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Abstract. Cerebral blood flow (CBF) is critical for the maintenance of cerebral function by guaranteed constant oxygen and glucose supply to brain. Collateral channels (CCs) are recruited to provide alternatives to CBF to ischemic regions once the primary vessel is occluded during ischemic stroke. However, the knowledge of the relationship between dynamic evolution of collateral flow and the distribution of regional blood flow remains limited. In this study, laser speckle imaging was used to assess dynamic changes of CCs and regional blood flow in a rat cortex with permanent middle cerebral artery occlusion (MCAo). We found that CCs immediately provided blood flow to ischemic territories after MCAo. More importantly, there were three kinds of dynamic changes of CCs during acute stroke: persistent CC, impermanent CC, and transient CC, respectively, related to different distributions of regional blood flow. Although there was the possible occurrence of peri-infarct depolarization (PID) during ischemia, there was no obvious significance about the onset time and duration of CCs between rats with and without PID. These results suggest that the initial arising of CCs does not ensure their persistence, and that collateral flow could be varied with distribution of regional blood flow in acute ischemic stroke, which may facilitate the understanding of collateral recruitment and promote the development of collateral therapeutics in the future. [DOI: 10.1117/1.JBO.17.12.125001]

Keywords: brain ischemia; brain imaging; optical imaging; cerebral blood flow; animal model; acute stroke.

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1 Introduction

Cerebral function needs a constant oxygen and glucose supply. Thus the regulation of cerebral blood flow (CBF) is critical for the maintenance of brain function. Inadequate blood flow will contribute to focal cerebral ischemia, possibly resulting in ischemic stroke.[1,2]

Collateral channels (CCs) can be immediately recruited to provide alternatives to CBF to an ischemic region once the principal supplying artery is occluded during ischemic stroke.[3,4] Collateral circulation plays an important role in ischemic stroke pathophysiology,[5,6] and its importance has been acknowledged for several years.[3,6,7] Direct collateral therapeutics have been developed but are largely untested or unproven clinically. Current clinical interventions for acute ischemic stroke still concentrate on vessel recanalization or penumbral neuroprotection. Therapeutics approaches with consideration for collateral circulation have been limited by the knowledge of the underlying process of collateral recruitment. To obtain richer understanding of collateral circulation, the refinement of current approaches will have to be required for the improved characterization of collaterals and details of collateral pathophysiology, collateral anatomy, and so on.[3] Improved characterization of collaterals in stroke may rely on the advance of noninvasive neruoimaging modalities with better spatial and temporal resolution to overcome some limitations in previous studies.[6,8]

Recently, a technique of laser speckle contrast imaging (LSCI)[9–13] with high spatial and temporal resolution has been introduced to continuously define dynamic evolution of CCs in ischemic rat cortex after mini-stroke[8] and middle cerebral artery occlusion (MCAo) models.[14] It has been reported that persistent and dynamic collaterals were recruited after vessel occlusion for 24 h in MCAo rats without reperfusion.[14] That is to say, the initial arising of CCs does not promise their persistence. Researchers suppose that hemodynamic fluctuations may influence the endurance of collaterals, possibly threatening CBF,[6] which suggests that there may be a relationship between dynamic evolution of collateral flow and the distribution of regional blood flow, deciding the fate of ischemic brain tissue. However, direct experimental evidence has not been reported. In this study, we used LSCI with high spatiotemporal resolution to map dynamic changes of CCs and regional blood flow and examine the relationship between them after MCAo. Insight may be gleaned from subtle details of this study, so that specific collateral therapeutics may be realized in the future.

2 Materials and Methods

2.1 *Animal Preparation*

Ten male Sprague-Dawley rats weighing between 250 and 300 g were used in experiments. Animal care and experimental procedures conform to the guidelines established by the Committee

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for the Care and Use of Laboratory Animals at Huazhong University of Science and Technology.

Rats were anesthetized with a mixture of α-chloralose (50 mg/kg) and urethane (600 mg/kg) and were maintained in a state unresponsive to toe pinching by supplements of one-third of an initial dose. Their body temperature was kept constant at 37.0 ± 0.5°C with a feedback-controlled heating pad. Arterial blood pressure, pH, pCO_2, and pO_2 were monitored, and all of them were maintained within normal limits throughout the experiments. Each rat head was fixed in a stereotaxic apparatus. A longitudinal incision was made along the midline overhead. The skull bone over right parietal cortex was removed with a high-speed dental drill (Fine Science Tools) under constant saline and cooled, and then a 6.6mm × 9.0mm (medial-lateral extent by anterior-posterior extent, starting about 1 mm lateral to the midline) cranial window was formed with dura intact. This window was large enough to study the changes of CCs and CBF in the rat cortex related to MCAo. The cranial window was bathed with normal saline at 37.0 ± 0.5°C.

