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Research report

Evaluation of chronic alcohol self-administration by a 3-bottle choice paradigm in adult male rats. Effects on behavioural reactivity, spatial learning and reference memory

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ABSTRACT

Chronic ethanol consumption is able to modify emotional behaviour and cognition in humans. In particular, the effects exerted by alcohol may depend on doses, time and modalities of administration. In this study we investigated, in adult male rats, ethanol self-administration and preference patterns using a 3-bottle choice paradigm with water, 10% ethanol solution, and white wine (10%, v/v), along a four-week period. The influence of alcohol free-access on novelty-induced explorative behaviour in the open field, and on spatial learning and reference memory in the Morris water maze was also evaluated. Our results indicate that: (i) rats show a higher preference for alcohol, in the first two weeks of the paradigm, displaying a higher consumption of 10% ethanol solution than white wine; in the last two weeks, they reduce their alcoholic preference, drinking the same moderate amounts of the two alcoholic beverages; (ii) at the fourth week of the free-access paradigm rats show a high explorative behaviour in the central squares of the open field and an improvement in spatial information processing in the new-place learning task of the Morris water maze. In conclusion our data suggest that, interestingly, rats exposed to the free-access paradigm were able to self-regulate their alcoholic intake, and indicated that a moderate alcohol consumption was able to induce an increase in behavioural reactivity and an enhancement in spatial learning flexibility.

1. Introduction

Among the several aspects and characteristics of ethanol, taste takes on particular importance in humans. The different alcoholic beverages vary, besides in alcoholic content, also in taste and flavours, and for some individuals they seem to be anecdotally important in their choice of an alcoholic brand. Thus, taste represents the main boost during alcohol approaching, whereas drinking behaviour is more correlated to the metabolic and central effects of ethanol [1–3]; subsequently, and in particular during alcohol abuse, rewarding effects play a priority role together with negative reinforcement [4,5]. Alcoholic drinks, such as wine, are produced by alcoholic fermentation of fruit simple carbohydrates; sugar fermentation by yeasts occurs in nature so that some ripe wild fruits contain traces of ethanol up to 0.6% [6]. Fruit-eating animals must then inevitably consume alcohol on a regular basis, as a part of the normal behavioural repertoire: this makes rodents an ideal subject for studying alcohol-drinking behaviour [7–9]. One commonly used approach for modelling human alcohol consumption in rodents is the alcohol preference study, in which animals are given a choice between water and alcohol solutions of various strength, and the amount of each fluid consumed is measured. Usually, at the beginning, rats prefer low-dose alcohol solutions (<6%), because of their "sweet taste" [8], then high-dose ones [10]. Animal models of drug self-administration are important in determining the behavioural effects of alcohol, as well as of other drugs of abuse, as they provide controlled environments in which the subject self-administers the compound. Furthermore, experimental studies of acquisition of drug self-administration in drug-naive animals are important to investigate factors that affect vulnerability to initiation of drug-abuse in humans. Given these preliminary remarks, the first goal of the present study was to examine ethanol intake and preference patterns in heterogeneous adult male Wistar rats, using a 3-bottle choice paradigm with water, 10% ethanol solution, and white wine (10%, v/v), along a four-week period, in order to assess whether the organolectic properties of white wine could play a role in the initiation and maintenance of alcohol voluntary drinking in rats.

It is widely reported that chronic ethanol consumption is able to modify emotional behaviour and cognition in humans: approximately 75% of alcoholic patients will show some cognitive deficits

