

Identifying transdiagnostic multimodal biomarkers for brain disorders

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The project leading to this application has received funding from the Innovative Medicines Initiative 2 Joint Undertaking under grant agreement No 115916. This Joint Undertaking receives support from the European Union's Horizon 2020 research and innovation programme and EFPIA.

Disclosures

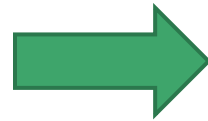
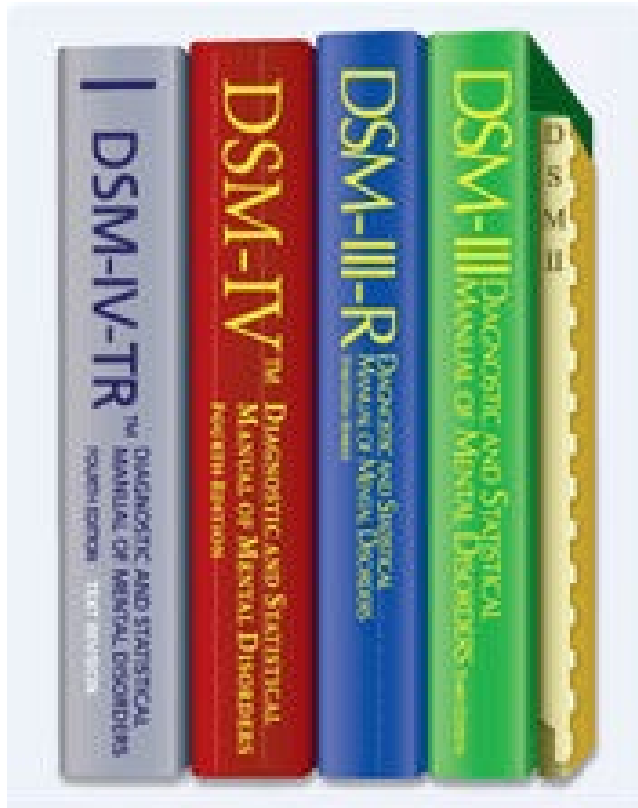


International Grants	Horizon 2020 project, CANDY (principal investigator) Horizon 2020 project, PSY-PGx (principal investigator) Innovative Medicine Initiative (IMI) EU grant, AIMS-2-Trials (principal investigator) Innovative Medicine Initiative (IMI) EU grant, EQIPD (principal investigator) Innovative Medicine Initiative (IMI) EU grant, PRISM and PRISM2 (project coordinator)
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Related Industrial Research Funding	Novartis
Board Member	Executive board member and President of the European College of Neuropsychopharmacology (ECNP)



