REVIEW OF CLINICAL PHARMACOLOGY AND
PHARMACOKINETICS INTERNATIONAL
EDITION 24: 140-141 (2010)

Region-dependent and Individual Differences in Glutamate Tissue Content Following Cannabinoids Administration

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Key words: Glutamate, cannabinoids, motor activity

S u m m a r y. Endocannabinoids modulate neurochemical processes in which a variety of neuro-transmitters are involved. The excitatory neurotransmitter system, including glutamate and aspartate, partakes in cognitive function and neuroplasticity but is also involved in neurotoxicity processes. The aim of the present study was to in-vestigate the effects of cannabinoids on tissue levels of glutamate in two rat phenotypes previously differentiated as High Responders (HR) or Low Responders (LR), according to their response to a novel environment. Our results have shown that HR displayed increased motor activity as compared to LR rats. Cannabinoids modified motor activity in a dose-dependent manner, indicating a biphasic behavioral profile. Concerning glutamate tissue content, cannabinoids induced notable differences in glutamate content in a region-, phenotype- and drug dose- dependent manner. This study addresses the role of cannabinoids in modulating glutamate function and reveals a drug dose-, phenotype- and region- dependent effect on glutamate status. These results contribute to the emergent evidence indicating that cannabinoids are implicated in a variety of physiological functions such as cognition and neuroplasticity as well as pathological states such as neurotoxicity.

INTRODUCTION

Endocannabinoids modulate neurochemical processes in which a variety of neurotransmitters are involved. The neurochemical effects of exogenously administered cannabinoids and endocannabinoids are mediated via stimulation of cannabinoid receptors. Amongst the neurotransmitter systems with which the endocannabinoid system interacts (and plays a modulatory role), is the excitatory. The excitatory neurotransmitter system partakes in cognitive function and neuroplasticity but is also involved in neurotoxicity processes. Two key players involved in this modulation are the excitatory amino acids (EAAs), glutamate and aspartate. In the present study, we investigated the effects of Δ^9- tetrahydrocannabinol (THC) and WIN55,212-2 (WIN), two CB_1 receptor agonists with distinct pharmacological profiles, on tissue levels of glutamate in two rat phenotypes previously differentiated as High Responders (HR) or Low Responders (LR), according to their response to a novel environment.

METHODS

Male Sprague – Dawley rats were differentiated based on the vertical activity into HR and LR phenotypes. Either THC, WIN or vehicle were administered intraperitoneally (i.p.) to both phenotypes. Ambulatory and vertical locomotor activities were automatically registered. Another subset of rats received THC, WIN or vehicle and glutamate tissue levels were measured in discrete rat brain regions using High Performance Liquid Chromatography with electrochemical detection.

RESULTS

Our results have shown that HR displayed an increased motor activity as compared to LR rats. THC and WIN modified motor activity in a dose-dependent manner, indicating a biphasic behavioral profile.

Concerning glutamate tissue content, THC modified glutamatergic status in a region-, phenotype- and dose-dependent manner. This neurochemical profile was similar to some extent following WIN administration.

DISCUSSION

This study addresses the role of cannabinoids in modulating glutamate function and reveals a drug dose-, phenotype- and region-dependent effect on glutamate tissue levels. These results demonstrate the ability of cannabinoids to produce distinct neurochemical events in EAA status which is greatly implicated in a variety of physiological functions such as cognition and neuroplasticitity as well as pathological states such as neurotoxicity.

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