Imaging cerebral neuroinflammation in acute and chronic cerebrovascular disease: a predictor of outcome and biomarker for guiding treatment

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Imaging cerebral neuroinflammation in acute and chronic cerebrovascular disease: a predictor of outcome and biomarker for guiding treatment

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Alzheimer's disease & other dementias

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Research Abstract

Acute stroke, vascular dementia and vascular cognitive impairment (VCI) are parts of the spectrum of cerebrovascular disease which has a high socioeconomic impact and is the most frequent neurological cause of permanent disability. There is an urgent need for more effective prevention and treatment. Although different in their presentation and time course, they share underlying disease mechanisms. There is extensive evidence that microglial activation is associated with the underlying pathological processes in both these diseases. Microglia are the resident macrophages of the central nervous system and play a key role in the brain’s reaction to ischemic insults. Experimental studies have demonstrated that microglia become activated within hours of the insult, initially within the ischemic core and later in the ischemic penumbra and anterograde neuronal pathways, especially the pyramidal tracts. Activated microglia contribute to the inflammatory processes that occur in the brain in response to ischemia by secreting cytokines which may exacerbate cellular damage, but may also contribute to removal of cellular debris. The inflammatory process in the brain also appears to be influenced by systemic inflammation. Previous data suggest that inflammation in the brain is associated with poor outcome but can be treated by specific drugs. Imaging the intensity and the extent of inflammation in patients will therefore help in predicting outcome and a may also serve as a surrogate biomarker for predicting response to treatment. While the biophysical consequences of ischemia, especially cellular and vasogenic oedema as well as blood-brain barrier damage, can be imaged by MRI techniques, imaging microglial activation requires molecular imaging techniques. Activated microglia express the translocator protein 18 kDa (TSPO) as a specific antigen which is not present in normal brain and can be imaged by positron emission tomography. Previous and current clinical research studies largely rely on 11C-labelled PK11195 as a tracer, which due to its short physical half-life requires a cyclotron on-site and therefore is not generally available in clinical medicine. Recently, new F-18 labelled compounds have been developed that can be used in clinical nuclear medicine departments. We therefore propose to study microglia activation in human brain using a novel 18F-labelled TSPO-ligand (18F-GE180) with PET in patients after mild to moderate stroke and VCI. In a staged approach, we will evaluate whether this technique is feasible and predicts outcome and clinical progression. We will also compare our PET findings with the extent of changes in proton diffusion and structural damage by MRI.

Lay Summary
Further information available at:

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