2.2 *Middle Cerebral Artery Occlusion*

Permanent focal cerebral ischemia was induced using the method of intraluminal suture middle cerebral artery occlusion.[15] In brief, a 1.5 cm longitudinal incision was made along the midline of ventral cervical skin. The right carotid artery tree was isolated, and the distal portion of the external carotid artery (ECA) was ligated. A smooth monofilament nylon thread (0.20 mm diameter), which had been coated with lysine, was inserted from the lumen of right common carotid artery (CCA) into right internal carotid artery (ICA), with an advanced length about 20 mm from the bifurcation of CCA until it reached at least the origin of the MCA.

2.3 *Laser Speckle Contrast Imaging*

Laser speckle contrast imaging (LSCI) was performed as described.[16] The cranial window was illuminated by a 660-nm laser diode in a continuous illumination mode. Raw speckle images (20 ms exposure time) were captured continuously by 12-bit charge coupled device (CCD) cameras (1024 × 1392 pixels, 2 × 2 binning, Pixelfly QE, PCO Computer Optics, Germany) attached to a stereomicroscope (Olympus SZX12 Zoom, Japan).

To get blood velocity images of high quality, laser speckle temporal contrast analysis (LSTCA) rather than laser speckle spatial contrast analysis (LSSCA) was used.[17] Speckle contrast factor K in LSTCA was calculated according to the following formula:

$$K_t(x,y) = \frac{\sqrt{\frac{1}{N-1}\sum_{n=1}^{N}\left(I_{x,y}(n) - \bar{I}_{x,y}\right)^2}}{\bar{I}_{x,y}}, \qquad (1)$$

where $I_{x,y}(n)$ is CCD counts at pixel (x, y) in the nth laser speckle image, N is the number of frames, and $\bar{I}_{x,y}$ is the mean value of CCD counts at pixel (x, y) over N images.

In our study, a frame of blood velocity image was obtained online by computing the speckle contrast of 100 consecutive raw speckle images by LSTCA based on a graphics processing unit.[18] We stored blood velocity images rather than raw speckle images to reduce whole data volume. Higher values in blood velocity images represented higher levels of blood velocity, and vice versa. The image acquisition commenced before the procedure of vascular occlusion (as a baseline) and continued immediately after MCAo for 180 min at intervals of 1 min. Relative change in CBF (rCBF) at each time in a region was expressed as percent change from its baseline.

2.4 *Measurements of Infarct by TTC Staining*

After optical imaging, rats were allowed to survive after ischemia for 1 h. Before sacrifice, they were deeply reanesthetized. The whole brains were quickly removed from the cranial cavity, sectioned into 3-mm-thick fresh slices in the coronal plane, and incubated in 0.5% 2,3,5-triphenyltetrazolium chloride (TTC) solution at 37°C for assessment of mitochondrial dehydrogenase activity. After 30 min, the coronal sections were viewed with a digital camera. In active tissues, colorless TTC is induced to red triphenyl formazan because of the dehydrogenase activity of the mitochondrial respiratory chain, while in infarct tissues, it is unstained by TTC. Therefore, it was regarded that TTC-stained tissue was viable and TTC-unstained brain tissue was infarct.

3 Results

All physiologic parameters were monitored within normal physiologic range during experiments: mean arterial blood pressure $= 98 \pm 11$ mmHg, $pO_2 = 145.3 \pm 14$ mmHg, $pCO_2 = 37.2 \pm 4.1$ mmHg, and $pH = 7.4 \pm 0.1$.

3.1 *Distribution of CBF Before and After Ischemia*

A blood velocity image over the parietal cortex before and after permanent MCAo was obtained by LSCI, and a representative result is shown in Fig. 1. In these images (pseudo color except the first one of the top row), regions with a higher level of blood flow are highlighted in red, whereas regions with lower velocity of blood flow are highlighted in blue. According to these, the CBF in rat cortex slightly decreased at 15 min after MCAo. Then, at 30 min after MCAo, there was a small region close to the lateral parietal cortex with very low blood flow velocity, shown as a dark blue area in Fig. 1. The size of this region increased with time during the first 3 h of ischemia, suggesting that the region with very low blood perfusion expanded with ischemic time.

3.2 *Dynamic Patterns of Collateral Channels after Stroke*

Before the occlusion of MCA, CC is difficult to identify because of low blood flow. However, after induced stroke in a representative experiment, these collaterals could be immediately recruited at 15 min after MCAo as shown in Fig. 1. More importantly, there were three kinds of dynamic changes of blood flow in these collaterals during the first 3 h of ischemia: persistent CC, impermanent CC, and transient CC. In persistent CC the collateral channel was initially patent after MCAo and persisted until the end of experiments (such as CC1 and CC4 in Fig. 1). In transient CC, the collateral could be also determined immediately after stroke, but it drastically disappeared after a short period and its duration was less than 90 min (for example, CC3 in Fig. 1). In impermanent CC, the collateral disappeared a bit later than that of the transient CC, and its duration was between 90 and 150 min (such as CC2 in Fig. 1).

