Researchers are programming a digital model of the brain that captures the key features of mental illnesses. The idea behind the digital brain twin is that in the future, schizophrenia and other conditions can be diagnosed earlier and treated in a more targeted way.

PHOTO: ADOBESTOCK

MIRRORING THE MIND

TEXT: CATARINA PIETSCHMANN

Long before the first outward symptoms appear, mental illnesses often become apparent through subtle changes in the body. However, the clues that lurk hidden in medical examination data cannot be detected with conventional analyses. That is why Nikolaos Koutsouleris at the Max Planck Institute of Psychiatry in Munich is turning to artificial intelligence. Together with an international research team, he is developing a digital model of the human brain. The hope is that it will help identify mental illnesses earlier and treat them in a more targeted way.

In some respects, the work of seismologists is not so very different from that of psychiatrists. The former record the tiniest tremors in Earth's crust and use the data to predict earthquakes and volcanic eruptions. The earlier this happens, the better; it's on this basis that people in at-risk areas can be warned and evacuated. Psychiatrists, for their part, seek to detect whether noticeable changes in behavior might be signs of mental illness. They also aim to detect the smallest psychological "tremors" as early as possible to assess the risk of a major "quake" in the form of a mental illness.

Another parallel is that both fields still struggle to make reliable predictions. Volcanic eruptions and earthquakes cannot be predicted with absolute certainty, nor can their magnitude. Psychiatry faces a similar challenge: "It remains very difficult to predict something like whether a single brief psychotic episode will develop into severe schizophrenia," says Nikolaos Koutsouleris, senior physician and professor of precision psychiatry at Ludwig Maximilian University of Munich and King's College London and research group leader at the Max Planck Institute of Psychiatry.

Yet given how schizophrenia can completely derail a person's life, such a prognosis would be crucial for them going forward. Many of those affected end up dropping out of school or university, withdrawing from family and friends, or dealing with unemployment or early retirement. The illness also carries a heavy social stigma, although, contrary to what the name (literally "split mind") suggests, it has nothing to do with a split personality. Instead, it manifests in delusions, restlessness, passivity, and difficulty concentrating – alongside abnormal movements such as freezing, grimacing, or an aimless urge to move. Acute psychotic episodes profoundly alter a person's perception and behavior and can last for weeks or months, sometimes never fully subsiding. →

Between 3 and 4 percent of the general population experience a psychotic episode at some point in their lives, with between 0.5 and 1 percent developing schizophrenia. In more than 80 percent of cases, schizophrenia manifests before the age of 30. Sometimes, however, symptoms can manifest in children as young as 10. In patients this young, the disorder can cause developmental delays, problems with coordination, and difficulties with thinking and speaking – and can also lead to difficulties with reading and spelling. "In these very early phases of the condition, the symptoms are hard to interpret, so diagnoses such as ADHD, autism, or depression are often made instead," says Koutsouleris.

The researcher wants to use AI to spare sufferers from misdiagnosis. "When I gave my first talk on mathematical models for the early identification of mental illnesses in 2008, only four people turned up. And they must have thought I'd been smoking something," he recalls. Today, thanks to the enormous progress in AI, the lecture halls are full. In January 2024, Koutsouleris helped establish the Virtual Brain Twin research platform, a digital model of the brain for the personalized treatment of mental illnesses, with a focus on schizophrenia. The four-year project brings together researchers from 18 European research institutions. It aims to make the diagnosis of schizophrenia more reliable, explore new treatment methods, and help tailor therapies to patients' individual needs. Currently, the team is still collecting data for the digital twin and refining the mathematical models. "We train AI models on MRI scans of patients with different degrees of illness severity. We then analyze what the models have 'seen' in the images. We pass the results on to the programmers, who use them as a blueprint for the individual digital twin," explains Koutsouleris.

SUMMARY

Researchers participating in the Virtual Brain Twin project are developing a digital model of the brain. It draws on AI analyses of MRI scans, blood test results, electroencephalography, and genetic data.

The aim is to correctly interpret the earliest signs of schizophrenia and to treat the disorder at an early stage.

