Cognitive profile of long-term abstinent alcoholics in comparison with non-alcoholics

Perfil cognitivo de los alcohólicos abstinentes durante un periodo de tiempo prolongado en comparación con un grupo de hombres que no consumen alcohol

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Abstract

Scarce studies have focused on the cognitive profile of chronic alcoholic men after long-term abstinence. Thus, we examined neuropsychological differences between long-term abstinent alcoholics for an average of 3.2 years (*n* = 40, LTAA; age = 45.55 ± 8.99) and matched for socio-demographic variables with non-alcoholic controls (*n* = 39; age = 42.05 ± 11.33). To this aim, we employed a neuropsychological assessment battery covered relevant cognitive domains: IQ, memory, attention, executive functions and empathy. LTAA presented deficits in abstract reasoning, speed processing, sustained attention, working and long-term memory (verbal and visuospatial), cognitive flexibility, inhibition and planning. Although our results must be interpreted with caution because of the cross-sectional nature of our study, it may offer a broader knowledge and understanding of alcohol-related socio-cognitive deficits after long-term abstinence. These deficits might entail risk factors for relapse in alcohol consumption, as they may interfere with recording therapeutic advice and internalizing the verbal material presented in rehabilitation programs. In turn, these impair the global efficacy of alcohol-relapse prevention programs. Hence, this knowledge could be applicable in guiding the development of early coadjutant treatments.

Keywords: Abstinence; Alcohol related-cognitive deficits; Alcoholism; Empathy; Neuropsychology.

Resumen

Solo pocos estudios han analizado el perfil cognitivo de los hombres con un trastorno por consumo de alcohol tras un periodo de abstinencia prolongado. Por tanto, este estudio tiene como principal objetivo analizar las diferencias neuropsicológicas entre un grupo de hombres con trastorno por consumo de alcohol pero abstinentes de forma ininterrumpida durante 3,2 años (*n* = 40, edad = 45,55 ± 8,99) en comparación con un grupo de hombres sin trastorno por consumo de alcohol pero con unas características socio-demográficas similares a las del grupo experimental (*n* = 39; edad = 42,05 ± 11,33) para establecer diferentes perfiles neuropsicológicos. Empleamos una batería neuropsicológica exhaustiva que evaluó los siguientes dominios cognitivos: CI, memoria, atención, funciones ejecutivas y empatía. El grupo de hombres alcohólicos abstinentes presentaron déficits en razonamiento abstracto, velocidad de procesamiento, atención sostenida, memoria de trabajo y a largo plazo (para información verbal y visuoespacial), flexibilidad cognitiva, y en las capacidades de inhibición y planificación. A pesar de que nuestros resultados deben interpretarse con cautela dado el carácter transversal de nuestro estudio, ofrece información relevante sobre el estado cognitivo de los hombres con un trastorno por consumo de alcohol tras una abstinencia prolongada. Estos déficits podrían estar implicados en las frecuentes recaídas en esta población. Del mismo modo, interferirían en la asimilación de contenidos teóricos de intervenciones psicoterapéuticas, lo que, a su vez, disminuiría la eficacia de las mismas. Por ello, estos resultados deberían ser empleados para el desarrollo de programas de rehabilitación cognitivos coadyuvantes a la psicoterapia.

Palabras clave: Abstinencia; Alcoholismo; Déficits cognitivos; Empatía; Neuropsicología.

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Several studies have demonstrated that long-term chronic alcoholism is associated with potentially long-term deleterious effects on neuropsychological functioning (Le Berre, Fama & Sullivan, 2017; Stavro, Pelletier & Potvin, 2013; Valmas, Mosher-Ruiz, Gansler, Sawyer & Oscar-Berman, 2014), but these deficits depends on variables such as drinking patterns (the amount, type, frequency...), the age of initiation of alcohol; the duration of the hazardous and harmful alcohol consumption and the alcohol abstinence (Bernardin, Maheut-Bosser & Paille, 2014; Sullivan, Rosenbloom, Lim & Pfefferbaum, 2000a; Sullivan, Rosenbloom & Pfefferbaum, 2000b; Rosenbloom, O'Reilly, Sassoon, Sullivan & Pfefferbaum, 2005). Given that alcoholic cognitive deficits are not evently distributed among individuals, it has been suggested that long-term alcohol abusers vary along of a continuum (Bates, Voelbel, Buckman, Labouvie & Barry, 2005; Oscar-Berman, Valmas, Sawyer, Ruiz, Luhar & Gravitz, 2014).

Unfortunately there are several limitations in the study of cognitive function in abstinence. In fact, it remains unclear the time of abstinence needed for normalization of cognitive function and which cognitive domains improve during this period of abstinence (Pelletier, Nalpas, Alarcon, Rigole & Perney, 2016). Although several studies have shown certain improvements in specific cognitive domains such as visuospatial capacity, memory, and executive function after the first months to one year of abstinence (Alhassoon et al., 2012; Bernardin et al., 2014; Erickson & White, 2009; Oscar-Berman et al., 2014; Pfefferbaum, Adalsteinsson & Sullivan, 2006; Sullivan et al., 2000a; Sullivan et al., 2000b), a recent meta-analysis suggested persistent dysfunctions in multiple cognitive processes after months of alcohol abstinence (Stavro et al., 2013). Impairments and/or improvements in each cognitive ability may differ depending on the recovery rate of each brain system, which underlie to these cognitive processes (Kish, Hagen, Woody & Harvey, 1980; Pelletier et al., 2016; Pfefferbaum, Sullivan, Mathalon, Shear, Rosenbloom & Lim, 1995; Stavro et al., 2013; Yohman, Parsons & Leber, 1985).

Alcohol-related cognitive deficits may explain why therapeutic programs are not adequately processed (e.g., low participation in therapeutic workshops, absence of recording of therapeutic advice…), which in turn affect the effectiveness of rehabilitation programs due to the complexity in therapy programs (Berking, Margraf, Ebert, Wupperman, Hofmann & Junghanns, 2011). Hence, a wider knowledge of cognitive and affective deficits could be employed to guide the development of early coadjuvant treatments, which allows to improve the affected cognitive domains and in turn reduce the rate of alcohol recidivism.

The current study was designed to address this gap in our understanding by investigating differences between long-term abstinent alcoholics (LTAA) and non-alcoholic individuals (control group), to establish differential neuropsychological profiles. In the light of previous findings regarding persistent cognitive impairments in patients with alcohol use disorders (AUD) after long-term periods of abstinence (Alhassoon et al., 2012; Fein, Torres, Price & Di Sclafani, 2006; Munro, Saxton & Butters, 2000; Nowakowska-Domagała, Jabłkowska-Górecka, Mokros, Koprowicz & Pietras, 2017; Pfefferbaum et al., 2006; Stavro et al., 2013; Yohman et al., 1985), we hypothesized that LTAA would manifest neuropsychological dysfunctions relative to controls. The analysis of these cognitive profiles in LTAA are crucial for the patient's participation in relapse prevention programs.

