**Objective:** To determine whether $^1$H MRS can detect cerebral metabolite abnormalities that reflect long-term neuronal and glial damage or loss in abstinent methamphetamine users.

**Background:** Methamphetamine abuse is a re-emerging epidemic in the United States and in many Asian countries. Clinical and preclinical observations suggest that methamphetamine may cause long-lasting injury to the brain. In humans, some of the psychiatric conditions, such as paranoid psychosis, may occur not only acutely during methamphetamine exposure, but may persist for months or even years after cessation of methamphetamine use (1, 2). In rodents, methamphetamine is toxic to dopaminergic and serotonergic neurons (3-5). However, little biological data is available on the possible toxic effects of methamphetamine on the human brain.

**Design and Methods:** MRI and localized $^1$H MRS was performed in 25 abstinent methamphetamine users with a history of methamphetamine dependence (median total cumulative lifetime exposure, 3,640 grams; median recency of last methamphetamine use, 4.25 months); and 25 healthy subjects without a history of drug abuse. The cerebral metabolite concentrations of N-Acetyl compounds [NA], total creatine [CR], total choline [CHO] and myo-inositol [MI], were determined in the frontal cortex, frontal white matter, and basal ganglia, using a protocol for absolute quantitation described in (6, 7).

**Results:** The concentration of NA, a neuronal marker, was statistically significantly reduced in all three brain regions of methamphetamine users compared to control subjects (Figure 1).

In the frontal white matter, the [NA] correlated inversely with the logarithm of the lifetime methamphetamine used (Figure 2). The methamphetamine users also showed significantly reduced total creatine in the frontal white matter and basal ganglia, reduced choline-containing compounds in the basal ganglia, and reduced myo-inositol (a glial marker) in the frontal gray matter and the basal ganglia (Figure 1).

**Discussion:** This $^1$H MRS study provides the first in vivo evidence for long-term neuronal damage, with reduced [NA], and glial abnormalities, with reduced myo-inositol concentration, in abstinent methamphetamine users. The persistence of the neurochemical abnormalities, even in subjects with more than 1 year abstinence, underscores the potential long-term impact of the methamphetamine epidemic on society and public health.

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**References**