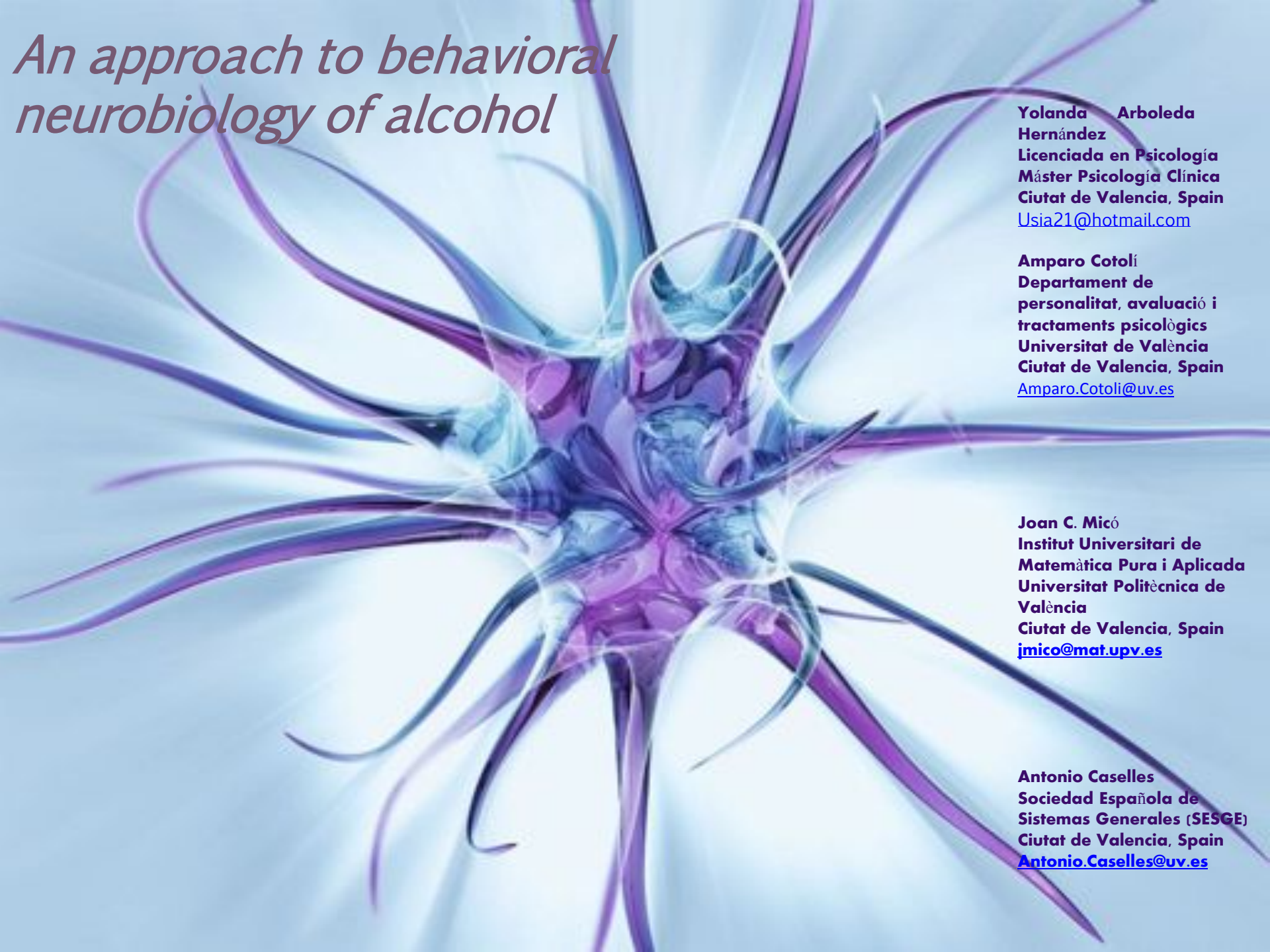
An approach to behavioral neurobiology of alcohol



