Neuropsychological predictors of alcohol abtinence following a detoxification program

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Abstract. Alcohol dependence syndrome has been associated to disfunctions of the pre-frontal cortex, with a negative impact on serveral areas of cognitive functioning, such as attention, memory and learning, visual-spatial synthesis, executive functions, and psychomotor functions. These changes in turn contribute to the perpetuation of the addictive behavior. We report a study with 249 recovering alcoholics assessed with neuropsychological tests pre- and post-treatment at an alcoholism rehab clinic, with follow-up for abstinence 3 and 6 months after treatment. We found that 3-month abstinence was associated to speed of psychomotor processing, whereas 6-month abstinence was related with decision-making, (lack of) impulsivity, speed of psychomotor processing, and emotional adjustment.[1]

Keywords: alcoholism, abstinence, neuropsychological assessment, predictors of abstinence

1 Introduction

Alcholic beverages have been produced and consumed for about 8000 years, but their consumption only became a public health problem from the industrial revolution onward, due to its mass sale [1]. Alcohol abuse is a progressive, chronic, and multifactor disease and public health issue. According to the World Health Organization (WHO) alcohol abuse is a lifestyle-related public health problem and alcohol is the most widely consumed drug in the World, being consumed by about two billion people [2]. In 2010, alcohol was responsible for 3.3% of deathers and 5.9% of working years lost; the European Union is the region of the world with highest per capita consumption (10.9 litres of alcohol per year) and worldwide, per capita consumption of

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over-15 year olds was 6.2 litres per year, or 13.5 grammes per day; and males consume more than females [3].

1.1 Causes and consequences of alcoholism

Alcohol dependence syndrome (ADS) is a chronic multi-causal disease, including genetic, social, cultural, and psychological causes. At the genetic level, research has identified a mutant allele (ALDH2*2/*2) that functions as a buffer against the development of the symptoms of alcoholism by accelerating the metabolization of toxic acetic aldeid, an intermediary substance based on metabolization of ethyl alcohol by the organism that is responsible for the symptoms of acute alcoholic intoxication. Individuals with this allele are thus more disposed to drink alcohol in larger quantities and develop dependency [4]. Social and cultural causes of alcoholism refer to the availability of alcohol and with the cultural and social norms and attitudes towards alcohol, and psychological or personality factors may include low self-esteem, sensation-seeking, escape from pain, and unfavorable family relations [5].

Alcohol consumption enhances the neurotransmission of monoamines such as Dopamine (DA), norepinefrine (NE) e serotonine (5-HT) in synapses by blocking the the uptake mechanism; the reinforcement effect of ethanol depends critically on DA, being implicated in the mesolimbic system [6]. Persistent stimulation of dopaminergic and serotinergic circuity, in particular in the aacumbens nucleus, has a motivational and emotional effect on alcohol addicts. [7, 8]. Adaptative and enhanced activity of the 5-HT2 receptors under chronic presence of ethanol may contribute to alcohol abstinence syndrome when this is withdrawn [9].

1.2 Treatments for alcoholism

Because ADS is a multifactorial disorder, its treatment should involve interventions at several levels: pharmacological, deep brain stimulation, or psychotherapeutic. Whatever the level of intervention, however, it will only be successful if alcoholics are in abstinence, which is the main goal of alcohol rehabilitation clinics.

Pharmacological intervention is mostly focused on alcohol abstinence syndrome (AAS), and uses medication such as dissulfiram that blocks the capacity to metabolize alcohol and produces nausea, naxeltrone that reduces pleasurable feelings produced by alcohol, and acamprosate that reduces alcohol craving, and more recently ondansetron and topiramato [10]. Research on the brain circuits that lead to alcoholism also opened up a path for Deep Brain Stimulation (DBS), use of this technique to treat alcoholism was hit upon by accident in 2007 as a by-product of a treatment for severe anxiety and depression, by stimulating the accumbens nucleus [11]. This technique has meanwhile been adopted for the treatment of several psychiatric disorders and addictions, including tobacco and alcohol [12, 13, 14]. Psychotherapy is also indispensable for alcoholics' ability to remain abstinent. Despite the fact that none of the many intervention methods has proven completely effective, they retain an important role in the psychological maturity and the social and family reinsertion of patients, through the establishment of strategies and essential goals for an effective treatment

[15]. Finally, a variety of research has shown that cognitive stimulation is effective in the recovery of the cognitive abilities of alcoholics [16, 17, 18, 19, 20, 21, 22, 23, 24]. The strategy of cognitive stimulation is based on the repetition of tasks that aim to stimulate the plasticity that the brain has to adapt to demanding environmental circumstances [25].