Furthermore, we registered the blood flow image with a rigid body transform and a B-spline interpolator[19] to overcome the slight translation of rat skulls during LSCI imaging. Thus,

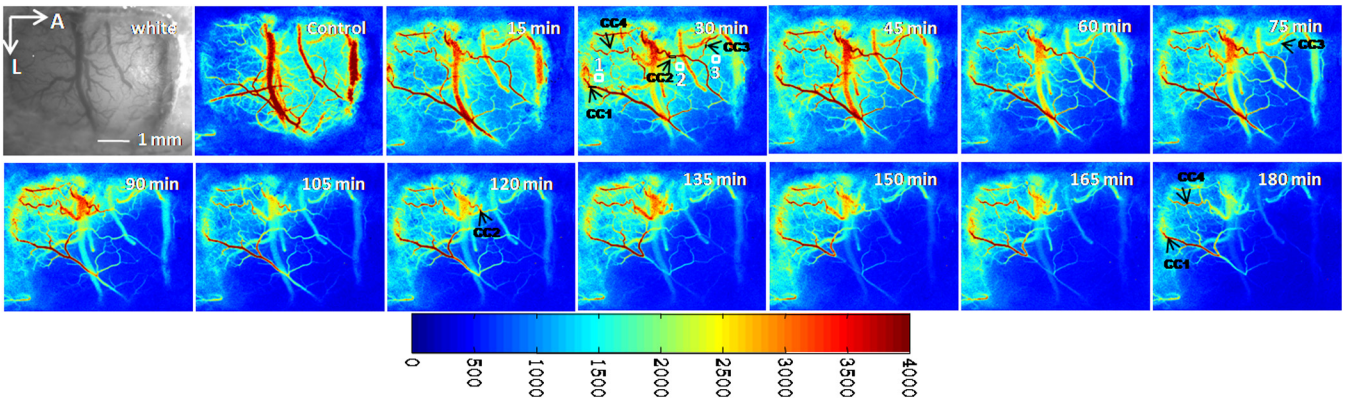

Fig. 1 Spatiotemporal evolution of the distribution of cerebral blood flow (CBF) in ischemic cortex by laser speckle contrast imaging (LSCI). After middle cerebral artery occlusion (MCAo), the region with low blood perfusion (blue-highlighted area) increased with time. There were dynamic changes in the blood flow of collateral channels (CCs). Some of them were persistent (CC1 and CC4); others disappeared with different durations (CC2 and CC3) (A, anterior; L, lateral).

more detail about the dynamic collaterals after MCAo was obtained. Four regions were selected, and each of them, respectively contained CCs described above. The sizes of the four regions were 60×61 pixels (including CC1), 56×69 pixels (including CC2), 58×66 pixels (including CC3), and 55×57 pixels (including CC4).

As shown in Fig. 2, there were two additional small collaterals (indicated by arrows) in the region, including CC3 at 15 min after MCAo, that were not obvious before MCAo (see control). Nevertheless, they did not persist and disappeared entirely at 90 min after MCAo. Similarly, two smaller collaterals were obviously recruited at 30 min post-stroke in the region containing CC2, but these collaterals were difficult to define at 165 min after stroke.

There were also two extra little collaterals in the region with CC4, and a tiny collateral channel in the region including CC1 at 30 min post-stroke (depicted in Fig. 3). The collaterals in both of regions persisted for the first 3 h of ischemia, and they did not vanish, distinct from those in Fig. 2.

3.3 *Dynamic Changes of Collateral Circulation in the Brain Area with Different Blood Perfusion after Stroke*

The ischemic infarct core always becomes stable after 2 to 3 h post-stroke.[20] Blood velocity images at 90, 150, and 180 min after stroke were superimposed on a blood velocity image at 15 min post-stroke that is the earliest image obtained after MCAo, and obvious CCs had been recruited at that time (see Figs. 1 and 4). Then ischemic threshold maps at 90, 150, and 180 min were obtained. Typical results in this study are shown in Fig. 4(a). In ischemic threshold maps, a red area