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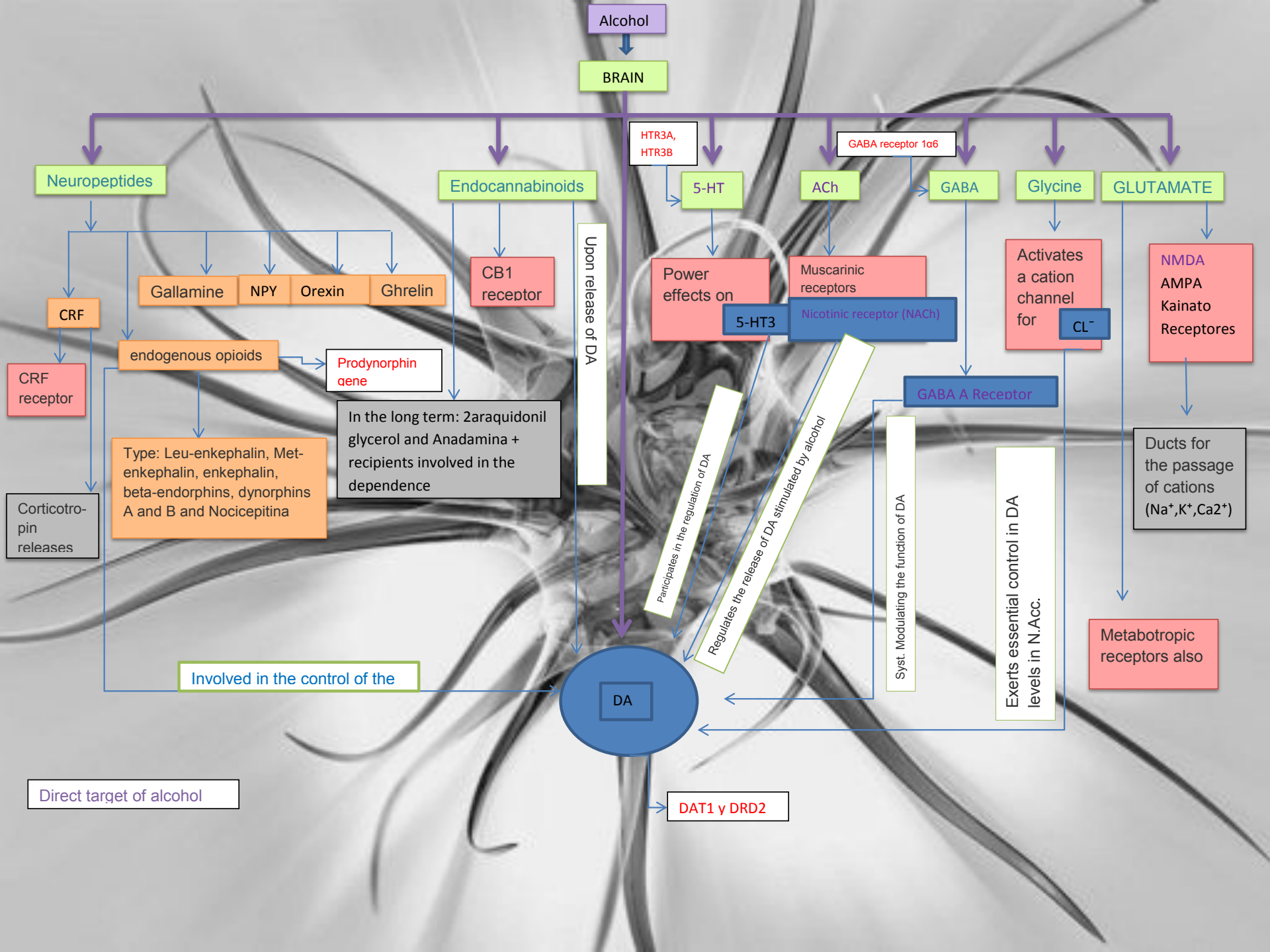
Today there is no doubt about intake of alcohol affects the brain neurotransmission. The biochemistry of the brain is reoriented and acts as a result of the new substance that invades the body. Its adaptive capacity is admirable, but there is a price to pay when that adjustment is performed consistently.

