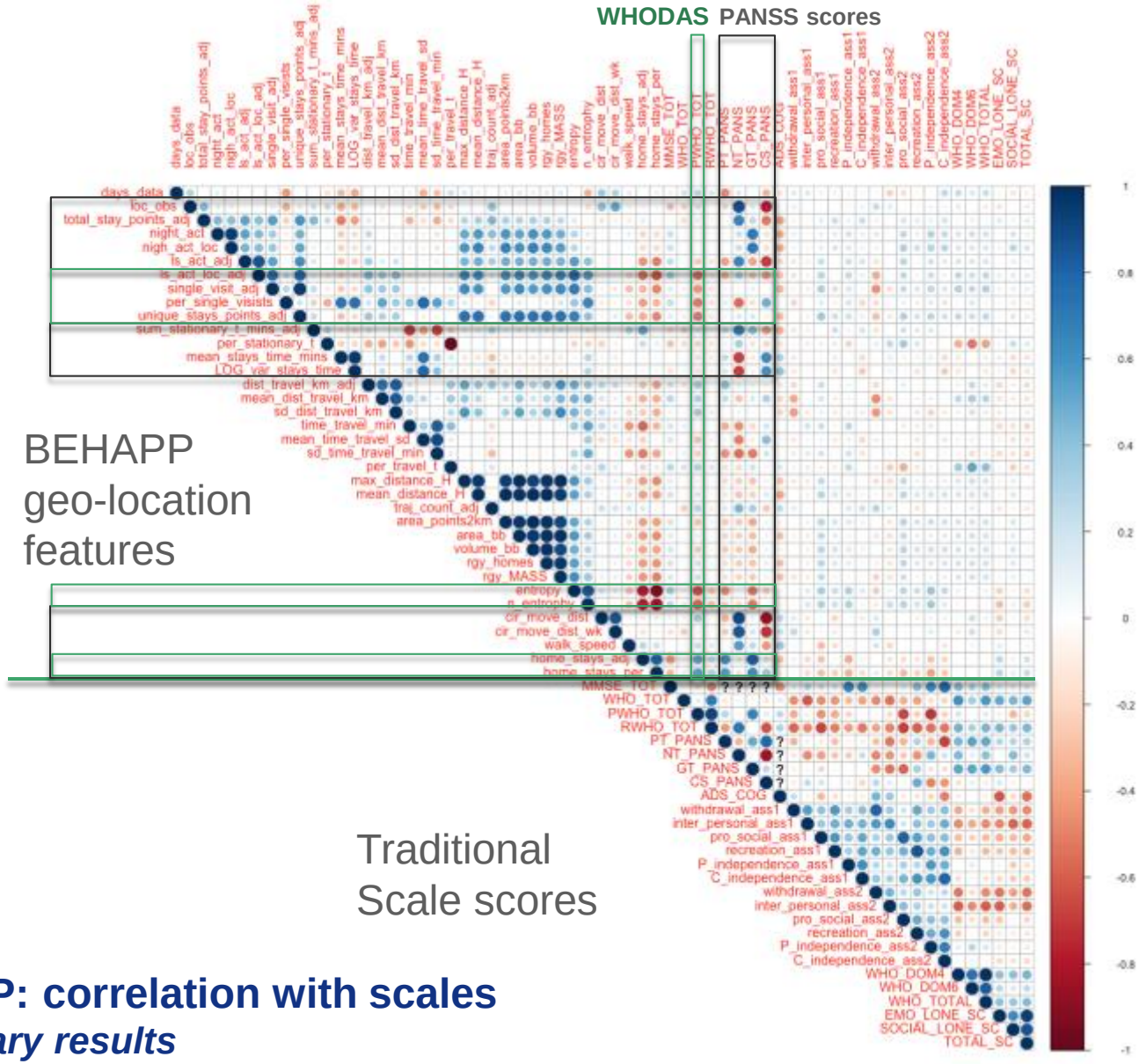

BEHAPP: correlation with scales

preliminary results

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Preclinical battery

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Alignment and harmonization of the pre-clinical and clinical behavioral test batteries