1.3 Impact of excessive consumption of alcohol at the individual and social level

Excess consumption of alcohol can lead to alcohol use disorder (AUD), which is characterized in the DSM-V by: prioritization of drinking over other spheres of life; uncontrolled, excessive and recurrent drinking; increased tolerance to alcohol; symptoms of abstinence and relief of abstinence through further drinking; and by concurrent social and professional problems linked to alcohol abuse [26]. The negative effects of alcohol use on brain functions are evident from the literature; the most obvious effects are on the pre-frontal cortex. The chronic consumption of ethanol is associated to changes in memory and learning, in visual-spatial analysis and synthesis, in psychomotor speed, in executive functions, in decision-making, in impulsivity and psychomotor lentification and information processing, and in some can result in persistent pathologies of memory and in alcoholic dementia, such as the Wernike-Korsakov syndrome [17, 27, 28]. Alcoholism is also associated to impulsivity [29, 30]. Impulsive individuals have difficulty in postponing rewards or an immediate pleasure, and are unable to wait for and understand future behaviors [31]. Alcoholics tend to exhibit changes in their decision-making process and make choices that do not take into account their future consequences [28]. Faced with the dilemma of drinking or keeping abstinent, patients' choice of immediate pleasure and relief of symptoms is due to changes in the pre-frontal cortex that damage an efficient decision-making process; most addicts show reduced decision-making process, suggesting an insensibility to future consequences [32].

These deficits in ADS patients are positively correlated with consumption patterns (i.e. social drinkers vs. alcoholics) [33] and the consequences of ethanol consumption extend to the neurological dimension, in particular at the level of the pre-frontal cortex: functional and morphological changes have an effect on the reduction glucose and blood flow and in neuropsychological deficits in executive control, impulsivity and attention, which reveal themselves as a pathology of the frontal lobe and alcohol disorder [34]. In fact, over half of the patients in alcohol recovery programs show some level of deficits in abstract reasoning, executive functions, spatial abilities, learning, and memory [22].

Conversely, alcoholics with greater changes in frontal functions, namely in inhibitory control and working memory tasks, tend to have worse prognoses and a higher relapse frequency during recovery programs. This suggests that executive functions such as inhibitory control and working memory are essential to maintain a consistent abstinent behavior. Executive functions are also crucial to maintain and achieve life projects, follow conversations (socialize) and in general for a sustainable day-to-day functioning. Therefore, cognitive deficits in alcoholics are both cause and conse-

quence of continuing dependency [17, 34]. Research also shows that frontal deficits in alcoholics have direct implications on the treatment itself, whether for the choice of strategy or for the prognose of patients [17, 27, 34, 35].

In previous studies [36] we have shown that cognitive training through serious games in recovering alcoholics can enhance the recovery of cognitive performance, namely mental flexibility. The current study is an extension of that work, in which we seek to identify neuropsychological variables that can predict abstinence in recovering alcoholics, refining the precision of prognoses for recovery with the use of neuropsychological assessment.

2 Method

2.1 Participants and procedure

249 patients aged 27 to 73 (M^{age} = 48.63yrs, 80.3% male, with an average 11yrs of formal education) diagnosed with alcohol dependence syndrome and undergoing a detoxification program at a Portuguese private clinic were randomly recruited for this study. Most participants (97.1%) were Portuguese, slightly less than half (44.5%) were employed, and only a third (33.3%) were married. All patients followed a medication regime including Diazepam, Triapride, and vitamins, to minimize abstinence symptoms and a deregulation of complex B vitamins.

Post-treatment mortality from the study was 139 participants 3 months after the end of the treatment, but only 88 after 6 months. Telephone follow-up by the nursing team at the clinic explains this lower mortality after 6 months compared to 3 months.