Structural, neurological and functional changes produce other changes on both cognitive and affective level in the person which consumes alcohol. We might wonder if certain forms of stable behavior, what we call "personality", can also be modified when the mild or moderate consumption becomes habitual

Research is needed to assess the subjective beneficial changes that manifest certain people. The problem of alcohol is its addictive power. When it is chronic and consumption increases, physical and psychological pathologies that can lead to death emerge.

In this work we present an organized recompilation of some recent findings about the brain biochemical markers over which alcohol impacts. Such markers are related to the biological basis of personality, such as glutamate, and to the variable extraversion/introversion.


Alcohol
BRAIN
Neuropeptides
Endocannabinoids
HTR3A, HTR3B
5-HT
ACh
GABA receptor 1α6
GABA
Glycine
GLUTAMATE
CRF
Gallamine
NPY
Orexin
Ghrelin
CB1 receptor
Upon release of DA
Power effects on
5-HT3
Muscarinic receptors
Nicotinic receptor (NACh)
Activates a cation channel for
CL⁻
NMDA
AMPA
Kainato
Receptores
CRF receptor
endogenous opioids
Prodynorphin gene
In the long term: 2araquidonil glycerol and Anadamina + recipients involved in the dependence
GABA A Receptor
Ducts for the passage of cations (Na⁺,K⁺,Ca2⁺)
Corticotro-pin releases
Type: Leu-enkephalin, Met-enkephalin, enkephalin, beta-endorphins, dynorphins A and B and Nocicepitina
Participates in the regulation of DA
Regulates the release of DA stimulated by alcohol
Syst. Modulating the function of DA
Exerts essential control in DA levels in N.Acc.
Metabotropic receptors also
Involved in the control of the
DA
Direct target of alcohol
DAT1 y DRD2

Summarizing, the outcome of the intake of alcohol is caused by the imbalance that occurs between inhibitory neurons (GABAergic neurons) and excitatory (Glutamatergic neurons) that break with its normal functioning. But also...

Dopamine, which is involved in mechanisms of reinforcement and reward, participates in the association of external stimuli with the consumption behavior. This fact is necessary for learning mechanisms to produce the reinforcement and maintenance of such behavior.

Serotonin is a key for functions such as regulation of mood, sleep/wake cycles or emotional behavior. Its recipients include the 5HT3 because it participates in the regulation of dopamine neurotransmission in the mesolimbic reward pathway (zone which is responsible for reinforcement) and it also seems that it takes part in the effects that alcohol can cause on the CNS.

The effect of acetylcholine is shown through two types of receptors: muscarinic and Nicotinic. These are points of action of alcohol and regulators of the dopamine released with the consumption of ethanol.

