Setting the stage for a better understanding of complex brain disorders

August 28 2023, by Christos Ntanos

Credit: AI-generated image (disclaimer)

We often compare the brain to a machine with wheels, cogs, and belts. In this analogy, when something breaks, the entire mechanism skips a beat or grinds to a halt. However, more often than not this isn't what happens with our brains. Instead, they're more like a theater. Here, neurons are the musicians, actors, and dancers, and they improvise a performance that shapes our thoughts and lives.

I'm an electronic and computer engineer at the DSS Lab of the National Technical University of Athens. In December 2019, Ioannis Stavropoulos, a neuroscientist at King's College London, introduced me to his colleague Elissaios Karageorgiou of the Neurological Institute of Athens. They wanted to talk about an idea they had about neurology and, in a way, theater, over coffee.

In any piece of theater, mistakes happen—a violin might miss a note, a drummer could skip a beat, an actor might muddle a line or a dancer stumble. Sometimes, many things go wrong simultaneously, and the audience is left wondering what's going on. Was it the singer who was off? Was it the pianist who hit the wrong chord? Did the lights go off at the wrong time and confuse them both?

Complex brain disorders (CoBraD) are very much like that. These include Alzheimer's disease, sleep problems, and epilepsy. We see their symptoms as performance missteps, yet it's hard to group, label, and know their causes. When multiple symptoms show up at once, diagnosis becomes particularly challenging.

It would be hard to know what's wrong in a musical or play by just listening to a second or two every half hour. Similarly, it's tougher to diagnose a medical problem if we only check the patient briefly, such as during occasional doctor visits. As a result, CoBraDs may stay under- or undiagnosed for a long time or be misdiagnosed. More than one can exist at the same time, and the diagnosis and treatment are expensive, at times inaccessible for patients, and often ineffective.

Paying attention to the whole performance

Much like how a piece of theater relies on each artist to play her or his part well for a captivating performance, diagnosing CoBraDs demands a wide range of accurate and harmonized data. Alzheimer's, sleep disorders, and epilepsy are among the conditions that Ioannis and Elissaios are studying and treating. Recognizing the limitations of traditional diagnostic methods, they turned their attention to real-world data (RWD), meaning data collected directly from patients not taking part in a clinical trial.

Data gathered from clinical trials are more reliable than real-world data—they're the result of experiments performed in strict and controlled conditions. However, they are often hard and expensive to get, limited in size, and they may not fully represent the complexity and variability of the real world.

In contrast, real-world data encompass a wider array of information sources, from electronic health records and patient visits to medical devices like MRIs and wearables. When aggregated, these diverse data points become "big data," offering a more comprehensive view of patient health. This holistic approach can reveal patterns and insights that might be missed in more conventional, narrower diagnostic methods.

Collecting significant amounts of real-world data is just the beginning. The real challenge lies in harmonizing and analyzing it all to extract meaningful insights and then finding ways to use them to diagnose and treat patients. To achieve this, we sought expertise from various scientific disciplines. What became our vision was to create a digital platform where neuroscientists could store and share large amounts of data, analyze them, and use them to devise new diagnostic processes and criteria that would be more complex and nuanced than what human clinicians can handle.

These processes would be built into the platform to support clinicians in making decisions for their patients when diagnosing or treating them.

These are called decision support systems, and when they use tools like artificial intelligence, enhancing the competences of human experts in a technical or scientific field, they're called expert systems.

Scientists have proposed numerous ideas hinting that faint clues and varied signals might point to early detection of CoBraD. Many remain unproven, and some are tough to track without computers. For instance, slight changes in sleep, coupled with specific MRI signs, could suggest an early brain disorder. Rather than waiting years for clear symptoms to emerge, doctors could act swiftly, improving the patient's prospects.

This is how the idea for the Multidisciplinary Expert System for the Assessment and Management of Complex Brain Disorders (MES-CoBraD) was born. Bringing together with experts in medicine, engineering, and computer science, we are building a software platform and performing medical research using it.

When doctors, practitioners, software engineers and AI work together

MES-CoBraD evolved into an EU-funded project that now includes 14 universities, companies, and hospitals across Europe. The underlying concept is straightforward: data and observations produced by clinical practice are used by medical research to enhance that very practice.

This continuous circular collaboration can use technology as a link and an enabler. Researchers and clinicians collect and anonymize patient data and upload them to the platform. The researchers form scientific hypotheses, analyze the data, train AI models, and test their hypotheses.

Should they achieve a breakthrough, clinicians would be able to directly use the platform's algorithms to diagnose patients and provide treatments. Related data would in turn will be anonymized and serve to test new hypotheses, aid new statistical analyses, train AI models, or refine existing ones.

The challenges are many. When designing new experiments, we must ensure our data are unbiased. We are also investigating and addressing the ethical implications of using artificial intelligence in medicine. For instance, how do we guarantee that its suggestions are understood by the clinician and can be explained to the patient? How can we be certain that they don't inadvertently favor one patient group over another, or prioritize cost savings over human life? If AI makes a mistake, who takes responsibility?

In MES-CoBraD, we have been venturing into some uncharted territory, but always with specific goals in mind. Although the platform is being made to work in multiple medical fields, the focus now is finding ways of using a very detailed picture of patients' health (a process called deep phenotyping) in conjunction with advanced analytics tools and AI to diagnose and manage CoBraDs. In essence, we aim to simultaneously tune the instruments, hone the actors' lines, and adjust the score.

A personal turn on the stage

Interestingly, my own life's "play" has its moments of dissonance, as I sometimes wake in the middle of the night and find it hard to get back to sleep. I don't think it's anything serious, but as a scientist and longtime researcher, I would never miss the chance to test our own methods and processes on myself. I thus signed up as a test subject for our sleep study and wore a device called "actigraph" on my wrist for a week, and it kept track of my activities, diet, and sleep. I took memory tests and answered questions, and finally there was the main event: I got hooked up with around 40 or 50 cables, tubes and sensors, and slept in the clinic for the night. As a bonus, I offered months of smartwatch health data, which was anonymized and included in the platform.

I am happy to report that for now my sleep issues are likely to be stress-related. However, if deep phenotyping and AI end up diagnosing something worse—say, an early onset complex brain disorder—the question for someone in my position would be: "Should I worry or celebrate the scientific breakthrough if it does?"

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