Patients who agreed to participate and signed an informed consent form underwent a neuropsychological assessment during their first days of treatment, after being cleared of withdrawal symptoms by the local psychiatrist (last author). All the participants again underwent the neuropsychological treatment 4 weeks later at the end of their treatment. They were then invited to attend follow-up appointments with the neuropsychological team at the clinic 3 and 6 months after the end of the treatment. Participants who attended theses appointments underwent a number of tests – Iowa Gambling Test (IGT) for decision-making, the SCL-90-R for emotional adjustment and the UPPS+P impulsivity scale. Participants were asked about their possible consumption of alcohol after the end of their treatment and contacted by telephone by the nursing staff of the clinic. Data on abstinence were registered at 3 and 6 months and coded dichotomically (no relapse vs relapse) as well as in more detailed form (some relapse, lower or higher consumption compared to pre-treatment, etc). About a third of the patients also underwent a cognitive stimulation program, but here we analyze the whole sample together.

2.2 Measures

Memory was assessed with the Wechsler Memory Scale (WMS) [37], which measure auditive learning memory, long-term retention, and working memory. In particular, working memory was assessed with the digit test (inverse order digit memory).

Mental flexibility was assessed with the Wisconsin Card Sorting Test (WCST) [38], which is commonly used to assess executive functions, such as strategic planning, abstract thinking, and perseverant behaviors. The correct responses and errors are registered during a maximum of 128 trials, which allows scoring the test for the number of correct responses, errors, perseverative errors, number of trials to complete first of six categories, and number of conceptual responses.

Decision-making was assessed with the Iowa Gambling Task (IGT) [28], which is a measure commonly used in the framework of addictions to detect impulsive decision-making behaviors. This test simulates a computer card game, where subjects choose cards that give money, or that give and take different amounts of money. The cards are divided into 4 decks, in which decks A and B are disadvantageous because losses are greater than gains in these decks, and decks C and D are vantageous because they give small amounts of money but the losses are lower in these decks. The test allows to study decision-making through the subtraction of vantageous by the disadvantageous decisions (NET), and the numbers of choices in each deck (RAW score).

The impulsivity was assessed with the UPPS+P [39, 40], which measures negative urgency, positive urgency, lack of premeditation, and lack of perseverance. The total score derives from the sum of the scores of all subscales, allowing to evaluate the general impulsiveness of the subjects.

Emotional disadjustment was measured with the SCL-90-R scale [41] which allowed us to discriminate nine dimensions of emotional disadjustment: somatization, obcessions/compulsions, interpersonal sensivity, ansiety, depression, hostility, phobic anxiety, paranoid ideation, and psychoticism, and also three general índex of emotional disadjustment: Global Symptoms Index (GSI) that comprises the number and intensity of total symptoms, the Total Positive Symptoms (PST) that reflects only the present symptoms, and the Positive Symptoms Disorder Level (PSDI) is a measure of intensity obtained through the number of positive symptoms.

Depressive symptoms were assessed with the Portuguese version Becks Depression Inventory II (BDI-II) [42, 43], which is a 21 mutiple choice-item self-report scale.

The Rey Complex Figure (CRF) [44] allows to test visuoconstructive functions, psychomotor speed and visual memory. The RCF consists of the reproduction of an abstract figure that is easily drawn. The test is made of two trials: copy trial that consists on visual reproduction, and memory trial that consists on a drawing after 3 minutes from the first trial. The first trial allows to measure visuoconstructive functions while the memory trial allows to measure visual memory ability. In two tasks the time spent is registered that allows to measure psychomotor processing speed in the copy trial.

3 Results

Simple correlation analyses indicate that regularity of consumption of alcohol is not very associated with cognitive performance, except for the Wechsler reverse numbers (r = .17) and the WCST number of conceptual answers measure (r = .16).

However, we used a relatively conservative measure of alcohol consumption and this produced a ceiling effect, which may explain the low correlations.

Specific measures of all the neuropsychological tests (1st and 2nd assessments, i.e. pre and post-treatment) were entered as independent variables in a series of four multiple linear regression analyses (stepwise method) with both complete abstinence and frequency of consumption at two moments – treatment plus 3 months and treatment plus 6 months – as dependent variables.

Complete abstinence 3 months after treatment was predicted by the percentile of time spent on the Rey Complex Figure (RCF) copy, 2nd evaluation ($F(1, 45) = 5.89$; $p = .019$), explaining 9.6% of the variance. No other variable had an independent significant effect.

