

Remediation therapy in patients with alcohol use disorders and neurocognitive disorders: A Pilot Study

Terapia de rehabilitación cognitiva en pacientes con trastorno por consumo de alcohol y trastorno neurocognitivo. Estudio piloto

CINDY FRÍAS-TORRES*, JOSÉ MORENO-ESPAÑA*, LLUISA ORTEGA*, PABLO BARRIO *, ANTONI GUAL*, LÍDIA TEIXIDOR*.

* Addictive Behaviours Unit. Clínic Hospital in Barcelona, Spain.

Abstract

Many alcohol-dependent patients suffer from cognitive impairment of variable severity, manifested by alterations in retrograde and anterograde memory, visuospatial processing, cognitive abilities and attention, some of which are reversible. In this context, cognitive remediation therapies could significantly improve patients' performance; therefore, these are considered a valuable alternative. The aim of this study was to implement cognitive remediation therapy in patients with alcohol dependence and cognitive impairment and evaluate its viability and effectiveness. The participants were sixteen abstinent, alcohol-dependent patients (mean age of 59 years, 63% males) from the Addictive Behaviours Unit of a tertiary hospital. Over 6 months, a nurse led 1-hour weekly sessions (24 sessions in total) during which exercises for improving functional, social and cognitive performance were completed. Patients were assessed at baseline, at the end of the study and 6 months later, using the Mini-Mental State Examination (MMSE) and the Memory Alteration Test (M@T). Their respective scores were 26.4 (SD 3.16), 29 (SD 1.67) and 27 (SD 3.1) for the MMSE and 38.7 (SD 6.81), 45.7 (SD 5.6) and 41.1 (SD 7.86) for the M@T. Changes were assessed with both Friedman and Wilcoxon signed-rank tests, with mostly statistically significant differences ($p < 0.05$). Assistance and satisfaction were high. Therefore, the therapy was viable, widely accepted and effective.

Key words: Alcohol dependence; Cognitive impairment; Cognitive remediation; Alcohol-related brain damage.

Resumen

El deterioro cognitivo es común en los pacientes alcohólicos. Éste se manifiesta por alteraciones en la memoria anterógrada y retrógrada, el procesamiento visual-espacial, y en las habilidades cognitivas y la atención, siendo algunas reversibles. Las terapias de rehabilitación cognitiva podrían mejorar el rendimiento de los pacientes, siendo una alternativa terapéutica de interés. El objetivo de este estudio piloto fue evaluar la implementación, viabilidad y efectividad de la terapia de rehabilitación cognitiva en pacientes con dependencia al alcohol y deterioro cognitivo asociado. Se trata de un estudio piloto con 16 pacientes (63% hombres, edad media de 59 años) seguidos en la Unidad de Conductas Adictivas de un hospital de tercer nivel. Siendo la abstinencia un requisito para la inclusión, durante 6 meses una enfermera realizó sesiones semanales de una hora (24 sesiones), realizándose ejercicios de psico-estimulación para la mejora del rendimiento cognitivo, funcional y social. Se evaluó a los pacientes al inicio, al final y pasados 6 meses, mediante las escalas MMSE (test Mini-mental de Lobo) y T@M (test de Alteración de Memoria). Sus puntuaciones medias respectivas fueron 26.4 (DE 3,16), 29 (DE 1,67) y 27 (DE 3,1) para MMSE y 38,7 (DE 6,81), 45,7 (DE 5,6) y 41,1 (DE 7,86) para T@M. Los datos se analizaron mediante la prueba de Friedman y se compararon los distintos periodos temporales mediante la prueba de rangos con signo de Wilcoxon, siendo la mayoría de comparaciones significativas ($p < 0,05$). La asistencia y la satisfacción fueron elevadas. Así pues, la terapia fue viable, ampliamente aceptada y mostró ser efectiva.

Palabras clave: Dependencia de alcohol; Deterioro cognitivo; Rehabilitación cognitiva; Daño cerebral asociado al alcohol.

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Send correspondence to:

Lidia Teixidor, c/ Rosselló 161 bajos, tel: 932275400, fax 932271750. Mail: lteixido@clinic.ub.es.

