Psychiatric Ratings using Intermediate Stratified Markers - Sofia ref.: 115916

Berichterstattung

Projektinformationen

PRISM

ID Finanzhilfevereinbarung: 115916

Projektwebsite

DOI
10.3030/115916

Projekt abgeschlossen

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SOCIETAL CHALLENGES - Health, demographic change and well-being

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EU-Beitrag
€ 8 080 000,00

Koordiniert durch
RIJKSUNIVERSITEIT GRONINGEN
Netherlands

Dieses Projekt findet Erwähnung in ...

4 Juni 2019

Periodic Reporting for period 3 - PRISM (Psychiatric Ratings using Intermediate Stratified Markers - Sofia ref.: 115916)

Berichtszeitraum: 2018-04-01 bis 2019-09-30

Zusammenfassung vom Kontext und den Gesamtzielen des Projekts

Most mental health conditions are still classified and diagnosed solely based on the symptoms observed. This stems in part from the fact that there are few objective, easily measured, biological parameters that aid diagnosis as compared to other conditions, such as diabetes (e.g. measuring blood sugar). Further, many neuropsychiatric disorders, as currently classified, share cardinal, diagnostic symptoms. Does this indicate that impact on different processes can lead to the same symptoms or that different disorders may in fact share perturbations to the same process but present differently?
This lack of understanding of the root biological causes is one of the reasons behind the dramatic slowdown in the development of new drugs to treat neuropsychiatric disorders. Historically, many of the major drug classes for psychiatric disorders were discovered as a result of chance observations. By contrast, modern drug design aims to reduce this risk of attrition by targeting a known biological process and then closely monitoring and quantifying the treatment effects.
The overall objective of this project is to develop a quantitative biological approach to the understanding and classification of neuropsychiatric disease with the goal to accelerate the discovery and development of better treatments for patients. The concept of our proposal is to define a set of quantifiable biological parameters for social and cognitive deficits to stratify and differentiate Schizophrenia (SZ) and Alzheimer's Disease (AD). The following specific objectives have been addressed:
1.) Proof-of-concept analyses to cluster and differentiate SZ and AD patients on the basis of quantitative biological parameters.
2.) Explore dimensional relationships between pathology and social withdrawal.
3.) Develop deeper understanding of the quantitative biology of social withdrawal using clinical data from SZ, AD and MD patients and by establishing a network of pre-clinical research sites able to

perform high quality back-translation studies.
4.) Develop a path towards recognition of social withdrawal as a registrable symptom across disorders.

Arbeit, die ab Beginn des Projekts bis zum Ende des durch den Bericht erfassten Berichtszeitraums geleistet wurde, und die wichtigsten bis dahin erzielten Ergebnisse

PRISM successfully identified quantitative biological parameters related to diagnosis (SZ and AD) as well as to social functioning irrespective of diagnosis, and provided a neurobiological framework for further validation. To reach that goal, 165 individuals, including SZ (N=56), AD patients (N=52), and age-matched healthy controls (HCs; N=57) underwent our deep phenotyping study. Unimodal analysis revealed that, out of 4,330 endpoints derived from MRI, EEG, and behavioral modalities, 139 endpoints showed a significant relationship with patient group status (AD, SZ, HC), whereas 183 endpoints showed a significant relationship with social functioning measures. The PRISM genetic study on social functioning outcomes revealed 604 genome-wide significant single nucleotide polymorphisms (SNPs) in 19 independent loci. In addition, a preclinical test battery was developed based on paradigms homologous to those assessed in the clinical study. This test battery allows effective back-translation of human clinical findings and thus expansion of our neurobiological knowledge. Finally, a novel digital tool for the quantitative assessment of social functioning was introduced. This provides objective social functioning characterization that transcends initial diagnostic classification and has been shown to be linked to quantitative neurobiological parameters assessed in PRISM. Based on 62 BEHAPP endpoints (e.g. total in- and outgoing phone calls and chats, GPS signal-derived unique visits of places, home stay time), novel insights in objective and real-world environment measures of individual social communication and exploration behavior were obtained. This analysis revealed three discriminable clusters that did not show a 1-to-1 mapping to the initial diagnostic groups and were not driven by participant age. This finding demonstrates the potential for novel and/or alternative nosologies to emerge from PRISM.

