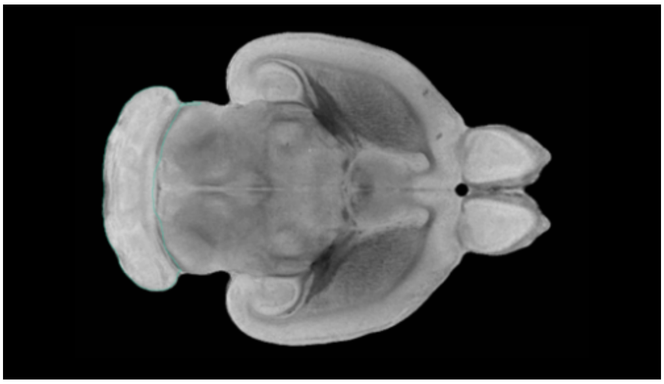
New 'pulsing' ultrasound technique improves drug delivery to brains of mice

26 March 2019



Cerebellum of CIVM postnatal rat brain atlas. Credit: Neurolex

Scientists currently use long-wave pulses of ultrasound to deliver drugs, which can cause side effects. These new findings from Imperial on shorter-wave pulses could have implications for how drugs are used to help patients of Alzheimer's and other neurological diseases.

Neurological diseases like Alzheimer's can be difficult to treat with drugs because they are often blocked by the protective membrane known as the blood brain barrier (BBB). The layer surrounds blood vessels in the brain and allows very few molecules to pass to the brain from the blood. This protects the brain from harmful substances but can also hinder drugs getting to where they can act.

One avenue of research involves prying open the BBB to let drugs into the brain. This is done by injecting mice with tiny bubbles, or 'microbubbles', before applying long-wave pulses of ultrasound radiation to the brain.

The ultrasound pulses change the pressure in the blood vessel, causing the microbubbles to expand and contract. As they do so, they gently pry open the BBB.

However, the long pulses last at least ten milliseconds at a time, which can cause side effects. The longer the BBB stays open, the more chance there is for tissue damage and for harmful molecules to reach the brain.

Now, in a new study published in *Radiology*, lead author Dr. James Choi and colleagues at Imperial compared long-wave ultrasound with shorter-wave, more rapid ultrasound pulses. They found their new technique was more effective and potentially much safer than current methods.

The research is led by Imperial College London and funded by Alzheimer's Research UK.

Lead author Dr. Choi, from Imperial's Department of Bioengineering, said: "We have now found a seemingly effective way of getting potentially effective drugs to where they need to be."

The researchers injected 28 mice with microbubbles, before using short-wave pulses on 14 mice, and long-wave pulses on the other 14.

They found that the short-wave pulses delivered drugs effectively throughout the brain without the surrounding tissue damage that can be caused by longer waves. The BBB also returned to its usual closed state within ten minutes, minimising potential damage.

Dr. Choi explained: "The blood brain barrier is relatively simple to open but current techniques are unable to do so safely—which is why we haven't been able to use them in humans without side effects."

The researchers say the new findings could eventually lead to new techniques for getting drugs to human brains in cases like Alzheimer's, brain cancers, and other disorders involving the brain.

Dr. Choi said: "Our new way of applying the ultrasound could, following further research, literally open up the brain to all sorts of drugs we had previously disregarded.

"Many potential drugs that looked promising in laboratory settings never moved on to use in people—possibly because they were blocked by the blood brain barrier when it came to using them in humans.

Dr. Sara Imarisio, Head of Research at Alzheimer's Research UK, said: "With over 550,000 people in the UK living with Alzheimer's and currently no treatment to slow down or stop the disease, we urgently need to see research to help deliver life-changing drugs.

"While the blood brain barrier protects the brain against damage and infection, it does make it very difficult to deliver treatments into the brain. Although this study exploring how we can penetrate the blood brain barrier was conducted in mice, it's a critical step before technology like this can be tested in people.

"Alzheimer's Research UK are committed to dementia drug discovery and it's vital we continue to explore all possible angles to help deliver real breakthroughs for people living with dementia."

More information: *Radiology*, doi.org/10.1148/radiol.2019181625

Provided by Imperial College London