Method

Participants

The final sample was composed of 79 men who participated voluntarily in the study: 40 LTAA and 39 individuals with no history of alcohol or drug consumption, as the control group. LTAA participants were recruited from Asociación Valenciana de Ex-Alcohólicos (*AVEX)*, which offer a psychoeducational treatment program conducted by two psychotherapists. Moreover, participants were also recruited from the community by postings at Alcoholics Anonymous (AA) meetings, mailings and subject referrals. Inclusion criteria in the current study were diagnosis of Alcohol Use Disorder (AUD) assessed by the DSM 5; participants who have been abstinent for a minimum of twelve months (Fein et al., 2006); age above 18 and less than 60 years old; and ability to understand and speak Spanish. Exclusion criteria were suffer from any neurologic or psychiatric disease such as Alzheimer's or any type of dementia, past history of stroke or brain injurys, encephalopathy, and refusal to participate. All the individuals who were candidate participants were interviewed by trained researchers (with extensive experience treating AUD) to assess their mental health. Cohen's kappa, used to assess inter-rater agreement between qualitative interviewers in the nine psychopathological dimensions evaluated (the same dimensions as the Symptom Checklist 90-R, SCL-90-R), ranged from .67 to .84. Regardless of the SCL-90-R scores, the interviewees were considered not to have any psychopathological signs and symptoms if they scored less than the mean for their age for each dimension. They were then considered eligible to participate if the qualitative interviews and SCL-90-R scores confirmed they were free of mental illness. Four LTAA participants and five controls were excluded because their results suggested psychological disorders and additional current drug abuse.

Controls were recruited via internet advertisements and posting flyers around our city from January, 2016 to August, 2016. They were matched on socio-demographic characteristics. Furthermore, it would be necessary that they present alcohol consumption lower than 30 g/day, and less than two DSM-5 symptoms of AUD. High alcohol consumption was operationally defined as alcohol intake higher than 30 g/day (Cao, Willett, Rimm, Stampfer & Giovannucci, 2015; Cho, Lee, Rimm, Fuchs & Giovannucci, 2012; Scoccianti et al., 2016).

All participants were right-handed and healthy, were properly informed about the research protocol and gave written informed consent. The research was conducted taking into account current ethical and legal guidelines on the protection of personal data and research with human beings in accordance with the Declaration of Helsinki and was approved by the University of Valencia Ethics Committee (H1348835571691).

Procedure

All participants attended three sessions at the Faculty of Psychology. In the first session, participants were interviewed to exclude those with organic diseases and socio-demographic data were collected through a semi-structured interview. Then, participants were asked about their consumption of alcohol and cigarettes, in terms of both the amount consumed and how long they had been abstinent. Moreover, it was employed a breathalyzer to assess whether participants present a 0,0% alcohol concentration. Subsequently, they completed an inventory based on DSM-5 to check for the presence of AUD, and the Fragerström test of nicotine dependence to assess addiction level. Lastly, they were asked if they had a history of traumatic brain injury, noting whether they had lost consciousness during the trauma; for example, had they been involved in fights, and if so, how often had this resulted in head injuries and had they had blackouts after these injuries. In fact, there were excluded those participants who suffered a severe TBI. Finally, other psychological tests were studied in order to complete participant's profile.

The second and third sessions spread over two consecutive days, a range of neuropsychological variables were assessed using traditional tests and also the computer-based Cambridge Neuropsychological Test Automated Battery (CANTAB) ordered as presented in table 2. This neuropsychological testing was build based on Ruiz-Sánchez de León, Pedrero-Pérez, Rojo-Mota, Llanero-Luque & Puerta-García (2011) recommendations. If any of participants was a smoker, he was asked to smoke previously to the neuropsychological assessment to avoid any bias related to the abstinence of nicotine

The end of the assessment was marked by displaying a sign saying "Thank you very much", participants were paid €20 for their participation and told that they could leave.

Frontal Behaviour

Spanish version of *Frontal Systems Behaviour Scale (FrSBe)* is composed of 46 items that measure frontally-based behavioural syndromes such as disinhibition (15 items), apathy (14 items) and executive dysfunction (17 items) (Pedrero-Pérez, Ruiz-Sánchez de León, Llanero-Luque, Rojo-Mota, Olivar-Arroyo & Puerta-García, 2009), all being rated on a 5-point Likert-type scale (1 = 'not at all' to 5 = 'very much so').

We used the translated into Spanish version of the Montreal cognitive assessment (MoCA) (http://www.MoCA-test.org/). The MoCA measures eight cognitive domains such as naming, attention, language, abstraction, delayed memory, orientation, visuospatial and executive abilities. The initially proposed normal MoCA score is ≥ 26, but a point must be added to the total score in participants with low educational level (less than 12 years of education).

IQ (abstract reasoning and processing speed) (table 1)

Abstract reasoning and processing speed were measured by the subtests matrix reasoning, digit symbol-coding, symbol search and similarities of the WAIS-III (Wechler, 1999).

Attention (table 1)

We employed the translated version into Spanish of the d2 test, which measures the ability to focus on relevant stimulus while ignoring irrelevant (Seisdedos, 2004). It consists in 14 lines with 47 characters each one, which contains letters such as «d» and «p». Participants should check during 20 seconds for each line from left to right, the contents of each line marking only «d» showing two little dashes (both above, below or one above and one below). Dependent scores for this study were: TR, overall answer; TA, number of correct guesses; O, omitted elements; C, commissions; TOT, total test effectiveness; and CON concentration index.

Attention Switching Task (ATS) measures the ability to switch attention between the direction of an arrow and its location on the screen and avoiding distracting events. It is a highly cognitive demanding test as participants should switch their attention between congruent (e.g., arrow on the right side of the screen pointing to the right) and incongruent stimuli (e.g., arrow on the right side of the screen pointing to the left) presentation. Dependent variables for this study were switch cost, percentage of correct responses and congruency cost (Cambridge Cognition Ltd, 2012).

Rapid Visual Information Processing (RVP) measures sustained attention. This test consists in a white box appears in the centre of the computer screen, inside which digits, from 2 to 9 are presented randomized. Subjects should detect specific target sequences of three consecutive digits (e.g., 2,4,6; 3,5,7 and 4,6,8). Dependent variable for this study was target sensitivity.

Choice Reaction Time (CRT) is a 2-choice reaction time test that assesses attentional ability and reaction times, which includes a practice stage of 24 trials and two assessment stages of 50 trials each. Dependent variables for this study were percentage of correct answers and mean correct latency (ms) (Cambridge Cognition Ltd, 2012).

Table 1. *Neuropsychological test battery.*

Neuropsychological test	
IQ	
Matrix reasoning WAIS-III	Abstract reasoning
Digit symbol-coding and symbol search	Processing speed
Similarities of the WAIS-III	Verbal reasoning
Attention	
d2 test	Sustained attention
Rapid Visual Information Processing (RVP)	Sustained attention
Attention Switching Task (AST)	Switch-attention
Choice Reaction Time (CRT)	Reaction times
Memory	
Word List WAIS-III	Immediate recall, delayed recall and recognition.
Rey–Osterrieth Complex Figure Test	Visuospatial constructional ability and visual memory
Logical Memory WMS-III	Short and long-term memory and recognition
Digit Span WAIS-III	Short-term memory, attention, and concentration
Letter-Number Sequencing WAIS-III	Simultaneously recall and organize stimuli (working memory)
Spatial Span WMS-III	Working memory capacity (visuospatial)
Spatial Span Test (CANTAB)	Working memory capacity (visuospatial)
Executive functions	
Semantic categorial evocation of animals and FAS verbal phonemic fluency	Verbal fluency
Stroop	Divided attention and resistance to interference
Hayling test	Verbal inhibition
Five-Point test	Design fluency
Wisconsin Card Sorting Test (WCST)	Abstract reasoning and the ability to change cognitive strategies in response to environmental changes (cognitive flexibility)
Zoo test and Key test	Ability to plan a strategy to solve a problema (planning)
One Touch Stockings of Cambridge (OTS)	Spatial planning and working memory
Cambridge Gambling Task (CGT)	Decision-making and risk-taking behaviour
Empathy	
Reading the mind in the eyes	Emotion decoding abilities

Memory (table 1)

Word List is a subscale of the WMS-III (Wechler, 1997). Participants must recall a list of words presented five times, and each time, the participant has to repeat the maximum number of words that he/she can recall. Moreover, there is an interference list. This test consists of three test conditions: immediate recall, delayed recall and recognition.