According to the original call text, PRISM has been anticipating a phase 2 project during which a sustainability roadmap will be implemented. As part of phase 1, the outline of this roadmap has been generated.

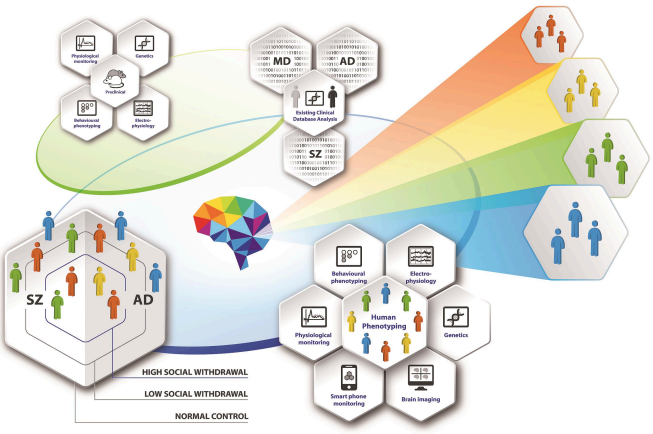
Fortschritte, die über den aktuellen Stand der Technik hinausgehen und voraussichtliche potenzielle Auswirkungen (einschließlich der bis dato erzielten sozioökonomischen Auswirkungen und weiter gefassten gesellschaftlichen Auswirkungen des Projekts)

PRISM addresses the treatment needs of the three most prevalent brain disorders in Europe. The economic burden of these three disorders is huge not least because of indirect impact of massive loss of productivity.

PRISM bridged the important translation gap between discovery and the validation of biomarkers and their associated technologies to a point where they can be deployed reliably and effectively across the network. The PRISM network established that quantitative biological parameters can be used to effectively stratify patients using biomarkers for social functioning.

Back-translation of human biological substrates for social and cognitive deficits has been performed using core technologies. Novel technologies have been implemented and validated to longitudinally assess social group behaviour and sensory processing deficits to provide better predictive preclinical model systems.
We have and continue to influence the thinking of patients, carers and the public establishing that neuropsychiatric disorders are ”real” with biomedical substrates similar to other physical illnesses thereby reducing the stigma associated with mental disorders. We have made real progress in encouraging the clinical community to consider neuropsychiatric disorders through a more quantitative lens (e.g. the journal Science highlighted PRISM’s project launch and feedback from stakeholders). Our quarterly Newsletter has been distributed to 20,000 stakeholders through ECNP, and presentations on the PRISM project were given at patient meetings and international conferences ensuring that we reach our target audiences. In addition, all PRISM procedures and feedback from stakeholders have been published in a special issue of Neuroscience & Biobehavioral Reviews on the PRISM project, including 13 manuscripts.
PRISM showed that using a smartphone-based app to measure social functioning across large populations containing subjects with neuropsychiatric diseases is feasible and could be more widely used in future research. PRISM has also initiated the dialogue with the EMA Innovation Task Force with respect to the qualification of a digital biomarker/endpoint for social functioning based on the BEHAPP smartphone data. The EMA ITF provided encouraging feedback, namely that we are progressing down to the path to being able to establish the app outcomes as a qualified biomarker.
The PRISM consortium presented the PRISM results at an EMA organized symposia at the 2019 ECNP Congress. Continuing the process is, therefore, clearly a key component to the strategy needed to deliver the concept of PRISM into an effective approach deployable by the various stakeholders for the benefit of patients across Europe.

Logo Prism



MD: Major depression AD: Alzheimer's disease
SZ: Schizophrenia

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