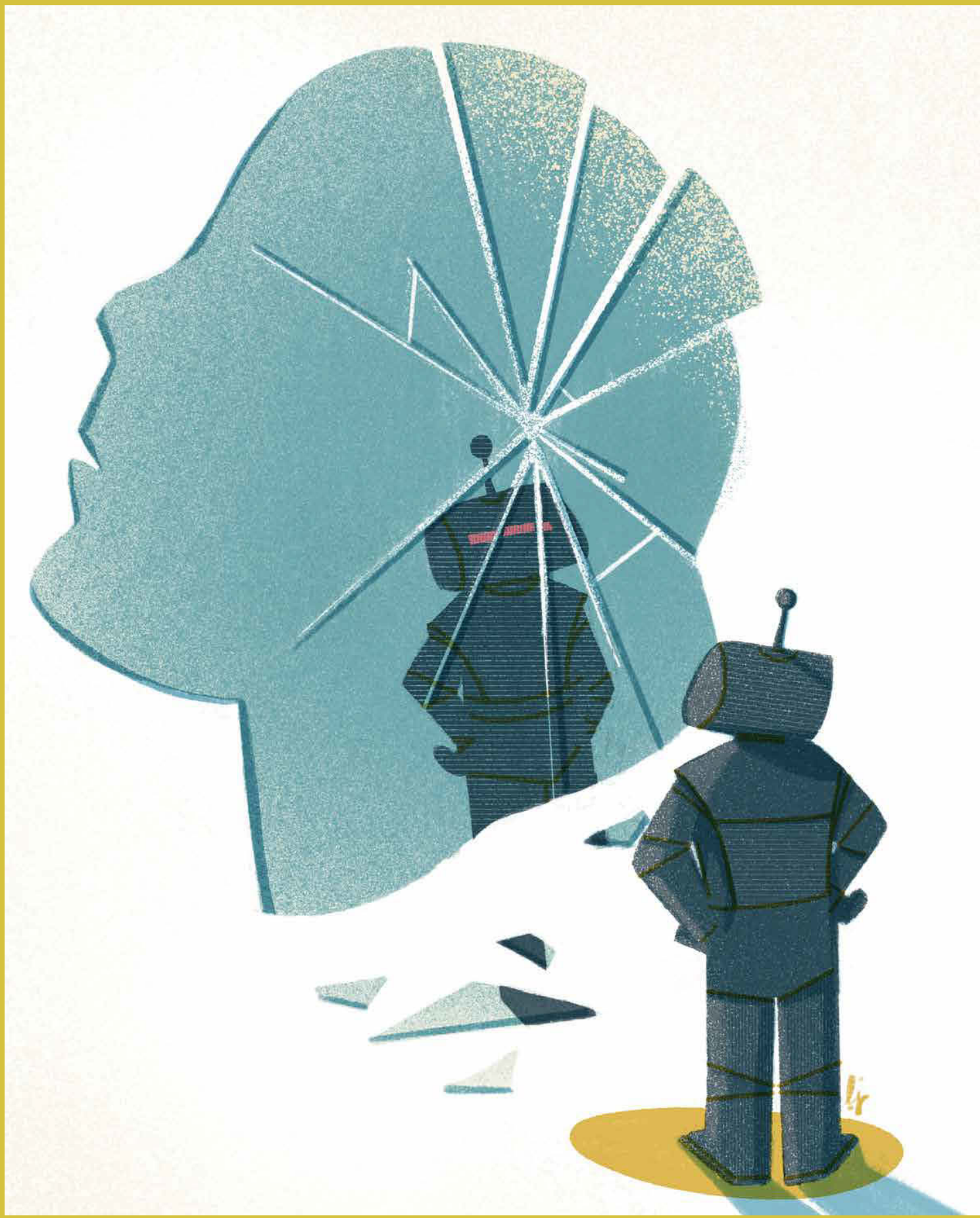

ILLUSTRATION: LUISA JUNG FOR MPG

SOFTWARE TO SCAN THE PSYCHE

TEXT: ANDREAS LORENZ-MEYER

Just tired? Or depressed? Introverted or autistic? Imaginative or schizophrenic? The symptoms of psychiatric illnesses are not always clear. Therefore, Nikolaos Koutsouleris, a fellow at the Max Planck Institute of Psychiatry, also relies on artificial intelligence for early detection. Algorithms are designed to supplement the doctor's expertise by detecting patterns in patients' genetic and physiological data.