Rey–Osterrieth Complex Figure Test assessed visuospatial constructional ability and visual memory. This test consists of three test conditions: copy, immediate recall and delayed recall. Initially, participants must copy a stimulus card. Afterwards, the card is taken away and they are instructed to draw what they remember of the figure. Finally, participants must draw the same figure once again after 30 minutes.

WMS-III *Logical Memory* evaluates short and long-term memory and recognition of two stories. Participants should remember as many ideas as possible from two stories (Wechler, 1997).

Digit Span is a subscale of the WAIS-III, which measures short-term memory, attention, and concentration. Participants are asked to repeat digits in direct and inverse order (Wechsler, 1999).

Letter-Number Sequencing is a subscale of the WAIS-III, which measures the ability to simultaneously recall and organize stimuli (working memory). Subject should repeat several series by repeating the numbers in ascending order, and then the letters in alphabetical order (e.g., 9-L-2-A; correct response is 2-9-A-L) (Wechsler, 1999).

Spatial Span is a subscale of the WMS-III, in which participants must copy a series of moves made by the evaluator with increasing difficulty. There are also two parts (direct and inverse order).

Spatial Span Test from the CANTAB measures working memory capacity. It has been presented white squares, some of which briefly change colour in a variable sequence. This test is stopped when the subject fails three consecutive trials at any specific level. The maximum number of boxes correctly defines the final score obtained (Cambridge Cognition Ltd, 2012).

Executive function tests (table 1)
Verbal fluency

Semantic categorial evocation of animals consists of asking the patient to say as many animal names as he can in about 60 seconds. It has been assigned 1 point for each correct animal name evoked in that time interval, without a maximum score (Del Ser Quijano, Sanchez Sánchez, Garcia de Yebenes, Otero Puime, Zunzunegui & Muñoz, 2004). Moreover, in the F-A-S verbal phonemic fluency participants must produce as many words as possible with each of the three test letters previously presented during 60 seconds each one.

Inhibition

The Stroop color and word test measures the ability of divided attention and resistance to interference (Spreen & Strauss, 1991).

For the assessment of verbal inhibition we employed the Hayling test (Burgess & Shallice, 1997).

Cognitive flexibility

For *Design fluency* was employed the Five-Point test, which involves the uses of a structured background that consists of a sheet of paper with 40- dot matrices (five columns x eight rows). Participants should draw as many different figures as possible by connecting any numbers of dots from the 5 dots within each cell to create novel designs within 60 seconds (Lezak, 2004).

Wisconsin Card Sorting Test (WCST) measures abstract reasoning and the ability to change cognitive strategies in response to environmental changes. It consists of 4 stimulus cards and 128 response cards containing various colours (red, blue, yellow or green), shapes (circle, cross, star or triangle) and numbers (one, two, three or four) of figures (Heaton, Chelune, Talley, Kay, & Curtiss, 1993).

Planning

Zoo test and *Key test* are part of the Behavioural Assessment of Dysexecutive Syndrome (Wilson, Alderman, Burgess, Emslie & Evans, 1996).

One Touch Stockings of Cambridge assesses spatial planning and working memory based upon the Tower of Hanoi test. The participant is shown two displays containing three coloured balls. Dependent variables are problems solved on first choice, mean choices to correct, mean latency to first choice and mean latency to correct (Cambridge Cognition Ltd, 2012).

Decision making

Cambridge Gambling Task measures decision-making and risk-taking behaviour. It has been presented a row of ten boxes across the top of the screen, some red and some blue. Rectangles containing the words 'red' and 'blue' can be seen at the bottom of the screen. Participants then have to decide whether the yellow taken is hidden in a red box or in a blue box. A set of points to gamble with is shown on the screen, which are displayed in rising or falling order. Participants are allow to place whatever bet they want with the number of points provided in order to gamble on their confidence in this judgement. The participants are aske to earns as many points as possible (Cambridge Cognition Ltd, 2012).

Empathy (table 1)

Eyes Test measures emotion decoding abilities by identifying the emotion that best represents the expression of the eyes in 36 photographs that show the eye region of the face of different men and women. In fact, subjects must choose one of a set of four adjectives. Total score, which ranged from 0 to 36 points, is obtained by summing the number of correct answers (Baron-Cohen, Wheelwright, Hill, Raste & Plumb, 2001), being interpreted a higher score as indicative stronger emotional decoding abilities.

The Spanish version *Interpersonal Reactivity Index* measures empathic response (Mestre, Frías & Samper, 2004), which includes four subscales such as perspective taking and fantasy (cognitive empathy) and emotional empathic concern and personal distress (emotional empathy). Responses are given on a 5-point Likert scale. The total score ranged from 7 to 35 points in each subscale, and a higher score indicate higher empathic skills.

Alexithymia was assessed using the Spanish version of the Toronto Scale of 20 Elements (TAS-20) by Bagby, Parker & Taylor (1994). It is a scale of 20 Likert type reagents with 6 variation points per element (from 0 to 5).

Data analysis

The Shapiro-Wilk test was used for exploring whether the data were normally distributed. Due to the fact that the majority of variables did not meet the assumption of normality ($p < .05$), therefore, it was decided to carry out nonparametric tests for statistical analysis of the results. U Mann–Whitney test was used to check for significant differences between the groups in socio-demographic, questionnaire scores and neuropsychological test. In addition, chi square analyses were performed for categorical variables such as socio-demographic characteristics (nationality, marital status, level of education, employment status, etc.).

Data analyses were carried out using IBM SPSS Statistics for Windows, Version 22.0 (Armonk, NY, USA). P values < 0.05 were considered statistically significant. Average values are reported in tables as mean±SD.

Results

Sample characteristics

Descriptive characteristics for LTAA and controls are presented in Table 2. Regarding AVEX (85% sample) and AA patients (15% sample) there were not differences between clinical and socio-demographic characteristics. Groups did not differ in anthropometric or socio-demographic variables, personal history of traumatic brain injury, or temporary loss of consciousness. Nevertheless, they differed in self-reported executive dysfunction, (Mann–Whitney $U = -2.64$, $p = 0.008$), and apathy, (Mann–Whitney $U = -2.80$, $p = 0.005$), with LTAA obtaining higher scores than controls. Moreover, a significant effect for group was found in IQ matrix Reasoning, (Mann–Whitney $U = -3.42$, $p = 0.001$), IQ similarities, (Mann–Whitney $U = -3.42$, $p = 0.001$), and IQ copy (Mann–Whitney $U = -3.03$, $p = 0.002$), having LTAA higher scores in all these scales than controls.

