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### Short Comunication

### Neuroimage

### *Comments on Books*

# Editorial

In his book *The Structure of Science Evolution*, Thomas Khum defines a paradigm as "a set of beliefs, values and accepted techniques that define the exercise of a scientific discipline". A new paradigm is a change of vision, a reconstruction of our knowledge in the light of discoveries; in the words of Socratics, "all cognition is a recognition".

The new paradigms arise from the exhaustion of the old ones, confronting followers and detractors in the controversy that between established knowledge and the latest discoveries there is a single tool to settle debates, the "scientific evidence". Without a doubt, "Cognitive Neuroscience" is the new paradigm of the last decades, which has allowed us to begin to understand the complex cognitive processes that occur in our brains. From Gazzaniga and Miller, through Kandel's contributions to the present, cognitive neuroscience has built a nucleus of "transdisciplinary" knowledge of excellent transforming power in various disciplines such as neurology, psychiatry and psychology; that has led it to a constant construction process, accepting challenges, adapting its techniques, defining its methodology and its theoretical frameworks.

Neuropsychology is the discipline that investigates the relationships between cognitive processes, underlying brain mechanisms, and pathological disorders. It was the beginning of today's applied cognitive neurosciences. The concern with the connections between the brain and the mind is almost as old as the world. Plato and Hippocrates (400BC) thought that the brain was the basis of thought. The latter defines the sacred disease (epilepsy) as a medical condition and not, as previously believed, a possession of the devil. Aristotle, a century later, convinced everyone otherwise, that the heart was the seat of the mental process, which lasted for several centuries. After the medieval scientific obscurantism, towards the 18th century, Franz Josef Gall's the Phrenology described cognition and behaviours related to the shape of the skull. Gall was the first to associate aphasia with a frontal injury, and he was probably the father of Neuropsychology. However, science never recognized him because his claims were unscientific, remaining at that time as a great charlatanism. After this failed attempt, neuropsychology was finally born in France with Paul Broca and his aphasia description due to a left frontal injury. Neuropsychology takes a significant boost with the locator school with names like Paul Broca, Karl Wernicke, Armand Trousseau, and Arnold Pick. At that time, in Europe, the psychologist school included authors such as John Hughlings Jackson, Pierre Marie, and Henry Head.

In the mid-20th century, Wilder Penfield in Canada reports on his cognitive studies

with brain stimulation. From the war wounded to the wounded patients, the neolocation took hold with the American neurologist Norman Geschwind who describes the disconnection syndromes. At the same time, in Russia, Alexander Luria developed the Pavlovian-influenced school of reflexology.

In the following years, neuropsychology addressed neurophysiology (EEG, evoked potentials, event-related potentials) and functional brain neuroimaging (functional magnetic resonance imaging-FMRI, positron emission tomography-PET).

Cognitive Neuroscience was born as a conjunction between cognitive psychology, which studies cognitive processes, and neuroscience, exploring the nervous system with different molecular, functional, computational studies and pathological aspects. Nowadays, the last step is developing the applied cognitive neurosciences that cover all human beings' activities (neurosciences applied to education, neuroeconomics, neuromarketing, sports, neuropolitics, etc.).

In Latin America, Neuropsychology born at the beginning of the 19th century with the role of Amusias by José Ingenieros (La nouvelle iconographie de la Salpetriere, 1906) reaching the golden age of the 90 with Andre Roch Lecous (Canada), Fernando Dalmás (Uruguay), Juan Azcoaga (Argentina), Julieta Heres (Mexico) and Alfredo Ardila (Colombia). They have been developed in parallel with international advances; however, most of the Latin American works have remained in the dark or have been published in local universities media or regional magazines in Spanish without global knowledge. Another difficulty from the region was the high publication cost of most of the indexed international journals.

In addition, the development of science in general and of neurosciences in particular has been accelerated in recent years in the region with several specialized university degrees in almost all countries and even doctorates in neurosciences such as those of the Universidad Maimonides in Argentina or that from the Universidad de la Costa in Colombia. In the last two years, the Ibero-American Forum on Cognitive Neurosciences has been developed with great success, which brings together researchers from the region.

All these situations lead to a conceptual shift in neuroscience communication reflected in the launch of the Journal of Applied Cognitive Neuroscience (JACN). This is the first scientific journal in Ibero-America, rigorously peer-reviewed with international standards, continuous biannual edition, free of charge, whose purpose is to make known the published content (in English) in relation to all fields of neuroscience cognitive in Ibero-America, from a transdisciplinary perspective, and with a continuous search for innovation to be shared worldwide.

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# Review

# Neuropsychological evaluations associated with workplace accidents: a systematic review

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*Abstract*

Most occupational accidents are evidenced by a loss of worker control over the procedures they carry out. Objective: To establish the neuropsychological tests used to assess the cognitive profile of workers as a measure to prevent workplace accidents. Method: An advanced and manual systematic search of databases (PubMed / MedLine, Web of Science, Scopus, Science Direct, Cochrane Library) was performed to evaluate the neuropsychological tests used in work settings. Results: The systematic review yielded 1777 articles, of which 150 were pre-selected according to what was reported in the abstract and 57 validated for complete reading. 21 articles were used for the narrative synthesis with a sample of two thousand eight hundred and fifty-four (2,854) subjects; and a range of 18 to 60 years. Conclusion: The limited number of investigations that establish the neuropsychological profiles associated with occupational accidents are evident.
**Keywords**: Systematic Review; Neuropsychological Evaluation; Occupational Accident; Cognitive processes

# Evaluaciones neuropsicológicas asociadas con accidentes en el lugar de trabajo: una revisión sistemática

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*Resumen*

Los accidentes laborales en su gran mayoría se evidencian por una pérdida del control del trabajador sobre los procedimientos que desarrolla. Objetivo: Establecer las pruebas neuropsicológicas utilizadas para evaluar el perfil cognitivo de los trabajadores como medida de prevención de la accidentalidad laboral. Método: Se realizó una búsqueda sistemática avanzada y manual en bases de datos (PubMed/ MedLine, Web of Science, Scopus, Science Direct, Cochrane Library) para evaluar las pruebas neuropsicológicas utilizadas en ambientes laborales. Resultados: La revisión sistemática arrojó 1777 artículos, de los cuales 150 fueron pre-seleccionados de acuerdo a lo reportado en el resumen y 57 validados para su lectura completa. Se utilizaron 21 artículos para la síntesis narrativa con una muestra de dos mil ochocientos cincuenta y cuatro (2.854) sujetos; y un rango de 18 a 60 años. Conclusión: Sevidencian el limitado número de investigaciones que relacionan el establecimiento de perfiles neuropsicológicos asociados a la accidentalidad laboral.
**Palabras clave**: Revisión Sistemática; Evaluación Neuropsicológica; Accidentalidad laboral; Procesos cognitivos

## INTRODUCTION

Occupational accidents are defined as a series of bodily or tissue damage, which can trigger the decrease or loss of either total or partial functions in any part of the body (Niza, Silva & Lima, 2018). In Colombia it is defined as "Sudden event that occurs due to or on the occasion of work, and that produces in the worker an organic injury, a functional or psychiatric disorder, disability or death" (Law 1562, 2012, art. 3); these accidents are characterized mainly due to the production of human suffering and economic losses at different levels of society (Nag & Patel, 1998).

There are different approaches to workplace accidents that allow us to explain their nature. The first is organizational; this approach refers to the process of social construction of risk, where resources, labor and work overload are taken into account (Clarke & Short, 1993). The second approach is the theory of human error, where the worker loses control over procedures due to insufficient training, stress, or fatigue (Jackson, 1995).

Occupational accidents can be attributed to immediate or basic causes, the immediate ones are generated directly, that is, by unsafe acts or inappropriate behaviors of workers in relation to the unsafe conditions of the facilities, infrastructure, equipment and tools that put at risk security (González, Bonilla, Reyes & Chavarro, 2016). On the other hand, the basic causes give rise to the immediate ones and are made up of personal and work factors, which, in control, could be factors that reduce the impact of the immediate causes (Chinchilla, 2002). Personal factors play a fundamental role in the motivation, suitability, and knowledge of safety standards by the worker (Huamán, 2017). Work-related causes refer to training workers in the use of machines and materials that comply with occupational health standards, optimal structural conditions with the legal extension of working hours and the establishment of organizational systems that can demonstrate the commitment of companies with the safety of their employees (Ortega, 2017).

Data provided by the International Labor Organization (ILO, 2019) suggest that workplace accidents cause around 380,000 deaths per year and 374,000,000 non-fatal accidents or injuries in the world. In Colombia, the Ministry of Labor (Mintrabajo, 2018) ensures that occupational accidents correspond on average to 7.2% of the population affiliated with the general occupational risk system, for that same year there were 483,560 non-fatal accidents or injuries in the workplace and 410 deaths. According to the previously reported figures, it is important to take into account that occupational accidents increase significantly according to the nature of the work, especially those that are called high risk. The Ministry of Social Protection of Colombia (Ley 2090, 2003) defines the High-risk work activities such as those in which the work or the place where they are performed represents a decrease in healthy life expectancy and a greater exposure or intensity compared to other work activities. Among those considered high-risk jobs are mining or those that involve performance in tunnels or underground, exposure to high temperatures, ionizing radiation, proven carcinogenic chemicals and in units of military forces, civil aeronautics, or similar entities.

Occupational accidents have different implications in relation to the parties, Feng, Zhang and Wu (2015) establish the

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subject, the family, society and companies as the focus of involvement. The social implications refer to the deployment of the necessary resources to attend to the accident through legal and health channels. For their part, companies go through financial losses, the temporary or permanent absence of the worker and the intangible costs of accidents (Ascuénaga, 2006). Family implications are non-material losses, in case of non-fatal accidents resulting in disability. The family must adapt to the new situation and take care of the worker who has suffered the accident, assumed by an external health assistant or internally by a family member (Navarrete & Zicavo, 2007). Overload in responsibilities and delicacy in care tasks can trigger burnout syndrome in the caregiver, manifesting symptoms associated with stress and anxiety (Caraguay, 2018).

Cognitive functions facilitate adaptation to the worker or subject to the environment and allow them to develop an active role (Dorado, 2012). These functions are linked to the level of performance, and a failure in any of them can be a predictor of an occupational accident, these failures are usually registered as human error, one of the main approaches in occupational accidents (Wadsworth, Simpson, Moss & Smith, 2003). Knowledge of this relationship seeks to promote health in the workplace as the main method of preventing this type of error. Behavior-based safety programs are currently being used which seek to reinforce safe behaviors in individuals so that they are maintained over time (Meliá, 2007). Neuropsychological evaluation is the tool that allows establishing an accurate diagnosis of the state of cognitive functions, establishing the necessary limits to objectify the neuropsychological profiles of the pathologies that may have been

triggers of occupational accidents (Mauri, Paletta, Colasanti, Miserocchi y Altamura, 2014).

Based on these positions, neuroscience has sought to improve the training of workers in behavior-based safety since the 1990s. One of the most recognized is the "SafeStart" project created by Larry Wilson, which seeks to avoid Work accidents focusing on the control that the worker may have over the relationship of the environment and their own body, this project establishes four causes of most work accidents: fatigue, haste, frustration and complacency, these alter attention and can generate loss of balance, traction or grip and leave the worker on the line of fire (Ciaffoni, 2019).

On the other hand, the National Institute of Health and Safety at Work (INSST, 2018) offers companies the prevention program FPSICO 4.0 that allows identifying the working conditions that present a psychosocial risk for workers, this method evaluates the time work, autonomy, work capacity, psychological demands, variety of work, supervision, interest, performance, and social support relationships. In the evaluation of psychological demands, this method assesses the cognitive demands, related to decision-making, memory, attention, and knowledge management required by the work being done; and the emotional demands that are produced by the work environment, work climate and the capacity for emotional control that a specific job requires (Aguilar-Soria, 2014).

Considering the importance of reducing the indicators of accidents at work and establishing the cognitive profiles that could increase these figures. The present review aims to establish the neuropsychological profiles associated with occupational accidents.

## METHODOLOGY

### Search strategy for the systematic review

A database of original articles was developed, based on systematic searches of electronic sources. The following databases were searched: PubMed / MedLine, Web of Science (WOS), Scopus, Science Direct, and Cochrane Library. All studies published from 2009 to 2020 that assess the relationship between cognitive processes and occupational accidents were identified.

The search was limited to literature in English and Spanish, no other languages were included. With the use of Boolean intercession operators ("AND" and "Y"). A cross search was carried out with the following strings: 1) Work accident (Industrial accidents OR work accident); 2) Cognitive processes evaluated (Cognitive processes OR Attention OR Memory OR Cognitive Assessment).

### Criteria for Inclusion and Selection of Articles

To be included in the review, the studies had to meet the following criteria:

1. *Participants*: Adult between 18-60 years old, and who did not present any neurocognitive, psychiatric or psychoactive substance abuse disorder.

2. *Labor relationship*: Formal.

3. *Method*: Use instruments for neuropsychological measurement of cognitive processes.

4. *Results*: Descriptive, correlational, or predictive analysis.

5. *Type of study*: research articles (quasi-experimental or experimental methods), excluding review articles, theoretical or single case studies and meta-analyzes.

### Qualitative Synthesis

From the included studies, the results indicate the tests used to evaluate cognitive profiles associated with occupational accidents, as well as the cognitive functions that are frequently evaluated. The PRISMA statement17 (Figure 1) was followed to inform the items of this systematic review.

## RESULTS

The findings of this review show the limited number of investigations that relate the establishment of neuropsychological profiles associated with occupational accidents. A separation of cognitive functions is seen in the different investigations, few establish a comprehensive profile as the object of study, some functions were evaluated in multiple investigations such as attention and memory, and others were evaluated in a lesser proportion such as cognitive flexibility and processing speed. It is important to point out that this review seeks to gather the greatest evidence that reflects the state of research and knowledge gaps in the study of the performance of cognitive functions in occupational accidents, since accidents in the workplace affect many spheres of work-business and personal life, implying a high financial and social cost.