The DSM-V (American Psychiatric Association, 2013) defines alcohol use disorders as a condition related with ongoing consumption of alcohol in excessive amounts or during a long period over one's lifetime; it is also associated with the appearance of behavioural and physical symptoms, including tolerance, abstinence, lack of control over use, and health, family and social problems (American Psychiatric Association, 2013; Schuckit 2009). The European Union, a region in which alcohol production and use is strongly rooted, has one of the world's highest per capita use rates (approximately 23 million adults/year are alcohol-dependent) (Rosón Hernández, 2008). In Spain, alcohol use has remained stable since the eighties, though the proportion of female drinkers has increased.

The World Health Organization (WHO) associates the disorder with physical and mental deterioration. This entails a significant increase of both mortality and morbidity (Varela-Rey, Woodhoo, Martínez-Chantar, Mato, & Lu, 2013), including neurological, cardiovascular, metabolic and neoplastic diseases.

Alcohol use disorder generates a socioeconomic impact, particularly low productivity and health-related expenses. In turn, the disorder is strongly correlated with sexual risk situations, injuries, suicide, homicide and automobile accidents, the costs of which are difficult to evaluate (Miller et al., 2008; Surkan, Fielding-Miller, & Melchior, 2012; Varela-Rey et al., 2013).

Alcohol-related brain damage (ARBD) is currently the focus of special attention (Soler-González, Balcells-Oliveró, & Gual-Solé, 2014). Behavioural alterations, cognitive deficits, amnesia and degenerative changes to the cerebellum are worth highlighting. Neuroimaging has related excessive alcohol use with the appearance of structural (e.g., loss of volume of brain and cerebellum tissue) and functional (e.g., dysfunction of the frontal and temporal lobes and their connections) changes (Glass et al., 2009; Yeh, Gazdzinski, Durazzo, Sjöstrand, & Meyerhoff, 2007). These changes have been related to alterations of episodic memory, attention, visuospatial processing, and emotional processing and decision-making (Pedrero-Perez, Rojo-Mota, Ruiz-Sanchez de Leon, Llanero-Luque, & Puerta-García, 2011). On this basis, a patient with alcohol use disorder may develop a Neuro-cognitive Disorder (NCD) characterized by deficits that last longer than the usual duration of acute abstinence, and which are more likely in older patients (Gongvatana et al., 2014). It is estimated that between 50-70% of alcohol-dependent persons have some degree of cognitive deterioration (Glass et al., 2009; Miller et al., 2008). The DSM-5 uses the categories "Mild (MND) and major neurocognitive disorders associated with substance abuse".

The more frequent MND entails difficulty in performing some daily tasks that require paying attention and

following instructions. Ongoing use, with the appearance of secondary brain damage, associated with lower neuronal plasticity and other age-related changes, could cause patients difficulty in learning and implementing new information (Pedrero-Perez et al., 2011). These changes are related to poor compliance with rules and guidelines, lower adherence to treatment, early relapses and few skills for refusing alcohol (Bates, Buckman, & Nguyen, 2013; Pedrero-Perez et al., 2011).

Executive functions and memory, given their close relationship with abstinence and the success of treatments for alcohol dependency, have been the most widely studied areas in the field of alcohol. Working memory and the capacity for inhibiting response (both based on frontal circuits) are highly vulnerable to alcohol use (Lawrence, Luty, Bogdan, Sahakian, & Clark, 2009). Other skills, such as conceptualization, abstraction and problem-solving are also frequently affected (Rupp et al., 2006). Despite the existing patterns as regards impact, it is absolutely necessary to emphasize the important heterogeneity among patients, due to the methodological limitations of published research, as well as to the numerous determinant factors underlying individual cognitive capacities, such as age, gender, cultural level or genetic influence (Bates, Bowden, & Barry, 2002).

Decades of research and clinical experience have focused current treatment for alcohol use on helping patients to reduce or stop their alcohol use through medication, behavioural therapies, brief interventions and social skills training (Huebner & Kantor, 2010). Studies with patients with alcohol use disorder and mild NCD show that the latter may interfere with treatment efficiency. Nevertheless, lost cognitive functions may be recovered, at least to a great extent (Rojo-Mota et al., 2009). To achieve this, continuous abstinence is a critical, though probably insufficient, element.

