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DESDE 1927 ANALES DE LA FACULTAD DE CIENCIAS MÉDICAS

ARTICULO ORIGINAL

Neurocognitive Assessment in Addictions

Evaluación Neurocognitiva en las Adicciones

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RESUMEN

Introducción: Este artículo pretende ofrecer una breve revisión de las pruebas recientes que consideran los factores cognitivos relacionados con la adicción. Las observaciones clínicas, la sabiduría convencional y los mecanismos teóricos bien razonados sugieren que el uso agudo y crónico de sustancias psicoactivas deterioraría el funcionamiento cognitivo de los individuos. Por lo tanto, la evaluación neurocognitiva de la adicción debería emplearse en la práctica diaria. Las intervenciones tempranas tienen como objetivo detectar los síntomas prodrómicos y proporcionar respuestas rápidas en las primeras etapas de los trastornos. **Objetivos:** Nuestro objetivo es resumir la información sobre la evaluación neurocognitiva en las adicciones para proporcionar una orientación general a los clínicos que trabajan con pacientes afectados por trastornos por consumo de sustancias. **Materiales y métodos:** La búsqueda de datos incluyó los principales motores de búsqueda (es decir, PubMed, Web of Science, PsycINFO y SciELO) y seleccionó artículos publicados en los últimos veinte años sobre la evaluación neurocognitiva basada en la evidencia en las adicciones utilizando las siguientes palabras clave: "(Evaluación neurocognitiva o neuropsicológica) AND (TUS o Farmacodependencia o Abuso) OR Alcohol OR Nicotina OR Adicción". **Resultados:** Este breve artículo destaca la importancia de evaluar el rendimiento cognitivo en la fase inicial de los trastornos mentales y, en concreto, las características cognitivas de los sujetos que consumen múltiples sustancias psicoactivas. Investigaciones posteriores deberían describir el

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resultado longitudinal de los rendimientos cognitivos entre estos pacientes a través de las diferentes etapas de la enfermedad: intoxicación, abstinencia temprana y abstinencia tardía. **Conclusión:** La evaluación de las habilidades cognitivas puede sugerir intervenciones de tratamiento adaptadas para la rehabilitación cognitiva temprana, de modo a reducir el impacto biopsicosocial del abuso de sustancias y promover la adherencia a estos tratamientos.

Palabras Clave: Trastornos por uso de sustancias; adicciones; perfil cognitivo; intervenciones tempranas; evaluación, rehabilitación.

ABSTRACT

Introduction: This paper aims to provide a brief review of recent evidence considering addiction-related cognitive factors. Clinical observations, conventional wisdom, and well-reasoned theoretical mechanisms suggest that the acute and chronic use of psychoactive substances would impair the cognitive functioning of individuals. Therefore, the neurocognitive assessment for addiction should be employed in daily practice. Early interventions are aimed to detect prodromal symptoms and provide prompt responses in the first stages of disorders. **Objectives:** We aimed to summarize information on neurocognitive assessment in addictions to provide general guidance to clinicians working with patients affected by substance use disorders. **Materials and methods:** Data search included the main search engines (i.e., PubMed, Web of Science, PsycINFO, and SciELO) and selected articles published in the last twenty years on evidence-based neurocognitive assessment in addictions using the following keywords: "(Neurocognitive OR Neuropsychological assessment) AND (SUD or Drug Dependence OR Abuse) OR Alcohol OR Nicotine OR Addiction". **Results:** This brief article highlights the importance of assessing cognitive performances in the early stage of mental disorders and, specifically, the cognitive characteristics of subjects using multiple psychoactive substances. Further research should describe the longitudinal outcome of cognitive performances among these patients through the different stages of illness: intoxication, early withdrawal, and late withdrawal. **Conclusion:** The assessment of cognitive skills may suggest tailored treatment interventions for early cognitive rehabilitation to reduce the biopsychosocial impact of substance abuse and promote adherence to these treatments.

Keywords: Substance use disorders; addictions; cognitive profile; early interventions; assessment, rehabilitation.

INTRODUCTION

Substance use disorder (SUD) is a severe health issue worldwide. SUD includes a pathological pattern of behaviors in which patients continue to misuse a substance despite experiencing significant related health problems. Generally, substances involved are psychoactive components such as alcohol, caffeine, cannabis, and synthetic cannabinoids, hallucinogens (e.g., lysergic acid diethylamide, phencyclidine, psilocybin), inhalants (volatile hydrocarbons (e.g., paint thinner, certain glues)), opioids (e.g., fentanyl, morphine, oxycodone), sedatives, hypnotics and anxiolytics (e.g., lorazepam), stimulants (e.g., amphetamines, cocaine), tobacco, and others (e.g., anabolic steroids). All these substances directly activate the human brain's reward system and generate a sensorial experience of pleasure. Activation may be so intense that patients may start craving the substance and neglect their usual activities to obtain and abuse it (1).