In the assessment of cognitive functions in the workplace, no specific neuropsychological batteries were found to be used consistently and uniformly for this purpose. On the other hand, tests and scales were found that are used to measure cognitive functions in different work environments such as aviation (Asmayawati & Nixon, 2020), military activities (Frings, 2011; Irgens-Hansen et al., 2015; Smith et al., 2019, Bell, Virden, Lewis & Cassidy, 2015), conduction (Horrey, Lesch & Garabet, 2009;
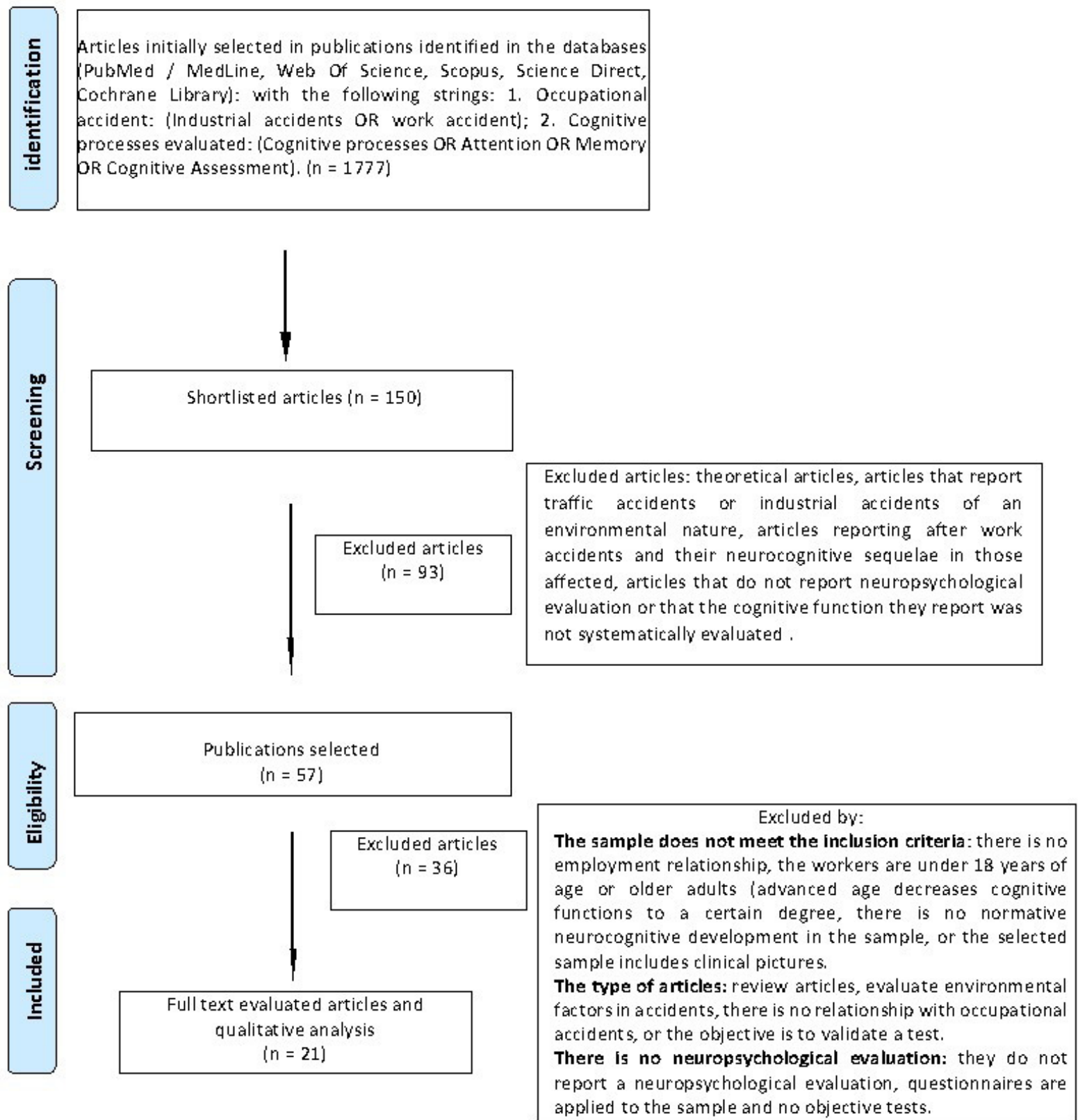
**Figure 1.** Prism Flow Diagram.
Source: Authors.

Cheng, Ting, Liu & Ba, 2015; De Oliveira et al., 2020; Chen, Chou, Su & Wen, 2019, Di Nocera et al., 2018, Adrian, Postal, Moessinger, Rascle & Charles, 2011; Elfering, Grebner & Haller, 2012), construction (Brossoit et al., 2019), service sector (Roll, Siu, Li & De Witte, 2019; Elfering, Grebner & De Tribolet-Hardy, 2013), industrial

operators and services (Kodappully, Srinivasan & Srinivasan, 2016; Muller et al., 2012) and other activities (Buodo, Patron, Benvenuti & Palomba, 2018; Askaripoor et al., 2019; Petitta, Probst, Ghezzi & Barbaranelli, 2019; Huang, Menozzi & Favey, 2019).

One of the most widely used scales is the Cognitive Failure Scale in the Workplace (WCFS) developed by Wallace and Chen (2005) that was used by different investigations (Petitta et al., 2019; Elfering et al., 2012; Elfering et al., 2013) this questionnaire assesses memory, attention, inhibition and praxis. On the other hand, Di Nocera, Ferlazzo and D´Olimpio (2014) propose a questionnaire of cognitive errors based on attention, which was used by Di Nocera et al. (2018). In this same line of cognitive questionnaires Wadsworth et al. (2005) report the Cognitive Failures Questionnaire.

However, the aforementioned investigations use short scales and even ecological assessments. On the other hand, some authors report the use of neuropsychological tests (Horrey et al., 2009; Adrian et al., 2011; Muller et al., 2012; Cheng et al., 2015; Irgens-Hansen et al., 2015; Buodo et al., 2018; Askaripoor et al., 2019; Chen et al., 2019; Smith et al., 2019; De Oliveira et al., 2020).

*Literature search*

The systematic cross-search of the two chains showed 1777 articles, of which 150 were pre-selected according to what was reported in the abstract and 57 validated for their complete reading (Figure 1). Among the articles included there are 10 experimental articles with descriptive analysis, 4 experimental with analysis of correlational scope, 4 quasi-experimental with correlational analysis, 2 experimental with linear regression analysis, 1 quasi-experimental article with analysis of descriptive scope.
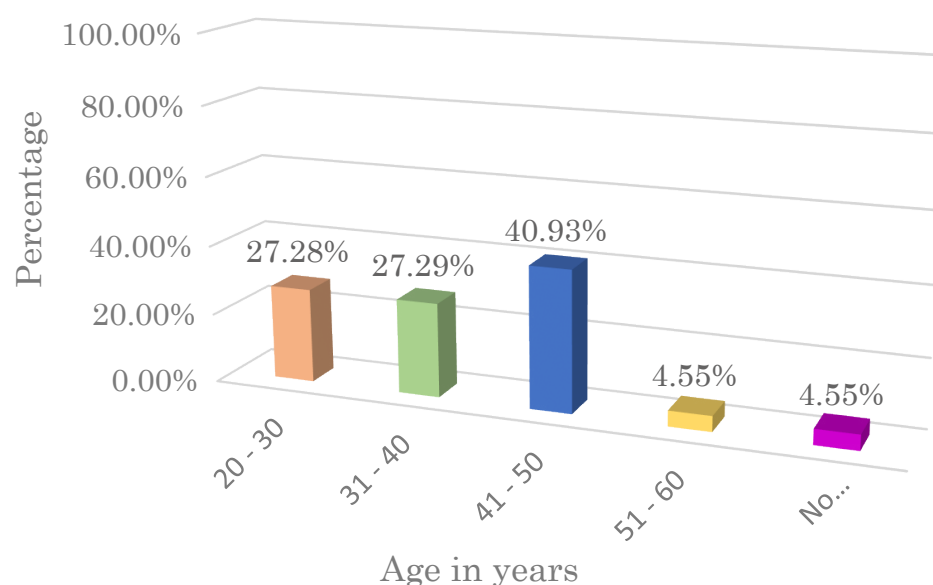


**Figure 2.** Age distribution.
Source: Authors.

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*Characteristics of the included articles*

In the systematic review, 21 articles were used with a sample of two thousand eight hundred fifty-four (2,854) subjects; and a range of 18 to 60 years, this range was different for each article, the most frequent ages of the subjects ranged between 31 and 50 years. As evidenced in Figure 2.

A quantitative and qualitative synthesis of the 21 articles included was developed and descriptive variables were analyzed. Since no unified data were found on the performances in the subtests of the neuropsychological tests used in each investigation. It should be noted that more than 50% of the articles included are from 2018 onwards. On the other hand, an important participation of the USA, the United Kingdom and Switzerland is observed in the work of the variables analyzed.

According to what was found, this set of neuropsychological tests, questionnaires, and scales to evaluate cognitive functions in correlation with occupational accident rates is evidenced (Table 1).

### DISCUSSION

This review includes 21 articles, which report one or more cognitive functions evaluated by different types of questionnaires or neuropsychological tests. The findings of this review show the limited number of investigations that relate the establishment of neuropsychological profiles associated with occupational accidents. Unified evaluations are evidenced and few establish a comprehensive profile as an object of study, some cognitive functions most evaluated in reported investigations were attention and memory (Buodo et al., 2018; Asmayawati & Nixon, 2020;
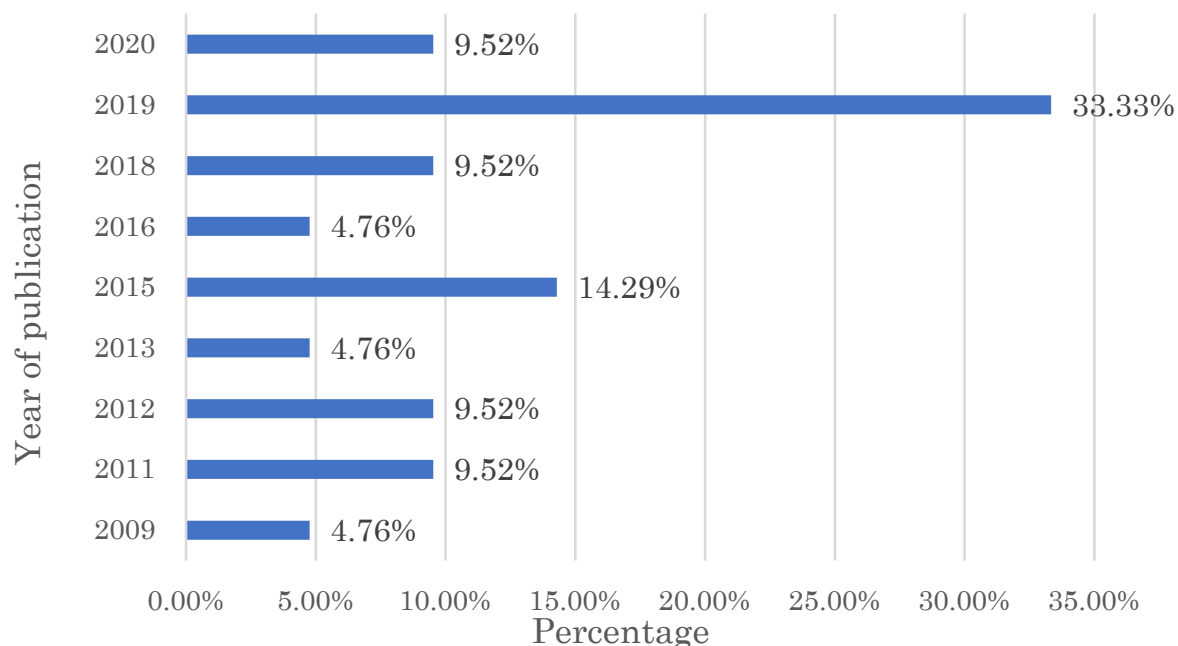


**Figure 3.** Distribution of articles by publication date.
Source: Authors.

TABLE 1.
*Reported instruments*

| Authors | Year | Measuring instrument | Evaluated functions |
|---|---|---|---|
| Buodo, Patron, Benvenuti and Palomba. | 2018 | Trail Making Test (TMT; Reitan, 1958; Italian adaptation by Giovagnoli et al., 1996). | Executive functions. |
| | | | Attention. |
| | | Test d2 (Brickencamp & Zillmer, 1998). | Visual perceptual skills. |
| Asmayawati and Nixon. | 2020 | Critical Decision Method Interview (MDL) (Klein, Calderwood & MacGregor, 1989). | Decision making. |
| | | | Problem solving |
| Frings. | 2011 | Troubleshooting test (8 items extracted from Luchins & Luchins, 1969). | Decision making. |
| | | | Cognitive flexibility. |
| Cheng, Ting, Liu and Ba. | 2015 | EGG-IGT (Simulated decision making). | Impulsiveness and Decision Making. |
| De Oliveira, Barroso, Leopoldo, Gouvea, Castaldelli-Maia and Leyton. | 2020 | The sustained attention test (TACOM-B) (Tonglet, 2007). | Sustained attention. |
| | | The Trace Color Test (CTT) comprises two forms (CTT1 and CTT2) (Santana et al., 2010). | Interference, divided attention. |
| | | Test D2 (Brickenkamp, Zillmer & Balcar, 2000). | Sustained attention. |
| | | Stroop (Stroop, 1931). | Interference, divided attention. |
| Chen, Chou, Su and Wen. | 2019 | Attention-Related Driving Error Scale (ARDES) (Nucciarone, Poó, Tosi & Montes, 2012). | Attention. |
| Brossoit, Crain, Leslie, Hammer,Truxillo and Bodner. | 2019 | Workplace Cognitive Failure Scale (WCFS) (Broadbent et al., 1982). | Memory and Attention. |
| Huang, Menozzi and Favey. | 2019 | Test for screening visual skills (Huang et al., 2019). | Attention. |
| Roll, Siu, Li and De Witte. | 2019 | Attention scale related to cognitive error (Cheyne, Carriere & Smilek, 2006). | Attention. |
| Smith, Cooper, Merullo, Cohen, Heaton, Claro and Smith. | 2019 | task GO/NO GO (GNG), Automated NeuropsychologicalAssessment Metrics (ANAM4, version 4). | Sustained attention and Inhibición. |
| | | Visual task-backtrack, Automated NeuropsychologicalAssessment (ANAM4, version 4). | Attention. |
| | | Visual task adjustment - backtrack adapted measure of attention and working memory (Angelet, 2015). | Working memory. |
| Petitta, Probst, Ghezzi and Barbaranelli. | 2019 | Cognitive Failure Scale in the Workplace (CFQ) (Wallace & Chen, 2005). | Memory and Attention. |
| Askaripoor, Motamedzade, Golmohammadi, Farhadian, Babamiri and Samavati. | 2019 | Three-minute visual task GO/NO GO. | Divided attention. |
| Di Nocera, Ricciardi, Longo, Mastrangelo, Cutini and Bisaglia. | 2018 | Workplace Cognitive Failure Scale (WCFS) (Broadbent et al., 1982). | Attention. |
| Kodappully, Srinivasan and Srinivasan. | 2016 | Eye tracking applications. | Attention, Inhibition and working memory. |