Table 2. *Mean ± SD of descriptive characteristics for all groups (*p < .05).*

	Alcohol group (n = 40)	Controls (n = 39)
Age (years)	45.55 ±8.99	42.05 ±11.33
BMI (Kg/m²)	27.74 ±3.42	26.90 ±4.96
Nationality		
Spanish	34 (85%)	32 (82%)
Latin Americans	6 (15%)	7 (18%)
Marital status		
Single	15 (38%)	17 (44%)
Married	9 (23%)	9 (23%)
Separate/Divorced/Widowed	16 (40%)	10 (26%)
Number of children	.94 ±1.03	1.20 ±0.95
Level of education		
Primary/lower secondary	18 (45%)	18 (46%)
Upper secondary/vocational training	17 (43%)	17 (44%)
University	5 (12%)	4 (10%)
Employment status		
Employed	18 (45%)	18 (46%)
Unemployed	22 (55%)	21 (54%)
Income level		
1800€ – 12000€	25 (63%)	25 (64%)
12000€ – 30000€	12 (30%)	12 (31%)
> 30000€ – 90000€	3 (7%)	2 (5%)
Personal history of traumatic		
brain injury	13 (48.14%)	14 (40%)
Yes	14 (51.85%)	21 (60%)
No		
Temporary loss of consciousness		
Yes	8 (29.36%)	14 (40%)
No	19 (70.37%)	21 (60%)
Alcohol Use Variables		
Age started drinking	17.74 ±8.82	-
Age at first heavy use	22.75 ±7.92	-
Average lifetime drinking dose (gr/day)	202.84 ±148.69	
Duration of active drinking (years)	22.80 ±8.82	-
Time of alcohol abstinence (months)	40.72 ±77.40	-
Family members with AUD		
Yes	37%	-
No	63%	-
Cigarettes/day*	16.61 ±10.13	9.75 ±7.21
Fagerstrom test	4.84 ±3.91	3.17 ±1.11
Frontal Behavior test		
Executive dysfunction**	19.77 ±9.54	13.14 ±7.14
Apathy**	10.33 ±5.77	6.25 ±4.94
Desinhibition	9.33 ±4.47	7.05 ±3.51

Neuropsychological assessment
Attention and memory (table 3)

Attention

We checked group differences and observed a number of differences that approached significance in the D2 Test, especially the total number of characters processed (Mann–Whitney U = -3.42, p = 0.001), total correctly processed (Mann–Whitney U = -2.97, p = 0.003), total number of errors (Mann–Whitney U = -2.83, p = 0.005), total performance (Mann–Whitney U = -3.42, p = 0.001) and concentration performance (Mann–Whitney U = -3.37, p = 0.001), while LTAA had a lower number total number of characters processed and total correctly processed, worse D2 and concentration performance and made more errors than controls. Regarding RVP, a significant group effect was found (Mann–Whitney U = -2.32, p = 0.021), LTAA performing less well in detecting the target sequences than controls.

Memory

Regarding the Wechsler Memory Scale-III Word List subscale, the difference between groups for the total number of words remembered (Mann–Whitney U = -4.19, p > 0.001), the number of words remembered in the first trial (Mann–Whitney U = –3.19, p = 0.001), short-term memory (Mann–Whitney U = -2.32, p = 0.020), the interference list (Mann–Whitney U = -4.19, p > 0.001) and recognition (Mann–Whitney U = -2.74, p = 0.006) were significant. LTAA remembered and recognized fewer words than controls.

For the ROCF test, "group" proved to be significant for copy time (Mann–Whitney U = -3.12, p = 0.002), short-term memory score (Mann–Whitney U = -3.17, p = 0.001), and long-term memory score (Mann–Whitney U = -3.48, p = 0.001), with LTAA needing more time to copy the figure and remembering the figure less well (both short-term and long-term) than controls.

Regarding the Logical Memory subscale, a significant effect of group was found in the first time that text A was read (Mann–Whitney U = -2.85, p = 0.004), text A units (Mann–Whitney U = -2.93, p = 0.003), and text B units 1, (Mann–Whitney U = -2.57, p = 0.010), and topics 1 (Mann–Whitney U = -2.12, p = 0.034) and text B units 2, (Mann–Whitney U = -2.05, p = 0.040), and topics 2 (Mann–Whitney U = -2.07, p = 0.039), LTAA remembered fewer units and topics than controls. Therefore, there were also group effects for delayed recalled of text A units (Mann–Whitney U = -2.06, p = 0.039) and topics, (Mann–Whitney U = -2.87, p = 0.004) and text B units (Mann–Whitney U = -1.97, p = 0.004), LTAA obtaining worse scores, meaning that they remembered both texts less well, than controls. There were also group effects for the recognition task (Mann–Whitney U = -3.72, p < 0.001), the LTAA group having lower scores than controls.

In the Digits Span subscale, though no significant differences were found between groups in direct scores, "group" was found to be significant in inverse order (Mann–Whitney U = -3.83, p < 0.001),, LTAA remembering fewer digits, especially in inverse order, than controls. Similarly, regarding the Letter-Number Sequencing subscale, there was a "group" effect (Mann–Whitney U = -3.83, p < 0.001), with LTAA remembering fewer letters and numbers than controls.

Tabla 3. *Mean ±SD of Memory tests of all grups (*p < .05)*

	Alcohol group (n = 40)	Controls (N = 39)
IQ		
Speed processing		
Symbol search	30.05 ±8.89	33.98 ±9.35
Abstract reasoning		
Digit Symbol - Coding		
Coding**	60.72 ±14.31	70.58 ±14.08
Incidental Learning Pairing*	10.21 ±5.39	12.50 ±4.96
Incidental Learning Free Recall	6.41 ±2.55	7.40 ±1.46
Copy**	103.51 ±23.16	117.40 ±18.76
Matrix Reasoning***	11.74 ±4.51	16.55 ±6.49
Similarities*	16.33 ±4.52	18.73 ±4.33
Attention		
D2		
TR***	387.18 ±95.94	485.70 ±79.37
O	23.92 ±22.64	30.55 ±31.00
C**	17.87 ±31.53	8.93 ±18.80
TA**	136.97 ±39.72	165.78 ±41.07
TOT= TR - (0 ± C)***	345.38 ±88.85	419.23 ±88.37
CON= TA –C***	119.10 ±42.93	156.85 ±51.49
E%= (100(O ±C))/TR	10.78 ±7.68	8.80 ±9.99
AST		
Switch cost	-146.33 ±136.41	-142.44 ±116.85
Percentage of correct responses (%)	89.31 ±11.24	93.03 ±6.73
Congruency cost	115.25 ±119.01	92.17 ±81.56
RVP Sensitivity (from .0 to 1.00)*	0.89 ±0.05	0.91 ±0.08
CRT		
Percentage of correct answers (%)	99.15 ±1.05	99.32 ±0.91
Mean correct latency (ms)	424.15 ±81.47	411.20 ±93.76
Memory		
Word Lists test		
Total words recalled***	28.91 ±5.38	34.64 ±4.99
Short-term memory*	7.51 ±2.00	8.36 ±1.94
Long-term memory*	6.76 ±2.14	7.72 ±2.16
First trial***	4.92 ±1.49	6.00 ±1.37
Learning curve	3.75 ±1.92	4.54 ±1.57
Interference list***	3.73 ±1.61	5.28 ±1.67
Omission	1.78 ±1.64	2.31 ±1.49
Recognition**	22.43 ±1.21	22.97 ±1.55
Rey Figure		
Copy score	34.86 ±1.39	35.31 ±1.23
Copy time**	152.24 ±59.70	118.93 ±44.86
Short-term memory score***	19.92 ±7.25	25.10 ±6.01
Short-term memory time	119.54 ±43.19	110.08 ±45.23
Long-term memory score***	19.19 ±6.21	24.46 ±6.38
Long-term memory time	95.77 ±33.82	93.46 ±32.57
Logical Memory test		
Delayed recall:		
Total score on the first try**	22.65 ±7.85	27.23 ±6.85
Text A		
Units**	11.93 ±3.45	14.15 ±3.84
Topics	4.60 ±1.99	5.41 ±1.27
Text B		
Units 1*	10.45 ±4.53	13.08 ±3.72
Topics 1*	4.45 ±2.36	5.72 ±1.10
Units 2*	10.45 ±4.53	10.45 ±4.53
Topics 2*	4.45 ±2.36	4.45 ±2.36
Delayed recall:		
Text A		
Units*	9.00 ±4.37	10.87 ±3.85
Topics**	4.10 ±2.01	5.38 ±1.37
Text B		
Units*	14.45 ±4.85	16.41 ±4.93
Topics	5.13 ±1.91	5.92 ±1.27
Recognition***	23.70 ±3.24	25.82 ±4.93
Digits		
Direct order	8.47 ±1.61	9.00 ±2.71
Inverse order***	5.06 ±1.53	6.90 ±2.19
Total score**	13.55 ±2.56	15.90 ±4.47
Letters and numbers		
Total score***	8.44 ±2.10	10.85 ±2.77
Spatial location		
Direct order	8.64 ±1.76	9.23 ±1.77
Inverse order**	7.14 ±1.59	8.38 ±2.18
Total score*	15.79 ±2.80	17.62 ±3.38