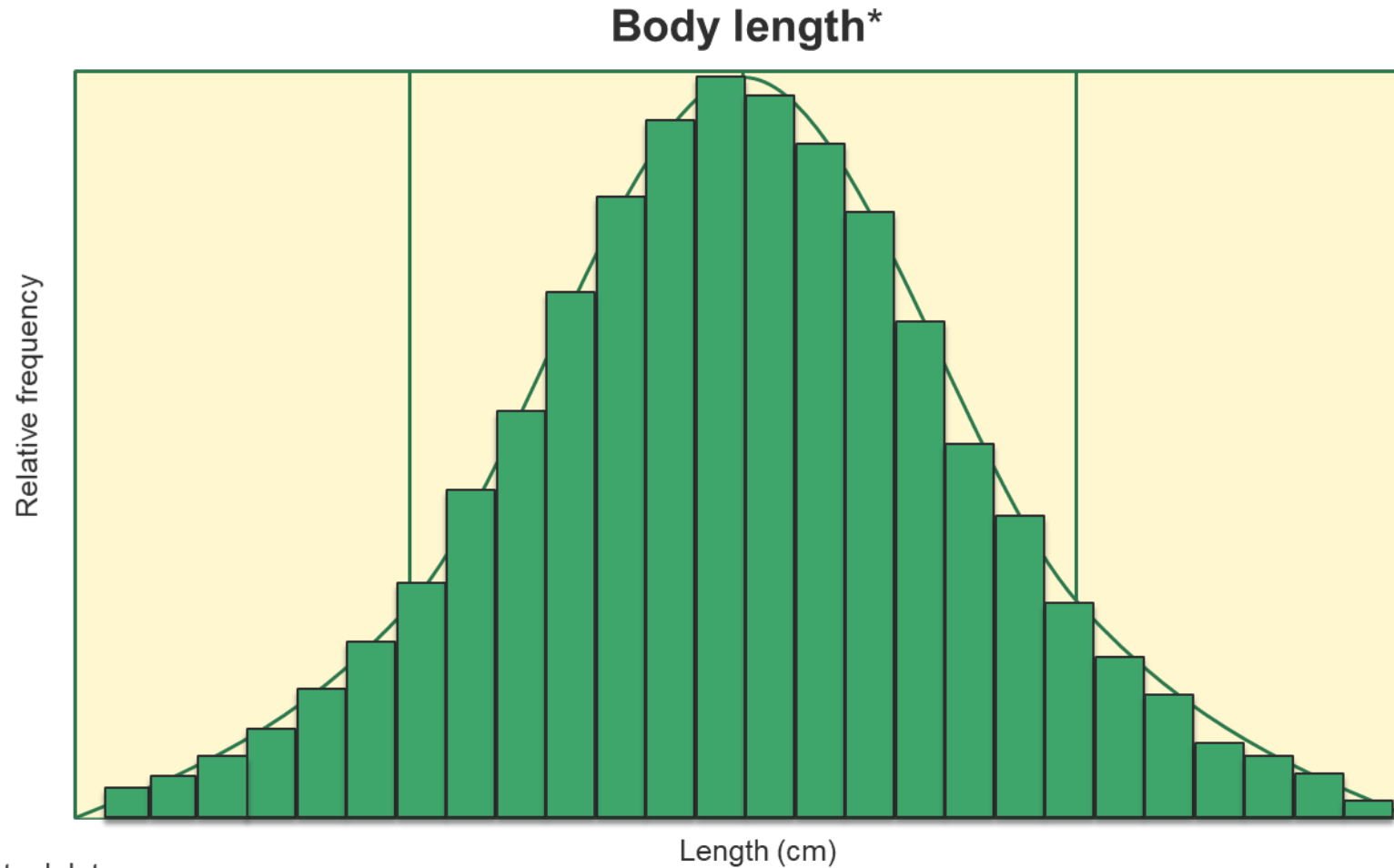
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From Diagnosis to Biology



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Dichotomous versus quantitative



