SCIENCE & TECHNOLOGY

Minimally invasive method tracks how the brain spends energy

Penn researchers have developed a new technique for monitoring the brain's metabolic rate of oxygen consumption, a measure of the brain's consumption of energy.

Our brains are charged with the task of directing most of the processes needed for our bodies to function. As such, they consume roughly 20% of our body's metabolic energy, even while we're resting.

This need for unremitting access to fuel is why brains are equipped with a dense and elaborate network of blood vessels that transport oxygen molecules to neurons. It's also why the cerebral metabolic rate of oxygen (CMRO2) consumption, a measure of how much energy the brain is using at a given time, is an important indicator of the brain's overall health.

In a paper published in *Neurophotonics* (https://www.spiedigitallibrary.org/journals/Neurophotonics/volume-9/issue-04/045006/Real-time-tracking-of-brain-oxygen-gradients-and-blood-flow/10.1117/1.NPh.9.4.045006.full?webSyncID=02c67125-9c3e-9c4b-7137-3766ea979c64&sessionGUID=0a36cbc9-b4bd-1721-6862-ddd3766101dd&_ga=2.149165374.905539366.1669912417-416458333.1669769298&cm_mc_uid=93627055553616697692982&cm_mc_sid_50300000=96254361669912416768&SSO=1), a team led by Penn researchers reports on a new, minimally invasive technique for monitoring CMRO2 in real time. The optical method relies on phosphorescent probes capable of tracking oxygen concentrations in and around the blood vessels in cerebral cortex in tandem with cerebral blood flow.

"This new approach is minimally invasive and allows for superior temporal resolution," says Sergei Vinogradov (https://www.chem.upenn.edu/profile/sergei-vinogradov), co-senior author of the paper and professor in the Perelman School of Medicine (https://www.med.upenn.edu/) and School of Arts & Sciences (https://www.sas.upenn.edu/). "It will create new opportunities for dynamically tracking and quantifying CMRO2, potentially even approaching the millisecond time-scale."

Figuring out a reliable way to quantify CMRO2 has long been a goal for scientists and clinicians. Better insights into this vital metric have major implications for improving understanding of how brains respond to stimuli and could even lead to new biomarkers for diagnosing and charting the progression of tissue damage in neurological conditions such as stroke, traumatic brain injury, and cancer.

Current methods of measuring CMRO2 rely heavily on techniques that make it difficult to get real-time readouts. Furthermore, CMRO2 values are usually derived from other blood dynamic parameters like cerebral blood flow, cerebral blood volume, and hemoglobin oxygen saturation.
"In our experiments, we directly measured oxygen concentration in brain tissue to calculate CMRO2," says first author Sang Hoon Chong, a postdoctoral researcher in the Department of Physics and Astronomy. "We obtained this information as a function of time at specific regions in the brain that were responding to a stimulation."

The researchers' technique uses two phosphorescent probes. One is placed in the brain's vasculature, a network of continuous blood vessels that supply oxygen to the brain cells, and the other is right next to brain cells in the brain interstitial space.

The two probes allow for oxygen levels to be monitored and compared, at the same time, allowing for improved readouts of the brain's oxygen gradient, which is the difference in oxygen concentrations between the two sites.

"What's exciting about this is that we get to see how brains directly respond to stimuli by charting the flow of oxygen between the circulatory system and the interstitial space," says Mirna El Khatib, co-author and instructor in the Perelman School of Medicine. "For the first time, we're able to get a real-time one-to-one quantification of how much oxygen is being depleted and how it is re-supplied."

The two probes have different colors, and by using two different lasers the researchers could measure the probes' signals simultaneously. The technique was applied to a rodent model, wherein the researchers stimulated the animal's paw and were able to demonstrate real-time computation and tracking of CMRO2. With the addition of a third laser and alternate imaging method, the researchers also succeeded in measuring cerebral blood flow in tandem with CMRO2.

"As technology develops, we anticipate that the method will become more broadly available for testing drugs and other effectors of brain metabolism," says Arjun Yodh (https://live-sas-physics.pantheon.sas.upenn.edu/people/standing-faculty/arjun-yodh), co-senior author of the paper and a professor in the Department of Physics and Astronomy, as reported by International Society for Optics and Photonics. "And, eventually, it should permit more rigorous examination of existing metabolism models."

Sergei Vinogradov is professor in the Department of Biochemistry and Biophysics (https://www.med.upenn.edu/biocbiop/)in the Perelman School of Medicine and a professor of biochemistry and biophysics in the Department of Chemistry (https://www.chem.upenn.edu/) in the School of Arts & Sciences at the University of Pennsylvania.

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Vinogradov and Yodh's coauthors were Penn Medicine's Yi Hong Ong, Srinivasa Rao Allu, as well as Joel H. Greenberg and Ashwin B. Parthasarathy in the Department of Electrical Engineering at the University of South Florida.

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