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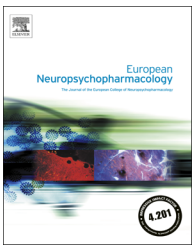

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REVIEW

The cannabinoid system and visual processing: A review on experimental findings and clinical presumptions

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Abstract
Cannabis is one of the most prevalent drugs used worldwide. Regular cannabis use is associated with impairments in highly integrative cognitive functions such as memory, attention and executive functions. To date, the cerebral mechanisms of these deficits are still poorly understood. Studying the processing of visual information may offer an innovative and relevant approach to evaluate the cerebral impact of exogenous cannabinoids on the human brain. Furthermore, this knowledge is required to understand the impact of cannabis intake in everyday life, and especially in car drivers. Here we review the role of the endocannabinoids in the functioning of the visual system and the potential involvement of cannabis use in visual dysfunctions. This review describes the presence of the endocannabinoids in the critical stages of visual information processing, and their role in the modulation of visual neurotransmission

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and visual synaptic plasticity, thereby enabling them to alter the transmission of the visual signal. We also review several induced visual changes, together with experimental dysfunctions reported in cannabis users. In the discussion, we consider these results in relation to the existing literature. We argue for more involvement of public health research in the study of visual function in cannabis users, especially because cannabis use is implicated in driving impairments.

1. Introduction

Cannabis use is very widespread in industrialized countries. In the United States, the lifetime prevalence of cannabis use is estimated at 42%, and the prevalence in the year preceding the interview at 21.5% (Degenhardt et al., 2008). In the European Union, some 75.5 million people aged 15–64 years old report having already smoked cannabis at least once in their lives, and 23 million Europeans used cannabis in the year preceding interview (European Monitoring Centre for Drugs and Drug Addiction, and Publications Office of the European Union, 2010). Regular cannabis use may have long-term health consequences. Part of these effects is comparable to that of tobacco, especially when smoked without a filter, such as bronchopulmonary cancers (Mehra et al., 2006), chronic respiratory diseases (Tetrault et al., 2007), arteritis (Sauvanier et al., 2002) and reproductive disorders (Holt et al., 2005; Vescovi et al., 1992). However, other outcomes are more directly linked to cannabis itself, such as psychiatric and cognitive effects. For example, higher risk of developing schizophrenia is correlated with cannabis use (Casadio et al., 2011; Moore et al., 2007). In a recent cohort study, 20 years of regular cannabis use was found to result in a significant intelligence quotient (IQ) decrease and major impairment in executive functions and processing speed (Meier et al., 2012). More specifically, the best-documented cognitive impairments due to regular cannabis use involve executive functions (Bolla et al., 2002; Pattij et al., 2008; Verdejo-García et al., 2006), memory (Bolla et al., 2002; Solowij and Battisti, 2008), and attention (Solowij et al., 1995). Studying the impact of cannabis use on these cognitive functions is particularly relevant from a clinical point of view. However, the precise neural mechanisms underlying impairments due to cannabis use, in particular those in cognitive functions critical for car driving, are still being debated. Consequently, modeling the effects of exogenous cannabinoids on the human brain on this basis is problematic because these high-level cognitive functions are tightly integrated and involve many brain areas (Aggleton, 2014; Funahashi and Andreau, 2013; Somers and Sheremata, 2013).

Low-level vision may therefore be a good candidate for conceptualizing the neural impact of regular cannabis use for several reasons. Despite the evolution of mammals, the visual function displays good preservation of functional and anatomical characteristics across species (Yoon et al., 2013), thus allowing the translation of findings between animals and humans. A broad range of techniques – electrophysiological, imaging and pharmacological – can be used alone or coupled to each other to study anatomical details and physiological or molecular mechanisms of the visual system (Disney et al., 2007; Katzner et al., 2011). For example, pharmacological modulation of gabaergic and glutamatergic receptors by the administration of agonists or antagonists may be useful techniques. In the human being, studying the earliest stages of visual processing, for example at the retina level, has the advantage of being less sensitive to attentional variation during experimental measurements, thus eliminating the bias of nonspecific generalized attentional deficit, which is difficult to control (Knight and Silverstein, 2001). Besides this fundamental question, and considering that the visual function seems to be altered in cannabis users, it is now crucial to obtain more insight on how cannabis use may change visual perception, especially given the pervasive role of vision in human everyday life. For example, cannabis users drive, and so we need to know whether or not regular intake of cannabis affects the visual ability of drivers.

This review looks at the involvement of the endocannabinoid system in visual processing, and whether exogenous cannabinoids may affect visual function. We review human and animal studies that have examined the distribution of cannabinoid receptors and ligands, together with those that have investigated the involvement of the cannabinoid system in neurotransmission and synaptic plasticity of visual information processing. We also review studies that have shown visual changes and experimental visual dysfunctions following both acute and chronic cannabis use. These results are discussed on the basis of the existing data in the literature. Since cannabis constitutes the most prevalent illicit drug implicated in road fatalities, we also argue for more involvement of public health research in the study of visual function among cannabis users (Hartman and Huestis, 2013).

2. Experimental procedures

A search for relevant articles was conducted in the Pubmed and Google Scholar databases using the following keywords (“CANNABIS” OR “CANNABINOID” OR “MARIJUANA” OR “THC”) AND (“VISION” OR “VISUAL PROCESSING” OR “VISUAL SYSTEM” OR “VISUAL CORTEX” OR “RETINAL PROCESSING” OR “RETINA” OR “THALAMUS”). All results up to February 28, 2014 were examined for the selection process. Relevant publications were chosen through an individual independent selection of titles by three authors (TS, VL, RS). The articles selected had to be written in English and be related to the topic of the review. Additionally, a manual search was performed on the bibliography of each selected article.