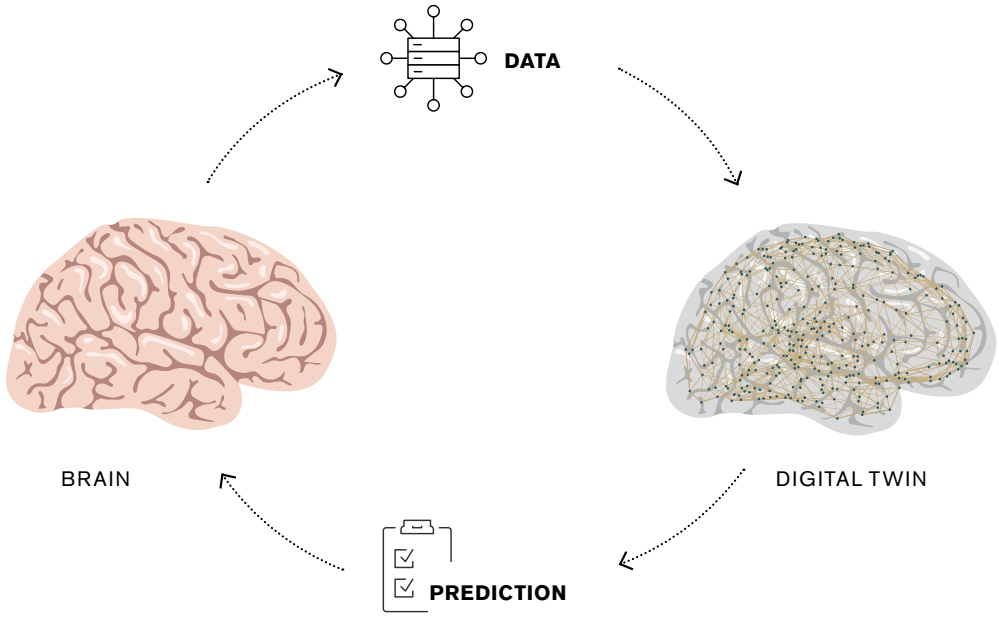
The digital twin is designed to simulate how different treatments would work in an individual patient and to identify the most effective therapy. The idea is also for the software to help develop drugs that act in a more targeted way against the various specific forms of schizophrenia.

The model could also help improve the treatment of disorders such as depression, Alzheimer's disease, and Parkinson's disease.

The platform builds on NeuroMiner, a software package developed by Koutsouleris and his team (MaxPlanckResearch 3/2021, p. 39). This program uses AI to analyze MRI brain scans together with other disease-relevant patient data and identifies subtle changes in brain structure that are invisible to the human eye and occur years before the onset of a mental illness. The digital twin goes a step further by using the computer to model a range of processes that play a role in mental illnesses. It is based on MRI scans that allow researchers to infer the activity of nerve cells in the brain; from the changes visible in

PHOTO: AXEL GRIESCH/MPG

As a student, Nikolaos Koutsouleris taught himself several programming languages. Later he realized that conventional statistical methods for predicting mental illnesses are not especially reliable, because they cannot detect complex patterns in individual patients' data. That is why he relies on AI for early detection and treatment.



GRAPHIC: GCO; BASED ON HUIFANG E. W. ET AL., "VIRTUAL BRAIN TWINS: FROM BASIC NEUROSCIENCE TO CLINICAL USE," NATIONAL SCIENCE REVIEW, VOLUME 11, ISSUE 5, MAY 2024.

The digital twin is fed with brain examination data. The program then uses these data to predict how the brain will respond to a therapy.

these images, they can reconstruct disrupted pathways. The model also incorporates MRI scans of healthy volunteers and patients taken before and after drug treatments at various doses. This teaches the program how a medication's effects differ from one patient to another. Blood values, electroencephalography readings, and genetic data are fed in, too. The AI system also draws on gene data, protein analyses, and information about how drugs work. Taken together, these data form a digital representation of an average human brain.

The digital twin can now adapt this "average brain" to the profile of each individual patient. It can, for instance, estimate how likely it is that a single psychotic episode will develop into schizophrenia or which drugs are likely to work for that specific person. With every new patient, the digital twin learns and improves. "Its predictive power will not reach 100 percent, however, because much about schizophrenia and how the brain works is still unknown," Koutsouleris adds. The program can also predict the effects of different drug doses and other forms of therapy. Just like a flight simulator recreates turbulence or storms, the digital twin runs through hundreds of scenarios for a single patient.

The researchers hope this will yield a wealth of new insights into how the disorder develops and how it can be treated. They might, for example, show why many antipsychotic drugs work in only 30 percent of patients. This low response rate is why many patients have to try one drug after another until they find one that helps. The fact that the same drugs can have such different effects suggests that there is not just one form of schizophrenia but rather several distinct types. Each form may have a different cause and would need to be treated accordingly. "In the future, the digital twin should be able to begin predicting the patient's response to a treatment, even before it begins. If we can then use it to describe the subtypes of the disorder, we will be able to develop new drugs that act far more precisely than anything we have today," Koutsouleris explains.

The digital brain twin could also improve the prognosis and treatment of other psychiatric and neurodegenerative disorders such as depression, Alzheimer's, and Parkinson's disease. "The effectiveness of Alzheimer's drugs depends heavily on things such as how far the disease has already progressed. If Alzheimer's could be detected just five years earlier than is usually the case today, medication might at least be able to slow the course of the illness," says Koutsouleris.

Study to Start in 2027

The first studies involving patients who display symptoms of schizophrenia are scheduled to begin in early 2027. If the digital twin is adopted in psychiatric practice, it would mark an important step toward personalized medicine, with therapies tailored to individual patients. In the future, the process of preventing small tremors in the psyche from escalating into a major quake may thus become much more reliable than it is today. ←