Effectiveness of Neuropsychological Rehabilitation in the Recovery of Executive Deficits in Patients with Alcohol Use Disorder: A Systematic Review Protocol

Eficácia da Reabilitação Neuropsicológica na Recuperação de Défices Executivos em Doentes com Perturbação por Uso de Álcool: Protocolo de Revisão Sistemática

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ABSTRACT
Introduction: Changes in executive functions associated with alcohol consumption are frequently found in alcohol use disorder. Neuropsychological rehabilitation can play an essential role as an effective treatment in the recovery from these deficits, leading to the maintenance of abstinence. However, there are still some uncertainties regarding its impact on the recovery of deficits in executive functions. Our purpose is to present a protocol for a systematic review aiming to assess which neuropsychological rehabilitation programs are effective in the recovery of executive deficits in patients with alcohol use disorder.
Methods: We will search the following databases: PubMed, Cochrane Library (CENTRAL), Web of Science, and Scopus, as well as the list of references of the identified studies. Screening, data extraction, and synthesis, as well as evaluation of the risk of bias, will be carried out by two reviewers independently, using ROBINS-I and RoB 2. Disagreements will be resolved using a third additional reviewer. Primary outcomes will correspond to changes in executive functions, following a neuropsychological rehabilitation program in patients with alcohol use disorder. The evidence will be synthesized using a narrative description of neuropsychological rehabilitation programs and the indicators of their effectiveness will be identified. The neuropsychological rehabilitation programs for executive functions will be assessed considering their different components and their impact on the recovery of these functions. The review described in this protocol will allow the development of guidelines for the design of more effective rehabilitation programs for clinical populations with alcohol use disorder.
Keywords: Alcoholism; Alcohol Use Disorder; Cognitive Rehabilitation; Executive Functioning

RESUMO
Introdução: Na perturbação por uso de álcool é frequente verificarem-se alterações nas funções executivas associadas ao consumo de álcool. A recuperação destes défices é essencial, podendo promover a eficácia dos tratamentos e levar à manutenção da abstinência. Apesar da reabilitação neuropsicológica poder assumir aqui um papel essencial ainda existem algumas incertezas em relação ao seu impacto na recuperação destes défices. O objetivo deste trabalho é apresentar um protocolo de revisão sistemática da literatura com vista a avaliar que programas de reabilitação neuropsicológica são eficazes na recuperação das funções executivas em doentes com perturbação por uso de álcool.
Métodos: Pesquisaremos nas bases de dados PubMed, Cochrane Library (CENTRAL), Web of Science e Scopus, bem como na lista de referências dos estudos identificados. A triagem, extração e síntese de dados, bem como a avaliação do risco de viés serão efetuadas por dois revisores de forma independente, utilizando o ROBINS-I e o RoB 2. Os desacordos serão ultrapassados com um terceiro revisor. As alterações nas funções executivas obtidas com a reabilitação neuropsicológica em pacientes com perturbação por uso de álcool constituirão os *outcomes* principais. As evidências serão sintetizadas por meio de uma descrição narrativa, sobre os programas de reabilitação neuropsicológica, identificando-se indicadores de eficácia. Serão analisados os programas de reabilitação neuropsicológica para as funções executivas, considerando as suas diferentes componentes e descrevendo o seu impacto na recuperação destas funções. A revisão definida neste protocolo permitirá o desenvolvimento de linhas orientadoras para a definição de programas de reabilitação mais efetivos para a população clínica com perturbação por uso de álcool.
Palavras-chave: Alcoolismo; Funções Executivas; Perturbação por Uso de Álcool; Reabilitação Cognitiva

INTRODUCTION

Alcohol use disorder (AUD) represents a serious public health problem, with multiple repercussions, causing liver disease, heart disease, psychiatric disorders (e.g., depression, anxiety, etc.), oncological diseases, and cognitive impairment,[1] affecting also the quality of life of individuals. In AUD the deficits in cognitive functioning are frequent, including those of executive functions, which may affect the treatment process by affecting motivation and decision-making.[2]

All these aspects may increase the risk of relapse.[3] In this context, significant changes in executive functions (EF) are present due to greater impairment in the prefrontal cortex,[4] both in recently detoxified individuals[5] and those with longer periods of abstinence.[6]

Some of the cognitive deficits tend to be restored over the course of abstinence,[4] although others can persist over time.[7] Some studies found improvements after one month of

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abstinence,[8] while others highlighted the presence of cognitive deficits after one and two years.[6,9] Variables such as psychiatric comorbidities, affective aspects,[10] the number of previous detoxifications,[11] age of cessation of consumption,[9] among others, may influence these aspects.

