Neurovascular Coupling

Neurovascular coupling (NVC) is the physiological mechanism by which neuronal activity is rapidly translated into localized changes in cerebral blood flow (CBF), ensuring proper delivery of oxygen and nutrients to active brain regions.

Core Mechanism

- **Neuronal activity** triggers the release of glutamate and other neurotransmitters.
- **Astrocytes** detect synaptic activity through receptors such as mGluRs.
- Intracellular **Ca^{2+} waves** propagate within astrocytes, particularly towards their **endfeet**.
- Astrocytes release **vasoactive molecules** (e.g., PGE2, NO, ATP), modulating arteriole and capillary tone.
- The result is **vasodilation** or **vasoconstriction** that adjusts local blood flow based on metabolic demand.

Key Cellular Players

- **Neurons** – Initiate the signal via synaptic activity.
- **Astrocytes** – Serve as intermediaries in translating neuronal signals to vascular responses.
- **Endothelial cells** – Respond to signaling and regulate vascular tone.
- **Pericytes** – Control capillary diameter.
- **Smooth muscle cells** – Control arteriole tone.

Experimental Tools

- **In vivo**:
    1. Laser speckle contrast imaging
    2. Two-photon microscopy
    3. fMRI (BOLD response)
- **Ex vivo**:
    1. Calcium imaging in brain slices
    2. Electrical/chemical stimulation with vessel recording

⚠ Pathological Disruption

- **Neurodegenerative diseases** (e.g., Alzheimer's, ALS)
- **Cerebrovascular disease** (e.g., stroke, small vessel disease)
- **Aging**
- **Traumatic brain injury**
- **Astrocyte dysfunction** (e.g., impaired AQP4 localization or SorCS2 mutation)

Key Molecules

- glutamate, mGluR3, AQP4, SorCS2
- Nitric oxide (NO)
- Prostaglandins (e.g., PGE2)
- Adenosine
- EETs (epoxyeicosatrienoic acids)

Clinical Relevance

- NVC is fundamental for:
    1. Functional neuroimaging interpretation (e.g., fMRI BOLD signal)
    2. Perioperative brain protection in neurosurgery
    3. Early detection of microvascular dysfunction
- Altered NVC may precede cognitive decline and neurodegeneration.

Related Pages

- neurovascular_signaling
- astrocytic_function
- astrocyte_dysfunction
- cerebral_blood_flow
- tripartite_synapse
- SorCS2

Revealing the structural and functional changes of microvasculature is essential to match vascular response with neuronal activities in the investigation of neurovascular coupling. The increasing use of rhesus models in fundamental and clinical studies of neurovascular coupling presents an emerging need for a new imaging modality. Here we report a structural and functional cerebral vascular study of rhesus monkeys using an ultrafast, portable, and high-resolution photoacoustic microscopic system with a long working distance and a special scanning mechanism to eliminate the relative displacement between the imaging interface and samples. We derived the structural and functional response of the cerebral vasculature to the alternating normoxic and hypoxic conditions by calculating the vascular diameter and functional connectivity. Both vasodilatation and vasoconstriction were observed in hypoxia. In addition to the change of vascular diameter, the decrease of functional connectivity is also an important phenomenon induced by the reduction of oxygen ventilatory. These results suggest that photoacoustic microscopy is a promising method to study the neurovascular coupling and cerebral vascular diseases due to the advanced features of high spatiotemporal resolution, excellent sensitivity to hemoglobin, and label-free imaging capability of observing hemodynamics [1)].

Impairment of neurovascular coupling (NVC) was recently reported in the context of subarachnoid hemorrhage and may correlate with disease severity and outcome. However, previous techniques to

evaluate NVC required invasive procedures. Retinal vessels may represent an alternative option for non-invasive assessment of NVC.

A prototype of an adapted retinal vessel analyzer was used to assess retinal vessel diameter in mice. Dynamic vessel analysis (DVA) included an application of monochromatic flicker light impulses in predefined frequencies for evaluating NVC. All retinae were harvested after DVA and electroretinograms were performed.

A total of 104 retinal scans were conducted in 21 male mice (90 scans). Quantitative arterial recordings were feasible only in a minority of animals, showing an emphasized reaction to flicker light impulses (8 mice; 14 scans). A characteristic venous response to flicker light, however, could observed in the majority of animals. Repeated measurements resulted in a significant decrease of baseline venous diameter (7 mice; 7 scans, $p < 0.05$). Ex-vivo electroretinograms, performed after in-vivo DVA, demonstrated a significant reduction of transretinal signaling in animals with repeated DVA ($n = 6$, $p < 0.001$).

To the best of Albanna et al. knowledge, this is the first non-invasive study assessing murine retinal vessel response to flicker light with characteristic changes in NVC. The imaging system can be used for basic research and enables the investigation of retinal vessel dimension and function in control mice and genetically modified animals [2].

1)
Qin W, Gan Q, Yang L, Wang Y, Qi W, Ke B, Xi L. High-resolution in vivo imaging of rhesus cerebral cortex with ultrafast portable photoacoustic microscopy. Neuroimage. 2021 Jun 9:118260. doi: 10.1016/j.neuroimage.2021.118260. Epub ahead of print. PMID: 34118393.
2)
Albanna W, Kotliar K, Lüke JN, Alpdogan S, Conzen C, Lindauer U, Clusmann H, Hescheler J, Vilser W, Schneider T, Schubert GA. Non-invasive evaluation of neurovascular coupling in the murine retina by dynamic retinal vessel analysis. PLoS One. 2018 Oct 4;13(10):e0204689. doi: 10.1371/journal.pone.0204689. eCollection 2018. PubMed PMID: 30286110.