| Authors | Year | Measuring instrument | Evaluated functions |
|---|---|---|---|
| Irgens-Hansen, Gundersen, Sunde, Baste, Harris, Bråtveit and Moen. | 2015 | Posner Reference Signal Paradigm in E-prime (version 2.0). | Response time, precision, and inhibition. |
| Bell, Virden, Lewis and Cassidy. | 2015 | Computerized Psychomotor Surveillance Test (PVT; Dinges, Mallis, Maislin & Powell, 1985). | Reaction time and attention. |
| | | STROOP Word-Color (Golden & Freshwater, 2002). | Cognitive performance. |
| Elfering, Grebner and De Tribolet-Hardy. | 2013 | Workplace Cognitive Failure Scale (WCFS) (Broadbent et al., 1982). | Memory and Attention. |
| Elfering, Grebner and Haller. | 2012 | Workplace Cognitive Failure Scale (WCFS) (Broadbent et al., 1982). | Memory and Attention. |
| Muller, Gunstad, Alosco, Miller, Updegraff, Spitznagel and Glickman. | 2012 | Integneuro computerized test battery TM (DuBois, Harb & Fox, 1990, Paúl, 2005): Digit Span, Choice Reaction Time, Verbal Interference and Executive Maze Task. | Memory and Attention. |
| | | | Executive functions. |
| | | | Reaction time. |
| | | | Spatial memory. |
| | | | Verbal interference: Inhibition of responses. |
| Adrian, Postal, Moessinger, Rascle and Charles. | 2011 | Stroop (Stroop, 1931). | Inhibition. |
| | | Incompatibility test (Zimmermannand & Fimm, 1994). | Visual attention. |
| | | The go / no-go test (Zimmermann & Fimm, 1994). | Inhibition. |
| | | Task plus-minus (Jersild, 1927). | Shifting. |
| | | Flexibility test (Zimmermann & Fimm, 1994). | Cognitive flexibility. |
| | | Letters and Numbers Task (Rogers & Monsell, 1995). | Working memory. |
| | | Trail Making Test A y B (Reitan, 1958). | Sustained attention and Inhibition. |
| | | Letter memory task (Morris & Jones, 1990). | Working memory. |
| | | Operation interval task (Turner & Engle, 1989). | Working memory. |
| | | Sequence of numbers and letters (Wechsler, 2000). | Working memory. |
| | | Bourdon-Wiersma test (Grewel, 1953). | Attention. |
| | | WAIS III Encoding Subtest (Wechsler, 2000). | coding. |
| | | Block design (Wechsler, 2000). | Viso-special and viso-constructive skills. |
| | | Search for symbols (Wechsler, 2000). | Processing speed. |
| Horrey, Lesch and Garabet. | 2009 | Paced auditory serial addition task (PASAT) (Brookhuis, De Vries & De Waard, 1991; Patten, Kircher, Östlund & Nilsson, 2004). | Working memory and Attention. |
| | | Guessing Task, Based on the Twenty Questions Quiz (TQT; Bruner, Olver, Greenfield & Rigney, 1966, Kafer & Hunter, 1997). | Decision making. |

Source: Authors.

Chen et al., 2019; Brossoit et al., 2019; Roll et al., 2019; Petitta et al., 2019; Askaripoor et al., 2019; Di Nocera et al., 2018; Kodappully et al., 2016; Irgens et al., 2015; Bell et al., 2015; Elfering et al., 2012; 2013; Muller et al., 2012; Horrey et al., 2009) were evaluated to a lesser extent as cognitive flexibility and processing speed (Frings, 2011; Bell et al., 2015; Muller et al., 2012; Adrian et al., 2011). It is important to point out that this review seeks to gather the greatest evidence that reflects the state of research and knowledge gaps in the study of the performance of cognitive functions in occupational accidents, since accidents in the workplace affect many spheres of work-business and personal life, implying a high financial and social cost (Feng et al., 2015).

In the evaluation of cognitive functions in the workplace, no neuropsychological batteries established specifically for this purpose were found, the tests and scales used to measure specific functions are diverse and there is no established relationship with a neuropsychological battery that can cover comprehensively the set of cognitive functions. One of the most widely used scales is the Cognitive Failure in the Workplace Scale (CFQ) (Broadbent, Cooper, FitzGerald & Parkes, 1982) which, in accordance with the above, assesses memory, attention, inhibition, and praxis, the first two being the most studied.

Despite the limited number of investigations, it has been shown that many of the work accidents are due to cognitive failures and that these can arise in the operationalization of the work environment (Almirall, 2001). The evidence presented may be useful for researchers and developers of strategies and / or training on safety and health at work to comprehensively evaluate cognitive functions and the direct implications that these have on worker behavior (Díaz-Cabrera et al., 2008).

The limitations in this study respond to the scarce scientific production on the incidence of the functioning of cognitive functions in occupational accidents, a limited number of databases were accessed for the collection of information and few studies were found with an approach / approach comprehensive of cognitive functions. Likewise, the articles included worked with small samples and their results are not conclusive enough to be extrapolated and faithfully represent the reality of the phenomena. Half of the articles included have a descriptive scope, meaning a low level of evidence. However, these information gaps represent an opportunity for new research, with cognitive functions being a crucial variable in worker performance and in the design of studies or projects aimed at increasing safety in the workplace and thus reducing accidents.

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Review

# Breathing technique in pain and cognitive function: a systematic review of the literature

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*Abstract*

Breathing techniques are key components of yoga, meditation and relaxation practices that are well known for reducing anxiety and improving overall well-being. To evaluate the efficacy of breathing techniques in pain and cognitive function. We conducted a literature review searching the main literature databases (medline, lilacs, Cochrane library) including randomized clinical trials. We assessed the risk of bias of the included studies using the methodology proposed by the Cochrane collaboration. In total, we found 16 studies that met the inclusion criteria, with an intermediate or unclear overall risk of bias. When combining the different breathing techniques vs control in the included studies, we found a statistically significant difference in terms of the visual analog scale (Difference of means, random effects; -1.21 [95% CI -1.75 to -0.68]; I2: 95%). Meditation-based breathing techniques would improve pain and cognitive function in patients with a painful entity or healthy volunteers.
**Keywords**: Breathing techniques; pain; cognitive function; systematic review; breath holding

## Técnicas respiratorias en dolor y función cognitiva: revisión sistemática de la literatura

*Resumen*

Las técnicas de respiración son componentes clave de las prácticas de yoga, meditación y relajación que son bien conocidas por reducir la ansiedad y mejorar el bienestar general. Evaluar la eficacia de las técnicas respiratorias en el dolor y la función cognitiva. Realizamos una revisión de la literatura a través de las principales bases de datos especializadas (medline, lilacs, Cochrane library) incluyendo ensayos clínicos aleatorizados. El riesgo de sesgo de los estudios incluidos se evaluó mediante la metodología propuesta el Manual Cochrane para las Revisiones Sistemáticas. En total, encontramos 16 estudios que cumplieron con los criterios de inclusión, con un riesgo general de sesgo intermedio o poco claro. Al combinar las diferentes técnicas de respiración versus control en los estudios incluidos, se encontró una diferencia estadísticamente significativa en términos de la escala analógica visual (diferencia de medias, efectos aleatorios; -1,21 [IC del 95%: -1,75 a -0,68]; I2: 95 %). Las técnicas de respiración basadas en la meditación mejorarían el dolor y la función cognitiva en pacientes con una entidad dolorosa o voluntarios sanos.
**Palabras clave**: Técnicas respiratorias; dolor; función cognitiva; revisión sistemática; contención de la respiración

## INTRODUCTION

Breathing techniques are key components of yoga, meditation, and relaxation practices that are well known for reducing anxiety and improving overall well-being (Arsenault, Ladouceur, Lehmann, Rainville & Piché, 2013; Chan et al., 2019; Mah, Turgeon, Loh, Tejani & Sweet, 2019; Mesgarpour et al., 2019). Slow breathing with focused attention to breathing is used in many interventions with the goal of inducing a state of relaxation (Arsenault et al, 2013; Wall, Magee, Campbell & Zed, 2019), including meditation (Warttig et al., 2019).

Slow and deep breathing techniques are also used in the treatment of many conditions such as stress, anxiety, panic disorder, and depression (Lewis et al., 2019; Zhang, Zhang, Grant, Wan, & Li, 2018). In such studies, these breathing techniques were found to alleviate anxiety, depression, daily stress, post-traumatic stress, and illness-related stress. Among the proposed mechanisms, the contribution to calm and alertness driven by the parasympathetic system, the stress response system, the release of neuroendocrine hormones, and thalamic generators are found. On the other hand, it has also been found that the group of respiratory exercises has a decrease in anxiety and depression, however the number of leukocytes did not differ between the groups; these findings suggest that relaxation breathing exercises improve anxiety and depression levels in the general population and in patients who will undergo hematopoietic cell transplantation (Lewis et al., 2019; Zhang et al., 2018).

Buddhist (*Anapama*) meditation practices have focused more on developing mindfulness of breath (Sud et al., 2018; Vojislav, Ramanathana & Mishraa 2020). However, even these mindfulness-based meditative practices have been shown to modify the respiratory rate and cycle (Choo, Simons & Sheikh, 2018; VojislavMaric, 2020). Suzuki Roshi, a practitioner of Zen Buddhism, describes this process: both the breathing and pulse will tranquilize afterwards a 5 or 10 minutes period of not being distressed by the mind (Connolly et al., 2018).

Many of these mind-body perception-based breathing techniques (Yoga, Reiki, Tai Chi, Quiqong) have also been used with some success to improve pain management (Aamann, Dam, Rinnov, Vilstrup & Gluud, 2018) and in a variety of associated clinical situations. with acute pain such as labor (Pollok, van Agteren & Carson-Chahhoud, 2018) or injections in children (Arsenault et al., 2013; Gilbert-Kawai, Mitchell, Martin, Carlisle & Grocott, 2018).

For these reasons, it is necessary to carry out a review of the literature that evaluates the effectiveness of the different breathing techniques in pain management and the evaluation of cognitive function.

## METHODOLOGY

Systematic review of the literature

*Criteria for including articles in this review*

*· Types of studies*

Randomized clinical trials were included. Cluster, crossover or before and after studies were excluded.

*· Types of participants*

Patients with any condition or pathology were included, as well as healthy participants 12 years of age and older.

### · Types of interventions

Any controlled breathing technique at any intensity or number of sessions.

### · Outcomes

*Pain*: Measured with any scale used in each study

*Cognitive function*: Including memory, attention and other measures of cognitive function measured in each study.

### Search methods to identify studies

### · Electronic searches

Studies meeting the inclusion criteria were identified in either English or Spanish.

Using a set of controlled and uncontrolled terms for "breathing techniques", "Pain" and "Cognitive function", with field labels (title and summary), proximity operators, and Boolean operators. Search strategies will be found in Appendix 1.

Specifically, the following databases were used:

- The Cochrane Central Register of Controlled Trials.

- (CENTRAL, Ovid platform): inception to present.

- MEDLINE®, Ovid platform: inception to present.

- MEDLINE® In-Process & Other Non-Indexed Citations.

- Ovid platform: inception to present.

- MEDLINE® Daily Update, Ovid platform: inception to present.

- EMBASE, embase.com platform: inception to present.

- LILACS, IAHx interface: inception to present.

### Data collection and analysis

### · Selection of studies

Evaluated the inclusion and exclusion criteria of all titles and abstracts found in the search strategy. All potentially relevant studies were evaluated in full text. The entire selection process was documented in a PRISMA flow chart.

### · Data extraction and management

An extraction format was designed for each study and collected the following information:

- Study design.

- Year of publication.

- Participants: characteristics.

- Number of participants in each group

- Loss to follow-up.

- Techniques used (intervention and control).

- Definition and frequency of outcomes in each group.

- Sources of funding.

### · Evaluation of risk of bias

The risk of bias of the included studies was independently assessed using the Cochrane Collaboration's risk of bias assessment that evaluates random sequence generation, concealment, blinding of the intervention to the participant and patient advisor, loss to follow-up, reporting bias, and other biases.

### · Effect measures

The studies were combined in a meta-analysis if possible, in cases where the studies could not be combined, a narrative synthesis was performed. A mean difference with a 95% confidence interval was used.

### · Evaluation of heterogeneity

Heterogeneity was assessed using an I2 and chi2 test, significant heterogeneity will be considered if it is greater than 40% in the I2 and the p value is less than 0.1 in the chi2.

## RESULTS

### Search results

When searching the different databases, we found a total of 1428 references, of which, when reviewed in text and abstract, a total of 29 eligible were left, which were read in full text, leaving 16 references included, of which 9 were combined in a meta-analysis (See Figure 1).

### Studies included

In total, 16 randomized clinical trials were included that compared some breathing pattern versus control.

Controls used include sham breathing techniques, different breathing methods (Wongwilairat, Buranruk, Eungpinichpong, Puntumetakul & Kantharadussadee-Triamchaisri, 2018) or social interaction (Ferreira, Tanaka, Santos-Galduroz & Fernandes, 2015).