The cognitive impairment and its interference in the day-to-day life of individuals with AUD point to the need to include neuropsychological rehabilitation (NR)/cognitive remediation in the traditional treatments for the disease to minimize its negative impact. This hinges on the premise that repetitive exposure to certain activities can help strengthen and restore cognitive function, facilitating the recovery trajectory compared to spontaneous evolution over time of abstinence.[10] Furthermore, NR is underpinned by neuroplasticity, which reflects the brain's capacity for self-repair, this being enhanced by the cognitively complex environmental experiences to which it is subjected, as is NR.[12]

As far as we know, there is some heterogeneity in results regarding the importance of NR in the recovery of cognitive deficits. Some data show that NR is associated with improved cognitive functioning, promoting recovery from alcohol-induced damage,[13-16] although others do not support this positive association.[17-19] In this area, it becomes increasingly relevant that the NR programs benefit the individuals' functionality, fitting in with their daily needs and demands. It is essential to make them more capable of managing their interpersonal relationships, daily life, and work tasks, as well as avoiding consumption.[20] On the other hand, it is thought that NR may contribute to better efficacy of treatments in AUD,[21] by promoting adherence to them. The protocol presented here describes the rationale, hypothesis, and methods to be followed for a systematic review aiming to assess which NR programs are effective in the recovery of executive deficits in patients with AUD.

METHODS

The protocol was structured, based on Cochrane[22] recommendations for systematic reviews of literature and Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA-P).[23]

Research question

We defined the following research question for the review: 'Which neuropsychological rehabilitation programs are effective in the recovery of executive deficits in patients with alcohol use disorder?'

Inclusion/Exclusion criteria

The inclusion/exclusion criteria[24] were defined as follows:

Study design: randomized and non-randomized controlled clinical trials, longitudinal studies (cohort), case-control studies, and cross-sectional studies.

Population: abstinent adults (≥ 18 years old) with previous history of AUD, with or without a history of other substance use, with different patterns and durations of consumption, and without brain damage. Individuals with traumatic brain injury and neurological conditions caused by alcohol consumption and psychiatric comorbidity will not be eligible, as well as other types of alcohol consumption other than dependence (e.g., binge drinking).

Intervention: all NR programs will be integrated, with no limitations in terms of intervention context, treatment phase, abstinence time, or trained executive functions. We will include different interventional strategies. Transcranial magnetic stimulation will be excluded.

Comparator: usual treatment in AUD and/or some type of NR with different characteristics (technical and frequency) of the experimental group, or cases of no intervention of any type.

Context: we will include all contexts of intervention in AUD, such as outpatient, inpatient, and therapeutic community.

Results: The main results will be assessed as changes (improvement/ worsening) in the EF with NR, particularly in inhibition, working memory, cognitive flexibility, planning, problem-solving, decision-making, and abstract thinking, using data from the cognitive tests used in the studies. We will also analyze changes in other cognitive domains or other EF components (transfer effect). As secondary outcomes, changes in alcohol consumption patterns will be described, such as reduction/increase in consumption or abstinence time and the number of relapses during treatment, based on reports and tests related to consumption.

Studies published in English, Spanish, French, Italian, and Portuguese will be included.

Only reports with empirical data will be included. We will exclude opinion or literature review studies, conference abstracts, and books or book chapters.

Information sources and research strategies

PubMed, Cochrane Library (CENTRAL), Web of Science, and Scopus will be used to conduct the proposed review. The only filter used in the research will be the language.

The search strategy will include text words, and search terms adjusted to the specificities of the different databases. Keywords or database-specific subject headings (e.g., MeSH) and the Boolean operators 'OR' and 'AND' will be used to combine the search terms. The keywords included will be 'alcoholism', 'alcohol', 'cognitive training', and 'cognitive remediation'. Keywords will be grouped into three combined free-text blocks, one on alcohol, one on cognitive domains, and another one on NR. An example of the

research strategy that will be used for one of the databases is presented in Appendix 1 (https://www.actamedicaportuguesa.com/revista/index.php/amp/article/view/19804/15224).

The reference list of systematic reviews and meta-analyses identified in this review, as well as from other papers that match the defined inclusion criteria will also be hand-searched.

