Introduction

Addiction is a burden disease that a ects a wide part of the world population and is the most harmful form of abuse for users and for society [1]. Nevertheless pharmacological treatment for alcohol use disorders (AUD) have a modest e cacy and none of the molecules accepted in North America and Europe (Disul ram, Naltrexone, Acamprosate, Sodium Oxibate, Nalmefene) can be considered a gold standard for the treatment of alcohol use disorders [2-7].

On the light of this consideration many researchers are underlying the importance of personali ation in pharmacotherapy by matching patient features with drug hallmark as a strategy to improve the e cacy of the treatment [3,6]. In the perspective of personali ing treatments, the chance to include our neurobiological knowledge, though challenging, can't be overlooked.

Indeed, in the last years, thanks to neuroimaging non-invasive techniques, we had the chance to explore the central nervous system involved with the genesis of addiction and speculate on new interpretative models [8]. In particular the scientists agree on the presence of two complementary pathological neurobiological alterations: on one hand the improvement of positive reinforcement and negative reinforcement as drive mechanisms toward the use of drugs of abuse, and on the other hand the lack of control ability due to cognitive prefrontal control de cit and changes in thalamic-cortex circuitry of habit [9].

is article tries to match clinical features corresponding to speci c neurobiological pathological addiction and pharmacotherapy of alcohol use disorders as a new frontier of personali ation of treatment.

Personalization of pharmacological treatment

Between the few alcoholism pharmacological treatment guidelines, the most renowned are NICE (National Institute of Clinical Excellence) Guidelines [10] that identify Naltrexone and Acamprosate as the rst treatment line due to the presence of a high level of e cacy. Recent international reviews adopt the same position [5,11] but there are also other points of view that highlight the value of Sodium Oxibate and Disul ram for the treatment of AUD [6,12,13].

In particular Skinner review article concluded indicating the blind studies with placebo as an incorrect methodology to research Disul ram e cacy and, based on results with open-label studies, pointed out that Disul ram is a safe and e cacious treatment compared to other pharmacological treatments for AUD [13]. e Leone et Al Cochrane Review establishes that Sodium Oxibate is better than Naltrexone and Disul ram in maintaining abstinence and these side e ects are not statistically di erent from those with BZD, NTX or Disul ram [14]. Moreover Caputo et Al, analy ing 20 year of Italian physician experience with Sodium Oxibate treatment clari es that the drug is safe if it is used at therapeutically dosage and under medical supervision [15]. On the light of these considerations there aren't e cacy based criteria or side e ects based criteria for choosing between the four abovementioned molecules, that have got the same treatment indication (maintaining abstinence from alcohol or preventing relapse) but widely di erent mode of action. Personali ation of treatment is therefore suggested by many authors as the correct approach to alcoholism pharmacological treatment [3,6,16].

On the light of this consideration neurobiology of addiction and in particular of alcohol dependence can give us a key to di erentiate the clinical use of these four drugs and can be added to other matching variables for treatment personali ation as psychiatric and internal comorbidity and typology of alcoholism and craving.

Neurobiological Evidence

Behavioural control is not only a cognitive function but depends on

accumbens and associated ventral striatal areas [20] that initially mediates the grati cation e ect of drug and subsequently is able to increase salience and appetitive value of substance related stimuli [21]. is mechanism is called positive reinforcement of the drug. Alcohol related positive reinforcement is mediated by $GABA_A$ receptor activation that induces a disinhibition of GABAergic neurons in the VTA and subsequently a disinhibition of dopaminergic neurons that project from the VTA to the NAcc [22]. Moreover alcohol promotes the release of endogenous opioid peptides within the mesolimbic

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