In this regard, functional and cognitive rehabilitation therapy acquires increasing importance. To date, most programs have focused on improving executive functions, memory, and other cognitive skills (Alfonso, Caracuel, Delgado-Pastor, & Verdejo-García, 2011; Bickel, Yi, Landes, Hill, & Baxter, 2011; Houben, Wiers, & Jansen, 2011; Levine et al., 2011) with the goal of evaluating their effect on both cognitive skills per se, as well as with regards to their impact on variables associated with alcohol use. Recently, rehabilitation models based on changing automatic and implicit processes have also been proposed (Wiers, Eberl, Rinck, Becker, & Lindenmeyer, 2011). Alternative programs include the use of heart rate variability biofeedback (Bates & Buckam, 2013), aerobic physical training (Brown et al., 2014) or mindfulness (Chiesa, Calati, & Serretti, 2011).

Though the concept is not new, most studies on this issue are already relatively outdated (Allen, Goldstein, & Seaton, 1997; Goldman, 1990). Though some recent studies (Rupp, Kemmler, Kurz, Hinterhuber, & Fleischhac-

ker, 2012) contribute promising results, notable controversy arises as to these programs' real efficiency, structure and organization (Bernardin, Maheut-Bosser, & Paille, 2014). In addition, there is still important vagueness as to the real mechanisms implied in these rehabilitation programs' observed improvements, with different studies suggesting different mechanisms (Houben, Havermans, Nederkoorn, & Jansen, 2012; Houben & Wiers, 2009). We must also mention the critique of both methodologies applied and external validity of cognitive rehabilitation programs in the field of alcoholism (Houben et al., 2011; Houben & Wiers, 2009). Altogether, this suggests that evidence on this issue is far from conclusive, and further research is required.

A wide range of health professionals manage these programs, but nurses deserve special attention because they assume a key role in both detecting and treating alcohol dependency. Patient care by nurses combines psychosocial interventions, where mental health nurses assume leadership, given their more direct and frequent contact with patients (Ryan & Rothwell, 2010). When providing orientation, the nurse takes advantage of the therapeutic relationship to boost the patient's motivation and interest in rehabilitation therapy.

The purpose of this pilot study was to evaluate the implementation of rehabilitation therapy within the framework of nursing, in alcohol-dependent patients with associated cognitive deterioration, and to evaluate the therapy's viability and effectiveness.

Resources and methods

Pilot study to evaluate the implementation, acceptability and preliminary efficiency of a cognitive rehabilitation program for patients with alcohol dependence and mild NCD. Longitudinal prospective design without control group. The study was comprised of a total of 24 alcohol-dependent patients seeking treatment through outpatient visits to the Addictive Behaviours Unit (see inclusion criteria) upon agreeing to participate and signing the informed consent.

Criteria for participation in the study was as follows. Inclusion criteria: outpatient services patient, alcohol use disorder (DSM-5) with a minimum of 6 months of abstinence beforehand, significant NCD: M@T below 43 and MMSE below 28. Exclusion criteria: Serious NCD or any other condition (per clinical diagnosis) that prevents correctly participating in, or assimilating, the cognitive therapy.

During 6 months, the Unit nurse led a total of 24, 1-hour weekly sessions. The group was comprised of 8-9 patients who always held group sessions with the participation of all of its members in each. Mental stimulation resources and exercises were used to improve cognitive, functional and social performance. Written language (prints) and

spoken language (recall of participants' names, previous tasks, etc.) were alternated. The tasks were completed in a classroom specifically adapted for group work, and the patients occupied the same place to facilitate name retention. The contents of the resources used were adapted to the patients to the extent possible, regardless of their sociocultural level.