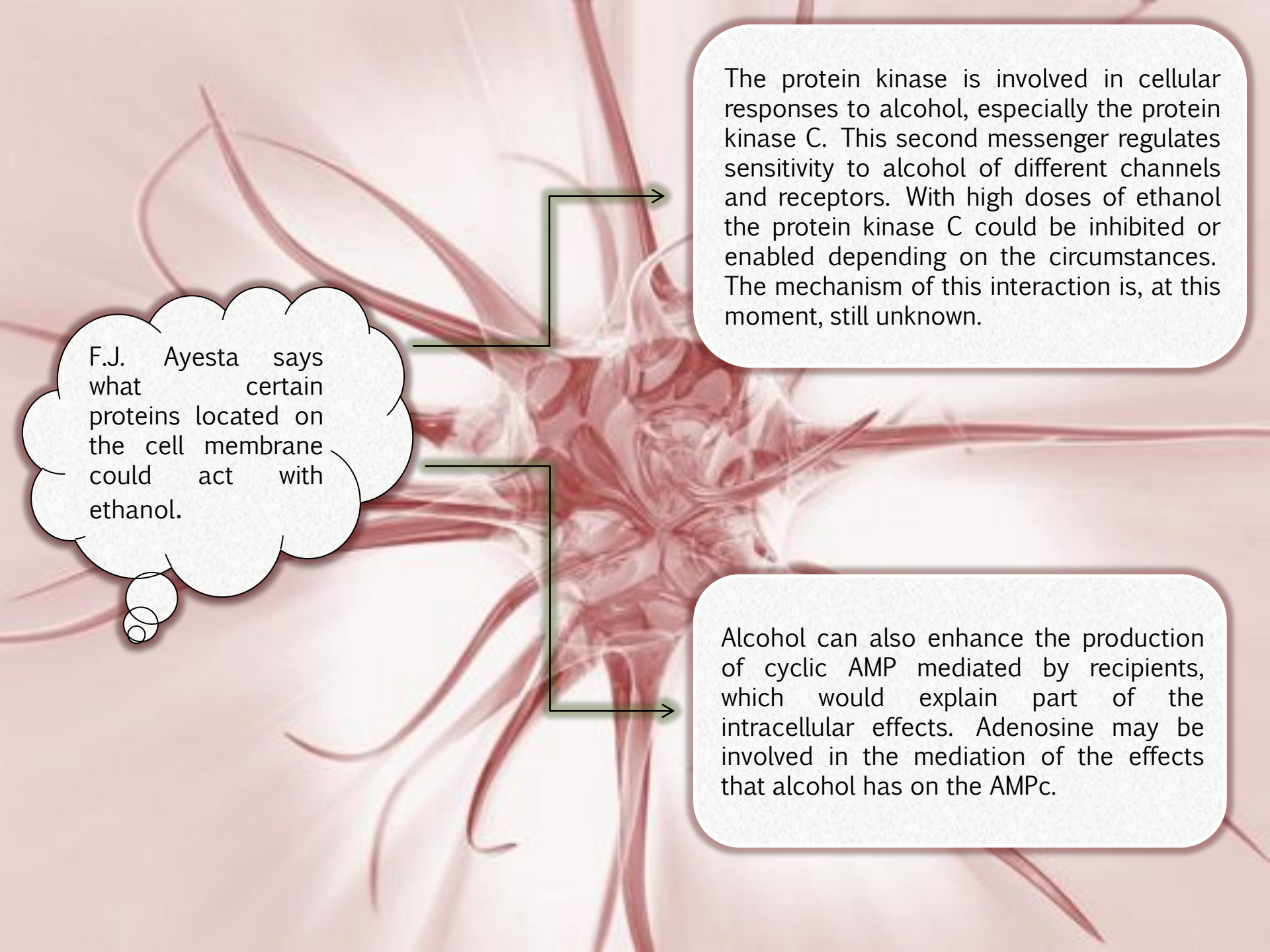
Glutamate, in addition to acting on metabotropic receptors, focuses on three receptors: NMDA, AMPA and Kainate, which in turn are conduits for the passage of cations Na^+, K^+ and Ca^2. This process assumes that the activation of the receptor gives rise to opening the channels, allowing the entry of cations, which produces a hyperpolarization of the membrane, which leads to a decrease in the excitability of the neuron and, consequently, a decrease of its functional activity

GABA, amino acid that has different brain functions related to its Union with specific receptors, has as receiver to the GABAA, which is considered as a direct target of alcohol as well as a modulator for the dopamine function.

Glycine is another amino acid that joining active a conduit for CL^-, its receptor cation.

Endocannabinoids and their receptors have been proved to be a good source of information for the understanding of the brain mechanisms connected with the Neurobiology of dependencies. The cannabinoid system appears to be involved in the reward mechanisms related to the intake of alcohol, which are conditioned by the release of dopamine and intervenes, in turn, on reinforcement mechanisms and rewards for alternatives to the dopamine pathways.

Opioid systems involved in the control of the alcohol-mediated dopamine activity. In addition, the ethyl alcohol stimulates the release of β-endorfinas. The endogenous opioids help pleasant impact that alcohol causes and consolidation of mechanisms for strengthening of the alcohol habit.


