Exploring the Neurophysiological Basis of Memory Deficits Associated with Psychological Trauma

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Background --- What’s the problem?

- Post-traumatic stress disorder (PTSD) is a psychological disorder characterized by recurrent, intrusive memories of a traumatic event (Keane et al., 2009).

- It is estimated by the National Comorbidity Survey that more than half of Americans will have a traumatic experience in their lifetime, and that 6.8% to 7.8% of all Americans will subsequently develop PTSD (Kessler et al., 2005).

- The costs of this disorder are both emotional and financial. PTSD is correlated with increases in social problems (e.g. marriage instability) and with economic problems (e.g. decreases in work-related productivity). It is estimated that $3 billion are lost each year as a result of PTSD-related loss of productivity (Keane et al., 2009; Kessler, 2000).

- Currently, the exact mechanism behind the onset and maintenance of PTSD is still unknown, and further research is required before new treatments/therapies can be developed.

Research Focus --- What will we try to determine?

- A variety of studies have shown that PTSD is associated with changes in how the brain processes fear information. Morphological and neurochemical alterations within the brain have been demonstrated, and are linked to altered fear memory maintenance.

- Imbalances in neural activity between three regions of the brain (hippocampus, amygdala, and prefrontal cortex) play critical roles in this adulteration of memory processing.

- We aim to investigate how glial cell dysfunction and differences in glutamate receptor subtype (GlutR) expression can induce this imbalance during traumatic experiences.

Proposed methods --- How will we do it?

- In vitro models will be used first to investigate the molecular events mediated by GlutRs (e.g. ERK and p38 MAPK pathways) that occur during stress. Our focus will be primarily on evaluating the extracellular influences of glucocorticoids on GlutR function in the hippocampus, amygdala, and prefrontal cortex. Analyses will include Western blots and RT-PCR, which will be used to determine functional differences of GlutRs in the different brain regions.

- Influences of inflammatory-like reactions (mediated by glial cells) upon these pathways will also be quantified biochemically.

- In vivo models of conditioned fear will be used following the biochemical studies to determine if preventing the glial-mediated inflammatory reaction can diminish changes in neuronal morphology and fear behavior associated with traumatic experiences.

References:

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