Human task	Rodent equivalent	Contribution by
Smartphone application	Social group behavior	RUMC, RUG, BI
Social Functioning scale	Social group behavior	RUMC, RUG, BI
Social incentive delay – MRI: 15 min. MID, incl. motivation – (outside the scanner)	Social conditioned place preference	RUMC, RUG, BI, Biotrial No task coupling to MRI
	Three chamber task	
Resting State eyes open and closed	Resting state EEG.	RUG, Eli Lilly, Janssen, Biotrial
MMN Auditory (passive)	MMN auditory	RUG, (Eli Lilly), Janssen, Biotrial
Steady-state auditory-evoked potential	Steady-state auditory-evoked potentials	RUG, Eli Lilly, Janssen, Biotrial
N-back – with fMRI	Odor Span Task	Biotrial, Eli Lilly
Arena Task- with fMRI	Morris Water Maze	Biotrial, Eli Lilly
Continuous Performance task	5C-CPT	RUMC

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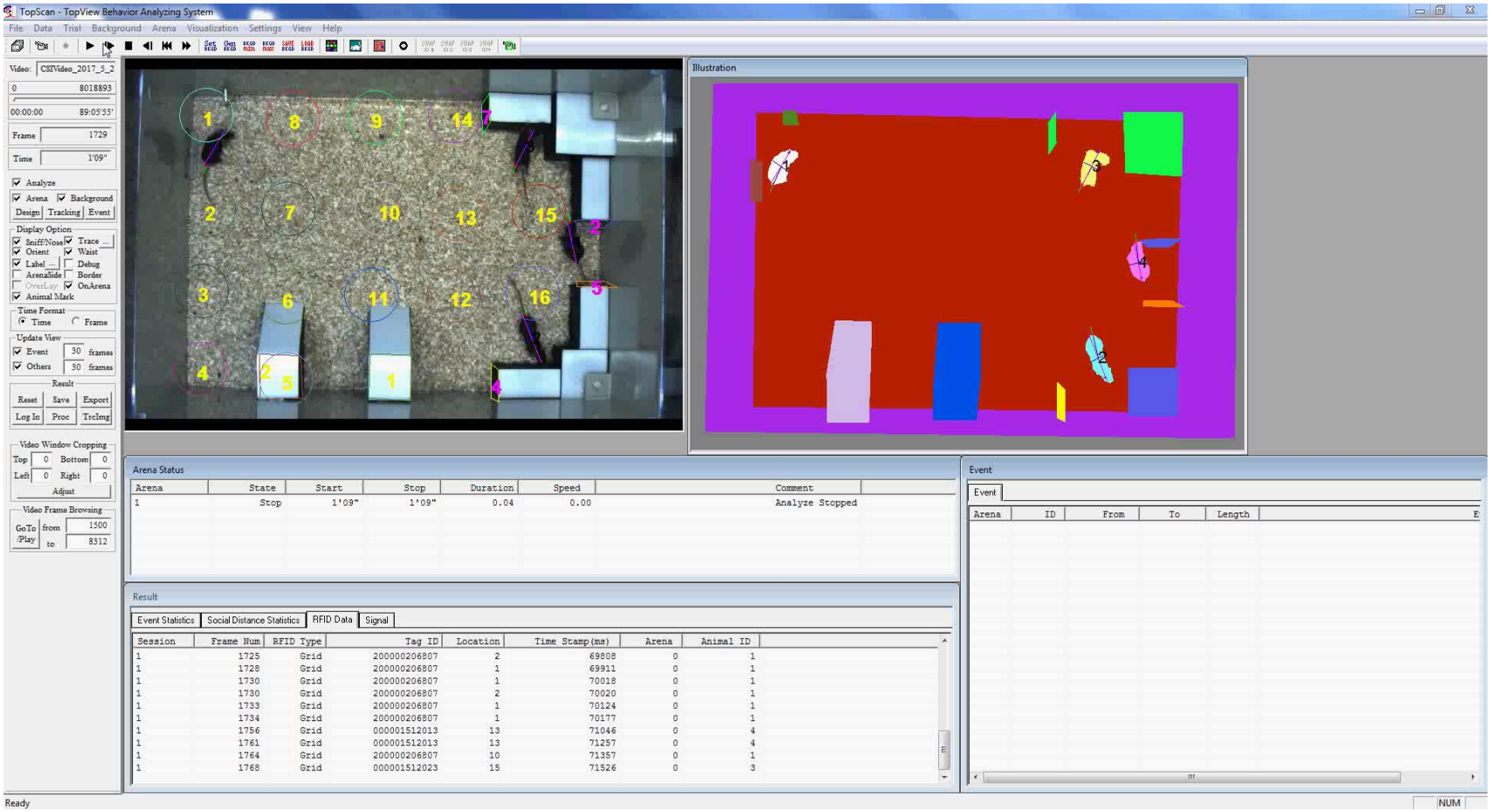
Automated longitudinal analyses of social behaviours