In contrast, three different independent variables predicted complete abstinence at 6 months, explaining 40.9% of total variance ($F(3,40) = 10,912$; $p < .001$). The first variable entered was percentile of time spent on the RCF copy, 1st evaluation, which alone explained 17.7% of the variance; the second was total score on the UPPS+P, 2nd evaluation, which explained an additional 11.9% of variance, and the third was the IGT Deck B Raw Score, 2nd evaluation, which predicted 11.3% of total variance.

Table 1. Multiple linear regression between neuropsychological variables and complete abstinence after 6 months

Steps	Ivs	Total Adj R^2	*B*
1	RCF copy percentile time spent 1st evaluation	.177	-0,009
2	UPPS Total 2 nd evaluation	.296	-0,009
3	IGT Deck B Raw Score 2nd evaluation	.409	-0,012

Frequency of consumption after 6 months was predicted by five independent variables, which explained a total of 53.2% of the variance ($F(5,35) = 10.095$; $p < .000$). The first variable entered was percentile of time spent on the copy of the Rey Complex Figure, which explained 13.5% of the variance, followed by the IGT Deck B raw score, 2nd assessment, explaining 13.6% of the variance, the total score on the UPPS+P, 2nd assessment, which explained 15.4% of the variance, general index of symptoms on the SCL-90, 2nd assessment, which explained 6.2% of the variance, and finally IGT net total raw score, 2nd assessment, which explained 4.5% of the variance.

Table 2. Multiple linear regression between neuropsychological variables and frequency of consumption after 6 months

Steps	IVs	Total Adj R2	β

1	FCR copy percentile time spent 2nd evaluation	.135	.411
2	IGT Deck B Raw Score 2nd evaluation	.271	.978
3	UPPS Total 2nd evaluation	.425	.254
4	SCL-90 General symptoms index 2nd evaluation	.487	.331
5	IGT Net Total Raw Score 2nd evaluation	.532	.581

4 Discussion

In this chapter, we report a study in which we tested the relation between neuropsychological functions and abstinence after an alcohol rehabilitation treatment. As we expected, we found that regularity of consumption had an effect on most of the measures of neuropsychological functioning. We also found effects of cognitive performance on abstinence, indicating that cognitive functions are at the same time a consequence and a cause alcohol abuse.

As regards cognitive functions and abstinence, in general, we found strongest effects on abstinence and reduction of alcohol consumption at 6 months, and these were predicted most precisely by cognitive performance during the second assessment (post-detoxification treatment). Participants who remained abstinent after 6 months had shown better short-term memory, better indicators of mental flexibility, less complaints about sensorial interference and anxiety, and better scores on premeditation on the impulsivity scale. Post-treatment, predictors of relapse before 6 months were complaints over sensorial interference, phobic anxiety, depression, psychoticism, paranoid ideation, and symptoms of the emotional readjustment scale, greater positive urgency, lack of premeditation and lack of perseverance in the impulsivity scale, mental flexibility, and depressive symptoms.

Some of our results indicate that the speed of psychomotor systems and visual-constructive abilitities is related to short-term abstinence (i.e. 3 months). Indeed, attention and speed problems can have negative impact on information learning during recovery, and thus negative consequences on the ability to choose abstinence. We also found that impulsivity control as measured by neuropsychological tests had an effect on abstinence.

What we have not analyzed in this chapter is the effect of cognitive stimulation on abstinence, even though a third of the sample underwent a cognitive stimulation rehab program. Cognitive stimulation has been found to be effective in recovering cognitive functions such as visual-constructive abilities, frontal functions, executive control, attention and mental flexiblity, memory and learning, and psychomotor processing [16, 17, 18, 19, 20, 21, 22, 23, 24, 36]. These capabilities in turn have been related to the abstinence of alcoholic participants [17, 34, 36]. In the current sample, we could not verify the direct effect of cognitive stimulation on post-treatment abstinence of participants. However, a cognitive stimulation strategy could contribute to indirectly to patients' abstinence [17, 27, 34, 35]. In future studies, the effects of cognitive stimulation on abstinence should be better clarified so as to develop a predictive model of the indirect action of stimulation, with the cognitive improvements that are produced by it, on abstinence.

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