Epilepsy research: will the digital doctor soon be assisting?

Neurologists want to use large datasets for early detection

By Anne Hardy

The healthcare industry sees great potential in consolidating medical data on one and the same person which is currently distributed across various practices and hospitals. This would not only save costs on repeating procedures; physicians also hope that artificial intelligence will help them identify new connections and thereby treat diseases earlier, or even prevent them.

It is somewhat reminiscent of »Brave New World«: in front of a wall full of monitors in the monitoring room of Ward 95-5 of the Epilepsy Centre at the Frankfurt University Hospital sit two medical-technical assistants and from here observe the patients in the hospital rooms. They simultaneously monitor their brain activities on the EEG (electroencephalogram). As soon as an epileptic attack occurs, Professor Felix Rosenow's team can find out what type of epilepsy it is, localize the seizure onset in the brain, and treat it with either medicine or an operation.

The people admitted to this ward usually have a waiting period of three months behind them. In Hessen, there are only two specialized epilepsy centres. At 13th place, the number of neurological practices in proportion to the population is ranked quite low in national comparison. It often takes years for epilepsy patients to get the right diagnosis. »The attacks could be controlled much more quickly for two thirds of the patients if they got the right therapy early on,« says Rosenow with regret.

Obstacles to telemedicine

In 2015, the Epilepsy Centre Rhine-Main was established in the Department of Neurology. Sections of EEG recordings from all over Hessen arrive here along with the question: does this patient suffer from epilepsy? Frequently, this cannot be answered on the basis of the data sent. Rosenow illustrates the complexity of an EEG by clicking on various curves recorded parallel to each other on a monitor. They represent the recordings of the electrical brain activity through 21 electrodes attached to the scalp according to a specific special configuration.

If the expert has the complete dataset, he can compare the recordings from individual electrodes over various brain regions with one another, create an image from the average of all electrodes, or filter out certain activities. »For an epilepsy diagnosis we require an average of eight to twelve montages,« Rosenow explains, while looking for noticeable high amplitude sharply contoured »spikes« in the ongoing brain activity.

Currently, there are difficulties in transmitting a complete EEG electronically. Although the data has not been recorded by pen for over 25 years, to this day there are no universally accepted international standards for electronic data storage and transmission of electrophysiological data. »Since the manufacturers do not make the source codes for their software public, I can't convert the data from a colleague who uses a different machine,« says Rosenow. This significantly complicates the exchange of data per telemedicine.

Negotiations on EEG standards

The International Federation for Clinical Neurophysiology is working on uniform EEG standards together with the DICOM, an international organisation for saving data in medicine. They have already created standards for numerous image-creating procedures such as X-ray, MRI and computer tomography. EEG standards from the DICOM organisation should now be published this year. »These are large files that state which channels, data sources and types of electrodes are used, and how the data should be stored,« explains Rosenow, who is a member of the respective DICOM working group #32.

This represents significant progress for the telemedicine project on epilepsy, which Rosenow began in 2017 using state funds. Currently, hospitals in Eschwege, Kassel and Bad Homburg, as well as the children's hospitals in Limburg are connected. At the end of the pilot phase, ten Hessian hospitals and ten practices should have the capability to send EEGs to the Epilepsy Centre and, as in a medical council, ask the experts questions. This is particularly important for the children's hospitals, since many forms of epilepsy appear during childhood and very few hospitals still have neuro-paediatricians with expertise in EEG evaluation.

IN A NUTSHELL

- Currently, DICOM standards for recording and storing EEG data for epilepsy are being developed. The goal is an optimisation of telemedical communication.
- Doctors hope that the consolidation of health data and their analysis by learning AI systems will enable early diagnoses and individualised treatments.
- In tests with animals, AI systems can identify developing epilepsy in the EEG, even before the first seizure takes place.

Enhancing valuable data for the neurosciences

It is also important to standardise data so that the currently existing large data volumes can be used more intensively. The Federal Ministry of Education and Research, and the German Research Foundation want to enhance this potential in the context of the National Research Data Infrastructure (NFDI). »When we talk about data as the raw material of the future, then the NFDI is a refinery in which data is processed and made available – and thus usable – to everyone,« says Federal Research Minister Anja Karliczek.

The German Society for Clinical Neurophysiology and Functional Imaging (DGKN), of which Rosenow is Vice President, has applied for a consortium in the NFDI. »Our goal is to consolidate the datasets that are stored throughout Germany in doctor's offices and hospitals and make them usable,« Rosenow explains. The server on the epilepsy ward currently has storage space for approximately 100 terabytes. This is equal to the capacity of about 100 external hard drives.

Rosenow enumerates the advantages for epilepsy research that come from the analysis of large, anonymized data volumes: »At this time we are studying how certain forms of epilepsy are distinguishable through the basic rhythm of the brain waves. We can determine whether the signals have a looser or tighter connection in various brain regions. In this way we can locate epilepsy sources,« Rosenow explains.

Recognising new connections with artificial intelligence

Far beyond brain research, the intitiave Medical Informatics in Research and Medicine – MIRACUM for short – seeks to consolidate all the medical data on patients that has been collected by different doctors and hospitals. For this comprehensive task, which is being funded by the Federal Ministry for Education and Research with 3.8 million euros, five consortia joined forces in 2017. Goethe University and its hospital are among them. A file of patients is planned, through which any doctor providing treatment can access all of the medical data that was ever collected on this person. »Today, the best case is if this data has been gathered by the family doctor, although he or she is not a specialist in its analysis,« comments the neurologist.

