Title: From hypertension to neurodegeneration: the microglial culprit

Collaborators:
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Proposal (250 words)

Introduction:
Vascular Cognitive Impairment (VCI) encompasses all the cognitive disorders associated with cerebrovascular disease, from frank dementia to mild cognitive deficits. While it is known that hypertension is a major risk factor for the development of VCI, the pathological cascade that lead to neurodegeneration remains elusive. While microglia, the resident immune cells of the brain, protects the brain from neurodegeneration under healthy conditions, they can acquire a proinflammatory phenotype under pathological conditions. Our recent study has shown that a prolonged hypertension induced a dysfunction of the blood brain barrier in association with local microglial activation and cognitive impairment (submitted).

Hypothesis:
Hypertension switches microglia into a pro-inflammatory phenotype that initiates a neurodegenerative process.

Key objectives:
1) chronic hypertension induces microglial activation around sites of Blood Brain Barrier leakages;
2) activated microglia are locally associated with signs of neurodegeneration;
3) chronic hypertension changes the microglial phenotype to a pro-inflammatory state.

Setting and Methods:
We will employ state-of-the art brain clearing techniques to image brains from normotensive and hypertensive reporter mice. Two-photon and light-sheet microscopy techniques will be used to study the vascular, microglial and neuronal changes induced by hypertension in transgenic reporter mice. This innovative approach will allow the PhD candidate to characterize the microglial behavior in their 3D environment, and to assess their impact on neuronal integrity. In addition, microglia from hypertensive and normotensive mice will be isolated and further phenotyped by flow cytometry.

Impact:
We expect to unveil microglia as a major relay between hypertension and neurodegeneration. This will open perspectives to prevent and treat hypertension-related neurodegeneration.

Requirements candidate:
Good command of English; background either in cardiovascular or neuroscience fields; expertise in microscopy or flow cytometry is not required but is a plus.

Keywords:
vascular cognitive impairment; hypertension; ageing; microglia; neuroinflammation; brain clearing; microscopy

Selected publications: