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Integrated Phase Resolved Optical Coherence Tomography and Laser Speckle Imaging for Enhanced Cerebral Blood Flow Analysis in Mice under Hypercapnic Stress

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Abstract: Cerebral blood flow dynamics are crucial in understanding neurovascular disease. Here, we developed an integrated imaging system combining Optical Coherence Tomography (OCT) and Laser Speckle Imaging (LSI), offering detailed insights into cerebrovascular hemodynamic changes.

1. Introduction

Alzheimer's disease (AD) is a progressive neurodegenerative disorder, standing as one of the most significant challenges in modern medicine. Recently, more research has suggested that cerebrovascular factors, including changes in cerebral hemodynamics, may play a critical role in the onset and progression of AD [1].

Hypercapnia, a condition marked by elevated carbon dioxide (CO_2) levels in the bloodstream, can significantly impact cerebral blood flow (CBF) and metabolism [2]. When CO_2 levels rise, vasodilation occurs, resulting in increased CBF [2]. Recent studies have begun to reveal a potential link between hypercapnia and AD, as the hemodynamic changes caused by hypercapnia could influence amyloid-beta deposition, neuronal function, and overall brain metabolism, factors central to the development of AD [3].

Optical Coherence Tomography (OCT) and Laser Speckle Imaging (LSI) have emerged as potent imaging modalities in the analysis of CBF in hypercapnia studies. OCT is a noninvasive imaging modality that uses near-infrared light. One application of OCT, phase-resolved OCT, has been used to study cerebrovascular hemodynamic changes in animal models with high spatial resolution on a micrometer scale [4]. Concurrently, LSI provides rapid, wide-field imaging of CBF, capturing dynamic changes over larger areas with high temporal resolution [5]. While each modality possesses unique strengths, their integration may provide additional insights into hemodynamic studies. Here, we propose an OCT-LSI system that can obtain OCT and LSI images simultaneously, combining the advantages of phase-resolved OCT's microvascular detail and LSI's mesoscopic flow overview. The OCT and LSI setups share the same field of view, with simultaneous data collection, thus providing a comprehensive understanding of cerebral hemodynamics under hypercapnic conditions.

2. Method

2.1. System Setup

The OCT-LSI system comprises a swept-source OCT component and an LSI part (Fig. 1A). The OCT arm features a 50k 1310 nm swept source laser. The light is divided by a 2x2 optical fiber coupler with a 95:5 coupling ratio, directing 95% of the light through the sample arm and 5% through the reference arm. In both arms, two circulators redirect the back-reflected light to a 50:50 fiber coupler, leading to balanced detection. To improve the laser's phase stability, the generated light is synchronized with an external lambda trigger which is from Fiber Bragg Grating with a center wavelength of 1260 nm and through a fiber-based 99:1 coupler back to the acquisition system. The LSI arm uses an 809 nm laser diode to illuminate the sample. The backscattered light is cross-polarized relative to the incident light and collected by a CMOS camera. A computer controls the system, enabling manipulation and data acquisition.

2.2 Animal Model and Imaging Timeline

C57BL/6 female mice were used in this study. 4% isoflurane was used to anesthetize the mice. Mice underwent surgery at 2% isoflurane on a stereotactic frame. The scalp was retracted to approximately a 1 cm circular diameter to expose both hemispheres. A dental cement well was created around the periphery of the imaging window and filled with saline to maintain skull hydration and optical transparency. The imaging timeline is shown in Fig. 1B. During imaging, 1.5% isoflurane was used, where mice were ventilated with room air, then exposed to 5% CO_2 in balanced room air to induce hypercapnia, and finally returned to room air conditions for recovery.