Several authors have pointed out that multi-substances abusers may develop cognitive disorders with a relevant impact on functioning (2). Cognitive disorders can interfere with the motivation process to avoid misfit behaviors

in favor of a healthier lifestyle, can also limit patient's ability to fully benefit from treatments (in particular, psychoeducational and cognitive-behavioral therapies), and can lead to relapses. Therefore, a neuropsychological evaluation seems crucial to promote relevant clinical decision-making (3).

Neuropsychological assessment in the addiction should include two components (2, 4):

a) The evaluation of cognitive functioning through a neurocognitive evaluation

b) The impact of cognitive deficits on patients' daily personal functioning:

The study of neurocognitive alterations has become of interest in recent years (2, 4). Also, the neuropsychological assessment is highly recommended as a good practice in the early clinical approach to this set of disorders. It aims to tailor specific interventions in the early phase as well as in the maintenance of treatment, possibly oriented to the full functional recovery (5).

Bagnati et al. (2013) pointed out that a broader approach to substance use disorders is needed beyond the psychological and psychiatric aspects. In particular, the analysis of neurologic and neuropsychologic alterations involved in the pathogenesis of these disorders allows overcoming the reductionist model based on the clinical characteristics (4).

Substance abuse may be underpinned by some potential goals (6):

- Improve social interaction,
- Facilitate mating behavior,
- Facilitate coping with stress,
- Self-medicate neuropsychiatric disorders,
- Improve cognitive performance.

The cognitive impairment (attention deficit and hyperactivity disorder, affective disorders) may precede or be related to the poisoning and chronic use.

The first step assessment of the patient with SUDs should include (2):

- Clinical assessment, recording of the age of onset and frequency of substance use.
- Neurocognitive toolkit.
- Evaluation by an internal medicine specialist.

It has been documented that chronic drug use leads to changes in brain circuits underpinning the reward processes, motivation, executive functions, and decision-making, all involved in maintaining an addiction. In addition, the onset of cognitive symptoms may significantly decrease patient personal functioning as well as patient adherence to the therapeutic process (7).

Objective and data search method

This review aimed to identify and propose evidence-based practices on addiction neurocognitive assessment, summarize information on the application of neurocognitive assessment in addictions in order to provide general guidance to clinicians working with patients affected by substance use disorders. A neuropsychological evaluation is highly recommended as a good practice in the early clinical management of this group of disorders. It aims to tailor specific interventions both in the early phase and in the maintenance of treatment (5).

We employed the main databases (i.e., PubMed, Web of Science, PsycINFO, and SciELO) and selected articles published in the last twenty years on evidence-based neurocognitive assessment in addictions using the following keywords: "(Neurocognitive OR Neuropsychological assessment) AND (SUD or Drug Dependence OR Abuse) OR Alcohol OR Nicotine OR Addiction).

NEUROBIOLOGICAL ASPECTS AND COGNITION OF ADDICTION

It has been demonstrated that addictive behaviors are characterized by disengagement between three neural systems interacting with each other (8, 9): a) an impulsive system (neural dopaminergic – striated - amygdaline system), which mediates automatic, habitual, and salient behavior; b) a reflective system in the prefrontal cortex: abnormalities in this system are associated to poor awareness of established social conventions as well as poor decision making on personal matters (10); also, the frontal ventromedial region represents a link between an external event, categorized on the base of memory records, and the effector structures underpinning the emotional response (11, 12): alterations in this area may impact on decision-making. c) the neural system of the insula, which involves networks that intensify motivation and weaken behavior control (13, 14).

Although neuropsychological tests are suitable for evaluating functions related to the prefrontal cortex (executive functions), there is still a gap in the neuropsychological evaluation of some other functions related to the insula, which is involved in the maintenance of addiction and compulsive behavior: further research on the development of specific tools for the neuropsychological assessment is a challenge in the field of addiction (8, 9).

Cognitive Domains

The cognitive domains specifically altered in patients with SUDs are attention, memory, and executive functions (15). Thus, cognitive domains and processes to be explored in SUDs are (15):

- Processing speed
- Selective and sustained attention
- Alternating and dividing attention
- Attentional breadth and the central executive
- Memory
- Cognitive flexibility and fluency
- Inhibition of responses
- Planning
- Abstraction
- Decision making
- Theory of mind

Although it may be difficult to differentiate specific neuropsychological effects caused by any substance abuse, some of them are considered to be dose-dependent (direct effects of exposure) according to cross-sectional studies. However, these pieces of evidence are limited by potential pre-existing cognitive vulnerabilities or previous cognitive deficits as well as neuropsychiatric symptoms that may be observed in the outcome of substance abuse (16). Furthermore, good practice recommendations suggest an early neuropsychological evaluation (4) to characterize drug-induced cognitive phenotypes (5).

