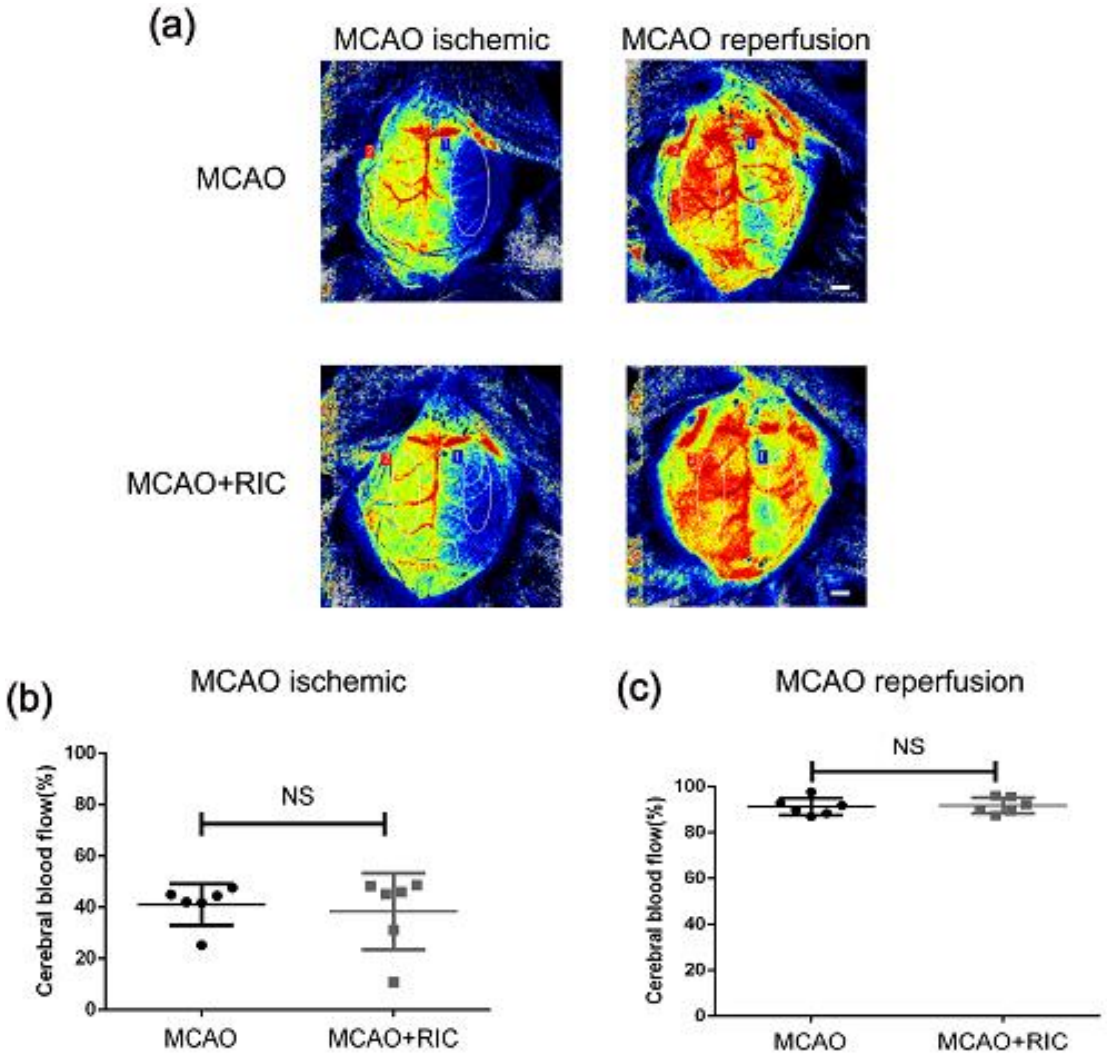
**Supplemental Materials**

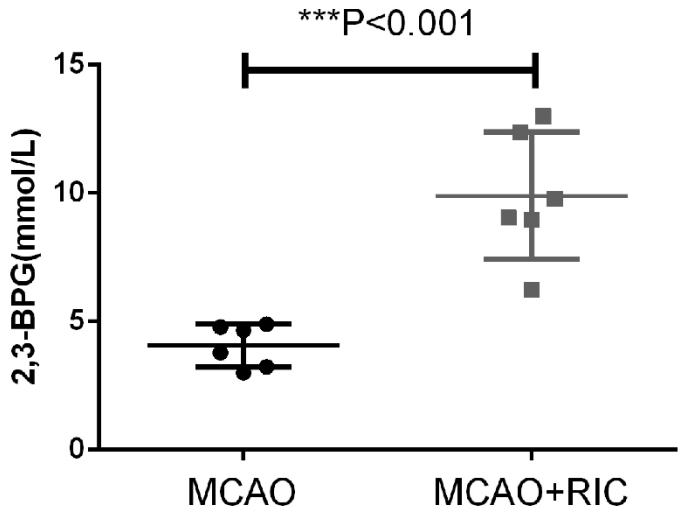
**Supplemental Figure 1**




**Supplemental Figure 1. Changes of cerebral blood flow (CBF) in mice after MCAO and reperfusion after MCAO.** MCAO mice were divided into two groups: MCAO only group (n=6) and MCAO + RIC group (n=6). The cerebral blood flow of all mice was examined 5 min after MCAO, or reperfusion after MCAO by a laser speckle blood flow imaging system (LSF, Perimed, Jarfalla, Sweden). A baseline cerebral blood flow of each mouse was acquired as well before MCAO. The cerebral blood