»If for example someone came to the hospital with memory loss, we could use the available datasets to find out which constellation of findings lead us to the possible diagnoses of alcoholism, depression, vascular dementia or Alzheimer's,« Rosenow says. With the aid of artificial intelligence (AI) he hopes to see new connections and be able to make diagnoses at an earlier stage of the disease, when treatment may be more sucessul.

On the basis of test results and images of the vascular system, for example, an algorithm could predict the risk for cardiovascular diseases. »Patient X has narrowed brain arteries and elevated blood fat values. The risk of a heart attack in the next three years is 80 percent. If he takes blood fat-reducing medicine it might take

half a year longer. And if he gives up smoking, he'll have a couple more healthy years.« The doctor hopes that individual therapeutic recommendations can also be derived this way. Perhaps one patient will benefit from cholesterol-reducing medicines, while anothers would do better to focus on their high blood pressure.

Early diagnosis, specific therapies

In the future, AI systems should also help to diagnose neurological diseases earlier. Patients with muscle tremors and movement disorders may suffer from either Parkinson's or multisystem atrophy, a progressive neurodegenerative disease whose symptoms are initially indistinguishable from Parkinson's. Neither the clinician nor the neuroradiologist can distinguish between these two diseases in their early stages. But perhaps it will be possible in the future to send image data sets to an AI platform that can discover hidden patterns. In this way, the patient could receive disease-specific therapy earlier.

The West German Teleradiology Network has proactively founded an AI platform on which various operators have made their algorithms available. The application possibilities go far beyond neurology. Even now, intelligent systems are finding application in forensic medicine for determining the age of underage criminals without IDs. The system is able to determine the age of the bones in an X-ray.

Artificial intelligence predicts epileptic attacks

It is the dream of every doctor to treat diseases before they exhibit severe symptoms or to prevent their occurrence altogether. »With epilepsy, the risk factors are often already present during childhood,« Rosenow explains. The risk increases if a febrile seizure lasts longer than 15 minutes, or if only one body half is involved. But many years may pass before the first spontaneous seizure occurs. »If we could predict epileptic attacks with a high degree of certainty, we could ideally prevent them with the right treatment,« says the neurologist.

Together with the physicist Professor Jochen Triesch from the Frankfurt Institute for Advanced Studies (FIAS), Rosenow recently demonstrated that this works in principle. In an animal model, the researchers stimulated certain areas of the hippocampus. Following this procedure, the animals developed temporal lobe epilepsy within about 21 days. In Rosenow's working group, EEGs of the test animals were recorded before and after stimulation.

An epileptologist studying these two datasets would hardly notice a difference. The physicists in Jochen Triesch's team then programmed a computer to recognise characteristic patterns or connections in the datasets with the help of deep learning algorithms – completely independent of any human input. The algorithm was then trained with the data of six rats. With a seventh rat, it was able to determine with 97 percent certainty if the animal was healthy or about to develop epilepsy.

Pairing specialised intelligence and common sense

»What's exciting about this approach is that we can then ask the system which characteristics it noticed. This could bring something new to the

In the monitoring room of the video EEG monotring ward, MTA-Fs and doctors have all 8 patients constantly in view and can be on the spot immediately. The large amount of EEG and video data that is recorded here make it possible to localize the seizure's origin in the brain and can later be analysed by artificial intelligence.

Image-creating methods such as magnetic resonance imaging (MRI) provide important data which, thanks to artificial intelligence, can be processed in order to make an early diagnosis of specific diseases possible.

surface,« says Triesch. There have been no surprises with regard to epilepsy so far, but in a joint project with Professor Elke Hattingen in neuroradiology, this kind of system recognised a relevant structure for a brain tumour that radiologists had not previously observed. These kinds of discoveries stimulate research.

And if the AI system makes a mistake? Can Triesch check the information given by his deep learning algorithm? »In a way, the AI system resembles a human expert who makes decisions based on experience. When it comes to deep learning systems, we know in principle how they work. But even though we are currently putting intensive effort into understanding their decisions, it will probably not be possible to do so a way that is completely satisfying,« the physicist admits.

The risk of errors in decisions and diagnoses can be minimised, however, if the system is used correctly. He recently showed a shoe to an app for identifying mushrooms, and it gave him the name of a mushroom. »This happens because these system have a very limited type of intelligence and no common sense. For this reason, a human expert will always have to be involved for the foreseeable future,« says Triesch.

Using mobile phones to diagnose epilepsy

Triesch and Rosenow cannot yet say when the epilepsy risk for humans can be also read from EEG data before the first seizure. »We want to examine more clinical data with artificial intelligence in order to collect additional characteristics that make the prediction more certain. To turn this dream into reality, we will then have to prove the connection in clinical studies. That will take at least another 10 years,« Rosenow estimates. It also has to be kept in mind that there is currently no treatment that can be used to prevent epilepsy. This means that high-risk patients will need to carefully consider whether they want to have this information in advance.

The doctors at the epilepsy centre are currently still struggling to prevent unnecessary suffering through early diagnosis and appropriate treatment. The telemedicine project should make a significant contribution toward this goal. But family members can help by filming the seizure with their mobile phones. »A doctor seldom sees a patient during a seizure. A video would be very helpful,« says Rosenow. It may possibly also spare afflicted individuals a longer stay at the at the video EEG monitoring unit at his ward. ●

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