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An Approach to the Effects of Cocaine and Alcohol in Astrocytes

Main Aims

- To elucidate which **astrocytic molecular pathways** have been importantly related with the abuse of some **addictive drugs**. Thus, two different types of drugs of abuse have been picked up as examples of substances that **stimulate** or **depress** the Central Nervous System (CNS).
- To evaluate whether **differences in their mechanisms** have been observed and to find out whether these effects have been related to **different consumption patterns**.

Methodology

This project has been made as a scientific review using principally original articles found in PubMed, Scopus, and Sciencedirect databases, also consulting some scientific journals (most used: *The Journal of Neuroscience*) , doctoral thesis and books and contacting with *Guerri, C.* (Principe Felipe Research Centre, Valencia). Articles used have been picked up considering their abstract, conclusions and concretion into the topic, as well as if they had been referred in previous articles read. Thus, approximately 50 publications have been read, although 35 have been finally used in the project writing. Main **key words** used: *cocaine AND astrocytes*, *alcohol/ethanol AND astrocytes, gene expression in alcohol/cocaine consumption, neuroinflammation AND cocaine/alcohol, glutamate AND cocaine/alcohol*, *astrocyte physiopathology.*

Introduction

Astrocytes Functions

Astrocytes are related to the reuptake and recycling of some extracellular neurotransmitters by using the gliotransmission. They also **supply energetic substrate** to neurons and have control of brain's glycogen and energy reserves. Actually, it has been reported that astrocytes show a high glycolytic rate that also results in a high production of lactate.

Nevertheless, astrocytes also play other roles in the **regulation of extracellular ions**, **pH**, **homeostasis** and **endothelial cells** by secreting angiogenic factors in order to regulate the blood brain barrier pressure, permeability and its blood flow in the CNS. So are the **immune system**, the extracellular matrix and a bunch of **neurotrophic factors** modulated.

Gliotransmission is described as the release of chemical transmitters from astrocytes to the brain environment. Reported transmitters most released by astrocytes are glutamate, ATP and D-serine contributing to the astrocyte-neuron communication as observed in several parts of the brain. Due to these secretions, gliotransmission has been shown to regulate synaptic transmission and plasticity.

Drugs of Abuse

Cocaine is an alkaloid and lipophilic molecule with neuropsychological stimulating effects that may produce euphoria in a short term and addiction in a long term.

Ethanol is a neuropsychological depressant and a small polar molecule that can easily diffuse into the brain. Initially, it causes inhibition, but depressive behaviour is presented in chronic consumption.

Thus, it seems reasonable that both drugs might affect astrocytes due to their wide distribution and metabolism interaction in the brain.

