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Research Report

Chronic methamphetamine abuse and corticostriatal deficits revealed by neuroimaging

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ABSTRACT

Despite aggressive efforts to contain it, methamphetamine use disorder continues to be major public health problem; and with generic behavioral therapies still the mainstay of treatment for methamphetamine abuse, rates of attrition and relapse remain high. This review summarizes the findings of structural, molecular, and functional neuroimaging studies of methamphetamine abusers, focusing on cortical and striatal abnormalities and their potential contributions to cognitive and behavioral phenotypes that can serve to promote compulsive drug use. These studies indicate that individuals with a history of chronic methamphetamine abuse often display several signs of corticostriatal dysfunction, including abnormal gray- and white-matter integrity, monoamine neurotransmitter system deficiencies, neuroinflammation, poor neuronal integrity, and aberrant patterns of brain connectivity and function, both when engaged in cognitive tasks and at rest. More importantly, many of these neural abnormalities were found to be linked with certain addiction-related phenotypes that may influence treatment response (e.g., poor self-control, cognitive inflexibility, maladaptive decision-making), raising the possibility that they may represent novel therapeutic targets.

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1. Introduction

Methamphetamine use disorder constitutes a major public health problem, associated with high rates of attrition, crime, relapse, and mortality. Although the prevalence of illicit methamphetamine use in the U.S. declined sharply in the late 2000s following legislation limiting access to precursors, the estimated number of current users has increased since 2010, totaling 595,000 in 2013 (SAMHSA, 2014a)). Furthermore, with 144,000 Americans estimated to have tried methamphetamine for the first time in 2013 (SAMHSA, 2014a) and established supply connections to Mexican cartels (Shukla

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et al., 2012), the problem may continue to grow. Methamphetamine has also become more prevalent throughout Asia and the Pacific region in recent years, leading to it being ranked as the primary or secondary drug of use in 13 of the 15 countries from that region surveyed in 2012 (UNODC, 2013). Although many users seek treatment for methamphetamine abuse, which accounts for well over 100,000 admissions to drug treatment facilities annually in the U.S. alone (SAMHSA, 2014b), the vast majority relapse (Brecht and Herbeck, 2014; McKetin et al., 2012). Still, despite their poor therapeutic efficacy, generic behavioral interventions (e.g., cognitive behavioral therapy, contingency management, motivational interviewing) remain the mainstay of treatment for methamphetamine use disorder.

Chronic abuse of methamphetamine is often associated with a constellation of behavioral problems (e.g., Cartier et al., 2006; Cohen et al., 2003; McKetin et al., 2008; Zweben et al., 2004), including mood disturbances (London et al., 2004; Newton et al., 2004; Shen et al., 2012), persistent craving (Zorick et al., 2010) and psychosis (Grant et al., 2012). Cognitive deficits are also common among individuals with a history of methamphetamine abuse, particularly involving executive functions (e.g., mental flexibility, self-control), which are important for suppressing habitual behaviors (Dean et al., 2012; Monterosso et al., 2005; Scott et al., 2007; Simon et al., 2010). As outlined below, neuroimaging studies have demonstrated that methamphetamine abusers also typically display several signs of corticostriatal dysfunction. Moreover, these studies provide suggestive evidence that many of these corticostriatal abnormalities may underlie certain cognitive and behavioral phenotypes that can serve to promote compulsive drug use, raising the possibility that they may represent novel therapeutic targets.

2. Structural brain imaging of methamphetamine users

Structural magnetic resonance imaging has provided evidence for cortical and striatal gray- and white-matter abnormalities associated with methamphetamine abuse. A substantial number of studies have linked structural brain abnormalities with cognitive dysfunction in methamphetamine users.

Methamphetamine users generally exhibit smaller cortical but larger striatal gray-matter volumes than non-users (Berman et al., 2008a). Following brief abstinence (< 3 weeks), gray-matter volumes in anterior cingulate cortex (ACC), dorsolateral prefrontal (DLPFC), orbitofrontal (OFC), and superior temporal cortices as well as the hippocampus are smaller than in never-users (Nakama et al., 2011; Thompson et al., 2004); and a bilateral deficit in gray-matter density of the insula has been observed with abstinence up to six months (Schwartz et al., 2010). In contrast, subjects who are abstinent from methamphetamine for an average of 3–4 months show greater gray-matter volume in the parietal cortex, caudate nucleus, lenticular nucleus, nucleus accumbens (Jernigan et al., 2005), putamen, and globus pallidus (Chang et al., 2005) than never-users. Putamen volume also is larger among non-abstinent users than non-users (Jan et al., 2012b).

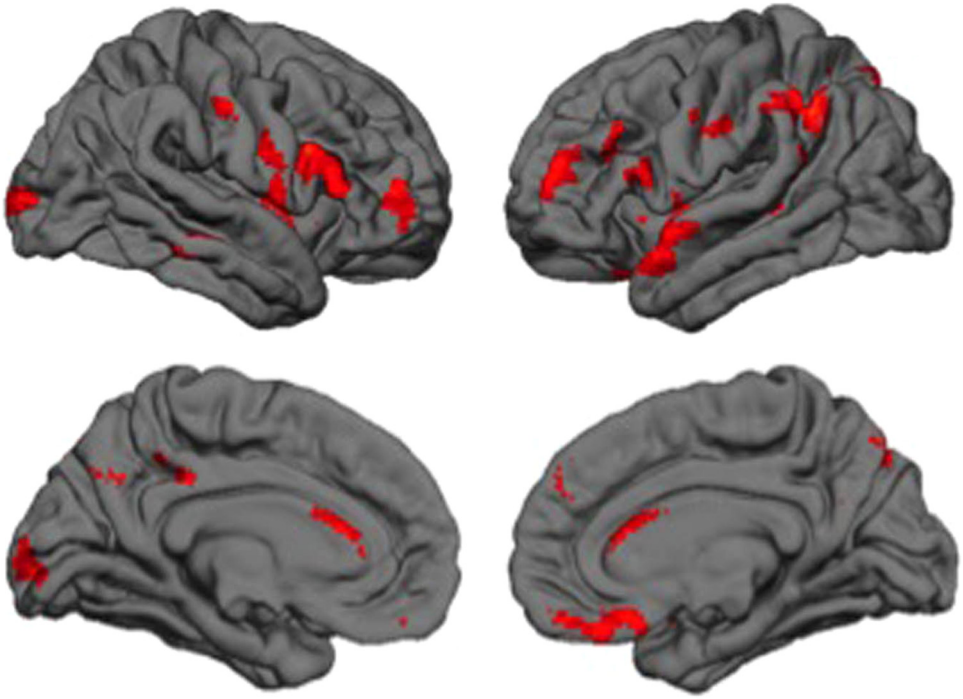

Fig. 1 – Changes in gray matter during early abstinence from methamphetamine.
In methamphetamine-dependent individuals, gray matter increased between the first and fourth weeks of abstinence from methamphetamine (results displayed at a statistical threshold of $p < 0.005$ uncorrected with a cluster extent > 200 voxels). No changes in gray matter were detected in healthy control participants who underwent two scanning sessions approximately one month apart. The left hemisphere is displayed on the left side of the image.