flow in ischemic brain tissue was calculated using the following formula:(cerebral blood flow of ischemic hemisphere/cerebral blood flow of nonischemic hemisphere)/(baseline cerebral blood flow of ischemic hemisphere/baseline

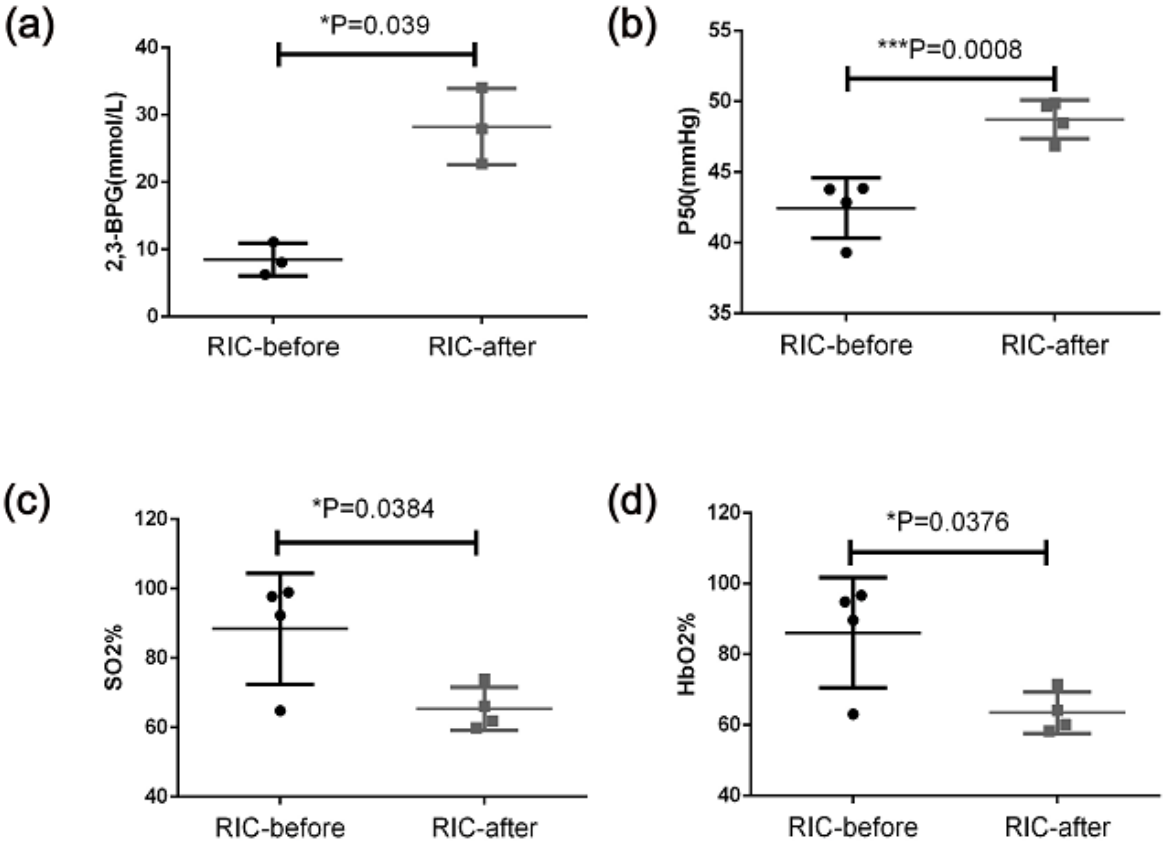
cerebral blood flow of nonischemic hemisphere)x100% (a) Representative imagines of different groups were shown (scale bar, 1 mm). (b) Summarized CBF data of two groups were shown and compared by Student *t* test. No significant difference between the two groups was observed after MCAO, or reperfusion after MCAO. NS: no significant difference.