*Not actual data

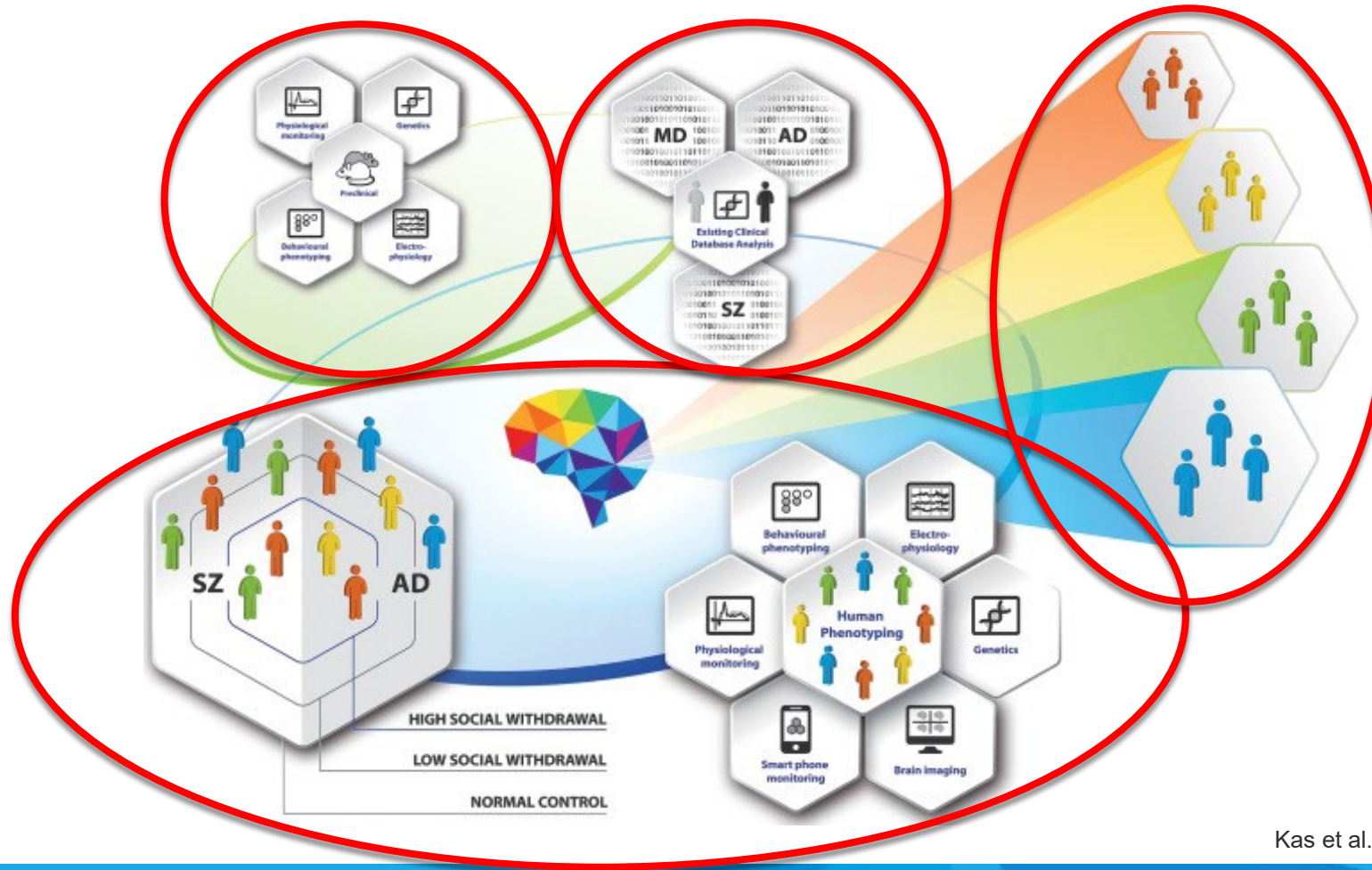


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PRISM project: a Precision Psychiatry approach



“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”



Kas et al., Neuroscience & Biobehavioural reviews, 2019



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Eli Lilly and Company	Boehringer Ingelheim
Novartis	Janssen
Takeda	Roche
Pfizer	P1 vital
Radboud UMC	öibersam
University of Bologna	EUFAMI
Biotrial	Drug Target ID
University of Exeter Medical School	SBGneuro
concentris research management	Leiden University Medical Center
Erasmus University Medical Center	University of Groningen
VU University Medical Center	University Medical Center Utrecht
European College of Neuropsychopharmacology	