The areas object of the intervention were:

1. Attention: practiced through visuospatial recognition exercises, word searches and differences between pictures.
2. Memory: different memory types were addressed:
 - a. Semantic memory: implying conceptual information, referring to aspects related to the meaning of the information, addressed in the group through exercises involving general knowledge without the recall of specific events, such as holidays and celebrations.
 - b. Episodic memory: worked on using information that allows for assigning dates and spatially locating information in relation to the patients themselves and to other events, specifying where and when a given information was presented in regard to one's personal biography. This was done by asking questions about each patient's life events, such as: "What did you do yesterday?" "What have you eaten for breakfast?" "What colour was the shirt you wore yesterday?"
 - c. Autobiographical memory: the recall of first-hand events experienced by each patient was addressed through the recall of specific episodes from their lives, based on personal and family photographs or objects.
 - d. Immediate memory: the recall and/or recognition of information received was addressed based on repeating word lists and describing previously presented images.
3. Language:
 - a. Automatic language: based on automatic verbal production tasks through exercises to recall the months of the year, numerical series, and popular sayings or proverbs in which the beginning of the saying was presented, and the patient had to complete the sentence and then try to explain its meaning.
 - b. Recall: to evaluate and work on aspects related with verbal fluency in which the person named the elements comprising a category (colours, animals, pieces of clothing, cities).
 - c. Spontaneous language: through exercises to describe images, prints, situations and occurrences.
 - d. Denomination: addressing the content of terms and words based on exercises that entailed naming objects and the components of objects.
4. Reading and writing: reading and writing exercises were completed based on reading newspaper articles, books and short texts.

5. Executive functions: practiced through exercises to detect similarities and differences, logical series and numerical processing exercises. Though the targets were attention and memory, other fields, such as language and executive functions, were alternated as well to maintain adherence and retention during the one-hour session.

Three evaluations were completed: at baseline, at the end of the sessions (6 months) and 12 months later. The initial evaluation gathered sociodemographic data, medical and psychiatric background and the level of cognitive deterioration using the MMSE (Mini-Mental State Examination) and the M@T (Memory Alteration) scales. The two latter ones were also evaluated at 6 and 12 months, as well as the patients' attendance in the therapy sessions and satisfaction (Annex 1).

Instruments

No specific validation exists for screening cognitive deterioration in patients with alcohol use disorder. Most published studies, as well as in clinical practice, use those tests that are most widely applied in other fields (such as dementias). In our case, we used the MMSE and the M@T.

MMSE: The Mini-Mental State Examination is a test for screening dementias, also used for follow-up of their progress. It is most commonly used to detect and evaluate the progress of a Cognitive Disorder associated with neurodegenerative diseases, like Alzheimer (Crum, Anthony, Bassett & Folstein, 1993). It includes five sections: orientation, attention, concentration and calculation, memory and language. The administration of this simple, structured scale requires no more than 5-10 minutes. The maximum, total score is 30 points. A score of < 23 points in a geriatric patient or of < 27 points in the general population is considered cognitive deterioration (Crum et al., 1993).

M@T SCALE: The Memory Alteration Test (M@T) is a cognitive screening test with high sensitivity and specificity for mild cognitive deterioration similar to amnesia, and for mild Alzheimer disease, among the general population. It is short, easy to administer and score. It evaluates several memory subtypes through five sections: immediate memory, temporal orientation memory, semantic remote memory, free recall memory, and recall memory with cues. Administration varies between 5-10 minutes for both healthy patients and those with mild cognitive deterioration. Correct answers are summed (1 point). A global score over the 50 maximum possible points of the test is recommended. A score of < 43 points represents significant cognitive deterioration (Rami, Molinuevo, Sanchez-Valle, Bosch, & Villar, 2007).

Data analysis

Microsoft Office Excel sheets were used to gather and analyse the data. SPSS (V.19) was used for statistical analysis. Given the sample size and non-normal data, the Friedman

test was used as a non-parametric method for repeated measures to evaluate the global significance of the study for both scales. Post-hoc analysis was completed with the Wilcoxon signed-rank test, comparing the baseline results with the results upon completing the therapy and with those 6 months later. A 95% confidence interval was used for data analysis for $p < .05$ to contrast the proposed hypothesis.