Table 4. *Mean ±SD of executive functions and empathy tests scores for all groups (*p < .05).*

	HA (n = 40)	LA (n = 39)
Verbal fluency		
Semantic (animals)	21.64 ±5.62	23.85 ±4.68
Phonemic (F, A and S)	37.33 ±12.11	40.38 ±13.82
Design fluency		
Part A***	15.26 ±5.15	19.38 ±5.53
Part B*	16.97 ±5.10	10.30 ±5.16
Inhibition		
Stroop 1*	100.23 ±14.34	108.38 ±14.52
Stroop 2	70.23 ±11.07	72.00 ±11.95
Stroop interference*	39.33 ±8.47	44.03 ±11.24
Hayling part A		
Time (sec)*	1.87 ±1.06	1.43 ±0.84
Score**	14.00 ±0.93	14.37 ±0.95
Hayling part B		
Time (sec)	4.65 ±3.82	3.83 ±3.09
Score	13.97 ±8.05	11.90 ±8.15
Cognitive flexibility		
Total trials***	113.32 ±19.41	93.40 ±21.17
Correct trials*	74.11 ±12.61	67.45 ±9.68
Total errors*	39.21 ±22.14	26.35 ±21.64
Perseverative mistakes*	21.71 ±13.07	13.90 ±13.57
Non perseverative mistakes*	17.39 ±11.79	11.87 ±10.22
Random not perseverative errors*	24.18 ±19.46	15.97 ±16.58
Completed categories*	4.34 ±1.79	5.33 ±1.56
Attempts to complete the first category	21.32 ±22.70	16.02 ±19.02
Failure to maintain the set**	1.37 ±1.65	0.40 ±0.95
Planning		
Zoo version 1		
Planning time (sec)	72.32 ±45.88	61.27 ±26.50
Execution time (sec)*	71.56 ±33.59	56.40 ±33.84
Errors	1.41 ±1.74	1.13 ±1.20
Total score version 1	3.15 ±3.45	3.97 ±2.81
Zoo version 2		
Planning time (sec)	32.51 ±19.03	23.19 ±12.72
Execution time (sec)*	45.23 ±20.14	35.37 ±18.66
Errors	0.59 ±0.97	0.36 ±0.67
Total score version 2	6.26 ±2.11	7.03 ±1.97
TOTAL SCORE	9.49 ±4.80	11.00 ±3.80
Key Test		
Planning time (sec)	20.76 ±29.39	14.94 ±14.53
Execution time (sec)*	36.51 ±36.23	32.64 ±26.18
Total score***	6.79 ±3.51	11.21 ±3.58
OTS problems solved on first choice* **	15.03 ±3.02	16.00 ±4.45
OTS mean choices to correct* **	1.71 ±0.53	1.63 ±0.46
Problems with:		
1 moves	1.17 ±0.53	1.12 ±0.22
2 moves	1.25 ±0.39	1.17 ±0.42
3 moves**	1.42 ±0.49	1.37 ±0.46
4 moves***	1.67 ±0.58	1.60 ±0.59
5 moves*	1.97 ±0.84	1.79 ±0.73
6 move***	2.79 ±1.15	2.72 ±1.08
OTS mean latency to first choice	14673.62 ±7265.36	18906.10 ±11429.33
Problems with:		
1 moves***	8747.65 ±3302.95	12087.74 ±9363.30
2 moves*	7082.91 ±22705.63	7825.22 ±23041.18
3 moves	8965.16 ±4337.98	10427.44 ±4870.10
4 moves	14439.84 ±11311.03	16357.72 ±9071.56
5 moves	24721.74 ±16877.17	26256.96 ±18742.32
6 move	24084.41 ±17827.82	40481.52 ±48533.45
OTS mean latency to correct		
Problems with:		
1 moves***	9313.49 ±3694.57	14111.03 ±11395.22
2 moves*	8902.96 ±3818.69	10136.43 ±7401.45
3 moves*	11758.40 ±8527.88	13884.02 ±8386.89
4 moves*	22097.44 ±24259.04	22477.01 ±13627.41
5 moves	35255.63 ±25785.04	35885.43 ±23406.45
6 moves	39906.75 ±28624.96	57317.70 ±51771.00
CGT		
Delay aversion	.19 ±.28	.13 ±.19
Deliberation time	2722.61 ±893.26	2587.29 ±801.52
Proportion bet	.50 ±.13	.51 ±.18
Quality of decision making	.88 ±.11	.85 ±.16
Risk adjustment	.95 ±.88	.78 ±.90
Risk taking	.54 ±.13	.55 ±.17
Empathy		
IRI		
Perspective taking	22.86 ±5.87	22.79 ±4.81
Fantasy	18.59 ±5.05	19.21 ±6.67
Empathic concern	25.47 ±4.17	25.95 ±3.54
Personal distress***	16.21 ±4.26	12.00 ±3.00
Eyes Test		
Total score	23.03 ±4.50	22.43 ±4.261
TAS* *	63.92 ±12.93	54.89 ±11.60

With regards to the Spatial Span subscale, "group" proved to be significant in inverse order (Mann–Whitney U = -2.65, p = 0.008), and total score (Mann–Whitney U = -2.13, p = 0.033), with LTAA being less able to repeat the series of movements made by the evaluator than controls. However, there were no significant differences between groups in direct order Spatial Span score.

Executive functions and empathic skills (table 4)

Cognitive flexibility

A significant "group" effect was found for the following WCST scales: total trials, (Mann–Whitney U = -3.83, p < 0.001); correct trials, (Mann–Whitney U = -2.89, p = 0.004); total errors, (Mann–Whitney U = -2.82, p = 0.005); perseverative errors, (Mann–Whitney U = -3.29, p = 0.001); rate of perseverative errors, (Mann–Whitney U = -2.61, p = 0.009); non-perseverative errors, (Mann–Whitney U = -2.34, p = 0.019); completed categories, (Mann–Whitney U = -3.02, p = 0.003), and failures to maintain the set, (Mann–Whitney U = -3.54, p < 0.001). LTAA needed more trials, made more errors, completed fewer categories, and more often failed to maintain the set than controls (Table 4).

