1-LBS-07 Late-Breaking Session

NOX1/NADPH in the hypothalamus regulate anxiety-like behaviors in mice

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The involvement of reactive oxygen species (ROS) in psychiatric disorders has been reported. However, the source of ROS has not been identified yet. NADPH oxidase is a superoxide-generating enzyme composed of multiple subunits including a membrane-spanning catalytic subunit, NOX. We investigated the role of NOX1/NADPH oxidase in the anxiety-like behavior using mice deficient in *Nox1*(NOX1-KO).

When anxiety-like behaviors were evaluated in elevated plus-maze and open field tests, no difference in anxiety levels was observed between wild-type mice (WT) and NOX1-KO. Increased anxiety-like behavior was demonstrated in WT subjected to two hour-restraint stress, but it was markedly ameliorated in NOX1-KO. Delivery of miRNA against NOX1 to the hypothalamus suppressed the anxiety-like behavior in WT. An increase in oxidative stress induced by restraint stress was blunted in the hypothalamus of NOX1-KO. Concomitantly, elevated levels of plasma ACTH as well as corticotropin-releasing hormone (CRH) and c-fos mRNA in the hypothalamus were significantly attenuated in NOX1-KO subjected to restraint stress. In hypothalamic slice cultures, the increase in CRH mRNA induced by a protein kinase A activator, forskolin, was suppressed in NOX1-KO. Moreover, the levels of phosphorylated CREB in the hypothalamus caused by stress were ameliorated in NOX1-KO.

Taken together, NOX1/NADPH oxidase appear to play a key role in stress-induced anxiety,possibly by regulating activation of the PKA-CREB pathway in the hypothalamus.