23 Public and Private Partners from 8 European Countries

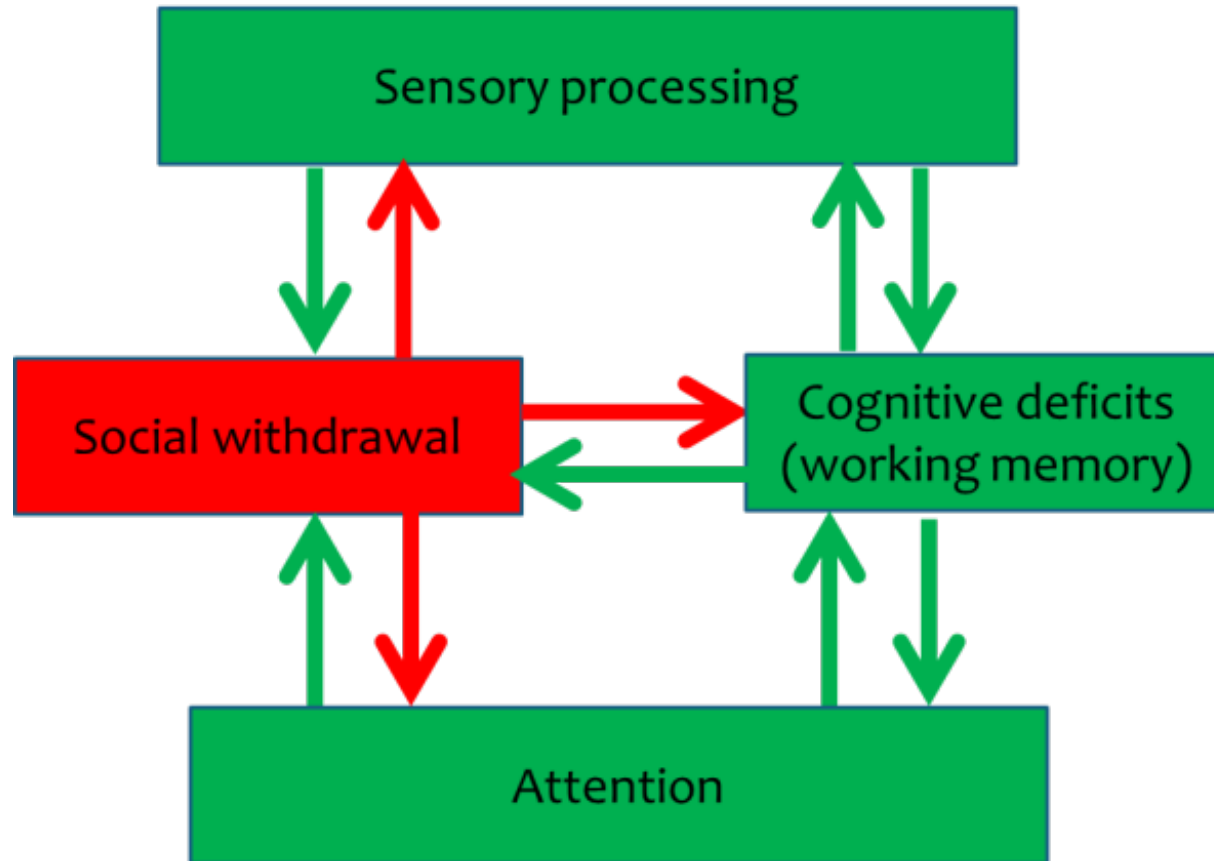


Psychiatric Ratings using Intermediate Stratified Markers (PRISM) Partners.
Available at: <https://prism-project.eu/en/about-prism/partners/>. Last Accessed:
May 2022.



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Human and Rodent Homologies

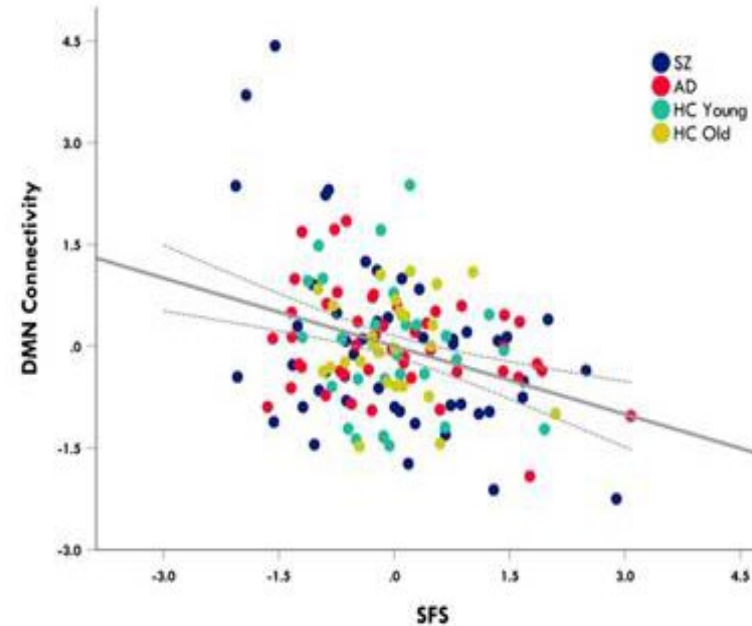
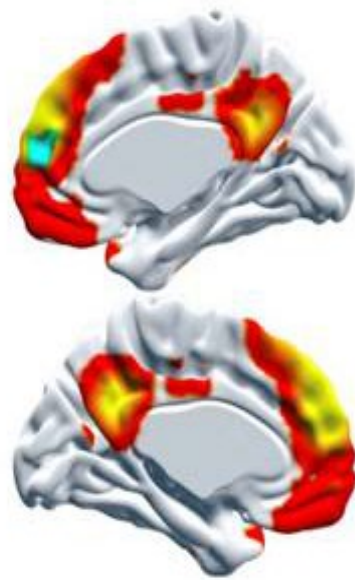


