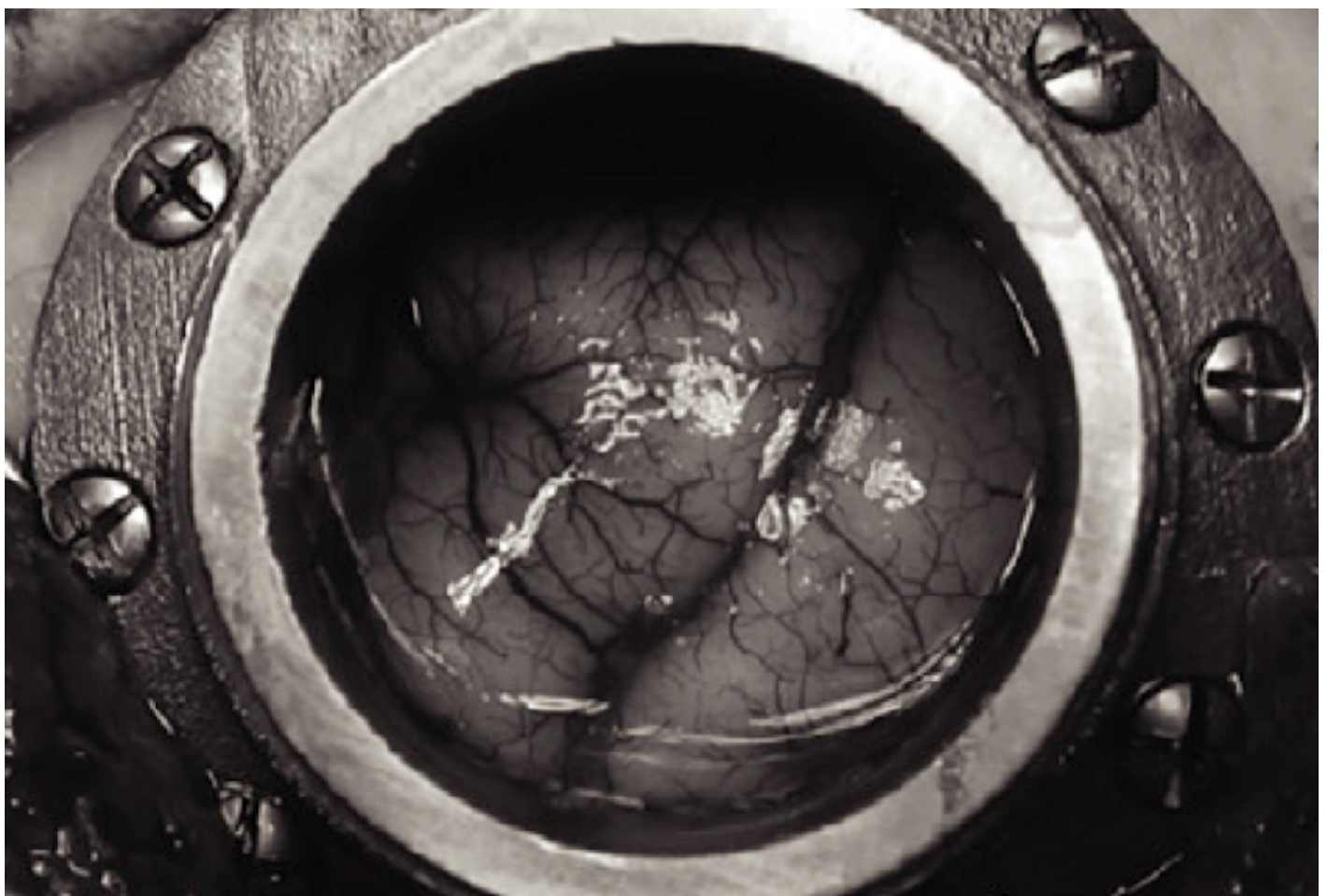


TOOLBOX

New tool offers way to 'light up' cells in monkey brain

BY ANN GRISWOLD

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A new technique can stimulate and record activity across broad swaths of the monkey brain. The tool, described 2 March in *Neuron*, could shed light on brain circuits that underlie complex behaviors, such as social communication¹.

The method involves the use of lasers to activate light-sensitive proteins in neurons, **triggering the cells to fire**. By inserting the proteins into specific sets of neurons, such 'optogenetics' experiments in mice can highlight brain circuits thought to go awry in autism. But scientists have struggled to **apply the technique to larger animals** such as monkeys, whose social behaviors **resemble those of people**.

Part of the problem lies in the delivery of the light-sensitive proteins, called opsins. Researchers traditionally inject a virus that carries genes for these proteins into the mouse brain. The virus slowly diffuses from the injection site to invade cells as far as 2 millimeters away. The infected neurons make the viral proteins, allowing researchers to activate the neurons with light. However, in the case of a monkey brain, it takes multiple injections to cover the areas, and the opsin expression is uneven.

In the new study, researchers used a technique that pushes large volumes of a viral solution through an ultra-thin hose to direct a high-pressure spray toward specific locations in the brain. The combination of high pressure and volume spreads the virus to cells within 5 millimeters of the injection site, far more than the 2-millimeter spread with conventional methods.

Special delivery:

The researchers drilled a 25-millimeter hole in the skulls of two rhesus monkeys and plugged each hole with a custom-printed plastic cylinder. They inserted the hose through the cylinder and injected a viral solution at four sites in sensory and motor regions of the brain.

They performed the procedure in a magnetic resonance imaging scanner to confirm the spread of the virus particles up to 5 millimeters from each of the sites.

The researchers then replaced the plastic injection cylinder with a titanium one and added a clear silicone sheet at the bottom of it to create a see-through portal into the monkey brain.

The researchers waited three months for the cells to take up the virus and express the opsins. They then directed laser beams through the portal and used a video camera to visualize light absorbed by the opsins. Opsin expression spanned large parts of the areas they had targeted.

Using a transparent array of 96 electrodes, the researchers shined light into the brain and recorded the resulting brain activity. The custom-built array detected electrical activity, accurately picking up changes in neural activity in response to variations in the intensity of light and other parameters. The results confirm the tool's usefulness for studying monkey brains.

This light sensitivity lasted two years, meaning researchers could perform long-term studies of neural circuits without repeating any of the invasive steps.

Beyond offering clues about the brain circuits underlying monkey behaviors, the platform may hold promise for optogenetics-based therapies in people with neurological conditions, the researchers say.

REFERENCES:

1. Yazdan-Shahmorad A. *et al. Neuron* **89**, 927-939 (2016) [PubMed](#)