The two outcomes found in the studies were pain in labor (Boaviagem et al., 2017; Yuksel, Cayir, Kosan & Tastan, 2017), pain in general, cognitive function in terms of memory, abstraction, flexibility and attention (Ferreira et al., 2015; Larkey, Roe, Smith & Millstine, 2016) (See Table 1).
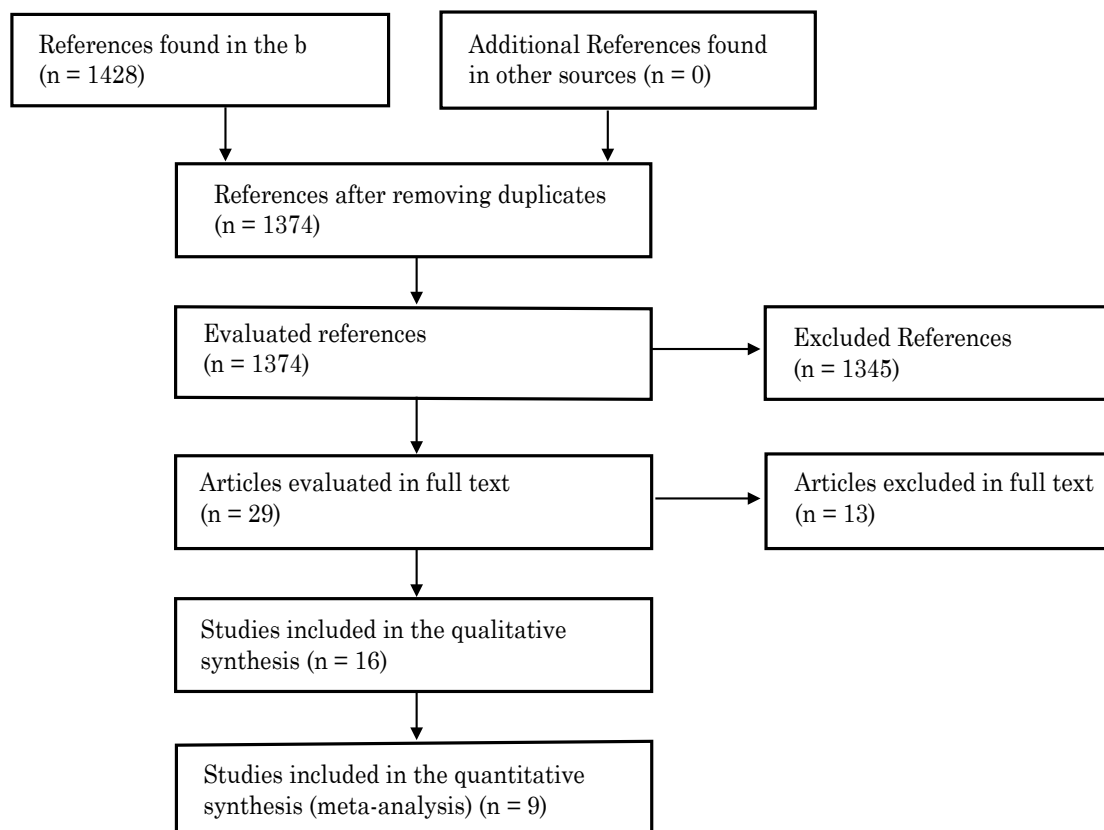


**Figure 1.** PRISMA flow chart.

TABLE 1.
*Summary of included studies*

| Reference | Population | Intervention | Comparator | Outcome | Intervention results | Control results | P-value |
|---|---|---|---|---|---|---|---|
| Boaviagem, 2016 (Boaviagem et al., 2017) | Women in labor, between 12 to 40 years old with a gestational age between 37 and 41 weeks. | Breathing pattern. N = 67 | Control. N = 73 | Maternal anxiety | 50.6+/- 1.8 | 49.3 +/- 1.5 | NS |
| | | | | Maternal pain | 8.8 +/- 0.3 | 8.8 +/- 0.3 | NS |
| Yuksel, 2017 (Yuksel et al., 2017) | Pregnant women between 37 to 42 weeks. | Controlled breathing. (n = 125) | Control. (N = 125) | Maternal pain | 88.2 +/- 6.3 | 90.5 +/- 7 | P = 0.000 |
| Tomas-Carus, 2018 (Tomas-Carus et al., 2018) | Women with fibromyalgia | Respiratory exercise program N = 18 | Control. N = 17 | Pain | 5.8 (5.16 a 6.43) | 7.93 (7.05 to 8.80) | p = 0.025 |
| Saoji, 2018 (Saoji, Raghavendra, Madle & Manjunath, 2018) | Healthy volunteers for yoga courses | Breath-based yoga interventions N = 56 | Control. N = 56 | Mind-Wandering Question-naire (MWD) | 1.89 +/- 0.76 | 2.41 +/- 0.89 | p <0.01 |
| | | | | State Mindfulness Attention and Awareness Scale (SMAAS) | 4.27 +/- 0.75 | 3.94 +/- 0.75 | p < 0.05 |
| Wongwilairat, 2018 (Wongwilairat et al., 2018) | Women with tension neck pain between 20 and 25 years old with normal BMI | Slow deep breathing exercise. N = 8 | Other breathing methods N = 8 | Pain | 0.75 +/- 0.71 | 0.75 +/- 1.49 | NS |
| Grubić, 2019 (Grubić, Babić & Štimac, 2019) | Multiple sclerosis patients | Home-based breathing exercise N = 9 | Control. N = 9 | Pain-according to sf36 outpatient | 80 +/- 27.4 | 79.0 +/- 28.8 | NS |
| | | | | Pain-according to sf36 non-ambulatory | 72.5 +/- 28.5 | 45.6 +/- 36.4 | NS |
| Park, 2019 (Park & Lee, 2019) | Low back pain patients aged 18 to 65 years with pain for at least 6 weeks | Breathing resistance training N = 23 | Control. N = 23 | Pain- NRS | 3.6 +/- 1.14 | 3.65 +/- 1.27 | NS |
| Tomas-Carus, 2019 (Tomas-Carus et al., 2019) | Women with fibromyalgia | Unsupervised breathing exercise program N = 16 | Control. N = 15 | Pain tolerance | 1.58 +/- 0.38 | 1.71 +/- 0.53 | NS |
| | | | | Pain | 6.8 +/- 1.69 | 7.78 +/- 2 | NS |
| Youn-Jung, 2020 (Oh, Park & Lee, 2020) | Women with low back pain between 40 to 49 years | Abdominal breathing maneuvers. N = 22 | Control. N = 22 | Pain (Quadruple Visual Analog Scale) | 4.58 +/- 0.46 | 4.45 +/- 0.42 | NS |
| Phattharasupharerk, 2018 (Phattharasupharerk, Purepong, Eksakulkla & Siriphorn, 2019) | Office workers with non-specific low back pain of at least 12 weeks. Between 20 to 40 years of age. | Qigong N = 36 | Control. N = 36 | Pain | 14 +/- 20.5 | 53.5 +/- 20.9 | < 0.001 |

| Reference | Population | Intervention | Comparator | Outcome | Intervention results | Control results | P-value |
|---|---|---|---|---|---|---|---|
| Peppone, 2015 (Peppone et al., 2015) | Women cancer survivors  2 to 24 months post-surgery | YOCAS. N = 75 | Control. N = 95 | Functional Assessment of Chronic Illness Therapy with Fatigue Subscale. Changes in FACIT-F–I have pain | -0.18 | 0.04 | 0.021 |
| | | | | Multidimensional Fatigue Symptom Inventory-Short Form. Changes in MFSI-SF–my muscles ache | -0.51 | -0.13 | 0.001 |
| Ferreira, 2015 (Ferreira et al., 2015) | Adults between 60 and 79 years | Breathing training. N = 34 | Control (Social interaction). N = 34 | Evocative / declarative memory | 21.0 (18.5, 23.6) | 25.4 (22.7, 28.1) | NS |
| | | | | Evocative memory | 17.5 (15.0, 20.0) | 22.8 (20.2, 25.4) | NS |
| | | | | Semantic memory | 28.3 (24.6, 32.0) | 38.5 (34.6, 42.3) | 0.01 |
| | | | | Short term memory | 5.2 (4.8, 5.8) | 5.0 (4.5, 5.5) | NS |
| | | | | Mental manipulation | 4.2 (3.8, 4.8) | 4.1 (3.7, 4.7) | 0.03 |
| | | | | Abstraction | 4.8 (4.2, 5.5) | 4.0 (3.3, 4.7) | 0.01 |
| | | | | Mental flexibility | 3.7 (1.8, 5.7) | 6.0 (4.0, 8.0) | 0.02 |
| | | | | Attention | 25.7 (22.9, 28.5) | 22.0 (19.1, 25.0) | NS |
| Sagkal, 2015 (Sagkal & Eser, 2015) | Women with cesarean delivery between the ages of 18 and 45 who do not use non-opioid analgesics. | Reiki. N = 50 | Control. N = 50 | Pain | 1.24 +/- 0.99 | 3.76 +/- 1.61 | 0.001 |
| Telles, 2016 (Telles, Sharma, Gupta, Bhardwaj & Balkrishna, 2016) | People with degenerative changes in intervertebral discs between 20 and 45 years old. | Breathing techniques in Yoga. N = 20 | Control. N = 20 | Pain | 4.68 +/- 2.3 | 6.1 +/- 2.19 | 0.04 |
| Sagkal, 2016 (Sagkal & Ciray, 2016) | Women with cesarean delivery between the ages of 18 and 45 who do not use non-opioid analgesics. | Reiki. N = 16 | Control. N = 16 | Pain | 26.8 +/- 21.3 | 37.2 +/- 19.1 | 0.001 |
| Larkey, 2016 (Larkey et al., 2016) | Women diagnosed with stage 0-III breast cancer | Breathing techniques with Tai-Chi and Qigong.N = 49 | Control. N = 52 | Cognitive function. FACT- Cog PCI | 1.01 +/- 0.75 | 1.1 +/- 0.66 | NS |

NS: Not Significant.

## Studies excluded

Out of the articles reviewed in full text, 13 of these were excluded, the most frequent reason for exclusion was that these articles did not assess pain or cognitive function (See Table 2).

## Risk of bias of included studies

The studies in general had an intermediate risk of bias (See Figure 2), this classification is due to the lack of blinding in some studies, specifically the blinding of the personnel evaluating the patients and the unclear risk of bias for the concealment of random assignment (See Figure 3).

Some studies had an unclear risk of bias in the generation of the random sequence secondary to the mention of the method, but how this sequence is performed is not explained (Grubić et al., 2019; Park & Lee, 2019; Phattharasupharerk et al., 2019; Telles et al., 2016; Wongwilairat et al., 2018) (See Figure 3).

TABLE 2.
*Excluded articles*

| Reference | Reason for exclusion |
|---|---|
| Frøkjær 2016 (Frokjaer et al., 2016) | Different outcome |
| Pettersson 2015 (Pettersson, Faager & Westerdahl, 2015) | Different outcome |
| Telles 2016 (Telles et al., 2016) | Different outcome |
| Rietberg 2017 (Rietberg, Veerbeek, Gosselink, Kwakkel & van Wegen, 2017) | Literature review |
| Smith 2015 (Smith et al., 2015) | Literature review |
| Janssens 2015 (Janssens et al., 2015) | Different intervention |
| Gunay 2016 (Gunay et al., 2016) | Different outcome |
| Nyer 2018 (Nyer et al., 2018) | Different outcome |
| Patrician 2019 (Patrician et al., 2019) | Different outcome |
| Smith 2017 (Smith & Norman, 2017) | It is not a clinical trial |
| Ratcliff 2018 (Ratcliff et al., 2019) | Different intervention |
| Seyyed-Rasooli 2016 (Seyyed-Rasooli et al., 2016) | Different intervention |
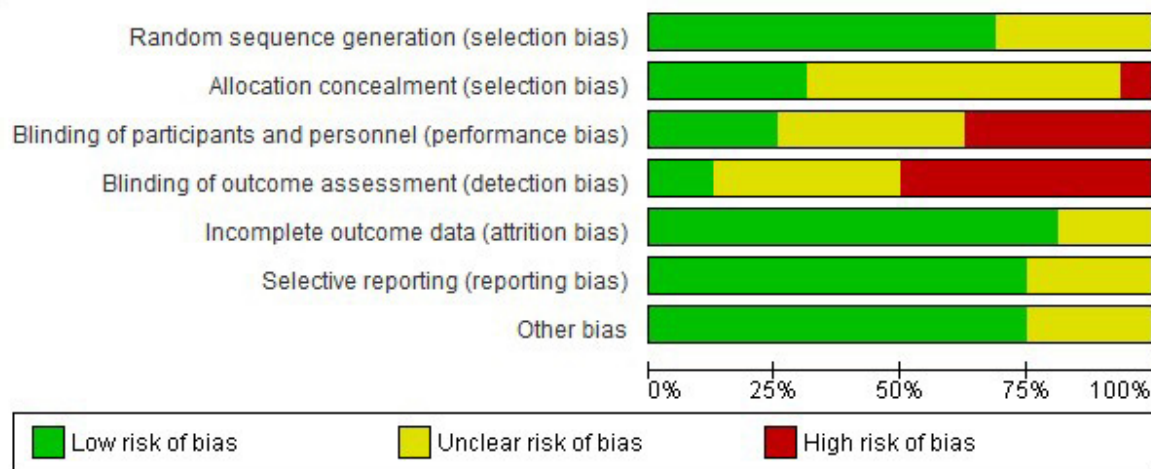


**Figure 2.** Summary of risk of bias.

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## Pain

### Breathing techniques in pregnant patients

The Boaviagem in 2016 study (Boaviagem et al., 2017) included women in labor between 12 to 40 years of age and evaluated the efficacy of breathing patterns during the active phase of the first stage of labor. The study did not find statistically significant differences between the intervention and the control for pain measured with the visual analog scale (8.8 +/- 0.3 vs 8.8 +/- 0.3).

Following the line of studies in pregnant women, the study by Yuksel 2017 (Yuksel et al., 2017) evaluated a controlled breathing method in pregnant women between 37 and 42 weeks. Patients in the intervention group received a respiratory exercise session in the first stage of labor. During training, all participants performed abdominal breathing during the second stage of labor. The main components of the breathing exercises were:

a. First, fill your stomach and then your lungs with air as you inhale;

b. Feel the expansion in your stomach;

c. Make sure the muscles from the stomach to the knee are relaxed, as if you were urinating while exhaling;

d. When there is pain, do deep abdominal breathing exercises, take a deep breath and hold as much as you can;

e. Try to push the baby down;

f. You can do this by holding your breath or exhaling very slowly through your mouth;

g. The most important point at this stage is that you do not have to fill your stomach with air, and you must push down to deliver the baby;

h. You should continue pushing until the pain is relieved.



**Figure 3.** Risk of bias of included studies.

### Effects of interventions

The results of each study are presented below (See Table 1).

When evaluating maternal pain with the visual analog scale, statistically significant differences were found (88.2 +/- 6.3 vs 90.5 +/- 7, p-value = 0.0001).

Similarly, Sagkal & Eser (2015) included 29 women with cesarean delivery between 18 and 45 years of age who did not use non-opioid analgesics, comparing Reiki vs control, finding a decrease in pain in terms of the visual analog scale (1.24 +/- 0.99 vs 3.76 +/- 1.61, p-value 0.001).

