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Title: Comparison of brain vasculature network characteristics between wild type and Alzheimer’s disease mice using topological metrics

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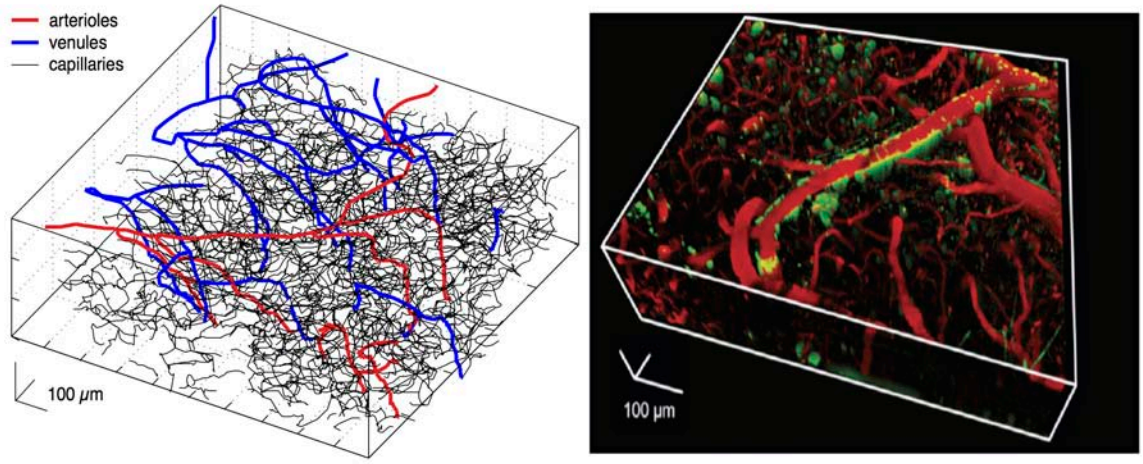
Abstract: There is a strong clinical correlation between Alzheimer’s disease (AD) and microvascular disorders. In mouse models of AD, our lab has found blood flow dysfunction in brain capillaries, suggesting the need to study the function of vascular networks at the capillary level. However, the ability to deliver blood flow continuously to all neurons also depends on connections between vessels, requiring that we also characterize the topology of brain vascular networks. Here, we use graph theory and topological metrics to characterize the connectivity of brain capillary networks in AD and control mice.

We imaged cortical vascular networks using *in vivo* two-photon excited fluorescence microscopy in APP/PS1 (AD) and littermate, wild type (WT) mice (3 mice per group; ~1,100 vessels per mouse; Fig. a). Then, we represented the vascular network using graphs in which individual vessels are defined by the path they take through the tissue and their connections to other vessels (Fig. b).

Two metrics suggested interesting differences between WT and AD mice. The average shortest path length is the mean of the smallest number of vessel segments that joins all pairs of vessel junctions. In AD animals this metric was 10.5 ± 0.6 vessels (mean ± standard deviation), which was just 8% lower ($p = 0.07$, t-Test) than in WT animals (11.4 ± 0.7 vessels). The average clustering measures the tendency of vessels in the network to group together; higher numbers imply that vessels and their neighbors have more connections to each other. In AD animals this metric was 37% ($p=0.09$) lower than WT animals. This metric is related to the redundancy of networks connections, which enables the vascular system to maintain blood supply even with occluded vessels, suggesting that capillary networks in AD mice are less connected and redundant than in WT animals.

In order to study how the brain blood flow is affected during the progression of AD, we developed a novel formalism to compare and describe the differences in the brain capillary vascular networks.



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