Role of neuropeptides in lung

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Severe influenza infection is characterized by a strong inflammatory response and profuse viral replication. These viruses, such as H5N1 avian flu, have a high rate of death and to date there are no effective treatments. Cross-talk between the autonomic nervous system and the immune system by means of sympathetic and parasympathetic pathways is a critical process in host defense. Activation of the sympathetic nervous system results in the release of catecholamines (CA) as well as neuropeptide Y (NPY). Here we investigated whether phagocytes are capable of de novo production of NPY, as has been described for CA. We show that synthesis of NPY and its Y1-receptor (Y1R) were increased in phagocytes in lungs following severe influenza virus infection. Genetic deletion of Npy or Y1r specifically in phagocytes greatly improved the pathology of severe influenza virus infection, which is characterized by excessive virus replication and pulmonary inflammation. Mechanistically it is the induction of suppressor of cytokine signaling 3 (SOCS3) via NPY-Y1R activation that is responsible for impaired anti-viral response and promoting pro-inflammatory cytokine production, thereby enhancing the pathology of influenza virus infection. Thus, direct regulation of the NPY-Y1R-SOCS3 pathway on phagocytes may act as a fine-tuner of an innate immune response to virus infection, which could be a therapeutic target for lethal influenza virus infection.