*Breathing techniques in other entities*

The study by Tomas-Carus et al. (2018) included women with fibromyalgia and compared a respiratory exercise program versus a control. The respiratory exercise program consisted of 30 min/ session for 7 times/ week for 12 weeks: 1 time supervised by an expert in breathing exercises, and 6 times/ week without supervision at home with audiovisual training through a versatile digital disc. Each session focused on breathing exercises that strengthened and lengthened the skeletal muscles of the thorax and abdomen, including five breathing exercises (3 min for each one), which were performed in the form of a circuit (2 circuits/session), including, a breathing awareness exercise: in a supine position, inhale through the nose and exhale through the mouth with the lips parted slowly; rib expansion exercise: in supine position, with the arms along the body with a cane held by the hands. Raise your arms and inhale and exhale and lower your arms; and three diaphragmatic breathing exercises: exercise (1) in the supine position, overlapping the hands on the diaphragm located in the abdominal region: breathe in through your nose and breathe out through your mouth slowly with your lips parted; exercise (2) in the prone position, with a folded towel under the diaphragm located in the abdominal region: breathe in through your nose and breathe out through your mouth slowly with your lips half closed; and exercise (3) in supine position, with a weight of 1 kg on the diaphragm located in the abdominal region: breathe in through the nose and exhale through the mouth slowly with the lips parted. The authors found statistically significant differences between the intervention and the control in pain measured by the visual analog scale (5.8 vs 7.9, p-value 0.025). The same author presented a similar study one year later (Tomas-Carus et al., 2019), where they also found no statistically significant differences in terms of pain measured by the visual analog scale.

Wongwilairat et al. (2018) included women with tension neck pain between 20 and 25 years of age with normal BMI, compared slow and deep breathing exercise vs other breathing methods, finding no statistically significant differences when measuring pain with the visual analog scale (0.75 +/ -0.71 vs 0.75 +/ -1.49).

On the other hand, Grubić et al. (2019) evaluated breathing exercises at home vs a control in patients with multiple sclerosis. For the breathing exercises, the basic principle was to inhale and exhale as fully as possible, but slowly to avoid hyperventilation and dizziness. Diaphragmatic or abdominal breathing (1.5 min) was performed to strengthen the abdominal muscles and the diaphragm, and thoracic breathing (1.5 min) to strengthen the intercostal muscles (3 × -20-s pause- 3 ×). When evaluating pain according to SF36, statistically significant differences were not found.

## Qigong

Park & Lee (2019) included patients with low back pain between 18 and 65 years old with pain of at least 6 weeks of progress and compared a respiratory resistance training vs a control evaluating pain with the visual analog scale, the authors found no differences statistically significant. Another similar study in women with low back pain (Oh et al., 2020) evaluated abdominal breathing maneuvers, finding no statistical differences between the groups. On the other hand, Phattharasupharerk et al. (2019) included office workers with non-specific low back pain of at least 12 weeks between 20 and 40 years of age. He compared Qigong vs control group. The Qigong group participants received an hour Qigong practice session each week for six weeks (Guan Yin Zi Zai Gong level 1, developed by Yang Pei Xen since 1995) at their workstation by a professional Qigong instructor from the Master Yang Qigong Center, Bangkok, Thailand. Fifteen minutes of Wu Chi meditation and 28 minutes of static exercise. In the pain outcome, the authors found statistically significant differences (14 +/ -20.5 vs 53.5 +/ - 20.9, p-value: 0.001).

## Yoga-based breathing techniques

Peppone et al. (2015) included women survivors of cancer 2 to 24 months after surgery, compared YOCAS vs control. The intervention includes 16 poses sitting, standing, transitional and supine. Breathing exercises includes low, controlled, diaphragmatic work of breathing coordinated by movements. Mindfulness exercises include meditation, visualization, and affirmation activities. The intervention is delivered in a group format taught by an instructor, twice a week, for 75 minutes each time, for 4 weeks which means a total of eight yoga sessions. Pain was evaluated using the FACIT F-I scale, finding statistical differences (p-value 0.021). In the same line of breathing techniques based on Yoga (Telles et al., 2016) used these techniques in people with degenerative changes in intervertebral discs between 20 and 45 years old, finding differences in the measurement of pain with the use of the visual analog scale (4.68 +/ -2.63 vs 6.1 +/ -2.19, p-value 0.04).

| Study or Subgroup | Técnica de respiración Mean | SD | Total | Control Mean | SD | Total | Weight | Mean Difference IV, Random, 95% CI |
|---|---|---|---|---|---|---|---|---|
| Boaviagem, 2016 | 8.8 | 0.3 | 67 | 8.8 | 0.3 | 73 | 14.9% | 0.00 [-0.10, 0.10] |
| Midilli, 2014 | 1.24 | 0.99 | 50 | 3.76 | 1.61 | 50 | 13.1% | -2.52 [-3.04, -2.00] |
| Midilli, 2016 | 2.68 | 2.13 | 16 | 3.72 | 1.91 | 16 | 7.4% | -1.04 [-2.44, 0.36] |
| Phattharasupharerk, 2018 | 1.4 | 2.05 | 36 | 5.35 | 2.09 | 36 | 10.2% | -3.95 [-4.91, -2.99] |
| Telles, 2016 | 4.68 | 2.3 | 20 | 6.1 | 2.19 | 20 | 7.5% | -1.42 [-2.81, -0.03] |
| Tomas-Carus, 2018 | 5.8 | 1.27 | 18 | 7.93 | 1.8 | 17 | 9.6% | -2.13 [-3.17, -1.09] |
| Tomas-Carus, 2019 | 6.8 | 1.69 | 16 | 7.78 | 2 | 15 | 7.9% | -0.98 [-2.29, 0.33] |
| Youn-Jung, 2020 | 4.58 | 0.46 | 22 | 4.45 | 0.42 | 22 | 14.5% | 0.13 [-0.13, 0.39] |
| Yuksel, 2017 | 8.82 | 0.63 | 125 | 9.05 | 0.7 | 125 | 14.8% | -0.23 [-0.40, -0.06] |
| Total (95% CI) | | | 370 | | | 374 | 100.0% | -1.21 [-1.75, -0.68] |

Heterogeneity: Tau² = 0.50; Chi² = 173.64, df = 8 (P < 0.00001); I² = 95%
Test for overall effect: Z = 4.43 (P < 0.00001)

**Figure 4.** Meta-analysis of pain, breathing techniques vs. control.

## Combination of studies

When combining the different breathing techniques vs control in the included studies, we found a statistically significant difference in terms of the visual analog scale (Difference of means, random effects; -1.21 [95% CI -1.75 to -0.68]; I2: 95%).

## Cognitive function

Three studies that measured cognitive function were included, one of these (Saoji et al., 2018) included healthy volunteers in yoga courses and compared breathing techniques derived from yoga vs. control, finding statistically significant differences with the scales used (See Table 1). The second study (Ferreira et al., 2015) found statistical differences in terms of semantic memory, mental manipulation, abstraction and mental flexibility when comparing breathing training vs social interaction in adults between 60 and 79 years old. The last of the studies did not find statistically significant differences in terms of cognitive function with the FACT-COG PCI scale when comparing breathing techniques with Tai-Chi and Qugong vs control in women diagnosed with breast cancer (See Table 1).

### DISCUSSION

An improvement in pain and cognitive function in intervention was found in most of the included studies in terms of breathing techniques accompanied by abstraction of ideas or the use of thoughts during the process of the same. This does not occur with studies that exclusively include breathing techniques.

The present findings appear to be consistent with other studies, which found that breathing techniques could reduce short-term and long-term pain intensity. It seems possible that these results are given because some techniques consist of three elements that could reduce pain: posture, deep breathing and meditation. The breathing techniques comprised various poses and movements that could strengthen the stabilizing muscles of the core. Also, deep breathing and meditation on breathing techniques help relax the body and mind, which in turn reduces muscle activity. In addition, meditation reduces the perception of pain (Abdallah et al., 2018; Abedi, Jahanfar, Namvar & Lee, 2016; Altenau, Crisp, Devaiah, & Lambers, 2017). A previous study by Sharon et al. (2016) demonstrated that meditation significantly reduces pain and cold stimulus-induced pain discomfort score in healthy adults. Interestingly, intravenous injection of naloxone, an opioid blocker, reverses this analgesic effect of meditation, suggesting that meditation modulates pain through the endogenous opioid mechanism (Sharon et al., 2016). Furthermore, a previous study by Movahedi, Ghafari, Nazari & Valiani (2017) showed that acupressure to specific points 3 times a week for three weeks reduced the severity of chronic low back pain (Babina, Mohanty & Pattnaik, 2016; Barnes, Mc-Donald, Smallwood, & Manser, 2019; Bayer et al., 2017).

A previous study showed that Qigong practice reduced stress and increased social interaction in the hospital staff (Knips et al., 2019; Larkey et al., 2016; Phattharasupharerk et al., 2019). Similarly, Skoglund y Jansson (2007) showed

that Qigong practice reduced the symptoms of low back pain and stress by reducing sympathetic activity. The results of this study showed that breathing exercises significantly reduced heart rate and respiratory rate compared to the reference and waiting list group. During meditation, the body enters a state of relaxation response by decreasing heart rate, respiratory rate, blood pressure, and muscle tone and increasing alpha brain waves, which in turn reduces stress (Lee, Gordon & Osadnik, 2018; Lee et al., 2016; Lee & Jang, 2019).

Among the limitations of this review, the small sample size of the included studies, is found, as well as the fact that several of these interventions were performed in an unsupervised manner and had short follow-up periods. On the other hand, the studies found are very heterogeneous clinically and statistically with each other; therefore, the combination of studies should be interpreted with caution and future studies could modify the interpretation of these results.

It is therefore suggested that randomized studies be carried out with sample sizes greater than those found in this review.We conclude then that meditation-based breathing techniques would improve pain and cognitive function in patients with a painful entity or healthy volunteers.

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APPENDIX 1.
*Search strategy*

Respiration/
respirat*.tw
Breathing.tw
Breathing Exercises/
Respiratory Mechanics/
Respiratory Rate/
Inhalation/
Inhaling.tw
Inspiration.tw
Exhalation/
Exhalation.tw
Expiration.tw
Exhaling.tw

Pain, Referred/
Pain.tw
Flank Pain/
Neck Pain/
Neck Aches.tw
Cervicalgia.tw
Pelvic Pain/
Low Back Pain/
Lumbago.tw
Abdominal Pain/
Colicky Pain.tw
Pain Measurement/
Analgesia Test.tw
Chest Pain/
Back Pain/
Backache.tw
Cancer Pain/
Headache/
Headache.tw
Cephalgia.tw
Hemicrania.tw
Myalgia.tw
Muscle Soreness.tw
Arthralgia/
Arthralgia.tw
Polyarthralgia.tw
Fibromyalgia/
Fibromyalgia.tw
Pain/
Ache.tw
Pain Management.tw
Acute Pain/
Musculoskeletal Pain/
Chronic Pain/
Nociceptive Pain/

Cognition/
Cognition.tw
Cognitive Function.tw
Neuropsychological Tests/
Neuropsychologic Test.tw

Source: Author.

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Review

# Interaction between domain-specific and domain-general abilities in math´s competence

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*Abstract*

This article is an approach to some viewpoints about interactions between domain-specific and general cognitive tools involved in the development of mathematical competence. Many studies report positive correlations between the acuity of the numerical approximation system and formal mathematical performance, while another important group of investigations have found no evidence of a direct connection between non-symbolic and symbolic numerical representations. The challenge for future research will be to focus on correlations and possible causalities between non-symbolic and symbolic arithmetic skills and general domain cognitive skills in order to identify stable precursors of mathematical competence.

**Keywords***:* Numerical cognition; cognitive development; approximate number system; working memory

## Interacción entre habilidades de dominio específico y dominio general en la competencia matemática

*Resumen*

Este artículo es una aproximación a diferentes puntos de vista acerca de la interacción entre las habilidades cognitivas de dominio específico y general involucradas en el desarrollo de la competencia matemática. Muchos estudios reportan correlaciones positivas entre la agudeza del sistema de aproximación numérica y el desempeño matemático formal, mientras que otro grupo importante de investigaciones no han hallado evidencias de una conexión directa entre las representaciones numéricas no simbólicas y las simbólicas. El desafío para las futuras investigaciones será focalizar en correlaciones y posibles causalidades entre las habilidades aritméticas no simbólicas, las simbólicas y las habilidades cognitivas de dominio general con el propósito de identificar precursores estables de la competencia matemática.

**Palabras clave**: Cognición numérica; desarrollo cognitivo; sistema de aproximación numérica; memoria de trabajo; precursores

## INTRODUCTION

Natural numbers are a critical tool for almost all human cultural achievements, they are everywhere and we deeply depend on them so, a central question for science is how they arise in our lives… which are the foundations that support numerical thinking.

Cognitive development depends on two types of essential tools, domain-specific and domain-general processes (Butterworth, 2019) and the way these abilities co-develop is crucial for understanding learning in general, and math learning in particular.

Domain-specific representations guide and constraint the cultural acquisition of novel representations (Carey, 2009; Piazza & Izard, 2009). The core knowledge systems are universally shared independently of formal education and engaged throughout lifetime (Spelke, 2017). For numbers, the neurocognitive startup tool are two preverbal and non-symbolic systems for numerical quantification to of the environment: the *Approximate Number System* (ANS) and the *Object Tracking System* (OTS) (Piazza & Izard, 2009; Piazza, 2010). But this nonverbal number sense may not be enough to develop verbal and exact math competencies and domain-general abilities could be involved.

Domain-general cognitive tools are necessary in a wide variety of tasks and refer to higher order cognitive variables that can predict the performance of several competencies (Fritz, Haase & Räsänen, 2019), for instance, Working Memory (WM) (Blankenship, Keith, Calkins & Bell, 2018) and Processing Speed (PS) (Clark, Nelson, Garza, Sheffield, Wiebe & Espy, 2014) or language (Butterworth, 2019).

## Domain-specific tools: ANS and OTS

The Approximate Number System (ANS) enables humans to represent and manipulate quantities in an approximate manner, it means that encodes an imprecise estimate of the numerical magnitude of a set (Nieder & Dehane, 2009; Nieder, 2019). This ancient and evolutionary number sense is shared with non-human animals and primates (Cantlon & Brannon, 2007) and is present from the very beginning, long before the acquisition of symbolic number.

Newborns are sensitive to the abstract numerical attributes of the environment and reacts to the cardinal values of sets presented in all sensory modalities, auditory or tactile, not only in a visual way (Anobile, Cicchini & Burr, 2016; Izard, Sann, Spelke & Streri, 2009) and they are able to discriminate between sets irrespective of the physical properties: surface area, density or contour length (Matejko & Ansari, 2016).

