The Effect of Glial Activation and Depression in Wild Type and Transgenic Mice

By: Liora Rahmani[1], Gavriella Jutan[1], Yosef Scher[2], Dr. Amit Lotan[3], Yoel Shor[3], Dr. Gilly Wolf[3], Reut Said[3], and Yarden Brock[3]

[1]Stern College for Women, Yeshiva University, New York, NY; [2]Yeshiva College, Yeshiva University, New York, NY; [3]Laboratory of Biological Psychiatry, Hadassah Hebrew University Medical Center, Jerusalem, Israel

Alzheimer's Disease (AD) is a neurodegenerative disease that is characterized by progressive cognitive and physical deterioration that leads to disability and dementia. Depression is a common, episodic and variable illness that diminishes quality of life and reduces psychological abilities, leading to a variety of emotional and physical problems.

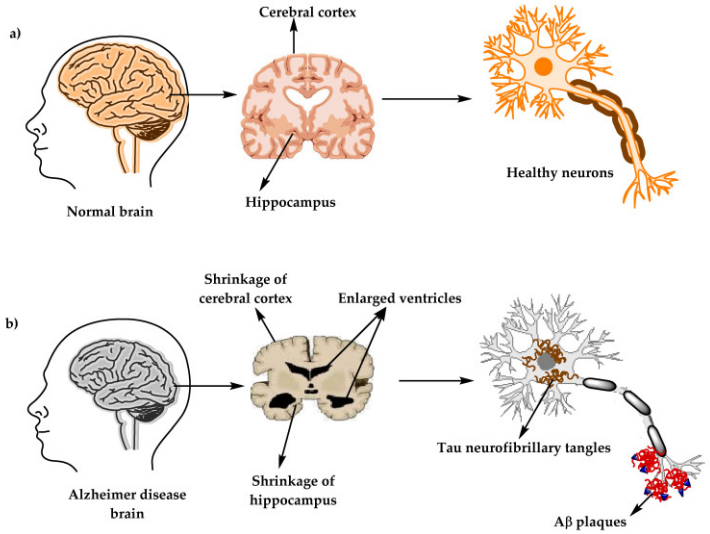

Figure 1: The physiological structure of the brain and neurons in (a) healthy brain and (b) AD brain

Depression is a major risk factor for AD and is highly prevalent among AD patients. 50% of AD patients suffer from depression symptoms and 20-30% suffer from Major Depressive Disease (MDD). The underlying mechanisms that connect both AD and MDD are unclear. As such, the purpose of the experiment was to determine the mechanisms that connect AD and MDD.

It has been hypothesized that neuroinflammation, which is present in both AD and MDD, is a possible link between the two diseases. The present study was designed to test this hypothesis, as it has gained much support in recent years. While both exhibit neuroinflammation, different effects are expressed. In AD, neuroinflammation leads to neurodegeneration, while this does not occur in MDD.

The activation of microglial cells causes neuroinflammation. Microglia possess many physiological functions, as they are essential for synaptic plasticity and neurogenesis. When neuroinflammation occurs, these physiological functions may be affected.

Dr. Amit Lotan's study was designed to test the effect of glial activation and depression in wild-type and transgenic mice. Sixty-four mice were used in the experiment. Half of the mice were transgenic to AD, while the other thirty-two mice acted as the control. The mice were then placed in stressful conditions through the chronic unpredictable stress protocol that consisted of various psychological stressors, which caused their emotions to mimic those of humans with MDD. A series of cognitive behavioral tests were then performed to test the cognitive function of the mice. A series of chronic mild stress (CMS) tests were administered, which included cage tilting, and exposure to many stressors including white noise, flashing lights, light during the night, and predator's urine. The behavioral tests administered included an open field test, various mazes, a fear conditioning test, and a forced-swim test. The different tests targeted different sections of the brain and represented certain psychological domains, including anxiety, depression, locomotor behavior, and cognition.

The affected brains were extracted and studied. The neurons and microglial cells were counted to compare the differences between the brains of mice with AD and those of wild-type mice, as well as the brain sections of stressed mice and the control group.

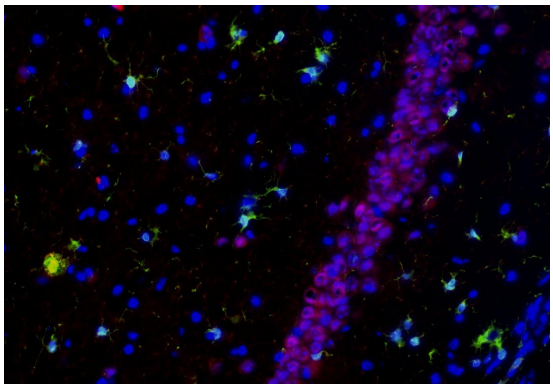

Figure 2: Example of microglia and neurons in segment of stained mouse brain

Dr. Lotan's lab is now studying whether there is an altered function in the brains of the mice that may correspond with an altered function of their behavior. The study is still in progress. It is hoped that the transgenic mice exhibit a greater amount of glial activation and fewer neurons, as this would mean that the chronic unpredictable stress protocols activates glial cells and induces neural decline.