Press release: PRISM Project

Major mental health project aims to uncover root causes of social withdrawal

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A major European funding initiative aims to unpick the biological reasons underlying social withdrawal, which is a common early symptom of, Schizophrenia, Alzheimer's disease and Major Depressive Disorder. The PRISM project (Psychiatric Ratings using Intermediate Stratified Markers), a €16.5m public-private cooperation, unites researchers from European academic centres, and major pharmaceutical companies.

Most mental health conditions are still classified and diagnosed solely based on the symptoms observed, as there are few objective biomarkers for these conditions as there are for other conditions, such as diabetes. Many different neuropsychiatric diseases share symptoms, which makes it difficult to understand what is the underlying biological cause of a specific disease. For example, we do not really have an idea how, if at all, the biological cause for social withdrawal in Alzheimer's disease differs from that in schizophrenia.

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 consequence of chance observations in human studies, an approach that suffers from a high rate of attrition and risk of drug candidate failures during development. Modern drug design aims to reduce this risk of attrition by altering a known biological process and closely monitor and quantifying the treatment effects of doing this. The emergence of new ways of measuring brain activity (e.g. functional Magnetic Resonance Imaging (fMRI) of the brain, which registers blood flow to functioning areas of the brain) is for the first time opening the door to applying this type of drug discovery to mental health conditions.

Now a €16.5 million project, supported by the European Innovative Medicines Initiative (IMI) has been launched to seek to uncover the biology behind social withdrawal. Social withdrawal is one of the earliest indicators of the onset of several common psychiatric and neurological disorders but it is a symptom that may be caused by very different neurobiological processes. People with social withdrawal tend to retreat from friends and family, as well as from social networks at their work places. No-one knows the real underlying causes and mechanisms.

As Pierre Meulien (IMI Executive Director) said:

'*Brain disorders place an immense burden on patients, their families, and society as a whole. By bringing together leading experts from industry and academia, the PRISM project is well placed to*

add to our understanding of the underlying causes of brain disorders, and this will help to pave the way for new, effective treatments that patients are waiting for.'

The IMI-funded PRISM project will take a mixed group of patients and measure the brain and behavioural activities using a variety of new and existing techniques, from fMRI, EEG and blood tests to behavioural apps on smartphones. The project will simultaneously correlate these activities with levels of social withdrawal, initially targeting Alzheimer's disease and Schizophrenia, but also looking at Major Depressive Disorder. This should allow scientists to understand exactly which biological parameters correlate with which clinical symptoms.

As project coordinator, Prof Dr Martien Kas (University Medical Centre Utrecht and University of Groningen, Netherlands) said:

"Mental health care needs a way of seeing beyond the diagnostic boundaries to the underlying biological causes – we need biomarkers for mental health that can be measured quickly and easily as we do this for example with blood glucose levels in diabetes. If we can use the available techniques to objectively measure and to pull out the causes of social withdrawal, then the project will open a whole new way of understanding the causes and treatment of mental illness. With this 'deep phenotyping' of the patients, we will be able to differentiate patients on the basis of distinct biological parameters and relate these to internal neurophysiology, biochemistry and genetics. This should allow us to identify specific biological targets for drug action. At the moment, we don't know what will drop out, but we hope that this new understanding will give us new drug targets, or even allow better targeting of old drugs."

Concerns in the pharmaceutical industry about the lack of a systematic methodology to develop drugs for mental health led EFPIA (the European Federation of Pharmaceutical Industries and Associations) to approach the IMI to investigate the problem. As Dr Hugh Marston (Lilly) the industry project leader of the consortium said:

"This project has grown out of a pharmaceutical industry initiative led by Boehringer Ingelheim (Dr Bernd Sommer) and Lilly. We now have 22 participant organisations, including 7 pharmaceutical companies each of whom are contributing between €1m to €2m. Other major participants include the ECNP, several academic departments, a patient body, and five small specialist companies. The whole project is brought together by the EU under the Innovative Medicines Initiative, which also supports the project. With this truly collaborative effort we stand an excellent chance of demonstrating for the first time that we can differentiate brain disorders based upon measurable biology rather than a classification based on the observed symptoms".

Commenting, ECNP (European College of Neuropsychopharmacology) President, Professor Guy Goodwin (Oxford) said:

"*ECNP were delighted to help create the academic network supporting this IMI with seed corn funding, and will participate enthusiastically in disseminating its results. The application of neuroscience is the key to solving the known and the unknown unknowns of mental illness. ECNP's mission is to increase the participation of the best neuroscientists in Europe in that effort.*"

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." **www.imi.europa.eu**

Notes for Editors

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