Study selection

The titles of the reports found in the different databases will be extracted and duplicates eliminated using Mendeley reference management software (keeping only the most recent versions, when applicable). Titles and abstracts will be independently assessed by two authors of this review in order to select the reports that potentially match the inclusion criteria [see Appendix 2 (https://www.actamedicaportuguesa.com/revista/index.php/amp/article/view/19804/15225)]. Disagreements regarding the eligibility of the reports will be resolved using a third researcher to reach a consensus. Reports with no full text available will be excluded. A list of the reports eliminated will be drawn up and the reasons for the exclusion will also be described.

Data extraction/synthesis

The extracted data will be included by one of the researchers in a standardized table and checked by another researcher. This table will include the article author's name, year of publication, study design, inclusion criteria, exclusion criteria, population and characterization of the participants (number, age, gender, comorbidity, type of consumption, other consumptions and participation rate), the NR characterization (objective, tasks, strategies, cognitive domains trained, intervention context, number of rehabilitation sessions/hours), simultaneous interventions, control group, transfer effect, follow-up, outcome measure (the instruments and moments of evaluation), the main outcome (changes in cognitive domains) and other outcomes, such as alcohol consumption pattern, emotional aspects, functionality in daily life.

The information described above will be included in a narrative synthesis, illustrated with tables because the diversity of interventions and comparators makes a meta-analysis difficult to perform.

Risk of bias assessment

Two reviewers will independently assess the methodological quality of the selected studies. The risk of bias in randomized controlled trials will be evaluated using the Cochrane Collaboration tool (RoB2). The risk of bias in non-randomized studies of interventions will be assessed using ROBINS-I.[25,26]

DISCUSSION

The proposed review is expected to aggregate a heterogeneity of results, some of which will point to the efficacy of NR on EFs,[13,14] while others will not highlight significant differences between baseline and follow-up data.[17,18]

On the other hand, it is expected that the NR of EFs may interfere with other variables in the daily life of this population specifically on the reduction of alcohol consumption[12] or the promotion of abstinence, which influences adherence and motivation for treatment,[2] as well as behavioral change. Neuropsychological rehabilitation for a particular cognitive function can improve the performance of that function and generalize the benefit of untrained tasks.[27]

Previous systematic reviews of the literature, despite not having controlled for some of the variables that may interfere with data analysis (inclusion of certain psychiatric conditions or the simultaneous use of pharmacological therapy), have shown improvement at the cognitive level with NR in AUD. However, the data does not appear to be robust, especially regarding the degree of impact of NR on cognitive functioning and/or functionality, in consumption and social adaptation of individuals with AUD,[27] causing the underlying mechanisms of those improvements not to be understood.[28]

The analysis of different NR programs, in different rehabilitative contexts and with different methodologies, in comparison with the usual treatments in AUD, may allow the identification of the most efficient interventions in this field. Nonetheless, the diversity found in studies, concerning the NR and the studied population, may constitute challenges in drawing conclusions regarding this issue. It is expected that this review may facilitate a better understanding of these aspects, by including structural elements of NR, specifically the duration/number of sessions and diversified interventional strategies, among others. Examining and better characterizing NR programs will allow us to assess whether there are methodologies with greater impact on the rehabilitation of executive deficits in AUD. This review will provide guidance for the design of more effective NR therapies for AUD and will identify possible profiles of individuals who may benefit from them, demonstrating their relevance in AUD therapeutic plans.

A possible limitation of this review relates to the risk of not including unpublished studies, which may not be covered by the search strategy. Furthermore, the risk of bias may persist, namely the difficulties in combining the various studies, with differences in the studied populations, interventions, and comparators, as well as methodological limitations of the primary studies, which may affect the analysis of results.

This review will examine the effectiveness of NR of EFs in AUD. Its strengths relate to the attempt to control

variables that may interfere with the analysis of the effectiveness of the NR programs, such as brain injuries or psychiatric conditions, attending to more structural elements of the NR, and facilitating the characterization of the rehabilitative processes. All these aspects may allow a more solid analysis of the NR in this population.

AUTHOR CONTRIBUTIONS

SF: Conceptualization, data curation, formal analysis, investigation, methodology, writing of the original draft, critical review.

AV: Conceptualization, formal analysis, investigation, methodology, writing and critical review of the original draft, supervision.

CR, SP, LBN: Writing and critical review of the original draft, supervision.

STUDY REGISTRATION

Submission to Prospero was carried out to record the systematic literature review (registration number: CRD42023393730).

COMPETING INTERESTS

The authors have declared that no competing interests exist.

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