Addiction Biology

HUMAN IMAGING BRIEF REPORT

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Reversible brain white matter microstructure changes in heroin addicts: a longitudinal study

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ABSTRACT

Previous neuroimaging studies have documented the structural damage in heroin addicts. However, little research has detailed the white matter microstructural changes in the human brain as a result of chronic heroin use and importantly, whether such changes can be recovered after short-term abstinence. Decreased fractional anisotropy values in frontal cortex were found in heroin users after 3 days of abstinence in comparison with controls. However, no significant difference was found between these heroin addicts and controls after 1-month abstinence. These results might better our understanding of the biological basis of drug addiction and provide insight into addiction treatment.

Keywords Cingulate gyrus, diffusion tensor imaging, fractional anisotropy, frontal gyrus, heroin addiction, white matter.

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Heroin addiction is a major burden to society, causing a range of negative consequences such as mortality, morbidity and crime (Hser *et al.* 2001; Tang & Hao 2007). Understanding the biological effects of chronic heroin use on the human brain may provide insight into the pathogenesis of heroin addiction and addiction treatment.

Difficulty to quit is a key problem in drug addiction treatment. Vast majority of relapses back to opioid abuse in out-patient treatment settings take place during the first weeks of abstinence (Kakko *et al.* 2003). Thus, it is important to understand the structural changes in the brain within this critical time period. The present study sought to explore the possible brain white matter microstructure changes in chronic heroin users during early abstinence and to examine whether such changes are transient. Diffusion tensor imaging, a novel non-invasive magnetic resonance technique, is used to investigate the white matter integrity by measuring the directionality of molecular diffusion.

Twenty right-handed heroin-dependent subjects were scanned twice, 3 days and 1 month after drug discontinuation. Twenty age-matched right-handed healthy subjects were also scanned twice (1 month apart) to serve as a control group (see supplementary materials for detailed information about subjects and methods).

There was no significant difference in age (heroin addicts 30.31 ± 6.65 versus controls 29.42 ± 5.33) or education (heroin addicts 9.64 ± 2.19 versus controls 10.11 ± 2.41) between the two groups (P-values > 0.2). The addiction group had used heroin 1.16 ± 0.72 g per day for an average of 4.05 ± 2.21 years. All participants were smoking. The heroin addicts (34.67 ± 5.16 cigarettes per day) smoked more cigarettes in comparison to the controls (18.66 ± 6.40 cigarettes per day), $t = 7.54$, $P < 0.001$.

After a 3-day abstinence interval, fractional anisotropy (FA) values in left frontal gyrus (−18,4,46, peak Z = 3.58, cluster size = 17, $P < 0.001$) and left cingulate gyrus (−18,0,30, peak Z = 3.43, cluster size = 32, $P < 0.001$) were significantly lower in the heroin abusers, compared with the healthy subjects (see Fig. 1). Importantly, after 1-month abstinence interval, there were no significant differences between heroin-dependent subjects and controls on FA values in any brain regions. Our study demonstrated that early abstinentheroin-dependent individuals had reduced FA values in the frontal gyrus and cingulate gyrus.

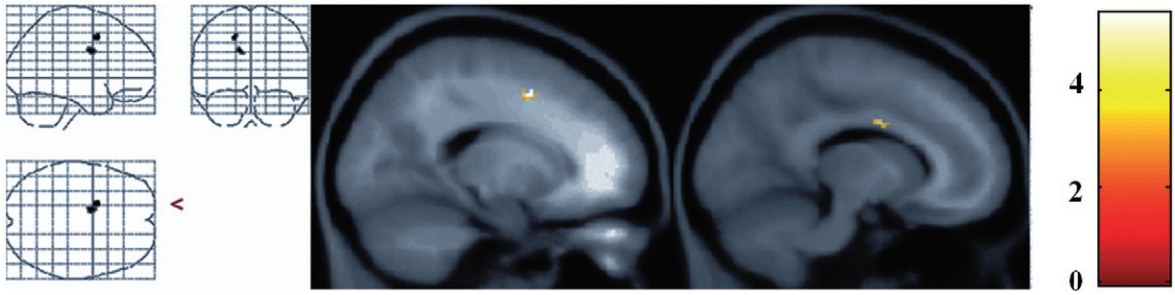

Figure 1 Brain maps of representative sagittal slices showing regions of abnormal fractional anisotropy in heroin group after 3 days abstinence in relation to healthy controls

Importantly, no significant difference between heroin-dependent subjects after 1 month of abstinence and the control subjects on FA values was found.

Drug addiction is characterized by a loss of control over drug intake. It has been proposed that dysfunction in frontal regions is a key neural mechanism underlying addiction (Goldstein & Volkow 2002). In accord with this hypothesis, we found that FA values in the frontal gyrus and the cingulated gyrus were smaller in early abstinent heroin-dependent individuals, which might underpin the cognitive control deficits in heroin-dependent subjects.

It has been proposed that drug abuse-induced neurocognitive deficits should be seen as recoverable limitations of neuronal plasticity rather than as permanent 'lesion effect' (Robinson & Kolb 2004). Rapeli *et al.* (2006) suggested that cognitive deficit during early abstinence from opioid dependence is partly transient. Our finding that there was no significant difference between the controls and heroin-dependent subjects after 1 month of abstinence on FA values suggest that the reversibility of white matter microstructural abnormalities might underlie the improvement in cognitive control.

Some limitations in our study are worth mentioning. First, the smoking status was not well matched. It was possible that the differences in FA values between 3 days abstinent heroin addicts and controls are related with nicotine use. Second, our study includes a relatively small sample size that may not be big enough to reveal the microstructural abnormalities in white matter between abstinent heroin addicts and controls after 1 month.

In summary, our study found that the FA values were reduced in frontal and cingulate regions for early abstinent heroin-dependent individuals in comparison with controls, and such abnormality disappeared after 1 month of abstinence. These findings demonstrate that heroin-dependent patients have microstructural disruptions in white matter and these changes are reversible after short-term abstinence.

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Authors Contribution

XW, RY, XZ, TL and WH designed the study and wrote the protocol. XW and XZ collected the magnetic resonance imaging (MRI) data. XW, JT, YL and BS undertook the MRI data analyses, and XW and RY wrote the manuscript. All authors have critically reviewed content and approved final version submitted for publication.

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SUPPORTING INFORMATION

Additional Supporting Information may be found in the online version of this article at the publisher's web-site:

Appendix S1. Methods.