Impact of Prenatal Stress on Pattern Separation: Role of Adult Hippocampal Neurogenesis

Stress is an unavoidable condition in human life. Stressful events experienced during infancy including in utero stress have been suggested as one major pathophysiological mechanism for developing vulnerability towards neuropsychiatric and neurodevelopmental disorders in adulthood. One cardinal feature of such disorders is impaired cognitive ability, which may in part rely on abnormal structure and function of the hippocampus. In the hippocampus, dentate gyrus (DG) represents the site of continuous renewal of dentate granule cells, a process called adult-hippocampal neurogenesis (AHN) that has been recently implicated in spatial pattern separation, a cognitive phenomenon of reducing the degree of overlap in the incoming information to facilitate its storage with minimal interference. However, both hippocampus and AHN are sensitive to pathological stimuli such as prenatal stress allowing us to hypothesize that the alteration in hippocampal neurogenesis due to in utero stress may possibly lead to impairment in pattern separation. To test this hypothesis, both control (C) and prenatally stressed (PS) mice were initially tested for contextual memory using simple contextual fear conditioning test and then the efficiency of pattern separation was investigated through contextual discrimination fear conditioning (CDFC). Further, the relative contribution of AHN to the CDFC test was determined using functional imaging of immediate early gene cfos, which is an indication of the recruitment of cells in response to the test. For the first time, we report here that PS mice are impaired in pattern separation process tested via CDFC compared to the C, while their contextual memory was unaffected, underlying the specificity of the observed effect. However, the immunohistochemical studies on AHN did not allow us to draw a clear conclusion regarding the involvement of adult-born cells in pattern separation process.

Key words: Prenatal restraint stress, Adult-hippocampal neurogenesis, Pattern separation, IdU cells.