Planning

Regarding the Zoo test, group proved to be significant in execution time (Mann–Whitney U = -2.27, p = 0.023), and execution time of version 2 (Mann–Whitney U = –2.92, p = 0.008), with LTAA spending more time planning than controls, which means that they had more problems developing logical strategies than controls.

There was a significant group effect for the total score on the Key test (Mann–Whitney U = -4.65, p < 0.001), LTAA being less able to plan a strategy to solve a problem than controls. Nevertheless, no significant differences were found between groups in planning and execution time.

A significant "group" effect was found in the OTS problems solved on the first choice (Mann–Whitney U = -3.84, p < 0.001), and in mean choices to correct total (Mann–Whitney U = -3.70, p < 0.001), third (Mann–Whitney U = -3.11, p = 0.002), fourth (Mann–Whitney U = -3.44, p = 0.001), fifth (Mann–Whitney U = -2.30, p = 0.022) and sixth (Mann–Whitney U = -3.77, p < 0.001) movements to correct, LTAA requiring more movements to finish the exercises and achieving less good performance than controls. Nonetheless, there were no significant differences in trials which only required one or two movements. Finally, a group effect was also found for latency to first choice (1 move) (Mann–Whitney U = -3.61, p < 0.001), (2 moves) (Mann–Whitney U = -2.52, p = 0.012) and latency to finish exercises correctly in exercises that need one movement (Mann–Whitney U = -3.84, p < 0.001), 2 moves (Mann–Whitney U = -2.35, p = 0.019), and 4 moves (Mann–Whitney U = -2.08, p = 0.038). Specifically, LTAA took more time to do the movements than controls.

Decision making

Regarding the CGT, no significant differences were found between groups in the proportion bets (Mann–Whitney U = -.13, p = 0.895), delay aversion (Mann–Whitney U = -1.26, p = 0.208), deliberation time (Mann–Whitney U = -.71, p = 0.474), quality of decision making (Mann–Whitney U = -.11, p = 0.914), risk adjustment (Mann–Whitney U = -.95, p = 0. 344) and risk taking (Mann–Whitney U = -.05, p = 0.953).

Empathy

A significant group effect was found in the IRI Personal distress (Mann–Whitney U = -4.29, p < 0.001), with LTAA presenting higher scores than controls. Nonetheless, groups did not differ in fantasy, empathic concern or perspective taking. With regards to the TAS, group proved to be significant (Mann–Whitney U = -2.94, p = 0.003), LTAA obtaining higher scores than controls. Finally, there were not found differences between groups in eye test.

The calculated type II error ranged from 1% to 12% in all the analysis.

Discussion

In the present study, we compared the neuropsychological performance on a computerized battery with pencil-and-paper tests of LTAA with non-alcoholic matched for demographic variables controls. We initially hypothesized that LTAA would manifest more neuropsychological dysfunctions, particularly memory and executive dysfunction, than controls. As expected, the LTAA group presented deficits in the abstract reasoning, speed processing, sustained attention, working and long-term memory (verbal, logical and visuospatial), cognitive flexibility, inhibition and time of planning. In addition, the LTAA had significantly more personal distress and alexithymic symptoms than the controls, though they did not differ from the controls in perspective taking, fantasy, empathic concern and emotional decoding skills.

Our study reinforces that certain cognitive skills such as abstract reasoning, speed processing, sustained attention, working and long-term memory (verbal, logical and visuospatial), cognitive flexibility, inhibition and time of planning might be persistently impaired after long term abstinence (Fein et al., 2006; Stavro et al., 2013). Additionally, LTAA also showed higher self-reported executive dysfunction, apathy, disinhibition and impulsivity in comparison with controls. In fact, it has been suggested that a result of chronic hazardous alcohol use could increase the risk of disinhibition and impulsivity, which entails a lack of concern for the consequences of inappropriate behaviours (Kravitz et al., 2015; Staples & Mandyam, 2016). These alcohol-related disinhibitory behaviors can be traced by neurobiological abnormalities such as prefrontal cortex, which is part of the substrate for executive control (Abernathy, Chandler & Woodward, 2010).

Based on WCST and OTS performance, LTAA presented less cognitive flexibility and weaker planning skills than controls. This means that they have problems to use negative feedback, suggesting they are less able to learn from aversive experience and modify behaviours in light of this learning. They also had problems developing logical strategies, with their abstract reasoning and they also need more time to planning their decisions and inhibit inappropriate responses than controls. It seems logical to conclude that these deficits could be explained by LTAA sustained attention and working memory impairments', which constrain the ability to learn, remember and adaptively utilize associations, reasoning, and problem solving.

Whether good decision making is a result of an accurate judgment of anticipated outcomes (Clark et al., 2011), attention and memory complaints may lead to ignorance of possibly advantageous choice alternatives or avoid unnecesary risks in decision-making situations. In fact, speed processing, attention and memory are important for these abilities, allowing focus on relevant stimuli and in inhibiting automatic thinking. Nonetheless, as LTAA did not differ from controls in CGT decision-making, we can't assume that LTAA make risky and/or impulsive decisions. Conversely, a previos research concluded that LTAA exhibited poor decision-making on the Iowa Gambling Task, which was attributed to their tendency to immediate reward than by delayed punishment (Fein et al., 2006). These differences between studies could be attributed to methodological reasons such as the neuropsychological tests employed in each study and/or by heterogeneity of AUD samples (time of abstinence, number of years of alcohol consumption, *polydrug* abuse, etc). However, it is important to note that in our study other cognitive processes requiring switch-attention, reaction times, verbal fluency, verbal inhibition, cognitive empathy and emotional decoding abilities seem well preserved. As the somatic marker model proposes that decision-making depends on cognitive and emotional processes (Gutnik, Hakimzada, Yoskowitz & Patel, 2006), the relatively well preserved cognitive and emotional abilities may help LTAA avoid unnecessary risks, but our data demonstrated that LTAA need more time to plan o make a choice than non-alcoholic controls. Therefore, our results underscoring the view that cognitive flexibility, inhibition or planning impairments are the main and determinant cause of decision-making deficits.

Several studies have been reported persistent deficits for processes related to social cognitive information, decoding of affective states, empathic ability, and in theory-of-mind in individuals with prolonged alcohol abstinence (Grynberg, Maurage & Nandrino, 2017; Maurage, Pesenti, Philippot, Joassin & Campanella, 2009; Stasiewicz et al., 2012). Additionally, sober alcohol patients tend to present difficulties to identify, differentiate, and express feelings (alexithymic symptoms) (Stasiewicz et al., 2012). Our results partially reinforced previous research in this field. Indeed, LTAA exhibited higher self-reported personal distress and alexithymic symptoms in comparison with controls. Conversely, they did not showed differences in cognitive empathy and emotional decoding abilities in comparison with controls. Based on or data, we could conclude that specific empathic measures did not present deficits after long-term abstinence, with the notable exception of personal distress and alexhitimia, on which alcoholism-related deficits remained. As regulate distressing emotional experiences and interpersonal difficulties to identify, differentiate, and express feelings has been associated with relapse after detoxification (Zywiak, Westerberg Connors & Maisto 2003), this suggest the importance to consider emotional and interpersonal difficulties in clinical treatment for alcoholics.