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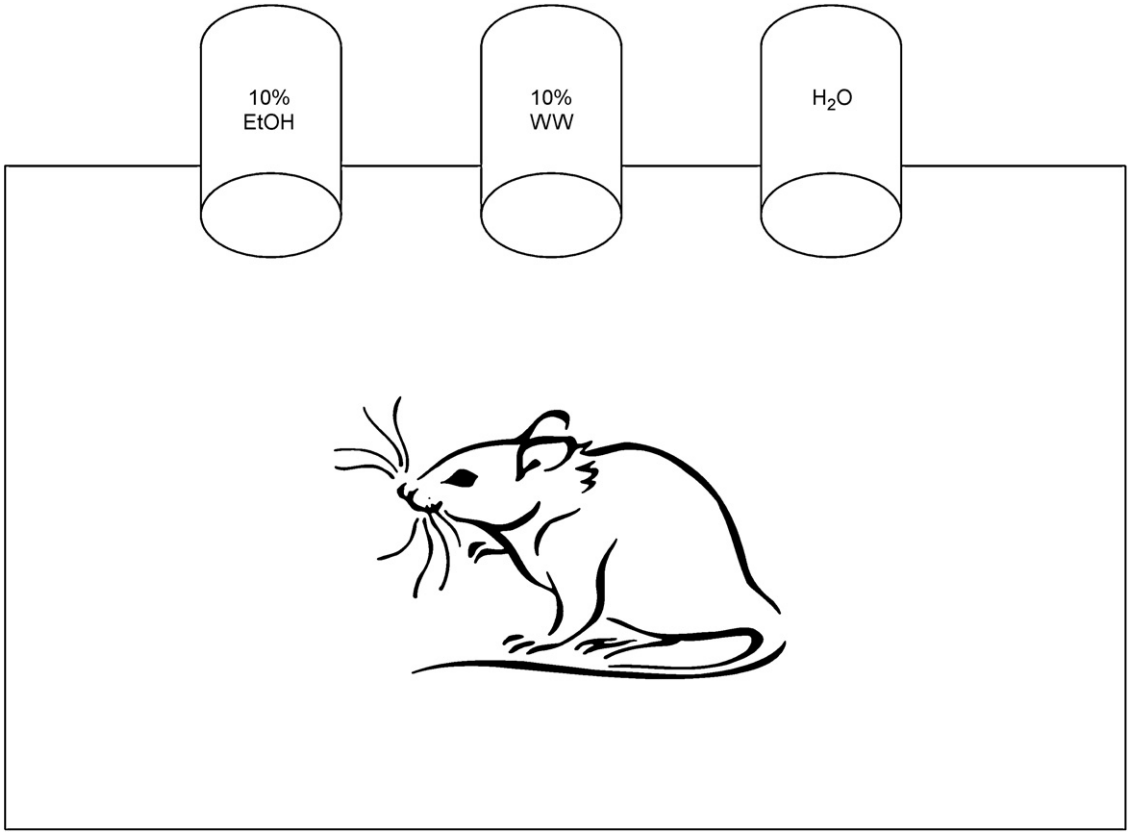

Fig. 1. Alcohol free access paradigm. Drinking behaviour was determined in individually housed male Wistar rats during 28 days in a 3-bottle paradigm with water, EtOH 10%, and white wine.

[11], such as impairments in intellectual function, memory, verbal and non verbal learning, visual-motor coordination, cognitive flexibility, executive functions, problem solving, decision-making, perception, information processing speed [12–16]. On the other hand recent reports suggest that moderate alcohol consumption may induce discrete beneficial health effects including lower risk for total and ischemic stroke [17], coronary heart disease [18–20], and dementia later in life [21], as well as a potentiation of visual and emotional memory traces [22,23]. Similarly, several reports on animal studies show a plethora of effects exerted by ethanol on different behavioural patterns, which depend on doses, time and modalities of administration. As a matter of fact, ethanol can have both stimulant and depressive behavioural effects [24,25]. In rodents the stimulant action of low doses of ethanol has generally been assessed using locomotor behaviour, [26,27]. Further studies show that anxiety-related behaviours are positively correlated with ethanol consumption [28–31], while other reports do not show this relationship [32,33]. Thus, in order to contribute to a further clarification on this argument, and taking advantage of the three-bottle choice paradigm, the second aim of this study was to investigate the possible influence of alcohol self-administration on novelty-induced explorative behaviour, assessed in an open field, as a measure of the emotional state of the animals [34].

It is widely described that high-dose ethanol exposure exerts detrimental effects on rat cognitive processes such as learning and memory [35–38]. However, some other reports show that chronic exposure to an ethanol containing diet can induce a better performance in discrete cognitive tasks depending on dosage and time of consumption [39,40]. Since alcohol does not affect all memory processes, in the same way it is useful to analyze the effects of chronic

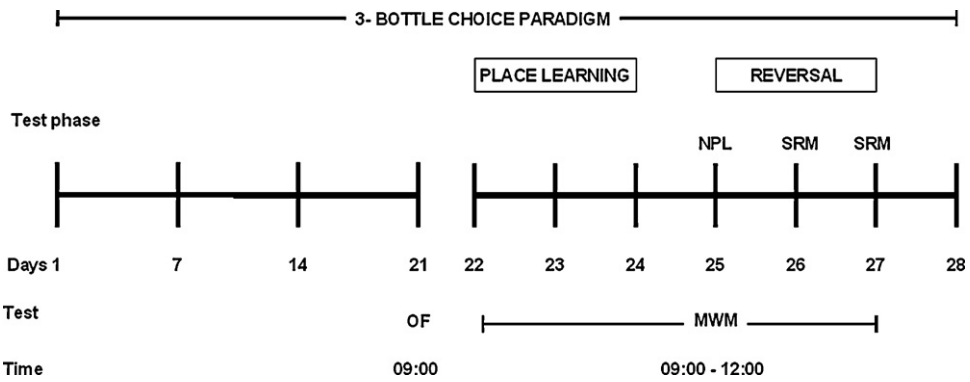

Fig. 2. Timeline showing days and time on which treatment and behavioural tests were conducted. OF: open field, MWM: Morris water maze, NPL: new place learning, SRM: spatial reference memory