

Utilizing cerebral oxygen and blood flow to provide insights into brain function, damage, and recovery *in vivo*

by Justin Croft

Introduction

The brain is undoubtedly a complex organ that controls thought, memory, touch, motor skills, vision, breathing, temperature, and most other processes that regulate the body. As such, it needs a large amount of oxygen to function. The fact is that in a resting state about a fifth of the body's total oxygen requirement is consumed through cerebral metabolism.

When the brain does not receive enough oxygen, brain cells can begin to die. Cell death can occur within 5 minutes of low oxygenation which quickly leads to various complications if oxygen is not redelivered. Since the brain is so complex and the process of hypoxia can occur so quickly, there is a great deal of preclinical research that goes into understanding these mechanisms and how to treat and mitigate damage due to cerebral hypoxia (or anoxia).

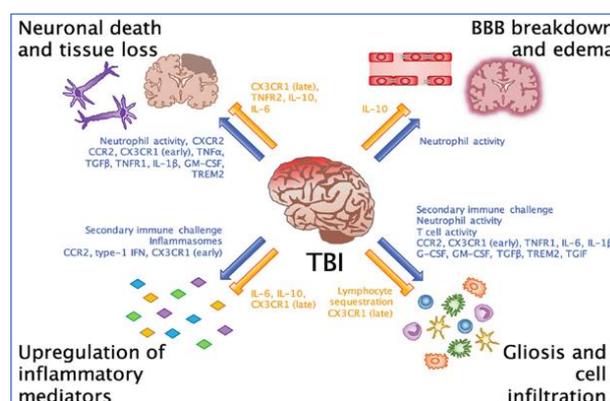
One way to investigate cerebral hypoxia caused by trauma (TBI) or lack of blood flow (stroke, MCAO) is to measure cerebral blood perfusion and pO₂ directly within the area of interest. We at Oxford Optronix have been supporting brain research for 30+ years and helping researchers to answer these questions with our tissue vitality monitors to assess both parameters in real-time. Sensors start at a very fine 250 μm diameter making them minimally invasive.

This article looks at some of the major application areas in brain research and the large and small animal models used. We describe how our OxyLite and OxyFlo systems have been employed and we provide some supporting publications as reference material for the reader. Please note these systems can be used separately to garner microvascular blood flow or tissue pO₂ information independently from separate tissue sites or in parallel using a unique combined sensor capable of reading pO₂, blood flow and temperature from a singular site. There are also implantable sensors available for chronic studies and specialized sensors for use in an imaging setting like MRI and CT. These are discussed towards the end of this article.

Traumatic brain injury (TBI) and tissue monitoring

Traumatic brain injury (TBI) is a sudden damage to the brain. It may happen when there is a blow, bump, or jolt to the head. Following head injuries there is reduction of cerebral blood flow (ischemia) which is detrimental to the brain's ability to recover following the injury. Depending on the nature and severity of the injury, different approaches are often studied in animal models (of different sizes) to assess the feasibility and efficacy of a specific treatment.

The OxyLite™ and OxyFlo™ products have been used extensively over many years in these types of studies to assess brain health prior to, during, and following TBI. To further assess a treatment or the effect of a drug a



Source: McKee and Lukens (2016). *Front. Immunol.*

researcher may look at the length of time it takes, following a traumatic event, for cerebral perfusion and brain pO₂ return to a normal baseline.

Malik H, Wolff MD, Teskey GC, and Mychasiuk R (2022). [Electrographic seizures and brain hyperoxia may be key etiological factors for postconcussive deficits](#). *J of NeuroPhys.* 128 (3), 727-737

Abutarboush R, Mullah SH, Saha BK, Haque A, Peter B, ... McCarron RN, Scultetus AH, Moon-Massat P (2018). [Brain oxygenation with a non-vasoactive perfluorocarbon emulsion in a rat model of traumatic brain injury](#). *Microcirculation* 25 (3), e12441

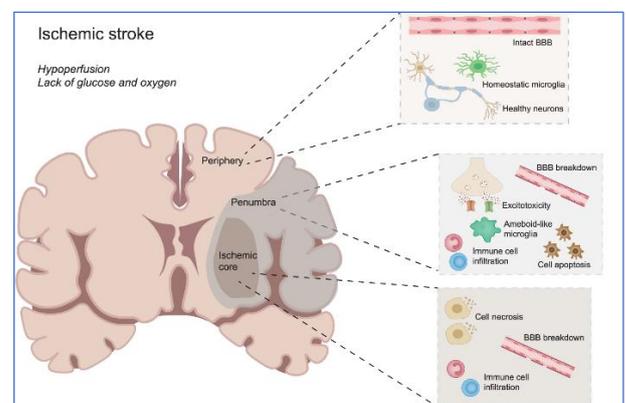
Schilte C, Bouzat P, Millet A, Boucheix P, Pernet-Gallay K, Lemasson B, Barbier EL and Payen JF (2015). [Mannitol Improves Brain Tissue Oxygenation in a Model of Diffuse Traumatic Brain Injury](#). *Crit Care Med* 43(10), 2212-8

Teranishi K, Scultetus A, Haque A, Stern S, Philbin N, Rice J, Johnson T, Aufer C, McCarron R, Freilich D and Arnaud F (2012). [Traumatic brain injury and severe uncontrolled haemorrhage with short delay pre-hospital resuscitation in a swine model](#). *Injury* 43(5), 585-93

Stroke/MCAO and tissue monitoring

A stroke, also known as a transient ischemic attack, happens when blood flow to the brain is blocked. This prevents a region of the brain receiving oxygen and nutrients from the blood. Without oxygen, brain cells begin to die within minutes.

