Visualization of Regional Cerebral Blood Flow Dynamics during Cortical Venous Occlusion using Laser Speckle Contrast Imaging in a Rat Model

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Background: Cerebral venous ischemia (CVI) is a rare but potentially significant complication of neurosurgical procedures. However, it is still unclear how cerebral venous occlusion (VO) affects regional cerebral blood flow (rCBF) dynamics. To elucidate its pathophysiology in detail, we examined the real-time perfusion dynamics during adjacent vein occlusions using laser speckle contrast imaging (LSCI) in a rat 2-vein occlusion model. *Methods:* Two cortical veins were occluded photochemically using rose Bengal dye in 6 male Wistar rats; rCBF was measured in real time with an LSCI before and after VO. Regions of interest were defined between the 2 veins (A) and on the opposite side of the first occluded vein (B) on semiquantitative pseudocolor images for off-line analysis. Histopathologic evaluation was performed 3 days after the procedure to assess the extent of infarction. *Results:* LSCI revealed a stepwise reduction in CBF, with a sudden decrease just after the first vein occlusion (∼20%) and a further decrease after the second (∼30%). Significant differences were observed between rCBF dynamics within regions of interest A and B ($P = .0004$). All rats exhibited infarcts in the superficial cerebral cortex histopathologically. *Conclusions:* This is the first report of LSCI specifically applied to the study of CVI. The extensive real-time measurement with high temporal and spatial resolution revealed the stepwise reduction in rCBF during sequential VO and the ensuing infarcts. **Key Words:** CBF dynamics—cerebral ischemia—cerebral venous ischemia—regional cerebral blood flow—laser speckle contrast imaging—cortical infarction.

Introduction

Cerebral venous ischemia (CVI) is a rare cause of cerebral stroke that differs substantially in mechanism and outcome from cerebral arterial ischemia but potentially a significant complication of neurosurgical procedures. Recently, there has been considerable interest in CVI because of the increasing number of neurosurgical procedures for elderly patients and the development of skull base neurosurgery.[1] Injury to cortical and bridging veins during surgery has been linked to poor clinical

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outcomes.[1] In such cases, cerebrovascular insufficiency can occur with a reduction of regional cerebral blood flow (rCBF). Although the pathophysiological mechanism of CVI has been examined experimentally,[2–5] a consensus is yet to be reached and the details are still unclear.

Laser speckle contrast imaging (LSCI) is widely used to measure rCBF in real time.[6] A number of recent technical advances have further improved the quantitative accuracy and temporal resolution of LSCI.[7] Moreover, LSCI offers a method for rCBF measurements over a larger field, which may reveal unexpected changes distal to the occlusion site.

To elucidate the pathophysiology of CVI in detail, we used LSCI to evaluate rCBF dynamics during photochemically induced cortical venous occlusion (VO) in rats (2-vein occlusion [2-VO] model).[8]

Materials and Methods

All experimental protocols were approved by the Animal Welfare Committee of Nara Medical University (Kashihara, Nara, Japan). Six male Wistar rats (CLEA Japan, Inc., Osaka, Japan) weighing 245 to 275 g were used in the study. The rats were housed and maintained on a 12-hour light-dark cycle with free access to food and water.

Surgical Procedures

The rats were anesthetized by intraperitoneal injection of chloral hydrate (36 mg/100 g bodyweight) after premedication with .5 mg atropine sulfate. The anesthesia was maintained by hourly administration of chloral hydrate (12 mg/100 g bodyweight) through a peritoneal catheter. All rats were intubated with silicon tubing (outer diameter, 2.5 mm) and mechanically ventilated (model 683; Harvard Apparatus, Holliston, Massachusetts). Body temperature was maintained at 37°C by a rectal thermometer and feedback heating pad (CMA 150; Carnegie Medicine AB, Stockholm, Sweden). Polyethylene catheters were inserted into the tail artery and right femoral vein. The arterial line was used for continuous monitoring of mean arterial blood pressure and arterial blood gas sampling, and the venous line was used to administer drugs. The PaO_2, $PaCO_2$, and arterial pH were measured with a blood gas analyzer (ABL 330; Radiometer Ltd, Copenhagen, Denmark), and blood pressure was continuously monitored through an intra-arterial catheter connected to a pressure transducer (Polygraph System RM-600; Nihon Koden, Tokyo, Japan). Each rat was mounted in a stereotactic frame (SR-6; Narishige Inc., Tokyo, Japan), and a left parietal cranial window was prepared using a high-speed drill to access the brain surface. The entire procedure was performed under an operating microscope (Carl Zeiss, Oberkochen, Germany). During craniectomy, the drill tip was cooled continuously with physiological saline to avoid thermal injury to the cerebral cortex. The dura was left intact.

Measurement of rCBF Dynamics during 2-Vein Occlusion

The left parietal cortex was visible through the dura matter, and rCBF was measured as earlier mentioned following the method described by Dusch et al.[9] A full-field laser perfusion imager (FLPI; Moor Instruments Ltd, Axminster, United Kingdom) was mounted perpendicular to and 25 cm from the dural surface, and the image focus was adjusted to cover the entire cranial window (Fig 1). During FLPI, 2 adjacent cortical veins were

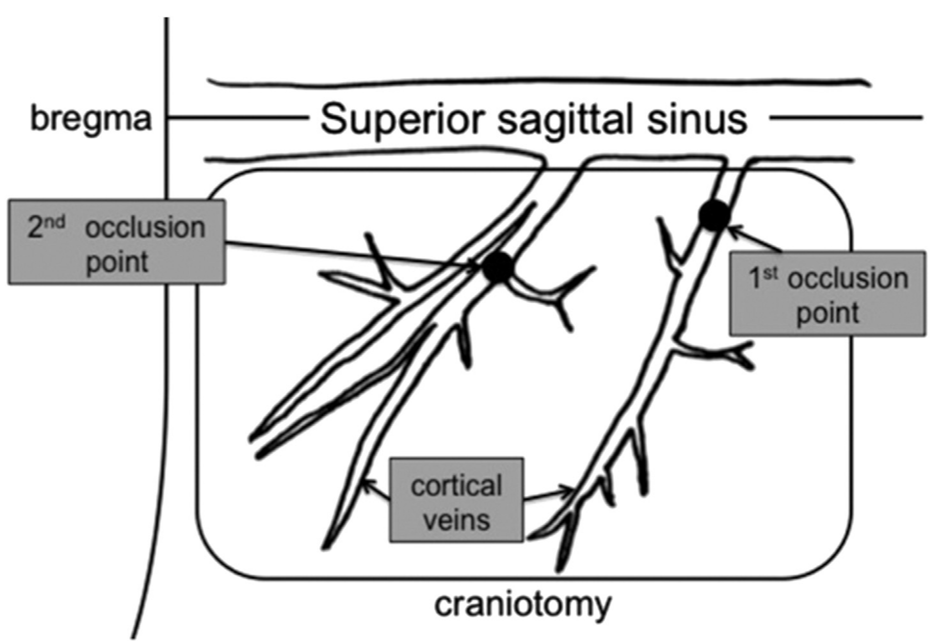

Figure 1. *Schematic drawing of rat superficial cortical vasculature showing the 2-vein occlusion model. A left parietal cranial window was made, and 2 adjacent cortical veins were photochemically occluded in series.*