Overview

Accumulating clinical evidence suggests that persistent cognitive impairment is one of the significant complications of COVID-19 infection. The underlying mechanism of such a long-lasting brain complication of COVID is still unknown, but the most compelling hypothesis is the contribution of excessive neuroinflammation induced by a systemic inflammatory response or cytokine storm on the blood-brain barrier, followed by subsequent activation of brain resident immune cells such as microglia and astrocytes. However, there is no published result to date presenting the association between persistent cognitive impairment from COVID infection and neuroinflammation in the living brain.

The _overall objective_ for this application is to collect preliminary evidence on the link between neuroinflammation and persistent cognitive impairments after recovery from COVID infection in a small group of older adults by positron emission tomography (PET) imaging. We will obtain [^{18}F]FEPPA PET scans from ten older adults with persistent post-COVID cognitive impairments for longer than six months after recovery from COVID infection. [^{18}F]FEPPA is a radioligand specific to 18-kDa translocator protein (TSPO) that is highly expressed in inflammatory cells including activated microglia in the brain, and Stony Brook Medicine is one of the leading institutes for using it in various clinical research studies. Our Center of Excellence for Alzheimer's Disease (CEAD) research team has been establishing a research cohort to study long-term neuropsychiatric symptoms following COVID infection and their public health impact. We will recruit participants from the cohort and utilize the extensive data resources such as neuropsychological testing results and the levels of blood markers for systemic inflammation.

Our _central hypothesis_ is that older adults with persistent cognitive impairments will show higher TSPO binding (thus higher neuroinflammation level) compared to the results from healthy individuals reported in the literature, and the binding level will be associated with the clinical severity of cognitive impairments and the levels of blood-based systemic inflammatory markers. The central hypothesis will be tested by pursuing three specific aims:

Aim 1: Determine the level of brain TSPO binding in older adults with persistent post-COVID cognitive impairments. Our hypothesis is that older adults with persistent cognitive impairments will have higher TSPO binding compared to the normal range of the similar age group reported in the literature.

Aim 2: Explore the association between brain TSPO binding and the severity of cognitive impairments in older adults with post-COVID cognitive impairments. Our hypothesis is that the TSPO binding is positively associated with the severity of cognitive impairments.

Aim 3: Explore the association between brain TSPO binding and blood inflammatory markers levels in older adults with post-COVID cognitive impairments. Our hypothesis is that the TSPO binding is positively associated with the blood inflammatory markers levels.

On successful completion of the study, preliminary neuroinflammatory PET image findings of persistent post-COVID cognitive impairments will be outlined, which will allow us to apply for a National Institute on Aging (NIA) R01 grant application. The proposed work has high socio-economic _impact_ because long-term complications of COVID infection in older adults will be a global health care issue in the future.