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Identification of biological substrates underlying transdiagnostic domains

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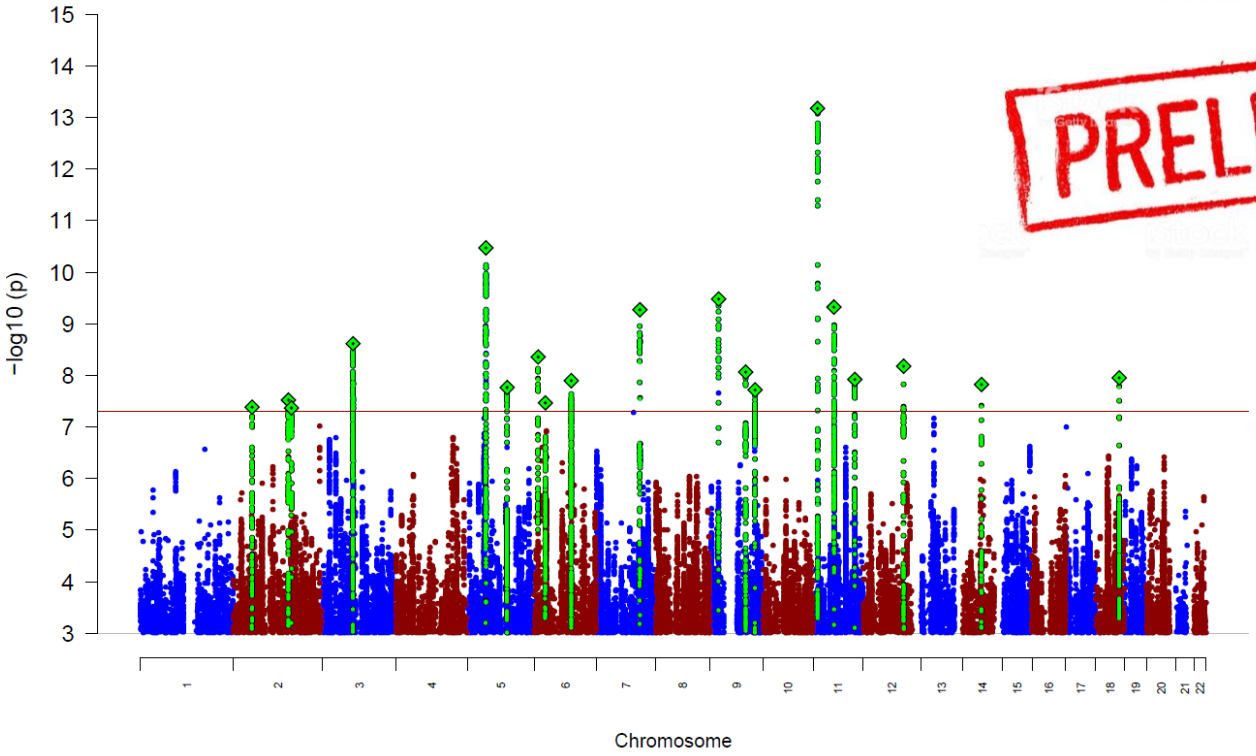
Genome wide association studies

= preliminary GWAS of a SW measure in 342,490 adult participants from the UK Biobank→ 584 genome-wide significant SNPs → 20 independent loci



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Some deliverable highlights

- Implemented a transdiagnostic clinical study that passed futility analysis
- Upcoming Neuroscience & Biobehavioural Reviews special issue on the PRISM project (with 9 manuscripts and 3 commentaries)
- Implemented a parallel preclinical test battery to enable the back translation of findings from PRISMs clinical study.
- Genetic studies of social withdrawal in humans revealing significant hits in known and novel pathways
- Starting discussions on initiating the regulatory path for a transdiagnostic biomarkers
- Excellent engagement with public, patients and researchers through ECNP led dissemination activities

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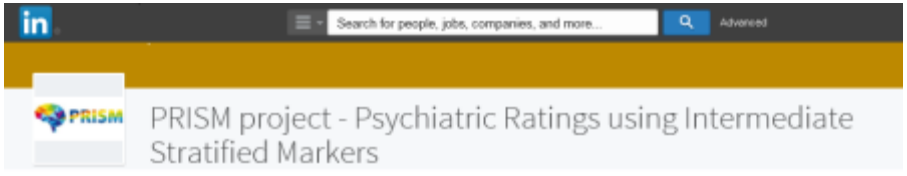
Stay tuned:

PRISM website: www.prism-project.eu

PRISM on LinkedIn and Twitter:



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