Novel imaging tools can identify the biological signatures of mental disorders

A novel MRI tool has enabled the IMAGEMEND project to shed some light on the biological markers characteristic of mental illnesses such as ADHD, bipolar disorder and schizophrenia. Although extensively used to study mental disorders and rule out other possible somatic conditions (lesions, tumours, etc.), MRI equipment in psychiatric hospitals is not yet exploited to its full potential. The problem, according to partners under the IMAGEMEND (IMAging GEnetics for MENtal Disorders) project, arises from the fact that diagnostics for illnesses such as schizophrenia (SZ), bipolar disorder (BD) and attention deficit hyperactivity disorder (ADHD) do not take biological readouts into account.

“There are no readouts from MRI, or any other biological modality, that are currently used to aid in the (differential)-diagnosis, staging, course prediction or therapy selection of psychiatric illnesses. This is primarily due to the inherent biological complexity of these conditions, which itself results in small effect sizes of individual biological markers and a substantial overlap of predictive signatures,” observes Prof. Andreas Meyer-Lindenberg from the Central Institute for Mental Health in Germany.

Integrating these biological markers into predictive, reproducible and robust algorithms, however, would allow for more accurate diagnosis. It would also enable earlier, biologically-based selection of intervention which in turn would result in improved patient outcomes. As Prof. Meyer-Lindenberg points out, the exploration of such biological characteristics may not only aid in the clinical management of psychiatric disorders, but ultimately help redefine these disorders based on their underlying biology. “This would have a substantial long-term impact on personalised medicine approaches and the development of novel, more effective therapeutics,” he explains.

To make this possible, IMAGEMEND partners spent four years building one of the largest multimodal databases on psychiatric illnesses, compiling data from approximately 13 000 patients. The latter combines neuroimaging, genetic and environmental risk, as well as clinical data to enable advanced computational identification of diagnostic and predictive signatures.

“The project contributed to several large-scale analyses showing robust differences between different groups and between patients and controls. However, a central conclusion is that whilst structural changes in the brain can reproducibly differentiate schizophrenia patients from healthy subjects, a lack of specificity against related illnesses such as bipolar disorder is currently limiting their clinical utility,” says Dr Emanuel Schwarz, co-coordinator of the IMAGEMEND project.

Besides, these structural changes are broadly distributed across the brain, which hints at global brain structural alterations rather than regional, well-defined effects. According to Dr Schwarz, this has important consequences for future studies and highlights the need for stratification approaches to identify subgroups with similar and potentially more regionally-focused...
changes of brain structure.

Besides advancing the biological understanding of mental disorders, IMAGEMEND has also helped develop neuroimaging-based therapeutic intervention with a real-time fMRI tool integrated into connectivity-based neurofeedback analysis software.

“We are currently informing the scientific community on the utility of using structural MRI for diagnosis of schizophrenia. We hope that this will lead to collaborative efforts, which in turn will result in the development of biologically-based diagnostic and predictive tools,” says Prof. Meyer-Lindenberg.

Such tools could ultimately change the clinical management of psychiatric illnesses to incorporate any biological readouts. Patients would then have access to more accurate diagnostics and more appropriate therapy, putting an end to repeated try-outs of medication, leading to faster remission and even preventing chronicity. Personalised therapeutic approaches would minimise side-effects linked to treatment, and the identification of high-risk profiles prior to illness would facilitate preventative measures.

**Keywords**

IMAGEMEND, mental disorders, MRI, fMRI, ADHD, bipolar disorder, schizophrenia, neuroimaging, prediction, biological readouts

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