Results

Table 1 displays sociodemographic data and the medical and psychiatric background of patients who attended therapy. A total of 24 patients participated, 58.3% were male and 41.7% were female. The average age was 62 years (minimum 41, maximum 83). Of these, 4.2% were single, 54.2% were married, 33.3% were divorced and 8.3% were widowed. As regards educational level, 54.2% had completed elementary schooling, and the remaining patients had completed secondary or upper education. As to employment, 45.8% were retired, 4.2% were currently unemployed but had worked previously, 33.3% had no paid job at the time, and 16.6% were currently employed. As regards socioeconomic level, 33.3% of the patients currently or previously experienced difficulties. As to household composition at the time of becoming a member of the therapy group, 29.2% of the patients lived alone, while the remaining lived with the family, mainly with a partner or children.

Patient health was assessed as to the presence or absence of cardiovascular risk factors (CRF), noteworthy neurological diseases and associated psychiatric diagnoses, independent of alcohol dependence. As to cardiovascular risk factors, 58.3% of the patients were smokers, and approximately one third of the sample showed dyslipidaemia. A lower percentage of patients had diabetes mellitus or obesity. No patients had primary neurological disorders. As to a history of neurological diseases, 20.9% of the sample showed some type of diagnosis; among these, two patients had a diagnosed cerebrovascular disease, one epilepsy and another Huntington's disease. A dual pathology diagnosis was common; 66.7% of the patients had a mental disorder, depression being predominant (33.3%), followed by personality disorder (16.75%), anxiety disorder (12.5%) and bipolar disorder (4.2%).

Table 2 displays the results of the MMSE and M@T scales over the course of the study. The global analysis of the Friedman test found statistically significant differences between the successive values of the MMSE ($X^2(2) = 22.86$; $p < .001$) and the M@T ($X^2(2) = 36.02$; $p < .001$). The post-hoc analysis was completed with the Wilcoxon signed-rank test and the Bonferroni correction, which established statistical significance at $p < .0125$. As regards the MMSE scale, the medians and interquartile range for the values at baseline, upon completion of the treatment, and 6 months later were 27 (from 25.25 to 28), 29 (from 28 to

Table 1. Sociodemographic data of the sample.

Variable	Characteristics of the sample Mean (SD) or percentage
Age	61,83 (12.25)
Gender (% female)	41.7%
Marital status	
unmarried	4.2%
married	54.4%
divorced	33.3%
widowed	8.3%
Level of education	
primary	54.2%
secondary	16.7%
occupational training	16.7%
3-year university degree	8.3%
5-year university degree	4.2%
Employment status	
unemployed	33.3%
unskilled worker	8.3%
skilled worker	8.3%
unemployment benefits	4.2%
pensioner	45.8%
Socioeconomic level	
lower class	33.3%
middle class	66.7%
Household composition	
alone	29,2%
spouse	41,7%
spouse and children	12,5%
children	12,5%
parents/siblings	4,2%
Comorbid psychiatric disorder	66,7%
Pharmacological treatments	
antipsychotics	20.8%
benzodiazepines	12.5%
antidepressants	33.3%
interdictor	37.5%
Smokers	41.7%

Note. SD = Standard Deviation.

30) and 28 (from 27 to 30). Significant differences were found between the values at baseline and at the end of the treatment ($z = -4.05$; $p < .001$), while no significant differences were found between the values at baseline and at 6 months after the end of the treatment ($z = -2.392$; $p = .017$). As regards the M@T scale, the medians and interquartile range for the values at baseline, upon completion of the treatment, and 6 months later were 40 (from 37 to 45.5), 47.5 (from 44 to 49) and 44.5 (from 40 to 48). Significant differences were found between the values at baseline and at the end of the treatment ($z = -4.3$; $p < .001$), as well as between the values at baseline and at 6 months after the end of the treatment ($z = -2.6$; $p = .009$).

Missed attendance was anecdotal: 7%. As regards satisfaction with the therapy, 3% of the patients was satisfied and 97% was very satisfied. During follow-up of the study, all of the patients remained abstinent, according to the usual urine tests and self-reports completed by patients and their family members.

Table 2. Values of the MMSE and M@T at baseline, end of treatment and 6 months.