F.J. Ayesta says what certain proteins located on the cell membrane could act with ethanol.
The protein kinase is involved in cellular responses to alcohol, especially the protein kinase C. This second messenger regulates sensitivity to alcohol of different channels and receptors. With high doses of ethanol the protein kinase C could be inhibited or enabled depending on the circumstances. The mechanism of this interaction is, at this moment, still unknown.
Alcohol can also enhance the production of cyclic AMP mediated by recipients, which would explain part of the intracellular effects. Adenosine may be involved in the mediation of the effects that alcohol has on the AMPc.

The CRF is a neuropeptide that releases adrenocorticotropic hormone. It is synthesized in the hypothalamus, but we can also find this hormone in areas such as the amygdala and the terminal Groove. The action of this neuropeptide in their CRF1 receptors regulates responses to stress and certain emotional States which are associated with more advanced States of alcoholism.

There is one greater variety of neuropeptides which has a role in alcoholism. The Orexin, which participates in the process of search and preference for alcohol, the gallamine, ghrelin, substance P and NK1 receptors are examples of this.
F.J. Ayesta, reflected in his work "Biochemical Bases and alcohol addiction neurobiological" details they **are interesting** for our research.

Neuropeptides are involved in the regulation of motivation and emotions. It also stimulates the appetite and has anxiolytics properties. In recent experiments with animals, it has been observed that an antagonist for one of their receptors, the NPY2, fails to reduce the intake of alcohol or episodes of relapse; but it significantly reduces the anxiety that appears associated with withdrawal syndrome.

Pérez-Rial, S., Ortiz, S. and Manzanares, J. suggest

They also provide novel data according to recent results in long term experiments of consumption. It has been known all of the neurochemical alterations, which occur in the brain after the intake of chronically therapeutic implications in the endogenous cannabinoid system, have been discovered. It is suggested that such chronicity could modify the activity of the endogenous cannabinoid system components. This new system of neurotransmission is composed of ligands of endogenous Anandamina (AEA) and 2-arachidonoyl glycerol (2-AG) that bind specifically to two types of cannabinoid receptors, both coupled to protein G, CB1y CB2.
Chronic exposure to vapors of ethanol induces a decrease both the density and the functionality of the CB1 cannabinoid receptor in the plasma membranes of the brain of the mouse.

The withdrawal could be due to an inhibitory overactivity of the neural Adaptive mechanism not offset by the effect of alcohol. There is an increase in the activity of the NMDA receptor by prolonged inhibition of glutamatergic mechanisms, which would increase the amount of calcium that enters the nerve cells. But although calcium is essential for neuronal function, an excess of it produces toxicity and cell death. In fact, repeated cycles of abstinence and alcohol can trigger brain damage by excess of neuronal calcium.

Using animal models based on chronic consumption, it also explains the abstinence neurobehavioral responses to alcohol that show a decrease in *GABA*ergic activity and a reduction of the number and sensitivity of the receptor GABAA, responsible for the increased levels of anxiety triggered.

The endogenous opioid system also intervenes in the decline in the activity of dopamine that occurs during the period of withdrawal syndrome; in fact apply opioid antagonists in the treatment of withdrawal to alcohol

The reinforcement and dependence on alcohol is due to stimulation of the dopamine in the mesolimbic system activity, which interacts with receptors glutamatergic

DA

GABAergic neurons also act on the dopaminergic modulating the reinforcement or enkephalinergic neurons act on opioid receptors located in same dopaminergic neurons. At the same time, these enkephalinergic neurons are enabled by serotonergic receptor 5HT3 contributing to the same reinforcing purpose.

The conditions that lead to excessive alcohol consumption in some individuals and not in others are complex because they involve interaction among environmental, psychosocial, genetic and neurobiological factors.

More research is needed to study the connections between the neurobiologial changes and behavioral changes.

Although consumption is low to be moderated, alcohol causes variations in the neurobiological mechanisms. These variations produce altered mental processes of learning, memory, motivation, emotion and personality changes.


THANK YOU