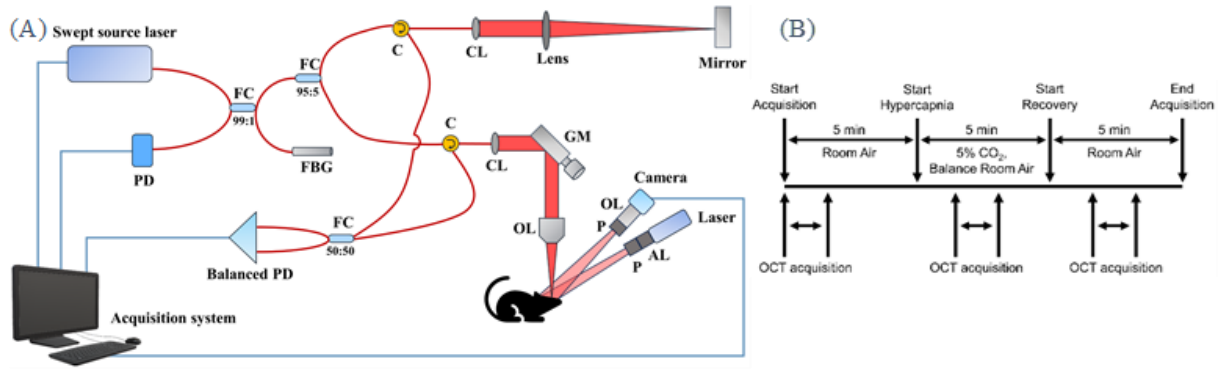

Fig.1 (A) OCT-LSI system setup. FC – fiber coupler, FBG – fiber bragg grating, C – circulator, CL – collimator, GM – galvo scanner, OL – objective lens, P – prism, AL – aspheric lens, PD - photodetector (B) Animal imaging timeline to induce hypercapnia.

3. Results

Fig. 2 shows results obtained from the OCT-LSI system. Fig. 2A presents the CBF maps calculated from the LSI spatial processing algorithm. Fig. 2B shows relative CBF, where a distinct increase in CBF is observed during hypercapnia. Fig. 2C and D correspond to the OCT angiography (OCTA) and phase-resolved projected image. The flow velocities calculated from the Region of Interest (ROI) in Fig. 2D are displayed in Fig. 2E and F, corresponding to room air and hypercapnia conditions, respectively. These are characterized by pulsatile blood flow changes due to each heartbeat. The mean velocity during room air conditions and hypercapnia were 8.8 ± 3.2 mm/s, and 10.0 ± 3.0 mm/s, respectively. These findings agree with the LSI results, indicating that blood flow velocity increases under hypercapnia conditions.

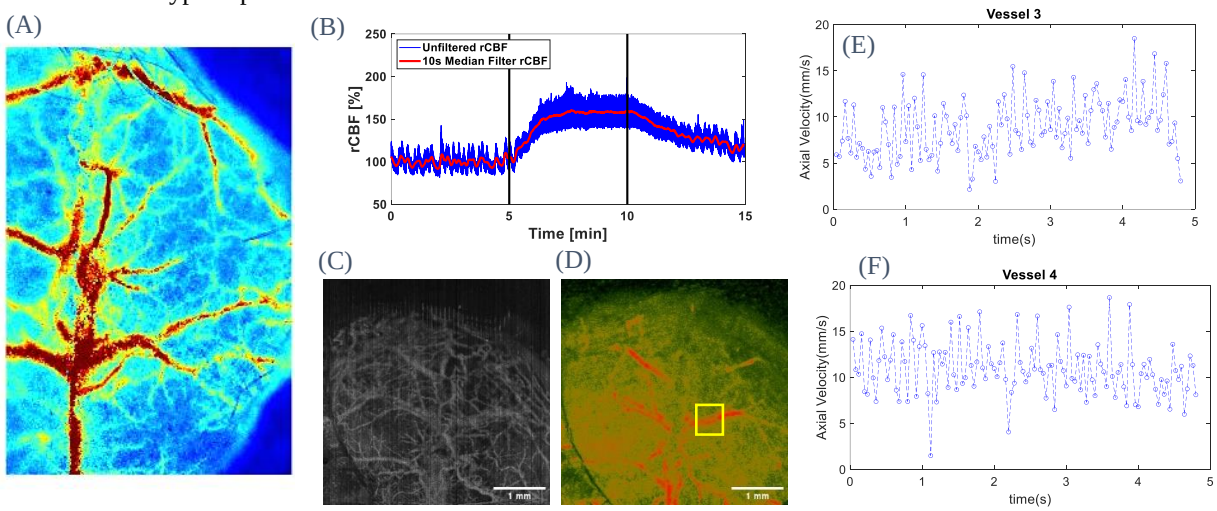

Fig.2 (A) CBF map from LSI; (B) relative CBF time course measured with LSI during hypercapnia; (C) OCTA (D) projection image of phase resolved OCT under hypercapnia condition. Actual axial velocity trend under (E) room air and (F) hypercapnia conditions.

4. Conclusion

In this study, we developed an integration of OCT and LSI. LSI offers high-speed imaging over a large field of view, while OCT provides quantitative flow velocities and detailed microvascular maps. With help of this OCT-LSI system, we are able to better understand hypercapnia-induced cerebrovascular changes. This may have important broader implications in neuroscience research and clinical applications.

5. References

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