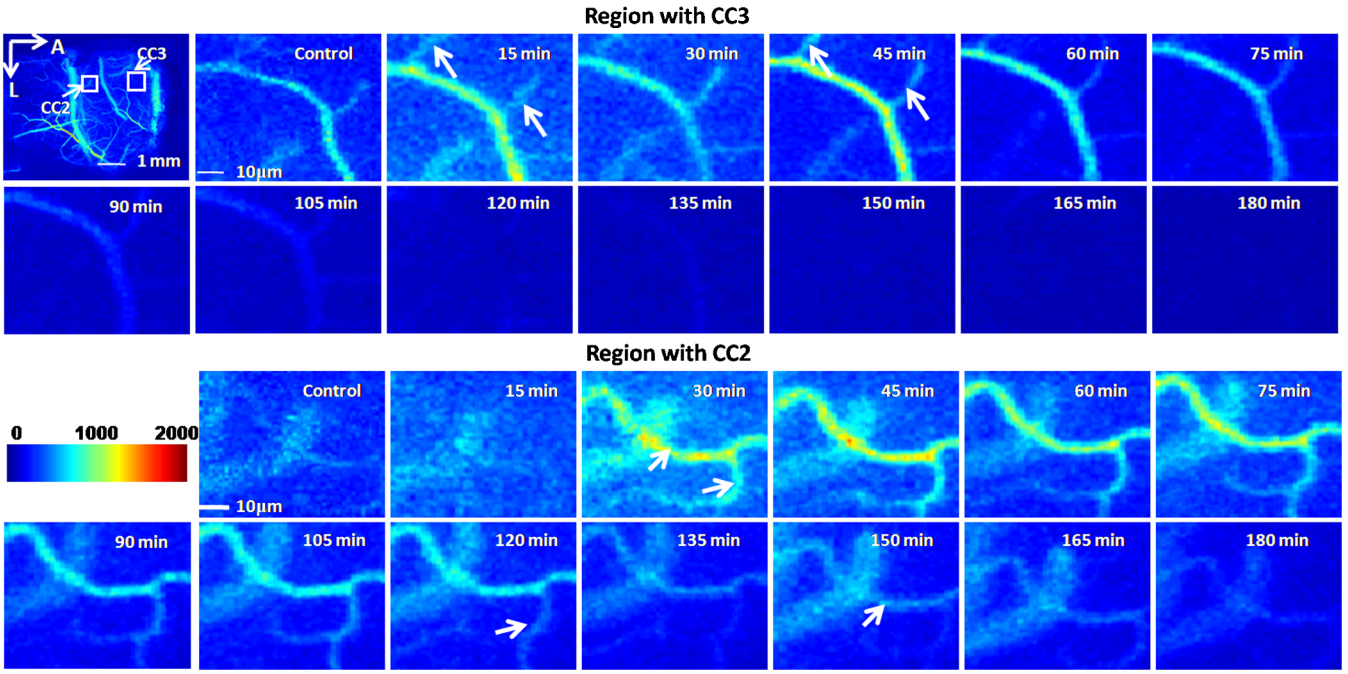

Fig. 2 Spatiotemporal evolution of CBF in unsustainable collateral channel. There were two additional small collaterals (indicated by arrows) in the regions including CC3 and CC2 at 15 min immediately after MCAo, but the collaterals in the region including CC2 disappeared a bit later than those in the region including CC3 (A, anterior; L, lateral).

