S 15-4

STRESS AND PREFRONTAL COGNITIVE FUNCTIONS IN RODENTS

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Stress is a biologically significant social-environmental factor that plays a pervasive role in our lives, from impacting our daily behaviors to producing and exacerbating myriad physical and mental illness. An accumulating body of evidence from human and animal studies reveals that while the acute response to stress (i.e., heightened cognition) is an adaptive mechanism, exposures to uncontrollable stress can subsequently produce detrimental neurocognitive effects, particularly in the hippocampus and prefrontal cortex. In rodents, the prefrontal cortex has been postulated to integrate spatial information from the hippocampus with key aspects of task rules to guide navigational decisions. In my talk, I will present data indicating that (i) stress, via altering both hippocampus-dependent spatial memory and prefrontal cortex-dependent working memory functions, exerts influences on decision-making processes on a spatial-reward navigational task; and (ii) the amygdala plays a crucial role in the emergence of neurocognitive stress effects.

S 16-1

DERANGED NEURONAL CALCIUM SIGNALING AND HUNTINGTON DISEASE

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Huntington's disease (HD) is an autosomal-dominant and fatal neurodegenerative disorder. Brains of early-grade HD patients display selective loss of striatal medium spiny neurons (MSN). HD is caused by polyglutamine (polyQ) expansion in the amino-terminal of cytosolic protein Huntingtin (Htt). A central question in the study of HD is how this polyQ-expansion of Htt leads to the neurodegeneration of MSN. Recently our laboratory discovered a direct connection between HD mutation in Htt and deranged neuronal calcium (Ca^{2+}) signaling mediated by intracellular neuronal calcium release channel - the type 1 inositol 1,4,5-trisphosphate receptor ($InsP_3R1$) (Tang at al (2003) Neuron 39:227~239). From these results we proposed that deranged neuronal Ca^{2+} signaling may be an underlying cause of MSN degeneration in HD (Bezprozvanny and Hayden (2004) BBRC, 322:1310-7). To test the "Ca^{2+} hypothesis of HD" we performed a series of experiments with cultured MSN from YAC128 HD mouse model. Obtained results supported a casual connection between Ca^{2+} signaling and neurodegeneration of HD MSN neurons (Tang et al. (2005) PNAS, 102: 2602~2607). In addition, a number of novel therapeutic targets and potentially useful compounds for treatment of HD have been identified in our studies with YAC128 MSN. Currently we are in the process of validating "Ca^{2+} hypothesis of HD" in whole-animal experiments with YAC128 HD mouse model.

Key Words: calcium signaling, neurodegenerative disease, transgenic mouse, polyglutamine