New insights into how vascular networks form in fish brains

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How the intricate network of blood vessels forms within the brain has long fascinated biologists. Though the human brain comprises only 2 percent of body weight it receives up to 15 percent of the cardiac output through this network, or vessel vasculature. The vasculature in the human brain consists of a complex branching network of blood vessels, in total some several hundred miles in length. The network is formed so as to distribute blood efficiently to all brain regions, and abnormalities can lead to various neurological disorders, including strokes, learning difficulties and neurodegeneration. Yet our knowledge of just how the brain vasculature develops remains relatively limited.

In this study, published August 14 in the open access journal PLoS Biology, Dr. Jiu-lin Du's research group at the Institute of Neuroscience, the Chinese Academy of Sciences, employed zebrafish as a simple vertebrate animal model and adopted a multi-disciplinary approach. They revealed that the 'vessel pruning' that naturally takes place during development (whereby the vasculature develops its optimum, relatively simplified final form through the disappearance of some vessels) is driven by brain blood flow, via lateral migration of cells that constitute the vessels.

Using high resolution microscopy that allows reconstruction of tridimensional images, the researchers analyzed larval zebrafish during the course of development to examine the exact nature of the pruning. They found that in early development the vasculature in the fish consisted of many loops, and that during development pruning tends to occur at these loop-forming segments—with some 45 percent of early-formed vessel segments pruned during the course of brain development. Comparing pruned and unpruned blood vessels, it was apparent that blood flow decreased in vessels prior to the onset of pruning, and when the researchers artificially blocked blood flow in specific vessels this led to vessel pruning—whereas increasing blood flow inhibited pruning in the vessels concerned. In investigating the molecular mechanisms that regulate this process, they found that vessel pruning was mainly mediated by the expression of Rac1, a protein known to drive migration of the EC cells concerned.

This study in fish brain development provides novel insight into how vessel segments are pruned in the development of the brain's network of blood vessels. The researchers trust it will spark further investigation in vascular research, offering further potential for understanding the importance of the vasculature system in areas such as cancer maintenance and metastasis.

More information: Chen Q, Jiang L, Li C, Hu D, Bu J-w, et al. (2012) Haemodynamics-Driven Developmental Pruning of Brain Vasculature in Zebrafish. *PLoS Biol* 10(8): e1001374. doi:10.1371/journal.pbio.1001374

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