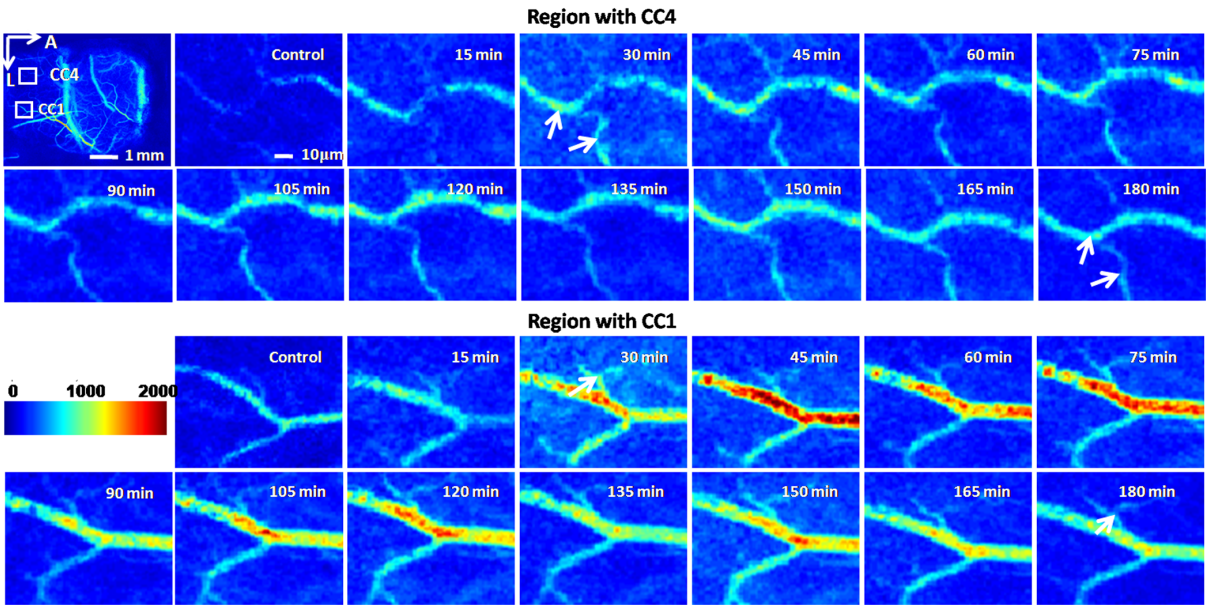

Fig. 3 Spatiotemporal evolution of CBF in persistent collaterals. The collaterals immediately recruited after stroke persisted in the regions including CC1 and CC4 (A, anterior; L, lateral).

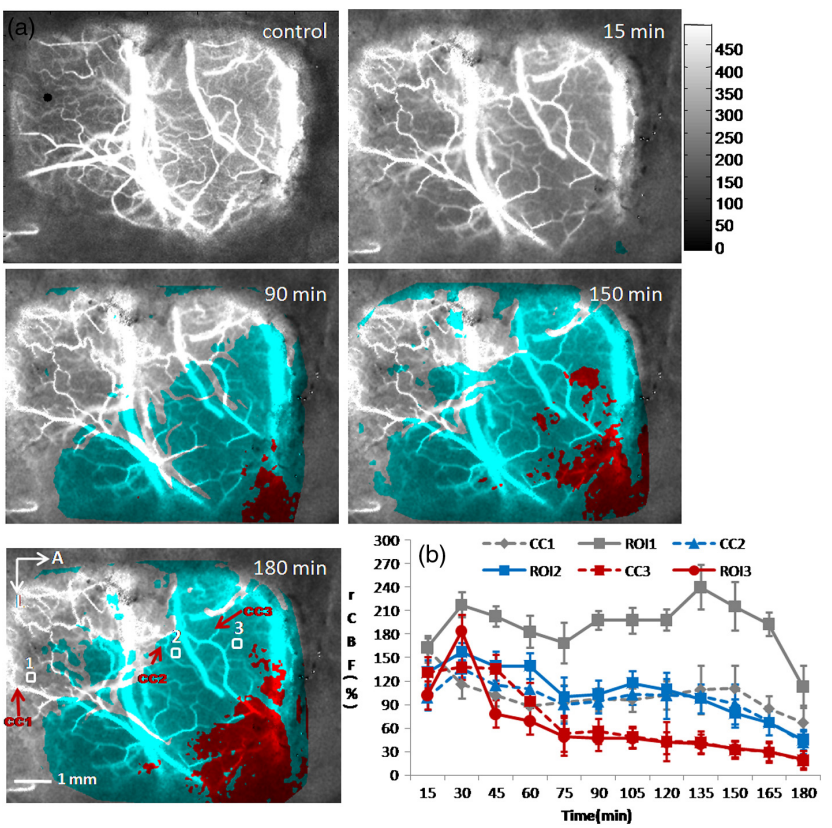

Fig. 4 (a) CBF maps before (control) and 15 min after MCAo, and ischemic threshold maps at 90, 150, and 180 min in representative experiments. Before MCAo, CCs are difficult to identify, but they could be immediately recruited at 15 min after MCAo. In ischemic threshold maps, the red area represents the threshold of rCBF (less than 20%, infarct core), the threshold of rCBF in the blue area was between 20% and 60% (ischemic penumbra), and the threshold of rCBF in the remaining area was above 60% (normal region). No CCs can be identified in the ischemic core, but obvious CCs can be observed in normal and penumbra areas. Also indicated is the expanding of areas with different rCBF values during the first 3 h of ischemia. Typical collaterals and the region close to each CC were selected. (b) Time courses of rCBF for the three kinds of typical CC and each ROI close to CC after stroke. The variation tendency of rCBF in each CC was similar to that of the ROI close to CC (A, anterior; L, lateral).

represents the threshold of rCBF less than 20%, the threshold of rCBF in the blue area was between 20% and 60%, and the threshold of rCBF was higher than 60% in the remaining area [Fig. 4(a)]. According to Ref. 21, these three areas, respectively belong to ischemic core (red), penumbra (blue), and normal area.