Just another day at the office. Suddenly a voice is heard: "You don't deserve this job!" The young woman turns to look, but no one is there. Her colleagues are all working at their desks. Did she just imagine that? Sometimes she gets the feeling the others are watching and controlling her and saying unkind things about her behind her back. She also feels they are secretly making insinuations and disparaging gestures about her performance. Although these thoughts are initially nebulous and easy to suppress, over time, they grow to ever more threatening proportions. Then, after ten months, the thoughts inside her head have become voices that seem to come from other people. They speak more and more often and harangue the 24-year-old. She stands up to them and argues with them. She is no longer able to concentrate properly, and she is making more and more mistakes at work. Is she going crazy? She finally seeks help. The diagnosis: schizophrenic psychosis. If the initial symptoms are as clear as in the case described here, an incipient psychosis can be easily detected. The onset of the disease can usually be prevented if only preliminary forms of delusions or hallucinations occur that the patient does not yet consider to be unshakeable reality. In other high-risk patients, however, the symptoms are more difficult to classify: they sleep badly, feel tired, are thin-skinned, unfocused and indifferent; they can barely cope with the everyday tasks of life and work, and they break off their social contacts. An incipient psychosis often remains undetected in such cases.

Nikolaos Koutsouleris wants to use artificial intelligence to better predict the risk of the future development of these types of psychiatric illnesses. Mathematical models aim to enable reliable prognoses to be made about who could become seriously ill and who can be

PHOTO: JARDUL/ISTOCK

The face is the mirror of the soul. But some people cannot correctly interpret this mirror image. Neuropsychological tests therefore form a part of the prognosis for psychiatric illnesses. A computer program factors in a person's ability to assign specific emotions to facial expressions when preparing the prognosis.

expected to be only mildly afflicted. The computer plays a supporting role in this. The objective here is not to replace the professionals, but rather to help doctors and psychotherapists detect correlations within the patient data that they might have missed. The most common form of schizophrenic psychosis is paranoid schizophrenia, which it affects 0.5 to 1 percent of the population. Patients experience hallucinations, delusions, and disrupted ego boundaries – in other words, the feeling of being controlled from the outside and the idea that thoughts can spread to acquaintances and to strangers. They believe that they are being persecuted or that others are stealing their thoughts. Those who are genetically predisposed are especially at risk. If both parents suffer from schizophrenia, their children have a 45 percent risk of developing the illness. However, the genes responsible for a person's schizophrenia have not yet been identified. Scientists are only aware of variants in the genetic makeup that increase the risk of a person developing psychotic disorders. These high-risk gene variants are compounded by environmental factors: stress and negative experiences such as the death of a loved one or the loss of a job can lead to the onset of psychosis.

SUMMARY

Some patients with a high risk of psychosis exhibit non-specific symptoms. The earlier a risk is identified, the better the chances for successful treatment.

In the future, artificial intelligence will improve early detection in those who are most likely to develop a psychiatric illness.

The NeuroMiner program can be used to create prognostic models that measure whether an individual at high risk will develop a psychotic disorder. The program evaluates psychiatric, medical and genetic parameters for this, while also factoring in the attending physicians' expertise.

The complex interaction of all these factors thus makes it difficult to offer a prognosis about whether and to what degree the illness could manifest itself. For example, if doctors knew that a patient was about to experience an acute psychotic episode, they could provide the person with targeted treatment. But this kind of reliable early detection does not yet exist.

Nikolaos Koutsouleris is working to change this. Fifteen years ago, he recruited and examined patients at the Ludwig Maximilian University in Munich for a study in the early detection of psychosis. "I was able to observe how mild symptoms in young patients who were in a high-risk state developed into severe illnesses and I could see the differences in their progress." But he also recognized that the traditional statistical prognosis methods did not help: "To this day, these methods don't work for calculating individual prognoses, because they cannot detect complex patterns. But this is exactly what would be needed for the early detection of mental illnesses – they can't be attributed to a specific gene or to specific damage to the brain." We still have insufficient knowledge about how the many different manifestations of psychosis are related to the spectrum of risk factors. "This is a Herculean task that can only be mastered using artificial intelligence," he explains.