ANS increases in acuity through childhood until around 30 years old (Halberda, Ly, Wilmer, Naiman & Germine, 2012) and varies across individuals (Piazza & Izard, 2009). ANS acuity is assessed with simple approximation number tasks of comparison of two sets, the performance depends on the ratio between the quantities. Because of ANS imprecision close quantities are more difficult to discriminate.

To solve an everyday decision making anytime counting is not possible, ANS representation is activated during both non-symbolic and symbolic approximations (Libertus, Odic, Feigenson & Halberda, 2020), the two systems remain intimately linked and mutually interact with each other.

The second core tool involved in number processing is the Object Tracking System, OTS (Dehaene, 2011), a visuospatial object-based attention system that allows a quick, effortless apprehension up to 4 items called *subitizing* (Ashkenazi, Mark-Zigdon & Henik, 2013). This is a mechanism to enumerate the number of sets at a glance and with high accuracy (Butterworth, 2019; Revkin, Piazza, Izard, Cohen & Dehaene, 2008) without counting. Similar to ANS, OTS varies across individuals and develops in a short period of time and babies reach the adult (like limit of 3-4 items in the first year of life). It´s most important constraint is that it´s limited to a small set (Piazza, 2010), for larger sets exact and serial but slower counting is the only possible mechanism because larger numbers can´t be tracked (Nieder, 2019). Subitizing is a precursor of counting and symbolic representations and the acquisition of a mental number line spatially left-right organization (Dehaene, 2011).

The approximate number system and subitizing are complementary mechanisms of the number sense. Together, enable the comprehension of cardinality and ordinality (Rapin, 2016). Similar to ANS, OTS varies across individuals and develops in a short period of time and babies reach the adult (like limit of 3-4 items in the first year of life). Around 4 years old, are assembled and children understand that sets may have a precise number, so 15 is a different concept from 13 (Dehaene, 2011).

The relation between ANS acuity and mathematical performance has been explored intensively but results remain unclear yet. In fact, several studies have shown that ANS acuity is meaningfully related to mathematical achievement and have also suggested that individual differences in this non-symbolic system predict symbolic mathematical skills (Libertus, Feigenson & Halberda, 2011; Bonny & Lourenco, 2013). For instance, on magnitude comparison tasks typical development children outperforming math learning disabilities children (Desoete, Ceulemans, De Weerdt & Pieters, 2012). So, ANS acuity may be helpful in designing diagnostic and intervention tools (Park & Branon, 2014).

ANS and the symbolic number system rely on each other in a sort of continuity of both representations, the way to acquire the meaning of symbolic numbers is linking with the preexisting innate representations of numbers. So, ANS may constitute the semantic foundation for the symbolic numbers (Dehaene, 2011; Mazzocco, Feigenson & Halberda, 2011).

Three meta-analyses confirm the positive relation between non-symbolic number acuity and math ability (Chen & Li, 2014; Fazio, Bailey, Thompson & Siegler, 2014; Schneider et al., 2016); however, many others studies failed to identify the relation between them (Chu, vanMarle & Geary, 2015; Vanbinst, Ghesquiere & Smedt, 2012; Zhou, Wei, Zhang, Cui & Chen, 2015).

Bugden & Ansari (2011) suggest that ANS acuity wouldn't be the foundation for early mathematical development but the basic symbolic competencies, numerals, number words and the relations among them. The notion of a direct link from non-symbolic to symbolic is challenged by the hypothesis that number symbols are not necessarily inextricably tied to non-symbolic quantities. Resents findings indicate that symbolic and non-symbolic abilities show different developmental trajectories in the first year of schooling but not a unidirectional relationship (Matejko & Ansari, 2016) and even divergent patterns of representation at the neural level (Goffin & Vogel, Slipenkyj & Ansari, 2020).

Possibly, both ANS acuity and the understanding of number symbols independently contribute to math learning (Fazio et al., 2014). ANS may facilitate children's explicit understanding of cardinal value and indirectly may influence early mathematical learning (Chu et al., 2015).

Undoubtedly, the experience with numbers and arithmetic of formal education enhanced the accuracy in the development of ANS (Lindskog, Winman & Juslin, 2014). For instance, there's evidence of higher ANS acuity in individuals who had formal education experience than without formal education or after ANS training (Nys et al., 2013; Honoré & Noel, 2016). Indeed, what it's relevant for teaching math is that ANS is refined through practice with the symbolic number system (Matejko & Ansari, 2016) and that acuity facilitates the acquisition of cardinal principle (Nieder, 2019), the core concept of succession of natural numbers.

Two concepts must be defined to avoid confusions: *cardinality* refers to set size, the last number produced when counting the set: 1, 2, 3, 4… 5 (Szkudlarek & Brannon, 2017), *symbolic number* includes the Arabic code and verbal code representations: 5 and five.

### *Domain-general tools: the case of WM*

According to Carey (2009) and Szkudlarek & Brannon (2017) improving math depends on a multifaceted approach so, ANS acuity is a foundational skill but insufficient. Many studies focused on different domain general abilities as predictors of children individual mathematical achievement: fluid intelligence and working memory (Blankenship et al., 2018; Geary, 2011; Xenidou-Dervou et al., 2018), processing speed (Clark et al., 2014; Kuzmina, Tikhomirova, Lysenkova & Malykh, 2020), vocabulary and word recall (Purpura & Ganley, 2014), inhibitory control (Gilmore et al., 2013) or in a combination of three: intelligence, central executive and reading achievement in a seven-year longitudinal study (Geary, Nicholas, Li & Sun, 2017).

Working Memory (WM) has shown to be a strong longitudinal predictor of various mathematical skills (Hornung, Schiltz, Brunner & Martin, 2014; Xenidou-Dervou et al., 2018). According to Baddeley (2012), WM is an attention-driven multicomponent cognitive construct, an active system for temporal storing and processing information in an online manner at service of complex cognitive tasks. The system includes four components: a) Central Executive (CE), the most complex, an attentional system which monitors, controls and regulates the workings of the others and is activated when visual, spatial or phonological elements need to be manipulated, b) a Buffer Store (BS) for integrating information from a range of sources into a multidimensional code, c) a Phonological Loop (PL) a brief store of phonological elements together with a means of maintaining information by vocal or subvocal rehearsal, and d) a Visuospatial Sketchpad (VSSP) for storing spatial and visual information.

WM span is considered essential to math skill but this seems to be content-specific: visuospatial rather than verbal WM skills correlate with math achievement (Clearman, Klinger & Szücs, 2017). In a recent systematic review, Allen, Higgins & Adams (2019) confirmed an evident positive effect of visuospatial WM on mathematics attainments and suggested to take into consideration the type of VSSP involved. It is possible to identify the individual con-

tribution of each component of the WM underlying different tasks (Fanari, Meloni & Massida, 2019), for instance, CE will be necessary in counting backward in twos from a certain number, whereas simply repeating the same number would not because it´s related to another component, the PL. In the case of atypical math development, researchers found difficulties in spatial WM tasks performance but not in visual tasks (Mammarella, Caviola, Giofrè & Szücs, 2018).

## Conclusions

In a way of reconciling discrepant findings about precursors of math competence, research proposes that interventions should focus on domain-specific skills but also general cognitive abilities (Träff, Östergren & Skagerlund, 2020) as apparently, they contribute to distinct aspects during math growth. Indeed, both are implied and interact in the early numeracy (LeFevre et al., 2010) with different weights and in different moments and perhaps different resources for similar tasks (Fanari et al., 2019; Hornung et al., 2014).

Siemmann & Petermann (2018) suggested an integral model that could help understanding learning math and identifying children at risk of struggling with mathematics. They describe three factors for arithmetic development: a domain-specific number sense, the *foundation* on which arithmetic development rest, a *scaffold* of domain-general skills that assist in linking abstract numerosity with symbolic representation, and *tools,* the early number competencies: ordinality, cardinality, counting that are involved in arithmetic.

This body of novel concepts from cognitive neuroscience on precursors of math development should be considered a valuable

contribution for educational interventions (Hellstrand, Korhonen, Räsänen, Linnanmaki & Aunio, 2020). It´s extremely important that educators improve their knowledge about factors related to healthy math competence. Teachers need this evidence-based guidance to make educational decisions about what to teach, why, how and when.

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## Original article

# COVID-19 resilience and neuroscience

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*Abstract*

Lately, neuroscience has proven key in providing scientific answers to research conducted in other disciplines. Resilience, from the point of view of neuroscience, takes on a new meaning due to the lockdown experienced under the COVID-19 pandemic. This article is the result of an investigation carried out during confinement in Spain, Mexico and Chile. It shows the preliminary results of the analysis of stress risk factors and resilience in neuroscience, identifying possible stress risk factors using socio-demographic data. A descriptive, cross-sectional, correlational and comparative study was conducted in a sample of 784 participants. The Connor-Davidson Resilience Scale (CD-RISC10) was used to identify resilience traits. The findings reveal a non-significant result among the countries, but statistically significant results in the level of education variable, which is associated with cognitive flexibility. The possible stress risk factors did not evince significant results. Thus, promoting resilience at an early age comes as a relevant finding. As argued by epigenetics, to immerse oneself in contexts where meaningful bonds are promoted, is essential to improve vital processes such as resilience and prevent potential stress risk factors.

**Keywords**: Covid-19; neuroscience; resilience; neuroeducation; well-being

## Resiliencia y neurociencia ante el COVID-19

*Resumen*

La neurociencia en los últimos años ha dado respuestas científicas a trabajos ya realizados desde otras disciplinas. La resiliencia desde la mirada de la neurociencia recobra nuevos significados ante la situación de confinamiento generada por la pandemia COVID-19. Este artículo es fruto de una investigación realizada durante el confinamiento en España, México y Chile, da cuenta de los resultados preliminares del análisis entre factores estresores y la resiliencia desde el enfoque de la neurociencia, identificando eventuales factores estresores a partir de datos socio-demográficos. Se realizó un estudio descriptivo, transversal, correlacional y comparativo con una muestra de 784 participantes. Se utilizó la escala de Connor - Davidson (CD-RISC10) para identificar conductas resilientes. Los hallazgos revelaron que la CD-RIC10 no presenta diferencia significativa entre los países, pero sí en el nivel de estudios; variable asociada a la flexibilidad cognitiva. Los potenciales factores estresores no arrojaron diferencias significativas. Por lo tanto, emerge la necesidad de promover la resiliencia desde etapas tempranas del desarrollo de los individuos como elemento clave de la epigenética, que apunta a rodearse de contextos enriquecidos para mejorar procesos vitales como la resiliencia y revertir eventuales factores estresores.

**Palabras clave**: Covid-19; neurociencia; resiliencia; neuroeducación; bienestar

## Introduction

A significant number of research has been conducted in neuroscience focusing on resilience. Authors such as Feder, Nestler & Charney (2009) and Burt et al. (2016) have analyzed the brain in the adaptation process. Similarly, Yang et al. (2016) have researched the areas of the brain that may be involved in resilience. Other studies, like Kong, Wang, Hu & Liu (2015) have investigated resilience's correlation to happiness. Therefore, it is possible to claim that the study of resilience in neuroscience is diverse and sometimes biased, for instance, when inspecting its link to anxiety in Clauss et al. (2014), or its connection with stress by Rothman & Mattson (2013).

Nevertheless, the question that should be posed is what concept of resilience is underlying these studies, as many of them take an individualistic and limited approach of the concept. As proposed by Grané & Forés (2019), neuroscience has been defining the neurological mechanisms associated with resilience. Even though resilience is seen as a professional motivational practice in social action rather than scientific evidence, in the last decades a great number of research has been carried out in the topic, which have provided scientific evidence to locate resilience in the neurological area. To go even further, neuroscience has yielded neurological evidence on the resistance to stress, trauma and recovery. This shows that neuroscience has endorsed to this day, the traditional perception of resilience. A prominent author from a neuroscientific view is Richard Davidson, who asserts that every person is characterized by an emotional profile composed of six styles: outlook (how long a positive emotion lasts), social intuition (ability to perceive social cues), self-awareness (to understand the body response to emotions), sensitivity to context (to adapt our emotional response to context), attention (ability to focus), and resilience (how fast or how slow we can respond to adversity). According to Davidson, these six styles reflect the findings of contemporary neuroscientific investigation (Davidson & Begley, 2012). As a consequence, resilience has been the object of analysis in the latest neuroscientific studies.

Based on what was previously explained, it seems imperative to investigate the neuroscientific findings of resilience in the COVID-19 pandemic context (Yıldırım & Arslan, 2020), with subjects from varied social, cultural, and economic contexts when having to experience mandatory confinement. This research seeks to scrutinize how resilience is connected to potential stress risk factors during lockdown.

## Methodology

The purpose of this investigation was to analyze from a neuroscience perspective, the relationship between resilience levels and potential stress risk factors with participants from Spain, Mexico and Chile during the social distance and confinement in the COVID-19 pandemic. A descriptive, cross-sectional, correlational and comparative study was carried out in June 2020. Another questionnaire response instance is scheduled to happen in December 2020 to the same subjects.

A nonprobability sampling technique was used with 784 subjects. Participants' ages ranged from 18 to 80 years ($M = 39.74$; $SD = 14.12$), 77.6% identified as female, and 22.7% as male. Participants come from 3 countries: Chile (n = 369), Spain (n = 194), and Mexico (n = 194). Subjects with incomplete or non-valid data were left out of the study. Other socio-demographic data are depicted in Table 1.

TABLE 1.
*Descriptive characteristics of the subjects*

| Country* | Frequency | Percent | Valid percent | Cumulative percent |
|---|---|---|---|---|
| Mexico | 194 | 24.7 | 25.6 | 25.6 |
| Spain | 194 | 24.7 | 25.6 | 51.3 |
| Chile | 369 | 47.1 | 48.7 | 100.0 |
| Total | 757 | 96.6 | 100.0 | |
| Level of education* | | | | |
| Uneducated | 2 | .3 | .3 | .3 |
| Primary school | 38 | 4.8 | 4.8 | 5.1 |
| Secondary school (mandatory) | 142 | 18.1 | 18.1 | 23.2 |
| College undergraduate | 171 | 21.8 | 21.8 | 45.0 |
| University graduate | 335 | 42.7 | 42.7 | 87.8 |
| Postgraduate studies | 96 | 12.2 | 12.2 | 100.0 |
| Total | 784 | 100.0 | 100.0 | |
| Marital status* | | | | |
| Married | 325 | 41.5 | 41.6 | 41.6 |
| Divorced/Separated | 83 | 10.6 | 10.6 | 52.2 |
| Widow/widower | 9 | 1.1 | 1.2 | 53.4 |
| Common-law relationship | 93 | 11.9 | 11.9 | 65.3 |
| Single | 271 | 34.6 | 34.7 | 100.0 |
| Total | 781 | 99.6 | 100.0 | 100.0 |

* The informed consent of the data was conducted in full agreement to Law 3/2018 of personal data protection and digital rights. Source: Authors.

