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Review

Characterizing the cognitive effects of cocaine: A comprehensive review

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ABSTRACT

Understanding the cognitive sequela of repeated cocaine use is a growing area of research and is crucial to the development of cognitive models of addiction. We systematically reviewed all available placebo-controlled and case-controlled studies on the acute and long term effects of cocaine on cognitive functioning. In order to compare the magnitude of cognitive effects across cognitive domains we conducted several meta-analyses on a subset of data from long term effect studies. Studies on acute cocaine administration suggest enhancement of response inhibition and psychomotor speed, while all other domains appear to be unaffected or not investigated adequately. Long term effects of cocaine show a wide array of deteriorated cognitive functions, indicating that long term cocaine use is characterized by a general cognitive impairment across functions, rather than with specific cognitive deficits. Literature on long-term cocaine effects is more substantial than literature on acute effects. This comprehensive review outlines possible dissociations and similarities of acute vs. long-term cocaine effects in the human brain. Atherosclerosis after cocaine exposure may underlie cognitive dysfunction suggesting involvement of several brain areas. Acute drug studies are important to the future development of addiction models.

Contents

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1. Introduction

Cocaine has been identified as one of the most powerful reinforcers currently known (Kuhar et al., 1991). After cannabis, it is the most popular drug of abuse in Europe. Cocaine has been used at Q2 least once in a lifetime by 4.3% of the general population (EMCDDA, 2011). Cocaine use is associated with an increased risk of a range of somatic, psychological and social problems; such as cardiac toxicity, psychosis, mood and anxiety disorders, aggression and crime (Gawin and Kleber, 1986; Kilbey et al., 1992; Kloner and Hale, 1993; Maraj et al., 2010) and a considerable risk of transition to addiction (Dhossche and Rubinstein, 1997; Gawin, 1991; Licata et al., 1993). Establishing cognitive alterations associated with cocaine use, may lead to a better understanding of mechanisms associated with this transition.

Cocaine belongs to the group of 'stimulant drugs', typically elevating mood, increasing feelings of well-being, energy and alertness Q3 (Boys et al., 2001). The pharmacological effects of cocaine at the synapse level are relatively well understood. Acute cocaine administration increases dopaminergic, serotonergic and noradrenergic neurotransmission by blocking pre-synaptic monoamine transporters in the central nervous system (Schlaepfer et al., 1997; Volkow et al., 1999b). Moreover, cocaine interacts with multiple neuromodulatory systems e.g. glutamate, endocannabinoid and GABA (Diaz et al., 2010). On the other hand, chronic cocaine use has a large impact on brain function related to downregulation of dopamine D2 (DRD2) receptors in the striatum (Volkow et al., 1999b), abnormalities in brain glucose metabolism (Baxter et al., 1988; Volkow et al., 1988) and vascular hypoperfusion in subcortical, temporal, and frontal regions (Strickland et al., 1993). Recently, it was suggested that cocaine dependent users show smaller gray matter volumes in dopaminergic regions including the striatum (Barros-Loscertales et al., 2011a) and that gray volume can be changed as a function of years of use and abstinence (Connolly et al., 2013). It should be noted that that the latter findings are not uniformly established and comparisons between studies show Q4 that results are still variable (Mackey and Paulus, 2013).

Establishing how these cocaine-induced aberrant brain processes relate to impaired cognitive changes in humans is of crucial importance in understanding and treatment of cocaine addiction and related impulse control problems. It is beyond doubt that, the field has greatly benefitted from a wealth of preclinical work in rodents and non-human primates, where it is possible to directly probe the neurobiological mechanisms responsible for impaired functionality (see for a review e.g. Bradberry et al., 2008). The field Q5 of *human* drug research has also greatly developed, due to more refined cognitive paradigms and the use of brain imaging.

The cognitive effects in humans following *crack* cocaine use, and following prenatal cocaine exposure has been established in recent reviews (Ackerman et al., 2010). Jovanovski et al. (2005) performed, to our knowledge, the latest review on long-term cognitive effects in humans. A systematic review into cocaine's effects on cognition that distinguishes between acute and long-term effects has not yet been published. This is in contrast with reviews on other classes of drugs such as cannabis and MDMA, on which various reviews have been published more recently (Crean et al., 2011; Dumont and Verkes, 2006; Kalechstein et al., 2007; Zakzanis et al., 2007; Zuurman et al., 2009). The cognitive effects of these drugs are also better understood. For example, acute cannabis administration has been consistently found to lead to psychomotor slowing (Dumont et al., 2011; Ramaekers et al., 2006b,a, 2009b), whereas chronic cannabis use has been repeatedly found to be associated with impaired short-term memory (Solowij and Battisti, 2008). Importantly, there is an increasing trend in the literature of considering the temporal evolution of development of addiction (e.g. Everitt and Robbins, 2005; Field et al., 2006). The evolution from acute to long term drug effects is an important feature of addiction models. Therefore, we will review both acute and chronic cognitive effects of cocaine. The review will be organized according to cognitive domains and concludes with discussing the differences and similarities between in acute and chronic term drug effects and discuss these in terms of their implications for treatment and future research.

2. Methods

2.1. Literature search and inclusion criteria

Included in the review were all identified studies that described cognitive effects associated with cocaine in human adult individuals. We systematically searched "PubMed" using the search terms "cocaine" and "cognition" OR "cognitive" OR "neuropsychology". Additional searches were performed with the terms 'cocaine' and each of the cognitive domains discussed below: 'attention, 'response inhibition OR inhibitory control', 'memory',

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