As a stroke can cause lasting brain damage, long-term disability, or even death, it's important to quickly mitigate the damage. This can be achieved by reperfusion (unblocking the stroke site) or using methods that extend brain cell survival, which is a focus for a large portion of translational research. Very much like in trauma studies where TBI researchers use the OxyLite™ and OxyFlo™ to assess brain health, in stroke models the same instruments and sensors can also be employed to assess (and quantify) the extent of the ischemic insult and to observe a potential or complete recovery to baseline following a drug or treatment intervention.



Source: Qin et al. 2022. *Signal Transduction and Targeted Therapy* volume 7

Nizari S, Basalay M, Chapman P, Korte N, Korsak A, Christie IN, Theparambil SM, Davidson SM, Reimann F, Trapp S, Yellon DM, Gourine AV (2021). [Glucagon-like peptide-1 \(GLP-1\) receptor activation dilates cerebral arterioles, increases cerebral blood flow, and mediates remote \(pre\)conditioning neuroprotection against ischaemic stroke](#). *Basic Res Cardiol* 116 (32)

Poon YY, Liu YW, Huang YH, Chan SH, Tsai CY (2021). [Postoperative Stroke after Spinal Anesthesia and Responses of Carotid or Cerebral Blood Flow and Baroreflex Functionality to Spinal Bupivacaine in Rats](#). *Biology* 10 (7), 617

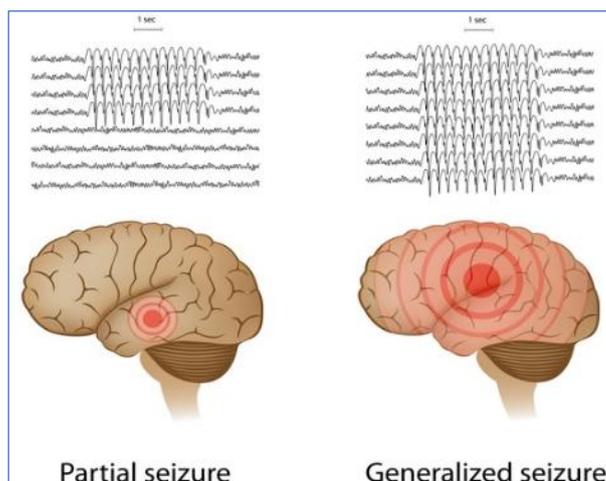
Chen CC, Chang CP, Yang CL (2019) [An adaptive fall-free rehabilitation mechanism for ischemic stroke rat patients](#). *Scientific Reports* 9, 984

Suh JY, Cho G, Song Y, Woo DC, Choi YS, Ryu EK, Park BW, Shim WH, Kim YR, Kim JK (2018). [Magnetic Resonance Imaging Biomarker to Assess Cerebral Oxygenation and Ischemic Damage in Stroke](#). *Stroke* 49, 3012–3019

Brain damage caused by other diseases or ailments assessed by tissue monitoring

Cerebral vitality assessment using the OxyLite™ and OxyFlo™ devices can also provide valuable surrogate data during trauma elsewhere in the organism or to other vital organs, e.g., during episodes of septic shock and/or resuscitation. Since the brain is such an important organ overall, monitoring it even peripherally can provide researchers with useful information on general health or on the efficacy of a specific treatment.

Other ailments, like hemorrhage, seizures, and epilepsy that originate in the brain can often cause a change in intracranial pressure, cerebral perfusion, and oxygenation. Being able to monitor these vital physiological parameters is potentially of great value to the clinical scientist in models of drug treatment or other intervention.



Source: National Library of Medicine article (NIH, USA)

Seizure

Malik H, Wolff MD, Teskey GC, and Mychasiuk R (2022) [Electrographic seizures and brain hyperoxia may be key etiological factors for post-concussive deficits](#). *J of NeuroPhys.* 128 (3), 727-737

Jansen NA, Schenke M, Voskuyl RA, Thijs RD, van den Maagdenberg J, Tolner EA (2019). [Apnea associated with brainstem seizures in Cacna1^{as218} mice is caused by medullary spreading depolarization](#). *J of Neuroscience* 39 (48), 9633-9644

Hemorrhage

Yang LY, Chen YR, Lee JE, Chen KW, Luh HT, Chen YT, Wang KC, Hsieh ST (2022). [Dental Pulp Stem Cell-Derived Conditioned Medium Alleviates Subarachnoid Hemorrhage-Induced Microcirculation Impairment by Promoting M2 Microglia Polarization and Reducing Astrocyte Swelling](#). *Transl Stroke Res*.