No CC can be determined in the ischemic core after permanent MCAo. But rats exhibited the patency of collateral connections in penumbra and normal area. Also in Fig. 4(a) is found the expanding of areas with different rCBFs during the first 3 h of ischemia. A representative CC was selected in penumbra (blue) and normal areas in Fig. 4(a), a subregion in each CC was chosen, and this subregion was always as close to the bifurcations of CC as possible. Relative changes in CBF at each time in this subregion of CC were expressed as percent change from baseline. The same process as described above was done in each experiment (including six rats). Statistical analysis was then performed on this dataset, consisting of six samples for each CC at each time point. The relative changes in CBF at each of the CCs were obtained by averaging over six samples, yielding three curves for the time courses of relative changes in CBF for the three CCs in three areas with different blood perfusion [see Fig. 4(b)].

From Fig. 4(b), the rCBF of CC1 in the normal area had some fluctuation over 180-min periods, ranging from 160% to 80% of the baseline from 30 to 165 min after stroke, and then declined to 66% at 180 min post-ischemia, which is always defined as the end of experiments. However, the rCBF of CC3 in the penumbra area was significantly different from other two CCs in Fig. 4(a). First, it increased from 130% at 15 min to 135% at 45 min after MCAo, then sharply decreased to below 60% at 75 min, and finally was less than 20% and difficult to define. As for CC2 in penumbra area, its rCBF change was always over 90% from 30 to 150 min after stroke, then it declined to 41% at 180 min post-ischemia.

3.4 *Relative Changes of CBF in Parenchyma Close to Collateral Channel with Different Dynamic Pattern after Stroke*

To investigate the relationship between dynamic collaterals and the blood perfusion of parenchyma in rat cortex after ischemia, probably hinting the influence of dynamic collateral flow on the fate of tissue in acute ischemic stroke, three regions of interest (ROIs) were selected and are shown in Figs. 1 and 4 by ROIs 1, 2, and 3. Their size was very small (about 15×15 pixels) and much closer to CC1, CC2, and CC3, respectively. Relative changes in CBF at each time in each ROI were expressed as percent change from baseline. The same process as described above was done in six experimental rats. Statistical analysis was performed, and the time courses of changes of rCBF in each ROI were also calculated, shown in Fig. 4(b). It was depicted that the rCBF in the ROI1 (neighbor to persistent CC1) was always higher than that of baseline after ischemia (Figs. 1 and 4). The maximum and minimum rCBF values were 240% and 113% of baseline, respectively; that is, the supply of blood flow in this region was kept normal or even hyperperfused; the decline of rCBF in ROI3, nearby transient CC3, was the most significant among these three ROIs. Its rCBF declined to 49% of baseline at 75 min post-stroke. At that time, CC3 was hard to define due to its rCBF drop. The rCBF in ROI3 was between 20% and 30% of baseline at 180 min after stroke (Figs. 1 and 4); the collateral close to ROI2 was impermanent CC2 (Figs. 1 and 4), which disappeared a bit later than CC3. The rCBF in ROI2 was increased briefly followed by a gradual decrease: between 157% and 103% of baseline from 15 min to 120 min post-stroke, over 60% between 135 and 165 min, and a gradual decline to 45% at the end of experiments.

3.5 *Collateral Channels in Rats with or without Peri-infarct Depolarization*

Among 10 experimental rats, all were successfully induced with permanent focal cerebral ischemia. Four rats did not have significant collaterals, so there were CCs recruited in six rats after stroke. We found that rats without significant collaterals were always accompanied with sharp decreases of CBF after MCAo and usually were dead due to severe brain ischemia before the end of experiments. Therefore the data from these rats were excluded. Among experimental ischemic stroke models, the intraluminal suture MCAO is the most frequently used,[22] but a range in infarct volumes is one of its disadvantages. This range was from around 5% to 50% of ipsilateral cerebral hemisphere.[23] We suppose that a more likely cause of this range was that the permanent MCAo model was induced by the same monofilament nylon thread (0.20 mm in diameter), but rats used in the experiments varied between 250 and 300 g and could have had different sizes of MCA (rats with the same weight may have anatomic differences). These may contribute to the different decreases of CBF after MCAo. Of course, we couldn't exclude the effect of subarachnoid hemorrhage, anaesthetic overdose, and so on.

Among six rats with recruited CCs, three had PID during brain ischemia. The onset time and duration of collaterals were analyzed statistically in penumbra ($20\% \leq \text{rCBF} < 60\%$, with two regions) and normal area ($\text{rCBF} \geq 60\%$ with one region) of these six rats. The total of collaterals (major ACA-MCA anastomoses) was 36, and among them, 10 (28%) were persistent; most collaterals failed within 3 h. This result was different from that reported by Armitage et al.[24] The likely reason is that the ischemia induced by the suture MCAo stroke model used in this study is more severe and less variable than that of the embolic MCAo model[25] used in the Armitage et al. study,[24] although the latter model closely mimics human stroke.[23] The focused time points after MCAo (the first 3 h with 15-min intervals) in this study were also distinguished from those of the Armitage et al. experiment,[24] which was focused on three time points: before and immediately after MCAo as well as 24 h after MCAo. Some dynamic CCs may be neglected between those later two time points.