The main limitation of the study is that the sample sizes were modest. For this reason, the findings should be considered preliminary, and further research is needed to explore these patterns in larger samples. Another limitation of the current study is the use of cross-sectional data rather than longitudinal data, and hence definitive conclusions cannot be drawn regarding the long-term effects of alcohol in these cognitive skills. Moreover, it would be possible that alcoholics present pre-existent cognitive deficits to alcohol consumption, which increase their proneness to alcohol abuse. Hence, we can not demonstrate cognitive recovery or impairments over time. Longitudinal studies are necessary to understand how duration of alcohol abstinence could contribute to scope and limitations of recovery of emotional and social abilities. Additionally, it would be necessary to specify the role of these cognitive deficits in alcohol-relapse. Another limitation, the neuropsychological tests employed to assess these deficits tend to measure broad categories of abilities without a homogeneous consensus on which specific attributes define these functions.

Finally, it seems logical that these deficits may interfere in workshops, and psychotherapy in alcoholic patients during the detoxification period. Indeed, the large amounts of verbal and complex material presented in therapy programs is not being adequately processed due to conceptual thinking and abstract reasoning impairments in alcoholics. Nevertheless, it should be mentioned that the absence of recording therapeutic advice or low participation in workshops might also reflects participants' non-engagement with the program and not necessarily cognitive deficits. It may be necessary to develop early coadjuvant neuropsychological rehabilitation program to existent psychotherapy programs after detoxification (Frías-Torres, Moreno-España, Ortega, Barrio, Gual & Teixidor López, 2018). Hence, this knowledge could be employed to guide the development of early coadjuvant treatments, which allows to improve the affected cognitive domains and in turn reduce the rate of alcohol recidivism.

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References

Abernathy, K., Chandler, L. J. & Woodward, J. J. (2010). Alcohol and the prefrontal cortex. *International Review of Neurobiology, 91,* 289-320. doi:10.1016/S0074-7742(10)91009-X.

Alhassoon, O. M., Sorg, S. F., Taylor, M. J., Stephan, R. A., Schweinsburg, B. C., Stricker, N. H.,... Grant, I. (2012). Callosal white matter microstructural recovery in abstinent alcoholics: a longitudinal diffusion tensor imaging study. *Alcoholism: Clinical and Experimental Research, 36,* 1922-1931. doi: 10.1111/j.1530-0277.2012.01808.x.

Bagby, R. M., Parker, J. D. & Taylor, G. J. (1994). The twenty-item Toronto Alexithymia Scale—I. Item selection and cross-validation of the factor structure. *Journal of Psychosomatic Research, 38,* 23-32. doi:10.1016/0022-3999(94)90005-1.

Baron-Cohen, S., Wheelwright, S., Hill, J., Raste, Y. & Plumb, I. (2001). The "Reading the Mind in the Eyes" Test revised version: A Study with Normal Adults, and Adults with Asperger Syndrome or High-functioning Autism. *Journal of Child Psychology and Psychiatry, 42,* 241-251. doi:10.1111/1469-7610.00715.

Bates, M.E., Voelbel, G.T., Buckman, J.F., Labouvie, E.W. & Barry, D. (2005). Short-Term Neuropsychological Recovery in Clients with Substance Use Disorders. *Alcoholism: Clinical and Experimental Research, 29,* 367-377.

Berking, M., Margraf, M., Ebert, D., Wupperman, P., Hofmann, S. G. & Junghanns, K. (2011). Deficits in emotion-regulation skills predict alcohol use during and after cognitive–behavioral therapy for alcohol dependence. Journal *of Consulting and Clinical Psychology, 79,* 307. doi:10.1037/a0023421.

Bernardin, F., Maheut-Bosser, A. & Paille, F. (2014). Cognitive impairments in alcohol-dependent subjects. *Frontiers in Psychiatry, 5.* doi:10.3389/fpsyt.2014.00078.

Burgess, P. W. & Shallice, T. (1997). The hayling and brixton tests. Bury St Edmunds: Thames Valley Test Company.

Cambridge Cognition Ltd. (2012). CANTABeclipse Test Administration Guide. Cambridge: Cambridge Cognition Limited.

Cao, Y., Willett, W. C., Rimm, E. B., Stampfer, M. J. & Giovannucci, E. L. (2015). Light to moderate intake of alcohol, drinking patterns, and risk of cancer: results from two prospective US cohort studies. *BMJ, 351,* h4238. doi:10.1136/bmj.h4238.

Cho, E., Lee, J. E., Rimm, E. B., Fuchs, C. S. & Giovannucci, E. L. (2012). Alcohol consumption and the risk of colon cancer by family history of colorectal cancer. *The American Journal of Clinical Nutrition, 95,* 413-419. doi:10.3945/ajcn.111.022145.

Clark, L., Dombrovski, A. Y., Siegle, G. J., Butters, M. A., Shollenberger, C. L., Sahakian, B. J. & Szanto, K. (2011). Impairment in risk-sensitive decision-making in older suicide attempters with depression. *Psychology and Aging, 26,* 321. doi:10.1037/a0021646.

Del Ser Quijano, T., Sanchez Sánchez, F., Garcia de Yebenes, M.J., Otero Puime, A., Zunzunegui, M.V. & Muñoz, D. (2004). Versión española del Test de los 7 Minutos. Datos normativos de una muestra poblacional de ancianos de más de 70 años. *Neurología, 19,* 344-358.

Erickson, C.K. & White, W.L. (2009). The neurobiology of addiction recovery. *Alcohol Treatment Quartely, 27,* 338-345. doi:10.1080/07347320903014255.

Fein, G., Torres, J., Price, L. J. & Di Sclafani, V. (2006). Cognitive performance in long-term abstinent alcoholic individuals. *Alcoholism: Clinical and Experimental Research, 30,* 1538-1544. doi:10.1111/j.1530-0277.2006.00185.x.

Frías-Torres, C., Moreno-España, J., Ortega, L., Barrio, P., Gual, A. & Teixidor López, L. (2018) Remediation therapy in patients with alcohol use disorders and neurocognitive disorders: A Pilot Study. *Adicciones, 30,* 93-100. doi:10.20882/adicciones.757.

Grynberg, D., Maurage, P. & Nandrino, J. L. (2017). Preserved affective sharing but impaired decoding of contextual complex emotions in alcohol dependence. *Alcoholism: Clinical and Experimental Research, 41,* 779-785. doi:10.1111/acer.13330.

Gutnik, L. A., Hakimzada, A. F., Yoskowitz, N. A. & Patel, V. L. (2006). The role of emotion in decision-making: A cognitive neuroeconomic approach towards understanding sexual risk behavior. *Journal of Biomedical Informatics, 39,* 720-736. doi:10.1016/j.jbi.2006.03.002.

Heaton, R. K., Chelune, G. J., Talley, J. L., Kay, G. G. & Curtiss, G. (1993). Wisconsin card sort test manual: Revised and expanded. Odessa, FL: Psychological Assessment Resources. Odessa, FL: Psychological Assessment Resources.

Kish, G.B., Hagen, J.M., Woody, M.M. & Harvey, H.L. (1980). Alcoholics' recovery from cerebral impairment as a function of duration of abstinence. *Journal of Clinical Psychology, 36,* 584-589. doi:10.1002/jclp.6120360234.

Kravitz, A. V., Tomasi, D., LeBlanc, K. H., Baler, R., Volkow, N. D., Bonci, A. & Ferré, S. (2015). Cortico-striatal circuits: novel therapeutic targets for substance use disorders. *Brain Research, 1628,* 186-198. doi:10.1016/j.brainres.2015.03.048.