Other

Wang CH, Huang CH, Tsai MS, Wang CC, Chang WT, Liu SH, Chen WJ (2022). [Inhaled Carbon Dioxide Improves Neurological Outcomes by Downregulating Hippocampal Autophagy and Apoptosis in an Asphyxia-Induced Cardiac Arrest and Resuscitation Rat Model](#). *J Am Heart Assoc.* 11(21):e027685

Boorman LW, Samuel, Harris SS, Shabir O, Lee L, Eyre B, Howarth C, Berwick J (2022). [Bidirectional alterations in brain temperature profoundly modulate spatiotemporal neurovascular responses in-vivo: Implications for theragnostics](#). *bioRxiv*

Other applications in brain research

Implantable sensors for tissue monitoring

For those performing chronic studies of the brain, implantable sensors offer a way to take serial measurements over time. In short, the sensors need to be surgically implanted into the brain. After a period of recovery measurements can be taken in awake, restrained, or anesthetized models by connecting the miniature exteriorized sensor ferrule to a dedicated adapter, itself attached to the OxyLite™ oxygen monitor.



Our chronic implantable oxygen sensor, supplied with calibration on iButton device

Yu LH, Thurston EMS, Hashem M, Dunn JF, Whelan PJ and Murari K (2020). [Fiber photometry for monitoring cerebral oxygen saturation in freely-moving rodents](#). *Biomedical Optics Express* 11 (7), 3491-3506

Malik H, Wolff MD, Teskey GC, and Mychasiuk R (2022) [Electrographic seizures and brain hyperoxia may be key etiological factors for postconcussive deficits](#). *J of NeuroPhys.* 128 (3), 727-737

Lee K, Bohnert S, Vair C, Mikler J, and Dunn JF (2020). [Cerebral blood flow and oxygenation in rat brain after soman exposure](#). *Toxicol Lett* 336, 50-56. doi: 10.1016/j.toxlet.2020.10.009.

MRI compatible sensors

Advanced imaging techniques, like magnetic resonance imaging, continue to be commonly used to examine the anatomy and physiological processes of the brain. Researchers using these imaging techniques commonly wish to validate their data. As the OxyLite™ and OxyFlo™ sensors utilize fibre optic technology, they are fundamentally MRI compatible, allowing for real-time blood flow and tissue oxygen measurement even during MRI. Dedicated, extended length sensors are available for this application.



Our combined oxygen and blood perfusion sensor type, including connector close-up

Suh JY, Cho G, Song Y, Woo DC, Choi YS, Ryu EK, Park BW, Shim WH, Kim YR, Kim JK (2018). [Magnetic Resonance Imaging Biomarker to Assess Cerebral Oxygenation and Ischemic Damage in Stroke](#). *Stroke* 49, 3012–3019

Schoennagel BP, Yamamura J, Fischer R, Tavares de Sousa M, Weyhmler M, Birkelbach M, Kooijman H, Adam G and Wedegaertner U (2015). [BOLD MRI in the brain of fetal sheep at 3T during experimental hypoxia](#). *J Magn Reson Imaging* 41(1), 110-6

Valable S, Corroyer-Dulmont A, Chakhoyan A, Durand L, Toutain J, Divoux D, Barré L, MacKenzie ET, Petit E, Bernaudin M, Touzani O and Barbier EL (2016). [Imaging of brain oxygenation with magnetic resonance imaging: A validation with positron emission tomography in the healthy and tumoural brain](#). *J Cereb Blood Flow Metab* 37(7), 2584-2597

Baskerville TA, Deuchar GA, McCabe C, Robertson CA, Holmes WM, Santosh C and Macrae IM (2011). [Influence of 100% and 40% oxygen on penumbral blood flow, oxygen level, and T2*-weighted MRI in a rat stroke model](#). *J Cereb Blood Flow Metab.* 31(8), 1799-806

Conclusion

There is good reason our OxyLite™ and OxyFlo™ platforms have been used so extensively in *in vivo* cerebral research. These systems, whether used independently or together provide incredibly useful real-time data that relays important physiological parameters to the scientist about brain health and function. These systems continue to be used and trusted by a worldwide user base in research institutes, universities, hospitals, pharma, CRO's, and military research.

If you have any questions about our OxyLite™ tissue pO₂ monitors, or our OxyFlo™ microvascular blood perfusion monitors, please do not hesitate to contact sales@oxford-optronix.com.



OxyLite Pro and OxyFlo Pro monitor stack for combined tissue oxygen and blood perfusion monitoring

Our closely knit team has over 25 years of experience in cerebral monitoring applications and is always available to discuss the complexities of any proposed studies.