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Heterogeneous changes in blood flow in response to single vessel blockages and MCA occlusion in rat parietal cortex as revealed by in vivo two-photon laser imaging

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Background: The microcirculation of blood flow during cerebral stroke is relatively uncharted. We use a new measure of microcirculation and ask if insults to the cerebral vasculature modulate flow and flow reversals in both arterial and venous vascular branches. Methods: The motion of red blood cells (RBCs) in individual vessels within parietal cortex of the urethane anesthetized rat is imaged with two-photon laser microscopy. RBC velocity is quantified for both small and large vessels in response to one of two perturbations. First, to examine the effects of complete blockage of blood flow in a small territory, we create stable thrombotic occlusions by the focal activation of rose bengal in single, targeted vessels. Second, to examine effects of flow reduction in a large territory, we use the filament model of reversible occlusion of the middle cerebral artery (MCA). Results: After photo-induced blockage of flow in single arterioles and veins, every blocked vessel showed nearly instantaneous reestablishment of blood flow in downstream branches distal to the clot (100 % of 15 vessels across 7 rats). In every case, the direction of flow was reversed in one or more of the downstream branches and compensatory flow was established distal to the blockage. After MCA occlusion, the majority of measured vessels showed a stable reduction in speed within the first 30 minutes post-occlusion (87 ± 9 % mean \pm SEM; 5 - 8 vessels per rat across 7 rats). A minority of vessels demonstrated increases in the speed of flow above baseline during the occlusion $(13 \pm 9 \%)$. Of interest, changes in the direction of flow occurred in several types of vessels, i.e., arteries, arterioles and one vein, with an overall incidence of 18 ± 9 %. Upon filament withdrawal, the speed increased in most vessels (85 ± 5 %; 5 - 8 vessels per rat across 6 rats). However, even after 2 hours of re-perfusion the flow in only a fraction $(26 \pm 10\%)$ of these vessels attained or exceeded their baseline values. Conclusions: These data demonstrate that persistent flow reversal occurs prominently and consistently after thrombotic single vessel blockages and can further occur more distally in the compromised vascular tree following MCA occlusion. Further, these reversals are not restricted to the arterial system but also are seen in veins. Author Disclosure Block: B. Friedman, None; N. Nishimura, None; C.B. Schaffer, None; D. Kleinfeld, None; P.D. Lyden, None.

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