**Supplemental Figure 2**




**Supplemental Figure 2. Effect of RIC on erythrocyte 2,3-BPG in MCAO mice**. MCAO mice were divided into two groups: MCAO only group (n=6) and MCAO + RIC group (n=6). RIC was performed immediately after MCAO surgery followed by blood collection. The erythrocyte 2,3-BPG were measured. Data of two groups were compared by Student *t* test.

**Supplemental Figure 3.**




**Supplemental Figure 3. Remote ischemic conditioning increases the 2,3-biphosphoglycerate (BPG) level in human RBCs and oxygen $P_{50}$ value, promotes tissue oxygen exchange with reduced SO2 and HbO2 levels in venous blood**. Three to four volunteers participated in this experiment after signing informed consent. RIC was performed bilaterally in the upper limbs of all subjects using a patented electric auto-control device (patent number ZL200820123637X, China) and consisted of five 5-min alternating cycles of inflation and deflation with an inflating pressure of 200 mmHg to temporarily block blood flow to the brachial artery of each upper limb. Blood was collected before and immediately after RIC. The 2,3-BPG level in RBCs and oxygen $P_{50}$ value were measured. The venous $SO_2$ and $HbO_2$ levels were measured before and after RIC. (a), 2,3-BPG levels in RBCs before and after RIC compared using the paired *t*-test (n=3). (b), The $P_{50}$ value measured before and after RIC and compared by the paired *t*-test (n=4). (c), The venous $SO_2$ in before and after RIC compared

using the paired *t*-test. (d) The venous $HbO_2$ before and after RIC compared using the paired *t*-test. The study protocol in humans was approved by the Institutional Review Board of Xuanwu Hospital, Capital Medical University. The volunteers in the study were required to be aged 18–65 years and in good general health. Subjects were excluded if they had a chronic or acute disease, had been taking any medication or supplement for more than 2 weeks, or had a body mass index <18.5 or ≥24. 2,3-BPG, 2,3-biphosphoglycerate; P50, partial pressure of oxygen at 50% oxyhemoglobin saturation; RIC, remote ischemic conditioning; blood $SO_2$, oxygen saturation; $HbO_2$, oxygenated hemoglobin.