Scientists were already using machine learning to diagnose neurodegenerative illnesses such as Parkinson's and Alzheimer's when Koutsouleris began his research. But at that time, no one had considered applying this technology in the field of psychiatry. However, Koutsouleris recognized the enormous potential artificial intelligence has for applying knowledge from basic research to psychiatric illnesses. At the same time, he also realized that he had to develop machine learning methods that would be easy for doctors to use, because current medical and psychology training programs do not yet include training in information technology.

NeuroMiner is a tool to help doctors and physicians

Koutsouleris was the perfect person to take on this project. As a specialist in psychiatry and psychotherapy at the University of Munich and as a computer programmer – he had taught himself several programming languages over the course of his doctoral research – he is at home in both worlds. Thus, in just over ten years, Koutsouleris has succeeded in developing NeuroMiner – a program that works with numerous algorithms. If it is uncertain which calculation method is the most appropriate, then the program simply applies several different methods. The results are compared and the best method is selected. The program also includes a meta-algorithm that combines different algorithms and then selects the combination that provides the most accurate prediction. Koutsouleris and his team are continuously developing the software further.

No programming experience is needed to work with NeuroMiner. "It can be used to analyze various data without any previous experience." First, the doctor feeds the program with data, e.g., from the genetic analyses and medical examinations of a psychosis patient. The doctor then selects an algorithm and trains it to detect the illness. NeuroMiner autonomously finds the settings for the selected algorithm that will ensure the optimum prediction of the psychoses. The general applicability of the learned settings is also tested. Can the algorithm make a reasonable prediction based on the input data? Does the "learned" decision function agree with the professional literature on the illness?

The training phase is then complete. The algorithm can now be used to calculate the risk of other patients developing a psychosis. Users can also share their models

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Psychiatry and IT – Nikolaos Koutsouleris is at home in both worlds. This is how he was able to develop machine learning methods for the prognosis of psychiatric illnesses. His goal: a digital mental health assistant.

PHOTO: AXEL GRIESCH FOR MPG

with colleagues and let them test their reliability. If the model also performs well in these cases, it is ready for clinical trials. NeuroMiner does not permit users to jump back and forth between steps, so as to ensure that they do not tailor their models too closely to the training data and therefore obtain inaccurate predictions.

New algorithm

Early this year, Koutsouleris published an algorithm that raises the use of artificial intelligence in psychiatry to a new level. It can be used to make reliable predictions for patients aged 15 to 40 in various high-risk states of paranoid schizophrenia or for people with depression. "Many affected patients in the high-risk state are already experiencing high levels of psychological strain and suffering distress. They experience "mental storms" or have difficulty distinguishing mere concepts from reality," Koutsouleris explains. If such high-risk criteria as mild psychotic symptoms or a family history of psychosis occur together with reduced performance, the risk of psychosis increases to between 14 and 20 percent. The algorithm can predict with an accuracy of 83 to 85 percent whether individuals will develop a psychosis within two years.

The algorithm follows several steps: doctors first interview their patients and perform neuropsychological tests. For example, the patients are tested on how well they can correctly recognize emotional facial expressions. The program uses these results to calculate the probability of the development of a psychosis. It also indicates if sufficient data are available for a conclusive prognosis. If not, the physicians enter their own evaluation data in the next step. The algorithm thus combines the expertise of humans and machines. If the prognosis is still not sufficiently certain at this point, genetic risk factors from a hereditary analysis are considered. The program identifies all mutations associated with the development of psychoses and weights them based on their relevance. The brain can also be

"Doctors and patients will trust the algorithm's results only when they understand how it works."

NIKOLAOS KOUTSOULERIS

examined using magnetic resonance imaging. "All of these factors have to be accounted for in 40 percent of patients; especially for those who from the start have been attested as having a high risk for developing a psychosis. As a result, the algorithm reduces the number of cases in which a psychosis would otherwise have been incorrectly predicted," says Koutsouleris.

