

Project Title: Assessing activation of brain microglia in chronic pain with simultaneous MR-PET

Abstract: Chronic pain is an enormous public health issue, with a prevalence of ~105 million individuals in the US. Until recently, pain disorders have been thought to arise primarily from the dysfunction of nociceptive neurons. This view, however, has been lately challenged by the demonstration that animal models of chronic pain present evidence of microglia activation (MA) in the central nervous system, i.e., an immune response traditionally known to occur in response to other pathological conditions (e.g., neuroinflammation). Importantly, increasing evidence indicates that MA is not simply an epiphenomenon co-occurring with pathological nociception, but is likely to have a causal role. Nonetheless, it is currently unknown whether microglia contribute to the pathophysiology of chronic pain in humans. In this project we will test the hypothesis that chronic pain patients present evidence of brain MA. We will use combined Magnetic Resonance/Positron Emission Tomography, a novel technology synergizing two leading imaging methodologies, and [11C]PBR28, a recently developed marker of MA with binding specificity far superior to that of other ligands targeting MA. The concomitant acquisition of PET and MR data will provide the unique opportunity to perform MR-based motion- and attenuation-correction of the PET images, and to assess the co-localization of MA and structural/functional/perfusion abnormalities during a single imaging visit. Recognizing the role of microglia in chronic pain would have tremendous clinical implications, including the development of much needed novel pharmacological approaches to pain. The data collected with the support of this Grant will represent an important foundation for future NIH grant proposals.