Pathophysiology of WMH and Implications for Treatment

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WMH are associated with disease in the small perforating arteries supplying the white matter and deep grey matter nuclei. A variety of arterial changes have been described including focal regions of micro atheroma and more diffuse arterial abnormalities, particularly seen in hypertensive individuals and referred to as lipohyalinosis. It is particularly the latter pathology that has been associated with WMH with focal atheroma more associated with isolated lacunar infarcts.

Hypoperfusion appears to play an important role in pathogenesis of WMH. They occur in internal border zone regions with lowest arterial perfusion. Reduced cerebral blood flow has been shown both within WMH and also in normal appearing white matter. Some studies have also suggested impaired cerebral autoregulation. Endothelial activation and dysfunction has been implicated and this could cause reduced cerebral blood flow via impaired vasodilatory responses.

More recently a role of blood brain barrier (BBB) leakage has been promoted. This could both exacerbate arterial damage and also lead to brain parenchymal damage. This is supported by both CSF studies and also MRI studies showing low grade leakage of gadolinium. It is possible that endothelial activation plays a role in BBB leakage. An additional process by which damage may be propagated within the brain is neuroinflammation which can now be studied by PK-III PET demonstrating glial activation. There are few effective treatments in SVD and developing better treatment approaches will require better understanding of the underlying disease mechanisms and potential molecular targets. However the above mechanisms do suggest some potential therapeutic interventions. For example in patients who have impaired cerebral blood flow and autoregulation is it better to run the blood pressure slightly higher? This is being testing in clinical trials. Do drugs which stabilise the BBB and reduce neuroinflammation delay disease progression?