A DRUG-PUSHING BRAIN IMPLANT FOR NEUROLOGICAL DISEASE

Dr Christopher Proctor

Fiona Dunlevy
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A team of researchers from the UK and France have developed a brain implant that pushes drugs directly into problem brain tissue, using a method called electrophoresis. In experiments, the implant successfully treated and even prevented seizures in mice with chemically induced epilepsy.

Getting into the brain

Neurological disease is one of the last frontiers in medicine – and that frontier is a physical one. The blood brain barrier is the brain's doorman, selecting what molecules are safe to let across the threshold. But this

In neurological diseases from epilepsy to Parkinson's, drugs that need to get from the blood into the brain are barred from entry by the blood brain barrier. Increasing the oral or intravenous drug dose can help enough of the drug to jump the fence, but high doses can lead to nasty side effects elsewhere in the body.

Dodging the doorman may be the best way to get drugs into the brain, according to the researchers behind the electrophoretic brain implant, led by Dr Christopher Proctor, a biomedical engineer now at the University of Cambridge, UK.

Selective drug delivery

Proctor's bioelectronics team developed a needle-shaped implant[1], known as a microfluidic ion pump, miniaturising it to the width of a few human hairs and studding the tip with sensors to monitor brain activity. The drug solution is loaded into a fluid channel in the middle, and the implant is inserted directly into the problem area in the brain.

When an electric field is applied, charged drug molecules (called ions) are pushed across a membrane at the point of the needle, directly into the brain[2]. "The device gives us good control over when and where we're delivering drug," says Proctor, "The amount of drug we deliver is directly related to the strength of electric field we apply."

Drugs are often dissolved in fluid for delivery to the target tissue, by injection for example. A benefit of electrophoretic drug delivery is that it delivers "dry" drug ions and avoids injecting fluid into the brain, which Proctor explains "would create a pressure increase at the delivery point and damage the very cells we want to interact with."

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Preventing seizures in mice

Proctor's teamed up with a group of neuroscientists at the Aix-Marseille University[3] in France to test the implant in epileptic mice. The team chose GABA as the test drug for their implant, a natural neurotransmitter that tells neurons not to fire, dampening or preventing seizures.

The device was implanted into the mouse's hippocampus and a chemical was injected at the same site to induce epileptic-like seizures. When the sensors at the tip of the implant detected the start of seizures, the researchers activated the electric current and pushed GABA directly into the malfunctioning part of the brain, stopping the seizures[4].

"After seeing the first seizure-like event we started delivering GABA, and after that we generally saw no further seizure-like events," says Proctor. Importantly, the team found that they could prevent seizures by pushing GABA into the brain before the epilepsy-causing chemical was injected.

Next steps

The long-term idea is prevention rather than treatment. “We wanted to model the local activity in the brain, so we know if a seizure is happening,” says Proctor. “Simple sensors monitor activity and there is circuitry that can initiate drug delivery when it detects a seizure. That drug delivery would prevent the onset of the seizure.”

The next steps are to fine tune the engineering of the implant to make it more robust, and to test safety and efficacy in longer studies. “We’re making our implant as minimally invasive as possible but we’re still talking about physically implanting something into the brain,” cautions Proctor, “so you have to thread carefully.”

The implant could also be useful in other neurological diseases such as Parkinson’s disease and brain tumours. “We see this as a platform technology that can be applied to many different scenarios,” says Proctor, “It can be relevant to neurological diseases where it’s very difficult to get drugs to where you need them, when you need them.”

Another route for improvement and modification is the electrophoretic membrane itself, which will have to be specially tailored to each drug, so that only the drug ions are pushed out when electricity is applied. “We’ve mostly been using materials that were never really designed for drug delivery,” explains Proctor, “Now that we have established that this is working well, we can design materials specially for this purpose.”

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A team effort

Originally from the USA, Proctor carried out most of this research at the University of Marseille before moving to the University of Cambridge last year. Taking this device through testing all the way to the clinic will take a lot of time, effort and teamwork. “It’s important to be in a supportive environment and be in an ecosystem where you can bring together engineers like myself, neuroscientists, clinicians and companies that have financial capital to back this,” says Proctor, “ethics considerations and patient groups are important. Understanding what is really needed is the best way to design the technology to make sure it is going to have the most benefit”.

REFERENCES

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