Imaging of the Human Brain in Health and Disease

Edited by:
Philip Seeman
Bertha Madras

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IMAGING OF THE HUMAN BRAIN IN HEALTH AND DISEASE

Edited by

PHILIP SEEMAN, BERTHA-MADRAS

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CONTENTS

CHAPTER ONE

Neuroimaging of Addiction

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1. INTRODUCTION

Scientific advances over the past 20 to 30 years have established drug addiction as a chronic brain disease (Leshner, 1997). Key evidence supporting this concept was produced by brain imaging studies of drug abusers obtained during or following various periods of drug exposure. These studies have provided information on drugs' neurobiological effects, helped explain the causes and mechanisms of vulnerability to drug abuse, and yielded important insights into abusers' subjective experiences and behaviors, including their difficulty to attain a sustained, relapse-free recovery. Clinicians may be able, in the not too distant future, to use brain imaging to evaluate the level and pattern of brain dysfunction in their addicted patients, helping them to tailor their treatments and to monitor their response to therapy.

The seven primary brain imaging techniques - structural magnetic resonance imaging (MRI), functional MRI, resting functional MRI, Diffusion Tensor Imaging (DTI), magnetic resonance spectroscopy (MRS), positron emission tomography (PET), and single photon emission computed tomography (SPECT) - reveal different aspects of brain structure and/or function (Bandettini, 2009; Detre and Floyd, 2001; Duyn and Koretsky, 2011; Johansen-Berg and Rushworth, 2009; Sharma and Ebadi, 2008). Individually, the techniques yield highly complementary information about brain anatomy and tissue composition; biochemical, physiological, and functional processes; neurotransmitter levels; energy utilization and blood flow; and drug distribution and kinetics. Together, and in combination with other research techniques they contribute to continuously improve our understanding of drug abuse and addiction.

2.1. MAGNETIC RESONANCE-BASED IMAGING TECHNIQUES

2.1.1. Structural Magnetic Resonance Imaging

Structural magnetic resonance imaging (sMRI) translates the local differences in water content into different shades of gray that serve to outline the shapes and sizes of the

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brain's various subregions. An MRI scanner delivers a specific radiofrequency that excites hydrogen atoms in the water molecule, which return some of this energy in the form of a characteristic nuclear magnetic resonance signal. Not all protons "resonate" in that way, but enough do such that the resulting computer-generated image constitutes a highly detailed map of the brain's tissues and structures. Thus, this tool can be used to discover the presence of abnormal tissue through the changes in tissue density or composition. Scientists examining an sMRI can readily distinguish between gray and white matter and other types of tissue—both normal, such as blood vessels, and abnormal, such as tumors—by their different shading and contrast with surrounding areas.

Such measurements can help scientists and doctors to home in on the regions that are most heavily affected by drugs. Importantly, these initial observations often guide additional investigations, using other research tools and techniques, to determine the reasons for the structural changes as well as their experiential and behavioral consequences. As explained below, sMRI studies have provided detailed evidence that chronic drug exposure can lead to both increases and reductions in the volume of specific brain regions.

Drug Exposure can Trigger Abnormalities in Prefrontal Cortex and Other Brain Regions

Numerous sMRI studies have documented that addictive drugs can cause volume and tissue composition changes in the prefrontal cortex (PFC), a brain region that supports logical thinking, goal-directed behaviors, planning, and self-control. These changes in turn are likely to be associated with drug abusers' cognitive and decision-making deficiencies. Related to this finding, another sMRI study found that individuals with a history of abusing multiple substances have smaller prefrontal lobes than did matched controls (Liu et al., 1998).

These findings add to the growing evidence associating prefrontal abnormalities with the abuse of various substances (Goldstein and Volkow, 2002; Stapleton et al., 1995; Volkow et al., 1991). For example, using sMRI, Schlaepfer and colleagues found that chronic substance abusers' frontal lobe tissues contained a lower proportion of white matter than those of matched controls did (Schlaepfer et al, 2006). Interestingly, similar deficits in white matter content have been found in individuals with other psychiatric disorders that tend to cooccur with substance abuse.

