

Research Brief: Mouse Brain Circulatory System Knows No Bounds

9 June 2013. Tiny blood vessels in the mouse brain crisscross the cortex, passing from one neural column to the next, like multiple streets between interconnecting city blocks. This surprising finding, published in the June 9 Nature Neuroscience online, contradicts a long-held hypothesis that blood vessels and neurons form discrete units in the sensory cortex, with few vascular connections between them.

Instead, capillaries from individual brain arterioles intermingle across multiple columns in the barrel cortex, the work suggests. However, neural columns rely heavily on input from the nearest arteriole, explaining why blockages in a single vessel are sufficient to cause mini-strokes. The researchers used a sophisticated imaging technique to map the blood vessels. The method might prove useful to researchers studying the vascular aspects of neurodegeneration and dementia.

Curious about the cartography of brain blood vessels, researchers led by David Kleinfeld, University of California, San Diego, mapped the cortical vasculature in fine detail. Joint first authors Philbert Tsai and Pablo Blinder, now moved to Tel Aviv University in Israel, examined the ins and outs of brain blood vessels in four mice, focusing on the neural columns that control the facial whiskers. Each of these specialized hairs connects to a single neural cluster, neatly segmented from the others. Researchers have thought that the vasculature for each unit might also form neat, walled-off sections, with one arteriole to bring blood in and one venule to drain it out. The new findings refute that assumption.

The researchers imaged the brains using an automated technique developed by Tsai and Kleinfeld. They stained the neurons and filled the blood vessels with a fluorescent gel, then imaged the sample as deeply as possible with light microscopy. After vaporizing the already imaged layer with a laser, they then scanned the tissue again (Tsai et al., 2003). The strategy protects finely sliced tissue samples from damage. By repeating these steps, the researchers built a precise map of the whisker control units. They found the blood vessels ran back and forth across columns in a three-dimensional meshwork. Jeffrey Iliff of Oregon Health and Science University in Portland, who was not involved in the work, called the study “definitive.”

While the vascular map suggests built-in redundancy, Kleinfeld and colleagues calculated that capillaries coming in from neighboring columns would be insufficient to replace blood lost if an arteriole was constricted. Venues would drain away too much blood, leaving the tissue starved of nutrients.

Iliff cautioned that one cannot necessarily extrapolate from this map to predict how neural networks are arranged in primates, including people. In fact, this cartogram only reflects the specific sensory cortex examined, and not other parts of the brain, added Costantino Iadecola of Weill Cornell Medical College in New York, who was not an author in the study. The most important element of the paper is the technique itself, said Iliff, as it could be useful to address many questions. For example, researchers interested in neurodegeneration could map blood vessels as they try to understand how vascular and neural function break down in disease states, Iliff said, and it should be possible to apply Kleinfeld’s methods to larger tissues such as the human brain. Tiny blood vessel blockages are a common element in vascular dementia, Iadecola said, and examining the vasculature in disease models might help scientists understand the relevance of those constrictions.—Amber Dance.

Reference:

Blinder P, Tsai PS, Kaufhold JP, Knutsen PM, Suhl H, Kleinfeld D. The cortical angiome: an interconnected vascular network with noncolumnar patterns of blood flow. Nat Neurosci. 2013 Jun 9.