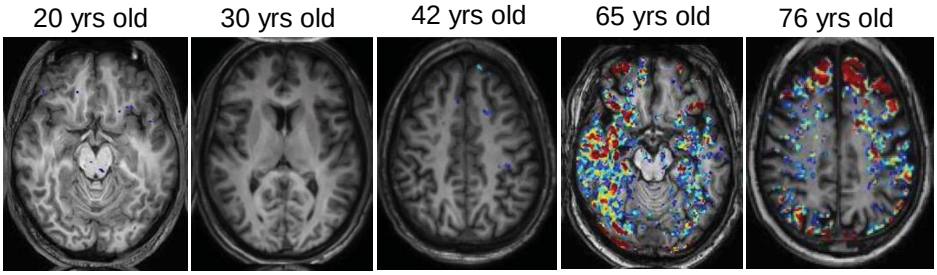
A Combined Therapy of FDA-Approved Drugs to Protect the Blood-Brain Barrier in Neurological Disorders

According to a recent WHO report, brain disorders are the major cause of disability in the modern world, affecting over 1 billion people worldwide. To this day, treatment of neurological disorders, including Stroke and Dementia is limited. While it is well recognized that the pathology of brain microvasculature is a key mechanism underlying neurological diseases, there is no clinically approved treatment for improving such pathologies. The blood-brain-barrier (BBB) is a highly specialized interface that separates the circulating blood from the brain's extracellular fluid in the CNS and transport between brain and circulation is allowed only by a highly selective molecular transport system. The BBB functions to protect the brain in a privileged environment. Break down of the blood brain barrier occurs in neurological disease such as Stroke, Alzheimer's, Epilepsy, Traumatic Brain Injury, Age-related Macular Degeneration (AMD), HIV associated dementia, ALS, Migraine and post-operative, post-radiation or hypertension-associated cognitive decline. BBB breakdown allows entry of neurotoxic blood products resulting in inflammatory response and a major damage to the brain. Therefore the integrity of the BBB and the ability to repair damages caused to its integrity are crucial.

The Technology

We have recently found that excessive release of the most common excitatory neurotransmitter, glutamate, leads to increased vascular permeability, through activation of N-methyl-D-aspartate (NMDA) receptors. We further showed that BBB pathology leads to transforming growth factor beta (TGFβ) pro-inflammatory signaling within the brain that further facilitates BBB opening. Our preliminary results confirmed that NMDA receptor antagonists improve BBB integrity following recurrent epileptic seizures, as well as in the peri-ischemic brain. More recently, we demonstrated the efficacy of combined NMDA-receptor antagonists and Losartan, an FDA approved TGFβ and angiotensin II (ATII) receptor antagonist, in improving BBB integrity following repeated seizure activity.



Advantages

- ✓ Combined Therapy with FDA approved drugs, known safety profile and validated activity.
- ✓ The treatment is relevant for many CNS indications such as Stroke, Alzheimer, ALS, Migrane, Epilepsy, Traumatic Brain Injury, AMD and multiple forms of Dementia.

Patent Status

Patent pending

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