Le Berre, A. P., Fama, R. & Sullivan, E. V. (2017). Executive Functions, Memory, and Social Cognitive Deficits and Recovery in Chronic Alcoholism: A Critical Review to Inform Future Research. *Alcoholism: Clinical and Experimental Research, 41,* 1432-1443. doi:10.1111/acer.13431.

Lezak, M.D., Howieson, D.B. & Loring, D.W. (2004). Neuropsychological assessment. 4 ed. New York: Oxford University Press.

Maurage, P., Pesenti, M., Philippot, P., Joassin, F. & Campanella, S. (2009). Latent deleterious effects of binge drinking over a short period of time revealed only by electrophysiological measures. *Journal of Psychiatry & Neuroscience, 34,* 111.

Mestre, E. V., Frías, M. D. N. & Samper, P. G. (2004). La medida de la empatía: análisis del Interpersonal Reactivity Index. *Psicothema, 16*, 255-260.

Munro, C.A., Saxton, J. & Butters, M.A. (2000). The neuropsychological consequences of abstinence among older alcoholics: a cross-sectional study. *Alcoholism: Clinical and Experimental Research, 24,* 1510-1516. doi:10.1111/j.1530-0277.2000.tb04569.x.

Nowakowska-Domagała, K., Jabłkowska-Górecka, K., Mokros, Ł., Koprowicz, J. & Pietras, T. (2017). Differences in the verbal fluency, working memory nd executive functions in alcoholics: Short-term vs. long-term abstainers. *Psychiatry Research, 249,* 1-8. doi:10.1016/j.psychres.2016.12.034.

Oscar-Berman, M., Valmas, M. M., Sawyer, K. S., Ruiz, S. M., Luhar, R. B. & Gravitz, Z. R. (2014). Profiles of impaired, spared, and recovered neuropsychological processes in alcoholism. *Handbook of Clinical Neurology, 125,* 183. doi:10.1016/B978-0-444-62619-6.00012-4.

Pedrero-Pérez, E. J., Ruiz-Sánchez de León, J. M., Llanero-Luque, M., Rojo-Mota, G., Olivar-Arroyo, A. & Puerta-García, C. (2009). Sintomatología frontal en adictos a sustancias en tratamiento mediante la versión española de la escala de comportamiento frontal. *Revista de Neurología, 48,* 624-631.

Pelletier, S., Nalpas, B., Alarcon, R., Rigole, H. & Perney, P. (2016). Investigation of Cognitive Improvement in Alcohol-Dependent Inpatients Using the Montreal Cognitive Assessment (MoCA) Score. *Journal of Addiction,* 1539096. doi:10.1155/2016/1539096.

Pfefferbaum, A., Adalsteinsson, E. & Sullivan, E. V. (2006). Dysmorphology and microstructural degradation of the corpus callosum: Interaction of age and alcoholism. *Neurobiology of Aging, 27,* 994-1009. doi:10.1016/j.neurobiolaging.2005.05.007.

Pfefferbaum, A., Sullivan, E. V., Mathalon, D. H., Shear, P. K., Rosenbloom, M. J. & Lim, K. O. (1995). Longitudinal changes in magnetic resonance imaging brain volumes in abstinent and relapsed alcoholics. *Alcoholism: Clinical and Experimental Research, 19,* 1177-1191. doi:10.1111/j.1530-0277.1995.tb01598.x.

Rosenbloom, M.J., O'Reilly, A., Sassoon, S.A., Sullivan, E.V. & Pfefferbaum, A. (2005). Persistent cognitive deficits in community-treated alcoholic men and women volunteering for research: limited contribution from psychiatric comorbidity. *Journal of Studies on Alcohol and Drugs, 66,* 254-265. doi:10.15288/jsa.2005.66.254.

Ruiz-Sánchez de León, J. M., Pedrero-Pérez, E. J., Rojo-Mota, G., Llanero-Luque, M. & Puerta-García, C. (2011). Propuesta de un protocolo para la evaluación neuropsicológica de las adicciones. *Revista Neurología, 53*, 483-93.

Scoccianti, C., Cecchini, M., Anderson, A. S., Berrino, F., Boutron-Ruault, M. C., Espina, C.,... Wiseman, M. (2016). European Code against Cancer 4th Edition: Alcohol drinking and cancer. *Cancer Epidemiology, 45,* 181-188. doi:10.1016/j.canep.2016.09.011.

Seisdedos, N. (2004). Test de atención d2. Madrid: TEA Ediciones.

Spreen, O. & Strauss, E. (1991). Controlled oral word association (word fluency). Spreen O, Strauss E. A compendium of neuropsychological tests. Oxford: Oxford University Press, 219-227.

Staples, M. C. & Mandyam, C. D. (2016). Thinking after drinking: impaired hippocampal-dependent cognition in human alcoholics and animal models of alcohol dependence. *Frontiers in Psychiatry,* 7. doi:10.3389/fpsyt.2016.00162.

Stasiewicz, P. R., Bradizza, C. M., Gudleski, G. D., Coffey, S. F., Schlauch, R. C., Bailey, S. T., ... Gulliver, S. B. (2012). The relationship of alexithymia to emotional dysregulation within an alcohol dependent treatment sample. *Addictive Behaviors, 37,* 469-476. doi:10.1016/j.addbeh.2011.12.011.

Stavro, K., Pelletier, J. & Potvin, S. (2013). Widespread and sustained cognitive deficits in alcoholism: a meta-analysis. *Addiction Biology, 18,* 203-213.

Sullivan, E.V., Rosenbloom, M.J., Lim, K.O. & Pfefferbaum, A. (2000a). Longitudinal changes in cognition, gait, and balance in abstinent and relapsed alcoholic men: relationships to changes in brain structure. *Neuropsychology, 14,* 178-188. doi:10.1037/0894-4105.14.2.178.

Sullivan, E.V., Rosenbloom, M.J. & Pfefferbaum, A. (2000b). Pattern of motor and cognitive deficits in detoxified alcoholic men. *Alcoholism: Clinical and Experimental Research, 24,* 611-621.

Valmas, M. M., Mosher Ruiz, S., Gansler, D. A., Sawyer, K. S. & Oscar-Berman, M. (2014). Social cognition deficits and associations with drinking history in alcoholic men and women. *Alcoholism: Clinical and Experimental Research, 38,* 2998-3007.

Wechsler D. (1999). Escala de inteligencia Wechsler para adultos (WAIS-III). 3 ed. Madrid: TEA.

Wechsler, D. (1997). Wechsler memory scale (WMS-III) (Vol. 14). San Antonio, TX: Psychological Corporation.

Wilson, B. A., Alderman, N., Burgess, P. W., Emslie, H. & Evans, J. J. (1996). Behavioural assessment of the Dysexecutive Syndrome. Bury St. Edmunds, UK: Thames Valley Test Company.

Yohman, J. R., Parsons, O. A. & Leber, W. R. (1985) Lack of recovery in male alcoholics' neuropsychological performance one year after treatment. *Alcoholism: Clinical and Experimental Research, 9,* 114-117. doi:10.1111/j.1530-0277.1985.tb05530.x.

Zywiak, W.H., Westerberg V.S., Connors G.J. & Maisto S.A. (2003). Exploratory findings from the Reasons for Drinking Questionnaire. *Journal of Substance Abuse Treatment, 25,* 287-292. doi:10.1016/S0740-5472(03)00118-1.