Differential effects of amphetamine exposure on neuroglia in vivo

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Abstract
Drug addiction is a major public health problem with wide range of negative health, economic, and social consequences. One of the most commonly abused types of drugs is amphetamine, a psycho-stimulant sometimes used as a performance enhancer to increase alertness and focus and induce anxiety and psychosis. Patients with history of heart disease or hypertension, and users of monoamine oxidase inhibitors may experience life-threatening complications if exposed to amphetamine. The effects of amphetamine use or abuse on brain development may last for many years, and chronic amphetamine exposure in animals and humans is known to cause hyperthermia and apoptosis, as well as random leakage of the blood-brain barrier (BBB). However, the effect of amphetamine on neuroglia is not well understood, and somewhat controversial. We chose to investigate the effect of amphetamine exposure on the neuroglia, as these cells play critical roles in modulating injury repair, neuronal migration, and axonal growth during nervous system development, and in facilitating neurotransmitter transport, BBB integrity, blood flow regulation, metabolic balance, iron homeostasis, and immune response. We investigated neuroglia in response to amphetamine exposure using antisense (AS) or sense (S) phosphorothioate-modified oligodeoxynucleotides (sODN) sequences that correspond to glial fibrillary acidic protein (GFAP) mRNA (AS-gfap or S-gfap, respectively) expression. The control is a random sequence sODN (Ran). Using cyanine 5.5-superparamagnetic iron oxide nanoparticles (Cy5.5-SPION) label, we observed a reduction in neuroglia population in the striatum, but the evidence of gliogenesis in the subventricular zone and the somatosensory cortex in vivo. The results confirmed autopsy report on methamphetamine users. The sensitivity of our unique gene transcript targeted MRI was illustrated by a positive linear correlation ($r^2 = 1.0$) between in vivo MRI signal changes and GFAP mRNA copy numbers determined by ex vivo TaqMan assay. The study provides direct evidence for targeting neuroglia by antisense DNA-based SPION-gfap that enables in vivo MRI of inaccessible tissue with PCR sensitivity. The results enable us to conclude that amphetamine induces toxicity to neuroglia in vivo, which may cause remodeling or re-connectivity of neuroglia.

Biography
Dr. Liu has completed his Ph.D. from Michigan State University and postdoctoral studies from the Department of Pathology, University of Washington Medical School. He is an associate biologist and Associate Professor of Radiology at Massachusetts General Hospital and Harvard Medical School. He has published more than 45 peer-reviewed papers in reputed journals.