A socio-demographic data questionnaire was used to collect data, as well as the Connor-Davidson scale (CD-RISC 10). The socio-demographic data was grouped in variables that could cause stress in confinement, such as number of people in the same household, marital status, and level of education. To measure the resilience level, CD-RISC 10 was used in its short version of 10 items to consider its validity and reliability (Notario-Pacheco et al., 2011; Serrano-Parra et al., 2013). Also, a unidimensional scale, with alternatives in Likert scale of 5 was employed. The questionnaire was self-administered and anonymous using Qualtrics.

### RESULTS

The descriptive and inferential statistics analysis of CD-RISC, incorporated as a dependent variable in the Anova and T-test to determine the differences between resilience and socio-demographic data such as level of education, number of people living in the same household, and marital status, were performed using the SPSS program.

In the first analysis, CD-RISC does not show a significant difference among the countries in the sample ($F$= 1.896, $p$> .05). There is a difference in the means, but it is not statistically significant: México (M = 39.56), Chile (M = 38.74), and Spain (M = 38.24).

The second analysis was performed with CD-RISC and the variable *level of education*, with the categories: primary school, secondary school, college undergraduate, university graduate, postgraduate studies. There was a significant difference among the groups ($F$ = 3.853; $p$ < .01) (Figure 1).
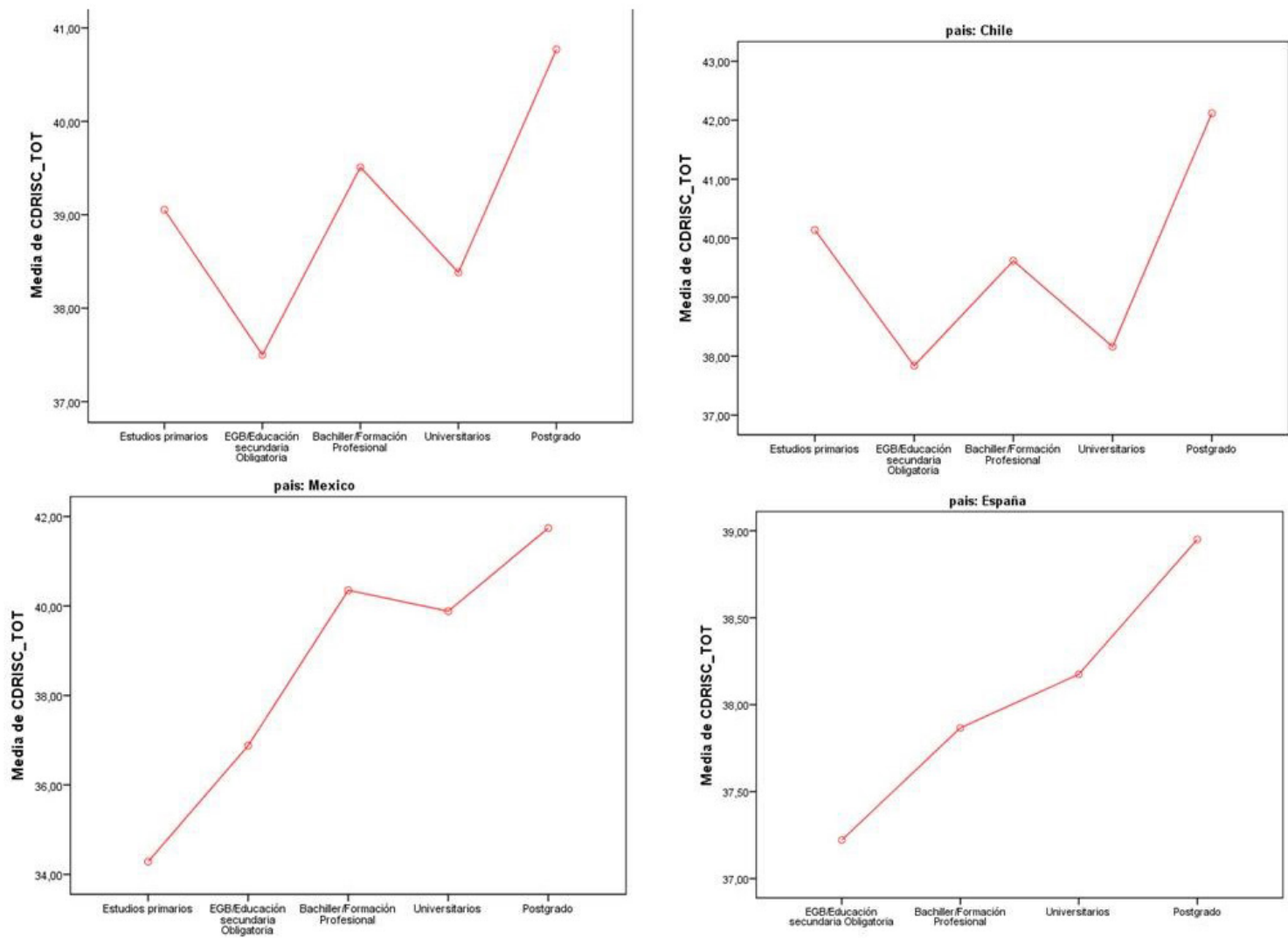
**Figure 1.** Level of education.
Source: Authors.

By analyzing these differences per country, it is possible to observe that Mexico reveals significant differences (F = 3.225; *p* < .05) in resilience levels depending on the level of education, according to a pairwise comparison, specifically between postgraduate studies and secondary school (*p* < .05).

The third analysis takes into account CD-RISC and the number of people in the same household during confinement. The descriptive results reveal a mean of 3.19 subjects (M = 3.19), with an interval from 0 to 12 people. Here, the correlation is not significant (r = .060, *p* < .05) in total, nor among countries. When comparing this data to marital status and performing a group analysis, the results indicate that single participants who live with more that

2 people show significant differences and a lower resilience level when compared to the other groups (*p* < .05).

### Conclusion

Promoting resilience from a neuroeducational perspective considers many internal, external, and community factors, as it has been revealed by this research paper. In the three participating groups the results are almost identical, with minimal statistically significant differences. This pseudo "non-significance" in the case of stress risk factors, as it is in the number of people living in the same household, evinces the role of resilience in the adaptation and flexibility when faced against stressful situations

such as confinement, regardless of context variables.

One interesting conclusion of this preliminary study, is that rather than confinement itself, the quality of the relationship among people living in the same household and the strategies they use to promote resilience to face confinement, is fundamental. In the same vein, the level of education can be interpreted as a protection variable associated with cognitive flexibility in a person.

In light of the findings of this research, it seems essential to establish a course of action that promotes resilience from an early age. As proposed in epigenetics, to immerse oneself in contexts full of meaningful bonds is key to improve vital processes, as it is the case of resilience.

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# Original article

# Executive Function evaluation in children with learning disabilities through a tablet assessment battery

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*Abstract*

Executive functions are a set of psychological processes that are necessary for the cognitive control of behavior: selecting and successfully monitoring behaviors that facilitate the attainment of certain goals. These skills are necessary to guide learning of new information. Core executive function (CEF) are inhibitory control, working memory and cognitive flexibility. They regulate and control other skills and behaviors, and also have influence on more basic skills such as attention, memory systems, and praxis. Executive functions allow setting goals and carrying them out through planning and monitoring, keeping inhibited thoughts, behaviors and emotions that interfere. This research consists of determining neuropsychological EF profiles in different clinical populations evaluated with tablet-based test. Two batteries developed by CEDETI UC were applied: Yellow Red and TENI (Infant Neuropsychological Assessment Test). The sample consists of 175 argentine children, between 7 and 12 years old, divided in two groups, clinical and control. The obtained scores show the importance of distinguishing profiles between these three CEF within the clinical population comparing with a typical developing group. The overall index obtained differentiates the groups best. Children with dyscalculia, autistic spectrum disorder and borderline intellectual disability obtain significantly lower scores having greater difficulties in EF.
**Keywords***: Executive functions; neuropsychological assessment; learning disabilities; tablet

## Evaluación de Funciones Ejecutivas en niños con dificultades de aprendizaje a través de una batería en formato digital

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*Resumen*

Las funciones ejecutivas permiten plantear metas y llevarlas a cabo a través de la planificación y el monitoreo de su desarrollo, manteniendo inhibidos pensamientos, comportamientos y emociones que interfieren. Son habilidades necesarias para guiar los procesos que permiten el aprendizaje de nueva información y están constituidas por el control inhibitorio, la memoria de trabajo y la flexibilidad cognitiva. Controlan y regulan otras habilidades y conductas, e influyen en habilidades más básicas como la atención, los sistemas de memoria y las praxias. Este trabajo de investigación consite en determinar perfiles neuropsicológicos en diferentes poblaciones clínicas a través de la aplicación de baterías de evaluación neuropsicológica en formato digital, que evalúan distintas funciones ejecutivas. Se aplicaron dos baterías desarrolladas por CEDETi UC: Yellow Red, y TENI (Test de Evaluación Neuropsicológica Infantil). La muestra consta de 175 niños de ambos sexos, entre 7 y 12 años, divididos dos grupos, clínico y control. Los puntajes obtenidos permiten determinar perfiles neuropsicológicos dentro de la población clínica. El índice global obtenido es el que mejor diferencia los grupos. Los niños con discalculia, trastorno del espectro autista e inteligencia límite obtienen puntajes significativamente más descendidos presentando mayores dificultades en las funciones ejecutivas.
**Palabras clave**: Funciones ejecutivas; evaluación neuropsicológica; dificultades de aprendizaje; tablet

## INTRODUCTION

*Executive Functions* (EF) comprise those skills that allow us to set goals and carry them out through permanent planning and monitoring during their development, keeping inhibit thoughts, behaviors and emotions that interfere with the achievement of their objectives. EF are critical to success in school, work, and in life. They are essential to carry out a reasoning, solve a problem, understand what we read or hear in a class, choose to be creative and self-regulate and flexibly adjust the information we receive (Burgess & Simons, 2005; Diamond, 2013; Espy et al., 2004; Miller & Cohen, 2001). EFs are needed when we have to concentrate and think, when acting on our initial impulse, relying on instinct or intuition, or going on automatic would be ill-advised, insufficient, or impossible. EFs depend on a neural circuit in which the prefrontal cortex plays a prominent role (Braver & Barch, 2002; Champod & Petrides, 2007; Miller & Cohen, 2001; Zanto, Rubens, Thangavel & Gazzaley, 2011).

EF are regarded as an umbrella term for top-down mental processes, which are necessary for all types of cognitive performance (Diamond, 2006; Diamond, 2013). EFs are able to predict the overall academic performance of student over time.

Core EF are formed by three specific cognitive abilities or functions: *working memory, inhibition* (self-control, resisting temptation and resisting acting impulsively) and *cognitive flexibility* (including creativity) seeing anything from different perspectives and quickly and flexibly adapting to changed circumstances (Diamond, 2013; Santa-Cruz & Rosas, 2017).

*Working memory* (WM) is the ability we have to hold in mind and mentally manipulate information over short periods of time. It is often thought as a mental workspace that we can use to store important information in the course of mental activities (Gathercole et al., 2008). This ability increases with age, and is essential to establish relationships between previous knowledge and new information (Carriedo, Corral, Montoro, Herrero, & Rucian, 2016), to establish non-obvious connections and to understand different types of expressions (Diamond, 2012; 2013). A sufficient capacity should have been acquired at the beginning of school to operate with the complexity required by the contents, particularly those related to learning the symbolization systems necessary to decode and to learn the numerical systems (Santa-Cruz & Rosas, 2017).

*Inhibitory Control* (IC) is the ability to ignore dominant, automatic or prepotent response that are irrelevant to task processing. It allows an individual to stay focused on the main task and prevents him from making automatic responses that do not fit the situation (Diamond, 2013). It distinguishes between cognitive inhibition, which is the control of emotions, thoughts and feelings that interfere with the course of thought or activity in the WM, and behavioral inhibition, which is the control exercised over actions. It directs consciously the attention, the course of thought, behavior and emotions. It has the effect of canceling both internal predispositions and the effect of the environment, which could lead us to carry out another task. Essentially, it consists of the ability to inhibit alternative thoughts, emotions and behaviors that distract us from the current task. It is therefore an attentional control measure (Diamond, 2013; Friedman & Miyake, 2004; Santa-Cruz & Rosas, 2017).

*Cognitive Flexibility* (CF) is the ability that allows an individual to adjust to the

demands of the environment efficiently (Miller & Cohen, 2001), creating and using alternative problem-solving strategies. In this sense, it allows a certain situation to be observed from multiple points of view (Diamond, 2012), changing behaviors directed towards a specific goal, the attentional focus or varying strategies according to the stimulus (McGowan et al., 2018). This skill includes a strong socio-affective component, as it includes the ability to understand solution strategies or understanding solutions that other people use. It is, therefore, a skill of both a cognitive and an affective nature. It has to do with empathy and creativity generating new solutions to solve a problem. (Santa-Cruz & Rosas, 2017). CF is also called set shifting, mental flexibility or mental set shifting, and it is built on WM and IC and it allows to change perspective and strategy to adjust to changes in external demands and take advantage of emerging opportunities (Diamond, 2012; 2016).

EFs monitor and control all behavior, and not just cognitive problem solving. The long and complex process of the development of the prefrontal cortex is related to the regulation of one's own emotions and social adequacy (Santa-Cruz & Rosas, 2017).

The evidence indicates that, from the age of 7, EF is progressively defined. Not until adolescence are children able to solve complex shifting tasks (Santa-Cruz & Rosas, 2017) nevertheless basic forms of CEF can be observed already in preschool years.

EF have an accelerated development during childhood, between the first and sixth year of life.

Also, a large body of research present evidence of a significant predictive effect of EF and academic performance (Reyes, Barreyro e Injoque-Ricle, 2015) and the importance of EF in learning processes (Fonseca, Rodríguez y Parra, 2016).

