*** 北米連携センター情報***

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●脳の内部を観察する新たな技術を開発

【Stanford University, 2014/08/06】

スタンフォード大の研究チームはレーザーとカーボン・ナノチューブを用いて生物の脳内血流を観察する技術の開発を進めている。

この技術はまだマウスを使った実験で効果が確認された段階だが、将来的には人体に応用することも可能と考えられており、脳梗塞や偏頭痛さらにはアルツハイマー病、パーキンソン病の研究に貴重な情報をもたらすことも期待される。

現在でも脳の働きを観察する手法は存在するが、開頭手術を用いる場合は脳の活動に影響を与える可能性があり、CT や MRI を用いれば全体像を眺めることはできるものの血管個々やニューロングループの活動を視覚化できない。

これに対して今回開発された近赤外線を使う「近赤外線-IIa 撮像法（NIR-IIa)」は水溶性のカーボンナノチューブをマウスの血流に注入した上で近赤外線レーザーを頭部に照射。これによりナノチューブは波長 1300～1400 ナノメートルの蛍光を発するので、これを検出することで血管構造を視覚化できる。この技術は頭皮の約 3mm 下で直径数ミクロンの毛細血管 1 本の活動を視覚化することが可能だという。

この技術を人間に応用するためにはまずレーザー光の浸透深度をさらに高める必要があり、カーボン・ナノチューブの臨床応用に承認を得なければならない。チームは他に使える蛍光物質がないかも探しているという。

（参考）本件報道記事

Stanford Report, August 6, 2014

Stanford scientists use lasers and carbon nanotubes to look inside living brains

A team of Stanford scientists has developed an entirely non-invasive technique that provides a view of blood flow in the brain. The tool could provide powerful insights into strokes and possibly Alzheimer's disease.

By Bjorn Carey

Some of the most damaging brain diseases can be traced to irregular blood delivery in the brain. Now, Stanford chemists have employed lasers and carbon

nanotubes to capture an unprecedented look at blood flowing through a living brain.

The technique was developed for mice but could one day be applied to humans, potentially providing vital information in the study of stroke and migraines, and perhaps even Alzheimer's and Parkinson's diseases. The work is described in the journal Nature Photonics.

Current procedures for exploring the brain in living animals face significant tradeoffs. Surgically removing part of the skull offers a clear view of activity at the cellular level. But the trauma can alter the function or activity of the brain or even stimulate an immune response. Meanwhile, non-invasive techniques such as CT scans or MRI visualize function best at the whole-organ level; they cannot visualize individual vessels or groups of neurons.

The first step of the new technique, called near infrared-IIa imaging, or NIR-IIa, calls for injecting water-soluble carbon nanotubes into a live mouse's bloodstream. The researchers then shine a near-infrared laser over the rodent's skull.

The light causes the specially designed nanotubes to fluoresce at wavelengths of 1,300-1,400 nanometers; this range represents a sweet spot for optimal penetration with very little light scattering. The fluorescing nanotubes can then be detected to visualize the blood vessels' structure.

Amazingly, the technique allows scientists to view about three millimeters underneath the scalp and is fine enough to visualize blood coursing through single capillaries only a few microns across, said senior author Hongjie Dai, a professor of chemistry at Stanford. Furthermore, it does not appear to have any adverse affect on innate brain functions.

"The NIR-IIa light can pass through intact scalp skin and skull and penetrate millimeters into the brain, allowing us to see vasculature in an almost non-invasive way," said first author Guosong Hong, who conducted the research as a graduate student in Dai's lab and is now a postdoctoral fellow at Harvard. "All we have to remove is some hair."

The technique could eventually be used in human clinical trials, Hong said, but will need to be tweaked. First, the light penetration depth needs to be increased to pass deep into the human brain. Second, injecting carbon nanotubes needs approval for clinical application; the scientists are currently investigating alternative fluorescent agents.

For now, though, the technique provides a new technique for studying human cerebral-vascular diseases, such as stroke and migraines, in animal models. Other research has shown that Alzheimer's and Parkinson's diseases might elicit – or be caused in part by – changes in blood flow to certain parts of the brain, Hong said, and NIR-IIa imaging might offer a means of better understanding the role of healthy vasculature in those diseases.

"We could also label different neuron types in the brain with bio-markers and use this to monitor how each neuron performs," Hong said. "Eventually, we might be able to use NIR-IIa to learn how each neuron functions inside of the brain."

The work was co-authored by Shuo Diao, Alexander L. Antaris, Changxin Chen, Bo Zhang and Su Zhao of Stanford's Department of Chemistry; Calvin J. Kuo and Junlei Chang of the Department of Hematology at the Stanford School of Medicine; Katrin I. Andreasson of the Department of Neurology and Neurological Sciences at Stanford School of Medicine; and Dmitriy N. Atochin and Paul L. Huang of Massachusetts General Hospital and Harvard Medical School.

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