Reliability and transparency

However, reliability as well as transparency are crucial for artificial intelligence to become an accepted diagnostic tool in the field of psychiatry. "This is critical for clinical applications! Doctors and patients will trust the algorithm's results only when they understand how it works." Although the patterns that the prediction algorithm has learned can already be traced, the researchers still cannot explain exactly how the program obtains its results. Koutsouleris and his team have therefore written software that calculates the weighting of the different parameters. This enables all of NeuroMiner's calculation steps to be followed.

Artificial intelligence could thus result in a paradigm shift in the care of people with mental illnesses: away from simply managing chronic illnesses and toward preventive medicine that seeks not only to treat defects or symptoms, but also to strengthen the patient's resilience. Outpatient clinics for early detection are still relatively inefficient, as they take too long to predict the risk of an illness. Artificial intelligence should greatly accelerate this process. Preventive psychiatry could soon provide a reliable prognosis of a patient's risk of developing an illness and offer treatment tailored for that specific patient. For example, a personal "digital mental health assistant" would give a patient access to e.g., a network of individualized support services.

The progression of the disorder described at the beginning could thus take a different turn with the aid of artificial intelligence. Shortly after the occurrence of the first diffuse symptoms, the primary care physician refers the patient to a high-risk outpatient clinic. There, the results of brain scans and genetic tests are analyzed on the computer and an 85 percent risk of developing an illness is determined. Doctors then recommend individualized treatment with behavioral therapy, lifestyle changes and low-dose antidepressants. From then on, the patient's risk of developing the illness is regularly checked in the outpatient clinic. The patient also uses an app to independently measure certain warning signals in real time. This provides a warning if symptoms and behavior patterns worsen and a progression of the illness can be anticipated.

www.mpg.de/podcasts/kuenstliche-intelligenz (in German)

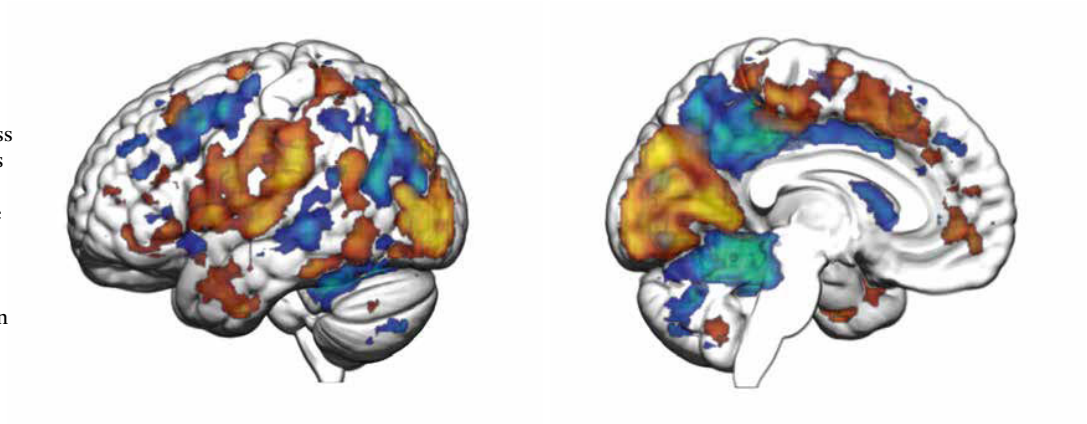

IMAGE: NIKOLAOS KOUTSOULERIS/MPI FOR PSYCHIATRY

A prognosis pattern learned by the computer: the algorithm predicts an increased risk of illness for patients who have less brain volume in the red areas and more in the blue regions: the more pronounced the pattern, the higher the risk. If the volume distribution is reversed, the risk of illness is low.

Several predictive models are now available that have been tested on independent samples. A clinical trial will now show whether their use results in more successful therapies. "The next few years will see many new projects testing the use of artificial intelligence in psychiatric clinical practice – such as for predicting psychiatric illnesses in high-risk and depressed patients, or to predict the probability of the success of magnetic stimulation treatment for schizophrenia."