It is also widely described that more than 80% of subjects with addiction drop out of the treatments in the clinical settings: this evidence may be due to a pattern of anosognosia or lack of insight regarding the severity of their disorder. It has been proposed that these aspects of denial are related to psychological mechanisms as well as to cognitive dysfunctions linked to insight and self-consciousness (17).

Verdejo-García highlights the grounds for e neurocognitive assessment in SUDs (18):

- Drugs may temporarily improve executive functions and emotional processing, and patients with cognitive deficits may be more inclined to use recreative drugs in order to enhance cognition, productivity, and well-being.
- Cognitive deficit is associated with poor adherence to treatments. People with poorer cognitive functioning are less likely to adhere to treatment and more likely to discontinue it prematurely.

- Risk of relapse. Disinhibition and impulsive decision-making contribute to relapse with a lower recovery rate and poor quality of life. Likewise, cognitive deficits may lead to chronic addiction.

Variability of the cognitive impact

Domínguez-Salas et al. (2016) reviewed prospective studies describing treatment retention and abstinence-related outcomes. They found that a battery of indexing speed / precision tests of general cognitive functioning during the attention and reasoning tasks (MicroCog) was a consistent predictor of treatment retention in SUDs, as well as uncertainty tests and risk-based decision making were robust predictors of relapse. However, the impact on cognition may vary depending on types of substance, combinations of substances, length of abuse, patient's cognitive baseline, patient's resilience and even cognitive battery used for the assessment (19).

For instance, an early cannabis use disorder in adolescence has been associated with decreased working memory and short-term memory, but with a high verbal IQ. Also, an earlier age of onset and frequent use from 14 years old has been associated with a neurocognitive decline in early adulthood. More specifically, adolescent cannabis use frequency and earlier onset were associated with lower high school graduation rates as well as with the neurocognitive decline in early adulthood, regardless of graduation from high school or not, concurrent use of cannabis with other substances, and externalizing behaviors (20). In addition, verbal IQ and tasks using trial and error learning were particularly impaired. These findings suggest two main areas of deficits, a "social" area related to school participation and a "biological" area related to potential neurotoxicity (20).

The high frequency of comorbidities in the clinical setting, for example, chronic smoking in patients with schizophrenia affecting cognitive impairment, emphasizes the importance of paying careful attention to both tobacco addiction and cognitive functioning in patients with psychoses (21).

Neuropsychological tools used in addictions

We carefully reviewed the available literature regarding the tools used in the clinical practice considered useful to assess impaired cognitive domains in addictions. The cognitive performance of patients with SUDs has been assessed using a wide range of neuropsychological batteries, such as the Cambridge Long-Term Neuropsychological Test. The MicroCog Short Form and the Neuropsychological Assessment Battery-Screening Module (S-NAB) are two screening batteries that can be used for cognitive assessment by clinicians and researchers. A main difference between the two batteries is that the MC Short Form is computerized while the S-NAB is administered in person. Both batteries assess attention, memory, and spatial reasoning/ processing, but the S-NAB also assesses language. In addition, the battery S-NAB does not evaluate impulsivity, inhibitory control, selective attention, and social cognition; these cognitive domains may be relevant in SUD (22).

The objectives of cognitive assessment in addictions are (2):

- Identify specific deficits and conserved functions.
- Determine the patient's ability to care for themselves, manage their finances, assist them in planning their return to work or study.
- Medico-legal assessments.
- Choosing and adapting the most appropriate treatment program.
- Objective method to evaluate the efficacy

of treatments and the patient's situation to prevent relapses.

When should neuropsychological evaluation be performed?

Now we know the importance of the cognitive status before, during, and after using drugs. We recommend an initial assessment, essential to achieve the best treatment plan, regarding the brain processing speed preservation, functional level of the semantic networks, memory systems, and executive functions. Addiction treatment involves cognitively-demanding psychotherapies, and people with cognitive impairment show problems in understanding or using efficient therapeutic interventions. Other authors have noticed a strong relationship between cognitive impairment and the risk of drug relapse. For these reasons, it is crucial to do a new assessment during the following patient evolution (e.g., 6-9 months after the first evaluation) (1, 23)

Which are the best initial tools to evaluate the patient with SUD?