In this study, we defined larger ACA-MCA anastomoses based on vessel anatomy in rat cortex and whether they can be easily observed in a blood velocity image after stroke. Although we can register the blood flow image with a rigid body transform and a B-spline interpolator to qualitatively describe relatively small collaterals, we cannot provide the statistic and quantitative analysis on smaller collaterals owing to a lack of objective and fair evaluation on which collaterals are smaller, which may be performed in a future study. Most collaterals immediately arose within 15 to 30 min post-ischemia in penumbra and normal areas. There was no obvious significance about the collateral onset time between the two areas based on data analysis with t-test ($P > 0.05$) [Fig. 5(a)], whether with or without PID. The duration of collaterals in the normal region was almost more than 150 min, but in penumbra, the duration

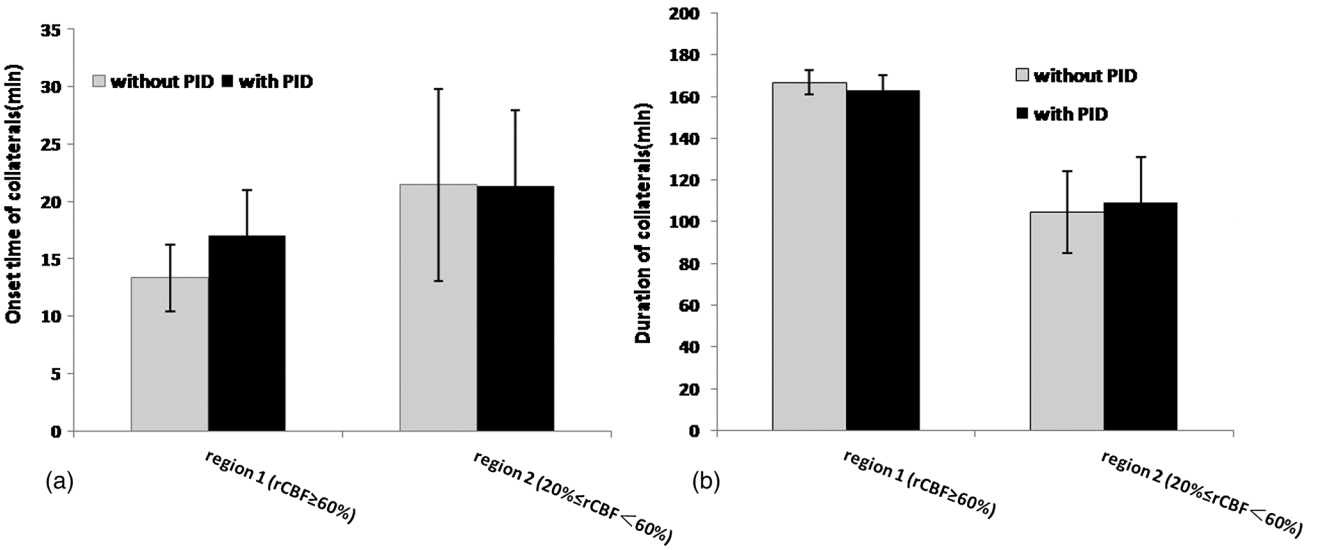

Fig. 5 The onset time and duration of collaterals in normal and penumbra areas with or without peri-infarct depolarization (PID). There was no obvious significance of the onset time of collaterals between normal region (rCBF > 60%) and penumbra (20% ≤ rCBF < 60%), with or without PID ($P > 0.05$) (a). Obvious significance on the duration of collaterals between normal and penumbra areas was found. However, the duration of collaterals in the same region between rats with and without PID was not significantly different ($P > 0.05$) (b).

Fig. 6 Ischemic infarct in brain was assessed by 2,3,5-triphenyltetrazolium chloride (TTC) staining. Rats had large infarcts (white area) incorporating a striatum as well as primary and secondary somatosensory cortices after MCAo.

of collaterals was less than 120 min. Obvious statistical significance on the duration of CCs was obtained between the normal and penumbra regions by *t*-test analysis ($P > 0.05$) [Fig. 5(b)]. However, the duration of collaterals in the same region between rats with and without PID was not significantly different ($P > 0.05$) [Fig. 5(b)].

3.6 *Infarct after Stroke*

The results from the brain tissue stained with TTC showed that infarcts were induced in MCAo rats. A representative TTC staining from a rat 4 h after MCAo showed ischemic infarcts (shown in Fig. 6). Rats had large infarcts (white area) incorporating striatum as well as primary and secondary somatosensory cortices after MCAo onset.