Results

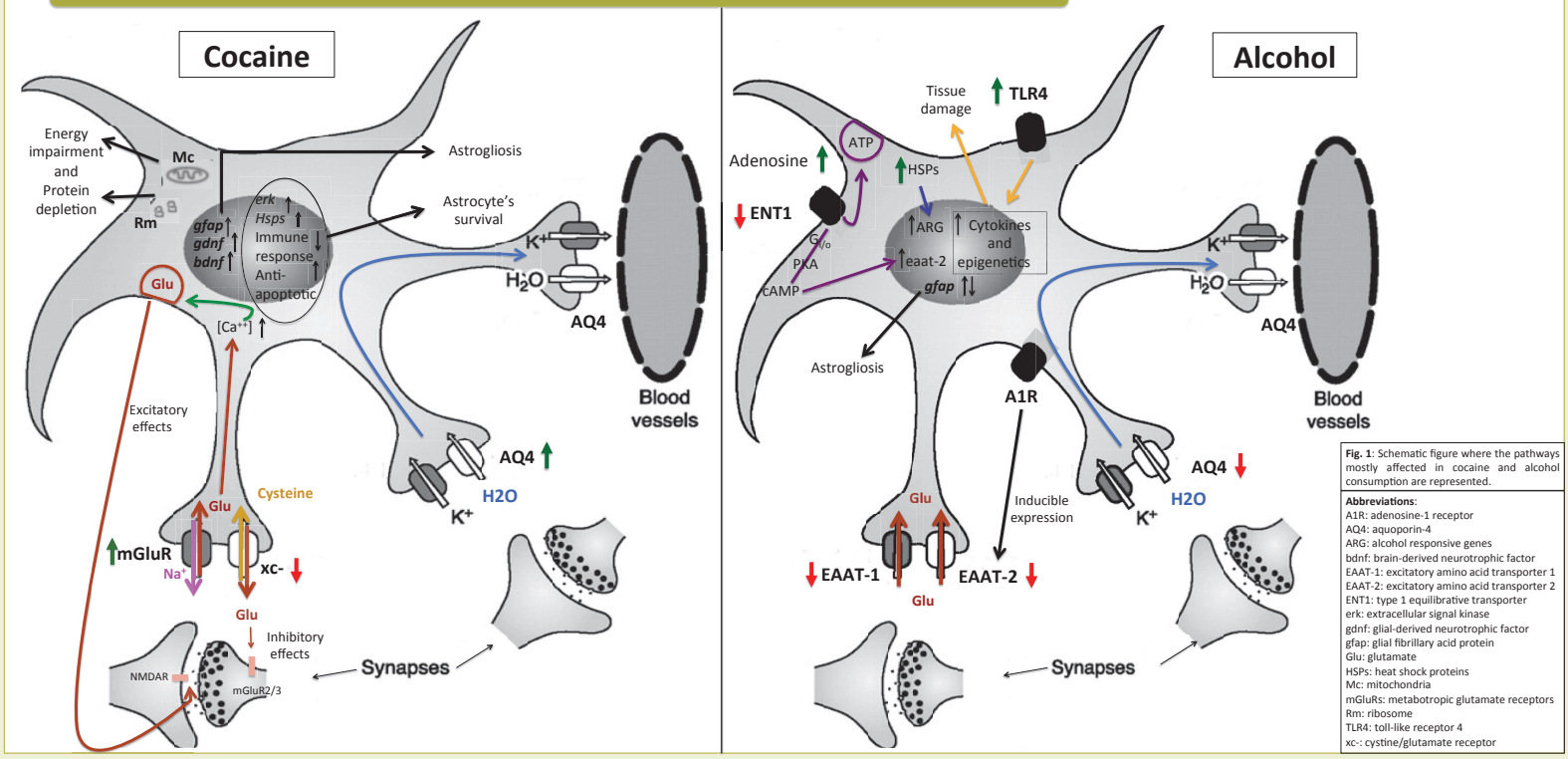

Fig. 1: Schematic figure where the pathways mostly affected in cocaine and alcohol consumption are represented.

Abbreviations:
A1R: adenosine-1 receptor
AQ4: aquoporin-4
ARG: alcohol responsive genes
bdnf: brain-derived neurotrophic factor
EAAT-1: excitatory amino acid transporter 1
EAAT-2: excitatory amino acid transporter 2
ENT1: type 1 equilibrative transporter
erk: extracellular signal kinase
gdnf: glial-derived neurotrophic factor
gfap: glial fibrillary acid protein
Glu: glutamate
HSPs: heat shock proteins
Mc: mitochondria
mGluRs: metabotropic glutamate receptors
Rm: ribosome
TLR4: toll-like receptor 4
xc-: cystine/glutamate receptor

Conclusions

- A great majority of studies carried out about the neuropathology of drug abuse have focused on the effects observed in neurons, especially in dopaminergic neurons and in specific brain areas. Moreover, the effects in other brain cell types have been much less studied and towards improvement seen in neurons experimental data. Despite this, **currently research in astrocytes knowledge may provide a new approach on how neuropathologies are studied.**
- Further experiments so as to better identify the **molecular pathways related to drug consumption** and astrocytes roles may contribute to better knowledge of addiction.
- After the large searching done in this project, we may conclude that astrocytes exemplify a case where a **fine regulation of the CNS** is observed and it may provide a better preclinical and clinical approach to a complex pathology. Therefore, several **targets** have been picked out and highlighted along this project such as anti-inflammatory drugs and transport agonists.