Scale	Baseline Mean (SD)	End Mean (SD)	At 6 months Mean (SD)
MMSE	26.58 (2,7)	28.92 (1,4)	27.71 (2,8)
T@M	39.79 (6,4)	46.00 (4,8)	42.21 (7,5)

Note. SD = Standard Deviation. MMSE = Mini-Mental State Examination. M@T = Memory Alteration Test.

Discussion

The results of this pilot study suggest how cognitive rehabilitation therapy, when integrated in the treatment for alcohol dependency, could facilitate improved cognitive functioning in patients with cognitive deterioration associated with alcohol use, in accordance with general cognitive screening tests, like the M@T and the MMSE. The data collected over the course of the study suggest that the improvement observed upon completion of the study tends to be lost at 6 months after the end of the intervention.

It is important to highlight the pilot nature of this study, implying the absence of a control group and a small sample size. This means that the observed cognitive improvements cannot be definitely attributed to the direct effects of the therapy. Any type of intervention that facilitates social interaction and fosters some cognitive effort could have caused improvements in the patients' cognition or mood state, and this could have acted as a confounding variable in our analysis. Furthermore, other secondary effects, such as a greater presence of or closer supervision by the health professionals in relation to the patients, also exist. We must also mention that part of the improved progress observed could be spontaneous, as it is known that some cognitive functions improve spontaneously during prolonged periods of abstinence. Even so, we consider that the fact that patients remained abstinent 6 months before and 6 months after the intervention increases the validity of the results. Again, given that this is a pilot study without a control group, conclusions cannot be drawn as to whether the observed improvement contributed toward maintaining abstinence in subsequent months, a fact confirmed by other studies (Rupp et al., 2012). Special mention must also be made of the use of instruments like the M@T and the MMSE, lacking high specificity and usually used as screening methods. Nevertheless, these are widely-used instruments validated in many contexts and have been shown to partially correlate with broader neuropsychological batteries (Rami et al., 2009), wherefore they may be considered an acceptable approximation of the cognitive state of the study's participants.

The fact that both levels of attendance and patient satisfaction were high suggests that the intervention was widely accepted. The fact that these patients' nurse led the

intervention could be an important variable in explaining this high satisfaction and acceptance. This could have significant implications as regards future research, suggesting that the implementation of the therapy by the patients' attending health professionals could improve its implementation and, therefore, facilitate or contribute toward achieving higher efficiency.

The study has major limitations derived of the criteria used for selecting patients to participate in the therapy. Based on the demand of patients and their family members as well as of professionals, with regards to the detection of cognitive impairment symptoms, the patient sample was quite heterogeneous, mostly in health-related issues. In this sense, the presence of patients with and without neurological disorders, as well as others with a dual diagnosis, could justify the scarce homogeneity of results in the MMSE and M@T scales. All of this hinders drawing conclusions on causality as regards the possible aetiology of the cognitive deterioration. Though it is true that all patients met criteria of alcohol dependency, it is quite likely that, in many cases, the observed deterioration had a mixed source. Another significant limitation is general and not study-specific: the absence of neurocognitive evaluation tests validated specifically in alcohol-dependent populations and which, furthermore, have proven their sensitivity to changes in the long term. Many authors have emphasized this, and it should be a focus of future research. Finally, given the pragmatic and exploratory study design, the effect of learning could not be controlled in patients in which it could have resulted of completing the same test several times over 12 months.

Conclusions

This pilot study shows how cognitive rehabilitation therapy in patients with cognitive deterioration and alcohol use disorder is viable and widely accepted by the patients. The study's important methodological limitations hinder obtaining valid conclusions about its efficacy. Nevertheless, preliminary exploratory data suggest that the intervention could contribute toward improving this population's cognitive functioning. The promotion of research in this field is of critical importance, given its potential positive impact on a highly relevant health problem. To this end, it would be convenient to first validate neurocognitive screening and evaluation tests in patients with alcohol use disorder that are sensitive to changes over time; then, to carry out prospective longitudinal studies with comparison groups for different rehabilitation approaches.

Conflict of interests

The authors declare the inexistence of conflicts of interest with regard to this study.

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