Pertaining to the abuse of stimulants, Kim and colleagues (Kim et al., 2006) documented a reduction in the gray-matter density in the right middle frontal cortex of abstinent methamphetamine abusers (Figure 1). A lower density correlated with a worse performance on a test that measures a person's ability to switch mental gears (Wisconsin Card Sorting Task). Gray matter was closer to normal in individuals who had been abstinent for >6 months than in others with a shorter period of abstinence.

In another sMRI study, cocaine abusers who had been abstinent for 20 days exhibited a reduced gray-matter density in the regions of the frontal cortex. Interestingly, no

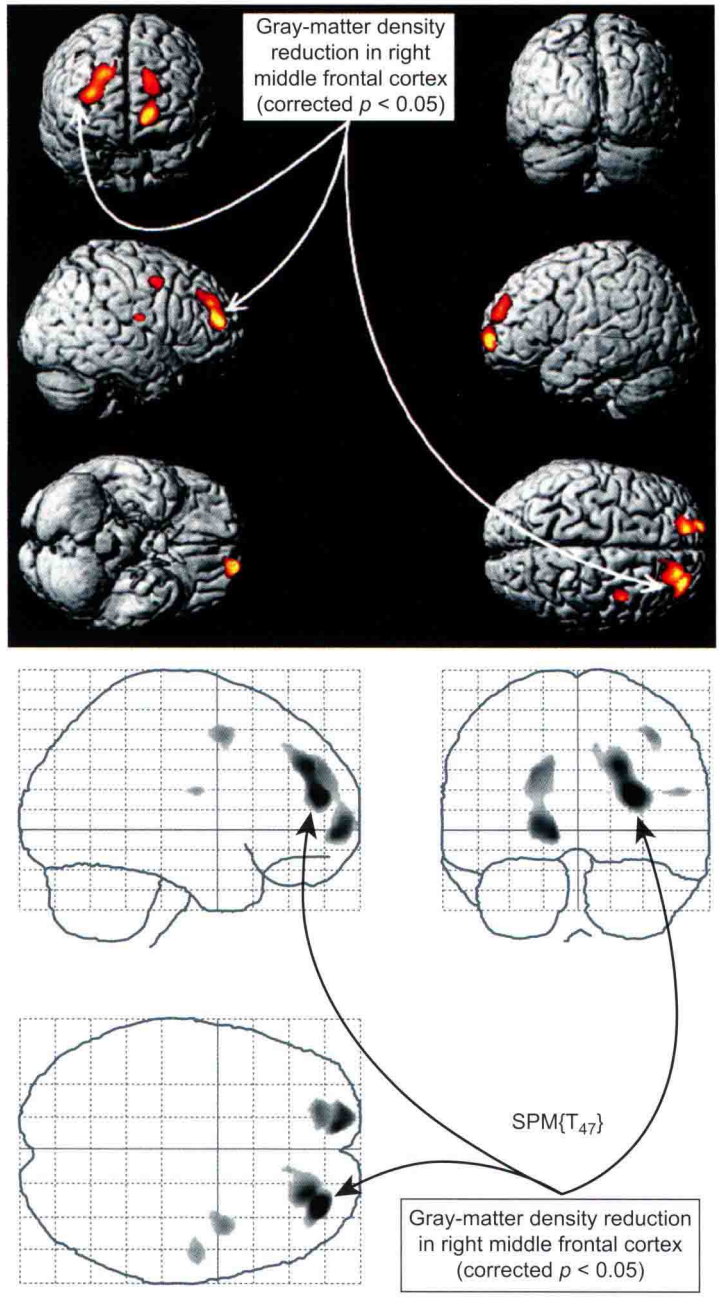

Figure 1 MRI: methamphetamine reduces gray matter. The yellow and red area in the central brain view indicates a reduced gray-matter density in the right middle frontal cortex. The same deficit is shown from other perspectives in the flanking views. *Reprinted with permission from Kim et al. (2006).*