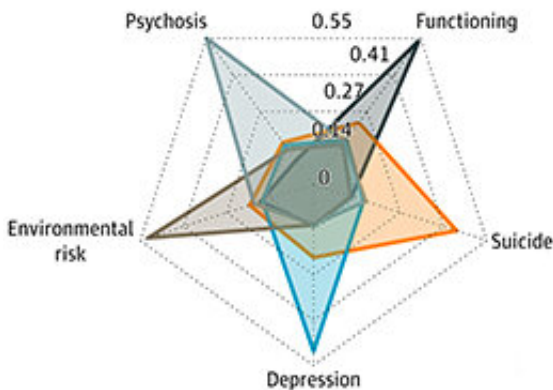# Five clearly defined subgroups could lead to better therapies for psychoses

February 24 2020

Five news subgroups of psychoses. Credit: AG Koutsouleris

Psychiatrists led by LMU's Nikolaos Koutsouleris have used a computer-based approach to assign psychotic patients diagnosed as bipolar or schizophrenic to five different subgroups. The method could lead to better therapies for psychoses.

Diagnostic methods capable of discriminating between the various types of psychoses recognized by psychiatrists remain inadequate. Up to now, doctors have assigned psychotic patients to one of two broad classes—bipolar disorder or schizophrenia—essentially on a symptomatic basis, focusing on shared elements of their psychiatric history, the range of symptoms displayed and the overall pattern of disease progression. This categorization remains a fundamental feature

of both clinical practice and psychiatric research, although detailed observations indicate that psychotic illnesses, and the underlying genetic risk factors, are more heterogeneous than the conventional diagnostic dichotomy suggests. Now researchers led by LMU psychiatrist Nikolaos Koutsouleris has carried out a longitudinal cohort study on a sample of 1223 patients over a period of 18 months. The results obtained enabled the team to divide patients into five well defined subgroups, thus providing a more differentiated picture of the pathology of psychoses, which has implications for therapeutic interventions.

Data from 756 of the 1223 patients enrolled in the study were used to establish the new classification scheme, which was then independently validated for the remaining subset of participants. All 1223 patients had been diagnosed with classical psychoses, based on assessment of a total of 188 clinical variables relating to the trajectory of the individual's condition, symptoms, ability to cope with the challenges of everyday life ('functioning'), and cognitive performance. The study set out to determine whether their high-dimensional clinical dataset covering a wide spectrum of psychoses could be decomposed into defined subgroups based on clustering of statistically correlated variables. The data-driven analytical strategy adopted is based on machine learning, which can discover patterns that reveal 'hidden structure' in large collections of multifactorial data. These patterns may in turn point to differences in causal relationships that are of diagnostic relevance. "Our study shows that computer-based analyses can indeed help us to re-evaluate how persons with proven symptoms of psychoses can be differentiated diagnostically," says LMU psychologist Dominic Dwyer, first author of the study, which appears in the journal *JAMA Psychiatry*.

The analysis ultimately led to the recognition of five clearly defined subgroups among the experimental population. "In addition to differences in their symptomatic and functional course, patients assigned to the different subgroups could also be distinguished on the basis of

defined clinical fingerprints," says Nikolaos Koutsouleris, who led the study. Members of one of the subgroups were also differentiated from all the others on the basis of their low scores for educational attainment, which is known to be a potential risk factor for psychotic illness.

The researchers used a mathematical approach known as non-negative matrix factorization to detect patterns in their statistical data. Using this procedure, they were able to reduce the starting dataset, comprised of 188 variables, to five subgroups defined by core factors. These factors encode hitherto unrecognized relationships between variables and uncover the functional links that connect them. "By evaluating the relative significance of these factors in individual cases, it is possible to assign patients to different groups on the basis of their overall scores," Dwyer explains. In this way, the authors of the study were able to define the following five subgroups of psychoses: affective psychosis, suicidal psychosis, depressive psychosis, high-functioning psychosis and severe psychosis.

"Each of these subgroups can be clearly delimited from all the others on the basis of the clinical data," says Koutsouleris. For instance, patients assigned to Group 5 are characterized by the core factors: schizophrenia diagnosis, significantly lower levels of educational attainment and low verbal intelligence. Most of the patients in this category were males and displayed marked symptoms of psychosis, but no indications of depression or mania. In Group 2, on the other hand, suicidal tendencies were clearly present. The results of the classification of this experimental population which provided the underlying data for the construction of the statistical model were confirmed for an independent group of 458 subjects.

The analyses suggested that unbiased, data-driven clustering may be used to stratify individuals into groups that have different clinical signatures, illness trajectories, and genetic underpinnings. In the future, such

computer-assisted categorizations may be integrated into clinical routine through the use of online tools. Koutsouleris and his team have developed a prototype of such an online tool that can be used to stratify new individuals into the same groups and predict outcomes that can be tested at www.proniapredictors.eu.

More information: Dominic B. Dwyer et al. An Investigation of Psychosis Subgroups With Prognostic Validation and Exploration of Genetic Underpinnings, *JAMA Psychiatry* (2020). [DOI: 10.1001/jamapsychiatry.2019.4910](DOI)

Provided by Ludwig Maximilian University of Munich