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Neurobiological underpinnings of sensation seeking trait in heroin abusers

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Abstract
Neurobiological investigation of heroin revealed that abusers of this highly addictive substance show dysregulation in brain circuits for reward processing and cognitive control. Psychologically, personality traits related to reward processing and cognitive control differed between heroin abusers and non-abusers. Yet, there is no direct evidence on the relationship between these neurobiological and psychological findings on heroin abusers, and whether such relationship is altered in these abusers. The present study filled this research gap by integrating findings obtained via magnetic resonance imaging (structural volume and resting-state functional connectivity) and self-reported personality trait measures (Zuckerman's Sensation Seeking Scale and Barratt Impulsivity Scale) on 33 abstinent heroin users and 30 matched healthy controls. The key finding is a negative relationship between high sensation seeking tendency and midbrain structural volume in the heroin users. Importantly, there was stronger coupling between the midbrain and ventromedial prefrontal cortex and weaker coupling between the midbrain and dorsolateral prefrontal cortex in heroin users. Our findings offer significant insight into the neural underpinning of sensation seeking in heroin users. Importantly, the data shed

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light on a novel relationship between the mesolimbic-prefrontal pathway of the reward system and the high sensation seeking personality trait in heroin abusers.

1. Introduction

Heroin abuse elicits rapid feelings of euphoria and adverse withdrawal effects. For these reasons, heroin is very addictive and its abuse highly resistive from long-term abstinence. The severe and persistent socio-economic burden caused by heroin addiction (Tang et al., 2006) highlight the significance of understanding the neuropsychological basis of heroin use. At the neurobiological level, heroin abuse is known for disrupting the mesolimbic-prefrontal pathway, which is an integral part of the brain reward system implicated in addiction (Everitt and Robbins, 2005; Goldstein and Volkow, 2011; Schultz, 2011). At the psychological level, sensation seeking and impulsivity traits are two personality constructs commonly associated with heroin addiction (Craig, 1979). One crucial and outstanding issue that needs addressing is the neural underpinning of these personality traits that characterize heroin abuse. Currently, information on such neurobiological basis of heroin use is scarce. This lack of information may be because the accessibility of the heroin-abusing population has been a challenge, even though the abuse of heroin is prevalent among substance abusers (Tang et al., 2006).

Regarding the long-term effect of heroin use on brain structure, a consistent finding is that abstinent heroin users have reduced gray matter volume in the prefrontal cortex (Liu et al., 2009a), among other brain regions (Lyoo et al., 2006; Yuan et al., 2009, 2010b). Regarding task-induced changes in blood-oxygenated level dependent (BOLD) signal, regions along the mesolimbic-prefrontal circuit (including the midbrain, striatum, amygdala, hippocampal, and prefrontal regions) have been most commonly found to alter in abstinent heroin users, especially in response to reward stimuli (Zijlstra et al., 2009) or cognitive demand (Lee et al., 2005). Resting-state functional connectivity studies found abnormal coupling in brain regions associated with reward processing and cognitive control (Liu et al., 2009b; Ma et al., 2010, 2011; Yuan et al., 2010a, 2010c), in either abstinent heroin abusers or individuals on methadone maintenance treatment (MMT). Although the vast majority of neuroimaging studies investigated heroin users in a state of abstinence, there are a few recent studies that examined the acute effect of heroin on heroin-dependent individuals enrolled in addiction treatment. These studies revealed that, compared to saline, heroin administration reduced BOLD signal in the prefrontal cortex (in response to cognitive demand) (Schmidt et al., 2013), the amygdala network (in response to emotional stimuli) (Schmidt et al., 2015a), and enhanced BOLD signal in the resting-state functional connectivity of the left putamen (in response to subjective pleasure) (Schmidt et al., 2015b). Furthermore, animal models of addiction demonstrated that the reward system is critically involved in heroin-seeking behavior (e.g., the nucleus accumbens; LaLumiere and Kalivas, 2008).

On a separate line of studies, the personality traits related to reward and cognitive control have been investigated among heroin users. Two personality constructs closely linked with heroin abuse are sensation seeking and impulsivity traits (Craig, 1979). Sensation seeking refers to need to seek intense sensations and the desire to engage in risky behavior associated with such sensations (Zuckerman, 1994). Individuals with heroin addiction scored higher on this trait compared to controls, even after adjusting for group differences in age, education, and intelligence (Platt, 1975). Impulsivity refers to the degree of behavioral control over novel or distracting stimuli and is known to underlie impulsive behavior in various forms of addiction (Patton et al., 1995). Both current and abstinent heroin users were reported to score higher on the impulsivity trait, relative to matched controls (Clair et al., 2009). Neuroimaging studies on healthy adults revealed that these personality traits are associated with the brain reward system. For instance, the novelty/experience seeking trait was found to correlate with the extent of glucose metabolism in the midbrain, parahippocampal region, and right prefrontal cortex (Youn et al., 2002), and with structural volume of the right hippocampus (Martin et al., 2007). A relatively recent study revealed that higher impulsivity trait is associated with lower structural volume of the ventromedial prefrontal cortex (Matsuo et al., 2009). Despite the theoretical postulations that the brain reward system underpins the pathological personality traits in people with addiction, there has not been any study that directly characterized this neuropsychological relationship in heroin abusers. This characterization is important because defining such neuropsychological abnormality would help refine theoretical models of addiction (Dalley et al., 2011; de Wit, 2009; Everitt et al., 2008; Schoenbaum et al., 2006). It would also facilitate the potential to utilitize neuroimaging measures as a biological predictor of personality pathology; and vice versa, in which trait measures act as a behavioral predictor of neuropathology.

To these ends, we recruited a group of currently abstinent heroin abusers and matched healthy controls to test for group difference in the relationship between brain and personality trait (sensation seeking and impulsivity traits) measures. A multimodal imaging protocol of structural volume and resting-state functional connectivity was used, as both imaging modalities have strong conceptual grounds for their ability to capture individual differences in cognition and behavior (Harmelech and Malach, 2013; Kanai and Rees, 2011). The Zuckerman Sensation Seeking Scale (SSS) and the Barratt Impulsivity Scale (BIS) were used for measuring sensation seeking trait and impulsivity trait respectively, as both have sound psychometric properties and are widely used self-report measurement scales (Clair et al., 2009; Lai et al., 2011; Patton et al., 1995; Zuckerman, 1994). Abstinent heroin users were