Slide provided courtesy of Martien Kas



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Social dysfunction correlates transdiagnostically with Default Mode Network connectivity



Subjectively reported low social functioning (based on the total score of the social functioning scale (SFS)) was transdiagnostically associated with decreased DMN connectivity across SZ/AD/HC participants. Higher values on the x axis indicate more severe social dysfunction.

Saris et al., World J Biol Psychiatry. 2022

Summary



- Capturing the complexity of brain functioning requires multimodal biomarker development and validation for brain disorders.
- Neuro-imaging, (digital) behavioural monitoring, and innovative statistical approaches are in place to deliver translational multimodal biomarkers for brain disorders using quantitative biological parameters.
- Multimodal biomarker development, validation, and completing the regulatory path requires a long-term team effort and commitment with synergistic expertise and knowledge from academia, industry, Small Medium Enterprises (SMEs), and patient organisations.



Cohen Veterans
Bioscience

The PRISM 2 project has received funding from the Innovative Medicines Initiative 2 Joint Undertaking (JU) under grant agreement No 101034377. The JU receives support from the European Union's Horizon 2020 research and innovation programme, EFPIA, and Cohen Veterans Bioscience (CVB). The presentation reflects only the authors' views and IMI JU, EFPIA, CVB, and the European Commission are not responsible for any use that may be made of the information it contains.

Main Objective 1:

Determine the reproducibility of the transdiagnostic and pathophysiological relationship between DMN integrity and social dysfunction in SZ and AD and its potential to generalise to Major Depressive Disorders (MDD).

Main Objective 2:

To test the causality between the quantitative variation in DMN integrity and social dysfunction.

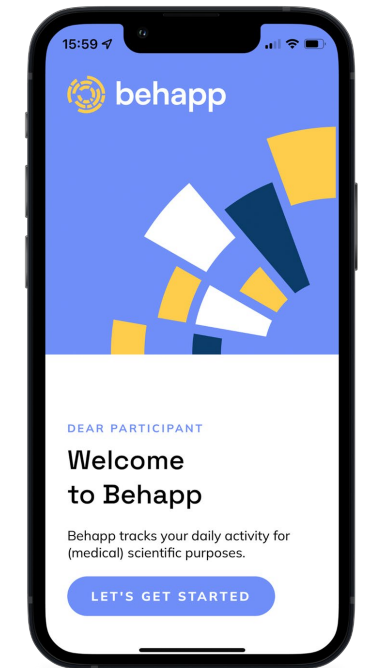
Main Objective 3:

Translate and communicate the project results for the benefit of stakeholders.

Development and validation of a digital endpoint for social functioning for EMA scientific advice opinion



- A linear combination of several Behapp features
- Correlates with Social Functioning Scale
- Statistically differentiates between patients and controls
- Connecting the digital endpoint and neuro-imaging data



www.behapp.com

Challenges for completing the regulatory path

- How to deliver transdiagnostic multimodal biomarkers in a regulatory framework that is focusing on the DSM-5 classification system?
- How to validate new quantitative multimodal biomarkers, for example, for social functioning, against the considered 'ground truth' that is usually based on patient report through questionnaires and that can be biased depending on disease severity?
- Limited availability for defining primary endpoints for transdiagnostic domains, such as social functioning. For example, current EMA guidelines do only include PANSS and cognitive endpoints as primary endpoints for schizophrenia.
- How to provide data on the ability to detect treatment effects and Minimal Clinically Important Differences (MCID), while there are no specific treatments for social functioning yet?