The assessment should focus on measuring sustained and selective attention, processing speed, the different domains of executive function, including fluency, response inhibition, cognitive flexibility and decision-making, social cognition, working memory, and episodic memory. In addition, particular emphasis should be placed on different aspects of impulsivity and decision-making, including reflection/ planning, delay discounting, risk-taking, and effort-based decision-making, since they will be directly relevant to clinical outcomes. Taking into account these valuable cognitive domains and their assessment, we list below the best tests that can be used in daily clinical practice for patients with substance abuse (1, 23, 24)

Processing speed (15, 25, 26)

- Processing speed index (PSI) of the Wechsler Adult Intelligence Scale (WAIS-IV): made up of the digit-symbol and Symbols Research (SR), coding and symbol searching subtests: it constitutes a measure of the ability to process visual information quickly.
- Execution time of the Trail Making Test Part A.
- Alternating verbal fluency task for one minute, in which the patient is asked to alternately produce a word that begins with 'p' and with "m" (that is not a proper noun).

Divided attention (26)

It is the ability to attend to more than one stimulus simultaneously. This type of attention occurs when we pay attention to several sensory channels at the same time.

- Trail Making Test Part B.
- Stroop Test

Sustained attention (27, 28)

It refers to focusing on the relevant, ignoring the irrelevant, and maintaining the attention focus over time. Failure in this domain is evidenced by a lack of concentration, distractions, errors due to inattention; all of these have been described in addiction.

- Digits in direct order - Wechsler Adult Intelligence Scale (WAIS IV).
- D2 Test: used to measure selective attention and concentration, which takes about 10 minutes. The processing speed, the following of instructions, and the execution of a task of discrimination of similar visual stimuli are evaluated, allowing the estimation of selective attention.

Attentional breadth and central executive (29)

They are framed in what is called Working Memory.

- Reverse order digits and digit sequencing - Wechsler Adult Intelligence Scale (WAIS IV): performance in the test is sensitive to the functioning of the 'articulatory loop' and the 'central executive' of the working memory model.

Cognitive flexibility (30)

- Wisconsin Card Sorting Test (WCST) to assess cognitive flexibility.
- PASAT (Paced Auditory Serial Addition Test): this test assesses auditory information processing speed and cognitive flexibility, as well as calculation ability.

Language (30)

- For the evaluation of semantic fluency, the subject can be asked to evoke the largest number of animals and vegetables in one minute. And for phonological fluency, the words that start with the letter "p" in one minute.
- The Multilingual Naming Test (MINT): a test of denomination by visual comparison

Decision making (31)

- Iowa Gambling Task.

Inhibitory control (15, 32, 33)

- Stroop interference.
- Five-digit test (5DT): also based on the Stroop interference paradigm. It is a test of selective attention and response inhibition. It was developed as an alternative to the Stroop test that minimizes the implication of schooling level in the performance of the test and significantly correlates with its equivalent sections.
- Go/no go task, in which the subject must respond by hitting the table once or twice according to conflicting instructions that require him to inhibit his motor responses.

Memory (34, 35)

- Copy immediate and delayed reproduction of Rey Complex Figure Test.
- WMS-III, logical memory subtest (verbal memory).
- Rey-Auditory Verbal Learning Test

Theory of mind (36, 37)

- The Faux Pas Recognition Test (adult version).
- Reading the Mind in the Eyes Test.

CONCLUSION

Our review highlights the importance of cognitive assessment in SUD. Unfortunately, impaired patients do not recognize it (anosognosia) or minimize it. Therefore, the inclusion of the evaluation in the clinical practice is a tool for measuring the global functioning of patients with SUD and tailoring treatments based on their cognitive functioning. A specific cognitive evaluation for SUD patients is missing, although the study of cognitive phenotypes in SUD will lead to selecting better diagnostic tools in the coming years. It will also be interesting to determine the functional consequences (social and occupational) of long-term abuse. Emerging evidence highlight the importance of cognitive consequences of substances abuse. Cognitive deficits impact patient daily functioning and

lead to a maintenance of consumption, as well as increase the probability of relapses. The clinical outcome of treatment is influenced by patient cognitive functioning, consequently. An assessment of cognitive deficits, as well as a clinical approach to them, is relevant in the early phase of addiction and in the treatment follow-up in order to improve the clinical outcome and identify an early rehabilitation program. Further research should address the identification of specific diagnostic tools in the clinical practice suitable for SUD, above all for adolescents, in order to tailor early interventions based on cognitive remediation and functional rehabilitation.

Authors' contribution statement

Marcela Waisman Campos, Cecilia Cervino, Pablo M. Bagnati, Julio César Torales, João Mauricio Castaldelli-Maia: conception and design of the study, analysis and interpretation of the results and conclusions, critical revision of the manuscript, final approval of the manuscript. Rodrigo Eduardo Navarro, Iván Barrios Coronel, Israel González-Urbierta, Oscar García Franco, Marcelo Gerardo O'Higgins, Antonio Ventriglio, José Almirón-Santacruz: collection/obtaining data/results, drafting, final approval of the manuscript.

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