4 Discussion

Collateral circulation not only defines the extent of ischemic penumbra[3] but also is an independent predictor of final infarct volume after ischemic stroke.[7] The fate of ischemic brain tissue is determined by the distribution of regional blood flow. Yet data remain sparse about what is the relationship between dynamic collateral flow and distribution of regional blood flow in acute ischemic rat cortex.

Laser speckle imaging has been widely used to describe relative changes in blood flow.[16,26–29] In this study, LSCI permitted high-resolution mapping of MCAo-induced dynamic collaterals and relative changes of CBF in cortical parenchyma to assess the relationship between the collateral flow and the distribution of regional blood flow in MCAo rat.

We found that the region with very low blood perfusion was expanded with time after stroke by LSCI. No recruited collateral channels can be defined in the ischemic core (with rCBF < 20%) in rat cortex, but they were patent immediately after MCAo in the normal and penumbra areas, and provided alternative blood flow to ischemic territories. More interestingly, the incipient recruitment of collaterals does not guarantee their persistence. These collaterals were dynamic, with three kinds of patterns, persistent CC, impermanent CC, and transient CC. The persistent CC was related to normal area, and the impermanent and transient ones were related to penumbrae with moderate and serious ischemia. Although Armitage et al.[24] have reported persistent and dynamic collaterals between ACA and MCA in MCAo rat without reperfusion, our possible findings of increased collateral dynamics relative to previous work was described as follows. One difference is the focused time point in the two experiments. Armitage et al.[24] focused on three time points: before and immediately after MCAo as

well as 24 h after MCAo. However, the observed time window in our study is before MCAo and during the first 3 h of ischemia. That is to say, we focused on the dynamic changes of collaterals over 3 h during acute ischemia. Reestablishment of perfusion after 3 h does not reduce infarct size in all animal models, and the first 3 h of ischemia is important for the clinic therapy in stroke patients.[30] The other difference is the key things to be observed. Armitage et al.[24] mainly presented the persistence and dynamics of larger anastamotic connections between ACA and MCA, whereas our study not only paid attention to the dynamics of larger collaterals between ACA and MCA, but also stressed the dynamic changes of smaller CCs among branches of MCA.

Although PID possibly occur during cerebral ischemia, its impact on collateral flow was not very significant. Therefore, dynamic change of collateral flow might be varied with different distribution of regional blood flow in the acute ischemic rat cortex.

CCs (including primary and secondary collaterals) stabilize CBF in cerebral ischemia when principal conduits fail.[6] Primary collaterals provide immediate diversion of blood flow to ischemic regions through existing anastomoses. Secondary collaterals such as leptomeningeal anastomoses, which require time to develop, are presumed to be recruited once primary collaterals at the circle of Willis have failed.[6] The capacity of these leptomeningeal anastomoses is a critical determination of the volume and severity of focal ischemic injury.[31,32] That is to say, as leptomeningeal anastomoses, which interconnect the distal branches of the cortical vessels, are anatomically present, they could mainly determine the dynamic influence of collaterals on CBF in ischemic rat cortex.

Improving blood flow to the ischemic tissue is one of the primary functions of the collaterals.[6] In this study, it was found that the supply of CBF in a region neighboring persistent collaterals was almost normal. That is partly because the persistent anastomoses could stabilize and offset the supply of blood flow to this region. On the contrary, in the other two regions, although the nearby collaterals were recruited immediately after stroke, the blood supply through them decreased with time and they closed and drastically disappeared. Accordingly, collateral blood supply could not suffice to maintain normal blood perfusion within these two regions, so the regions had gradually declined rCBF. Furthermore, with gradually declined rCBF, alterations in the endothelial cell wall result in leukocyte adherence and platelet rupture,[33] leading to potentially nonreversible intravascular injury within hours.[34] Because of alterations in the blood-brain barrier, cytotoxic edema results in increase in tissue pressure and closure of capillaries.[35,36] At the same time, activated leukocytes interact with the damaged abluminal endothelial wall, leading to plugging of microvasculatures.[35] All these effects lead to the continuous decline of rCBF during ischemia. Therefore, in penumbra zone, a region involved with earlier vanished collaterals showed sharp and significant drops in rCBF, and an area related to lately disappeared collaterals had a slow decline in rCBF. These results suggest that the fate of ischemic rat cortex tissue could be predicated based on the dynamic change of collaterals.

5 Summary

In this study, LSCI was introduced to map dynamic changes of collateral circulation and regional blood flow in rat cortexes. It was found that there were three kinds of dynamic changes in CCs, and different dynamic of collaterals flow could be varied with different distribution of regional blood flow in acute ischemic rat cortexes. These results may facilitate the understanding of collateral recruitment. However, the collateral channel remains largely unappreciated. Further study in the future should be performed for the understanding of the underlying pathophysiology of the collaterals.

Acknowledgments

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