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An "immunomodulatory" approach for the treatment of Methamphetamine addiction

Jennifer Loftis
Oregon Health & Science University, USA

The role of the immune system in regulating psychiatric and cognitive function, including in the context of substance use disorders, has attracted increasing attention over recent years. Chronic use of methamphetamine (MA), a highly addictive central nervous system (CNS) psychostimulant, is associated with neuronal injury, neuroanatomical alterations, and serious psychiatric and cognitive impairments that make dependence on the substance particularly challenging to treat. Preclinical studies show that MA injures neurons through multiple mechanisms including interfering with dopamine metabolism, altering glutamate processing by astrocytes, worsening oxidative stress, and increasing expression of pro-inflammatory cytokines [e.g., tumor necrosis factor-alpha (TNF-α) and interleukin 1-beta (IL-1β)] secreted from activated glial cells, neurons, auto-reactive T-cells, infiltrating macrophages, or other peripheral immune cells. These findings converge with clinical studies demonstrating the relationship between both peripheral and central inflammatory systems and neuropsychiatric function in individuals addicted to MA. In line with current models of Cytokine-induced depression and cognitive dysfunction, MA-associated immune dysregulation can influence neurotransmitter (e.g., Dopaminergic, glutamatergic, serotonergic) and neuroendocrine (e.g., corticotropin releasing factor, hypothalamic-pituitary-adrenal axis) systems and contribute to cognitive dysfunction and mood disturbances (e.g., impulsivity, depression, anxiety, and irritability)-neuropsychiatric consequences of drug addiction that persist during remission and hinder recovery efforts. To date, pharmacotherapeutic development for substance use disorders has primarily focused on neurotransmitter systems and results from related clinical trials continue to be modest. Our preclinical data suggest that an immunotherapeutic approach using partial major histocompatibility complex (MHC)/neuroantigen peptide constructs (pMHCs), which have therapeutic effects on cognitive function and inflammation, has the potential to safely and effectively treat MA use disorders in adults. New approaches of this kind are expected to augment the efficacy of traditional substance dependence and mental health treatments.

Biography

Jennifer Loftis earned a PhD in Behavioral Neuroscience from Oregon Health & Science University (OHSU) and completed a Postdoctoral fellowship in Molecular Microbiology and Immunology at OHSU. In 2008, she was awarded a career development award from the Veterans Health Administration (VHA) to study inflammatory mediators in depression and hepatitis C viral infection (HCV). As a VA career development award recipient, she identified a novel role for cytokines in the etiology of depressive symptoms in adults with chronic HCV. This finding has guided the testing of hypotheses regarding how circulating inflammatory factors affect central nervous system functioning and how immunotherapeutic strategies may help to treat these conditions. She is currently a Research Scientist at the VA Portland Health Care System and an Associate Professor of Psychiatry at OHSU, with over 50 publications in the fields of psychiatry, neuroscience, and immunology. To support her translational research program and investigation of the psychoneuroimmunological mechanisms contributing to substance abuse and neuropsychiatric impairments, she has received grants from local and national organizations such as the Northwest Health Foundation, VHA, and the National Institutes of Health.

jennifer.loftis2@va.gov

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