These studies evidence the relationship between cognitive skills and literacy learning and mathematical competences (Orbach, Herzog & Fritz, 2020; Risso et al, 2015)

The preschool stage represents a window of opportunity for intervention, enhancing the development of EF during childhood. This stage also has the advantage of being able to intervene through educational proposals in those children who, given the conditions associated with their SES, see the development of their EFs limited. It is from this perspective that preschool education has been proposed as a space where the development of skills and knowledge that facilitate the acquisition of learning in the later stages of schooling and subsequent socialization should be promoted (Blair, 2002). A series of studies has been found that relate the development of certain cognitive abilities with the subsequent development of executive functions, such as attention and language, as well as environmental factors such as socio-economic status and early experiences

Research lead by Colombo and Lipina (2005) with children in contexts of poverty, shows that these children present low performances in CEF tasks that require self-regulation, attention, inhibition, among others, and that it is important to develop preventive interventions in this regard (Colombo y Lipina, 2005; Lipina, 2008; Lipina y Segretin, 2015)

Attention is a construct closely linked to EFs and is cross-linked to them. Attention is a complex cognitive function, organized in a hierarchical way that allows filtering, selecting and inhibiting the information that is not relevant (Portellano, 2005). This cognitive function has been divided into focused attention, sustained attention, and divided attention (Posner & Petersen, 1990).

Bonifacci and Snowling (2008) compared speed and information processing in children in different groups (typical developing, dyslexics, and borderline intellectual disability groups). The children with borderline functioning were slower and more error prone compared to the other two groups and they showed greater variability in different tasks. Alloway (2010) found greater verbal and visuo-spatial WM deficits among individuals with borderline intellectual disabilities to typical developing children age 7 to11.

By assessing CEF by means of a tablet-based test in a large sample, the present research aimed to examine the role of CEF in different clinical groups.

## Purpose

The main goal of this study is to investigate the neuropsychological profile in different clinical populations through the Yellow Red and TENI assessment batteries, both in Tablet format, which evaluate different cognitive abilities related to EF and are within the paradigm of invisible evaluation through game (Rosas et al., 2015).

## Methodology

### Participants

Participants of the study were 175 children, (both girls and boys), between the ages of 6 and 12 years old.

They were divided in two samples, clinical sample and typical developing group (control group).

The clinical sample consisted of 135 children who have a clinical diagnosis including: Attention Deficit Disorder, Dyslexia, Dyscalculia, Borderline Intellectual Disability and Autism Spectrum Disorder.

Within the typical population, 43 children will be considered matched in age and sex with the clinical groups (Table 1).

### Procedure

The participants were assessed in a quiet room by trained researchers. Testing was completed in three sessions each lasting 35 minutes.

To confirm previous diagnosis the groups were tested specially.

TABLE 1.
*Sample Description.*

| Clinical Diagnosis | Frequency | Percentage |
|---|---|---|
| Control Group | 43 | 24,2 |
| TDAH | 36 | 20,2 |
| Dyslexia | 66 | 38,8 |
| Dyscalculia | 16 | 9,0 |
| ASD | 7 | 3,9 |
| Borderline Intelectual Disability | 7 | 3,9 |
| Total | 175 | 100 |

Source: Authors.

· *Dyslexia:*

Reading Fluency was assessed with PROLEC R (Cuetos, Rodríguez Ruano y Arribas, 2007) or LEE (Defior & Serrano, 2006) test in Spanish.

· *Dyscalculia:*

WISC IV Arithmetic subtest and WRAT 3 (Wilkinson, Helman & Ross, 1993), Math Achievement Test.
ADD (Attentional Deficit Disorder) SNAP IV (Grañana et al., 2011).
*ASD*: ADOS (Gotham, Pickles & Lord, 2009).

· *Borderline intellectual disabilities:*

WISC IV (Wechsler, & Corral, 2015). (IQ: 70-79). All children were previously evaluated with WISC-IV. Parents and guardians were contacted directly and signed the informed consent.

· *Core Executive Functions:*

Core executive functions were measured with the tablet-based Yellow Red Test (Rosas, Espinoza y Garolera, 2020).

*Yellow Red* is an assessment battery made up of 4 tasks specially designed to test the core EF. These tasks are focused both on the general evaluation of EF and on the specific evaluation of its different components: CI, WM, CF and the global index of EF (Figure 1).
The reliability (internal consistency) of the Yellow Red Test was $\alpha = 0.80$ to $\alpha = 0.86$. Higher values refer to higher abilities.
*TENI (*Infant Neuropsychological Assessment Test) is an assessment tool that consists of 6 sub-tests to establish a cognitive neuropsychological profile identifying strengths and weaknesses (Tenorio, Arango, Aparicio y Rosas, 2012). The participants were tested on two tasks that focus on attention skills, specifically sustained and focused attention (Figure 1).
Statistical analysis was performed using IBM SPSS Statistics (Version 24).

## Results

The significance of the Bonferroni tests (post ANOVA) of each neuropsychological profile with respect to the control group in the tasks evaluated by the YR battery are shown in the Table 2. A $p < 0.05$ was taken as a significant value. n.s. = not significant.

Table 2.
*Results.*

| Results | TDAH | Dyslexia | Dyscalculia | ASD | BID. |
|---|---|---|---|---|---|
| Trios-CF | n.s. | n.s. | n.s | n.s. | p = 0.017 |
| Binding WM | n.s. | n.s. | n.s. | n.s. | p = 0.022 |
| Arrows IC | n.s. | n.s. | p < 0.001 | n.s. | p < 0.001 |
| G & P EF global | n.s. | n.s. | n.s. | p = 0.007 | p = 0.002 |
| Gobal Index | n.s. | n.s. | p < 0.001 | p = 0.004 | p < 0.001 |

Source: Author.
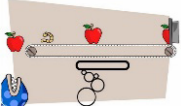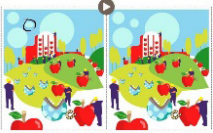
| YellowRed | |
|---|---|
| **Arrows**<br> | A big arrow pointing in one of four possible directions (up, down, left and right) was presented on the top of the screen Participants were instructed to press the smaller arrow in the bottom of screen. (out of three smaller arrows) that was pointing in the same direction as the big arrow. If the big arrow were pointing down the participant was not to press any button but was to wait until the next big arrow appeared.<br>The task included 36 items, of which 8 items were inhibition tasks. This task evaluates CI. |
| **Binding**<br> | Participants had to recall an increasing number of paired associations between numbers and images, which were visually presented for 5 s. To do so they had to push the correct number under the appropriate symbol or figure without a time limit. The order of the symbols/figures occasionally changed between the presentation and recall phases. The task comprised 27 items of increasing difficulty, a factor that was considered in the computation of scores.<br>This task assesses WM. |
| **Trios**<br> | Participants were instructed to select three out of four figures on the basis of similarity. Four different figures (square, triangle, circle, pentagon), in four different colors (blue, red, yellow, green) and two sizes (big, small) were presented. The task included four rounds (each round having 12 items) of changing categorization principles (shape → color → size → mixed). During the task, the categorization principle changed discreetly without any information to that effect being given. For each item the participants received a visual feedback, whether the item was correct or incorrect. CF. |
| **Cats and Dogs**<br> | A cat or a dog was presented on the right- or left-hand side of the screen participants were instructed to press the button on the opposite side the dog appears. The task procedure was rehearsed in separate trials before the assessment proper was begun. The stimuli were presented at one second intervals. This test is a global index of executive functions as it works with both WM, IC and FC. |
| TENI | |
| **Duno and the worms**<br> | A conveyor belt appears in the screen with apples passing by. The participant has to touch the screen each time he detects apples with a worm during a period of six minutes. Sustained attention is necessary to solve this task, identifying target and not target. |
| **Alternative Universes**<br> | Two pictures apparently equal are showed in the screen. The participant has to identify differences. The child must point out the differences between each pair of pictures and touch them. The difficulty increases item by item. The child has to quickly identify what the difference is. It is the indicator of attention focus (AC). |

**Figure 1.** Tasks description.
Source: Author.

| | Trios | Binding | Arrows | Catdog | Indice Global |
|---|---|---|---|---|---|
| Grupo control | 54 | 62 | 53 | 51 | 58 |
| TDAH | 53 | 57 | 50 | 48 | 53 |
| Dislexia | 53 | 56 | 51 | 49 | 54 |
| Discalculia | 47 | 52 | 42 | 43 | 44 |
| TEA | 41 | 53 | 48 | 35 | 41 |
| BID | 32 | 44 | 28 | 32 | 24 |
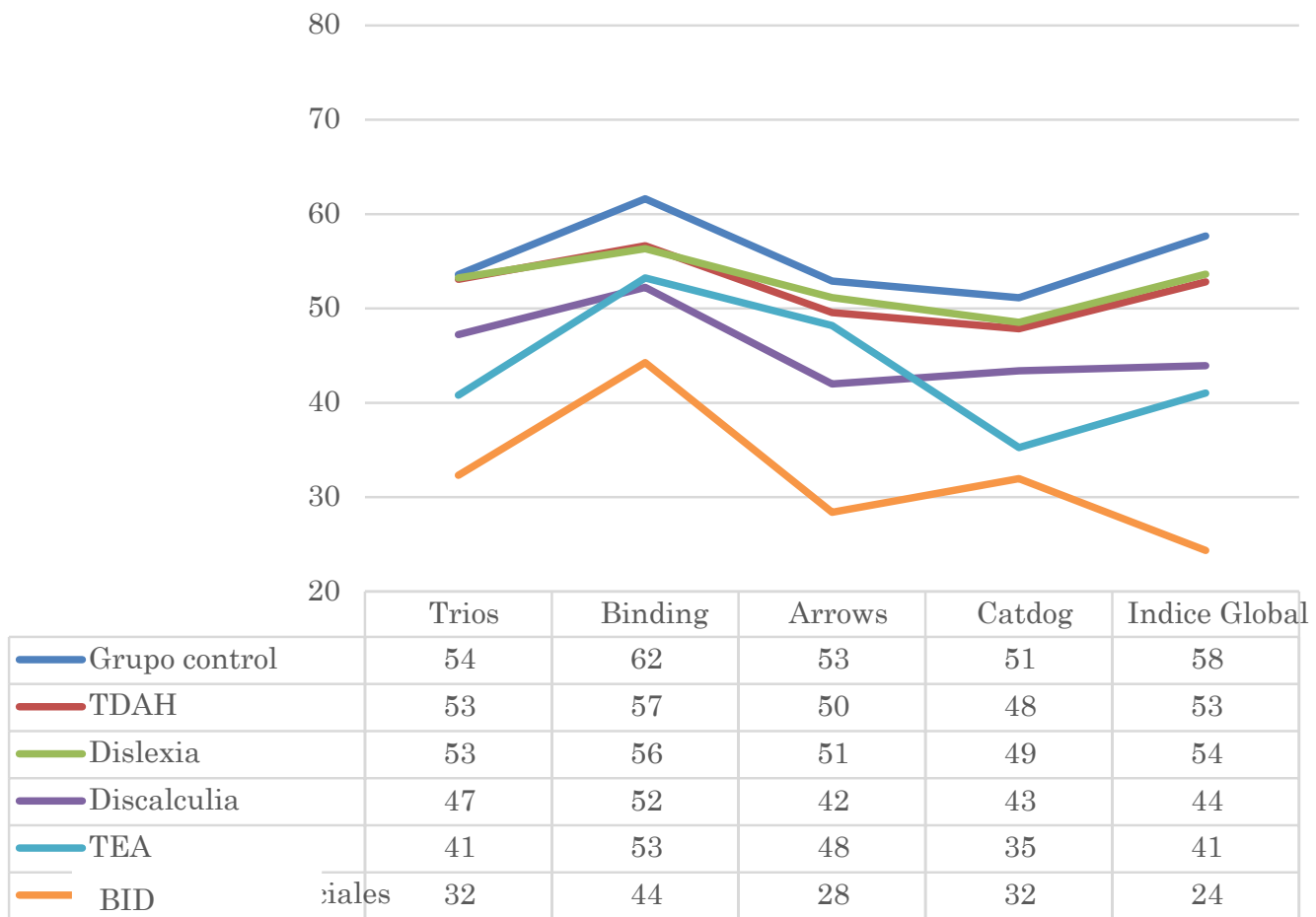
**Figure 2.** Comparison between groups with clinical diagnosis and control group
Source: Author.

For the comparison of different diagnoses and the control group, the standard test scores were used (Mean 50 and Standard Deviation: 10).

In order to better compare the different groups in each task, means are taking into account according to the different subtests in the different diagnoses and in the control group.

The Figure 2 above shows the comparisons of groups diagnosed with Attention Deficit Hyperactivity Disorder (ADHD), dyslexia, dyscalculia, Autism Spectrum Disorder (ASD) and Borderline Intellectual Disability (BID). For ADHD and dyslexia, the only test that shows a notable difference comparing the CG, are the WM test and the global index. In both populations, CF has not difference to the control group. In the case of dyscal-culia, all the tests are more than a half SD below the average, highlighting cognitive inhibition and the global index as the most significant measure. In the case of ASD, the two general indicators of executive functions (Cat and dogs, global index) are greatly diminished. CF is also greatly diminished, while WM is at a one DS under the control group and cognitive inhibition at a half DS. Finally, the participants with IL show a decrease of more than 1 SD in all indicators, reaching more than 3 DS low in average in the case of the global index.

## DISCUSSION

Results in this study illustrate the multidimensional nature of EF developing.

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According to the results, we can determine that within each neuropsychological profile there are differences in CEF comparing with typical development group.

The Trios (FC) and Binding (Nexos) (MT) tasks only show significant differences and are affected in children with BID. The Arrow Task (IC) only in children with Dyscalculia and BID. Cats & Dogs (FE) task in the ADS and BID profiles.

Regarding the Global Index, there are significant differences in children with Dyscalculia, ASD and BID, comparing to the typical development population scores.

Regarding the Dyslexia and ADHD profiles, no significant differences were observed with respect to the typical development group in these tasks evaluated in YR, although they did provide a notable difference in the working memory task and in the global Index.

Children with ADHD obtain scores close to CG, because the tasks contained in the YR (digital format, attractive and challenging) do not require attentional support, which is what is affected in children with this profile. It remains to establish what happens with these children in the data obtained with the Infant Neuropsychological Assessment Test-TENI (Tenorio et al., 2012), in tasks that evaluate selective and sustained attention, and its correlation with the Yellow Red.

When comparing the performance in each subtest in the different groups, it can be seen that the control group is the one that obtains the best results in all the tasks and is close to the average standard score of 50.

The performances of children with dyslexia and ADHD obtain results close to the CG and the difference between groups is less than one standard deviation in all the subtests and in the global index, obtaining a remarkable difference in the WM tasks and in the global Index.

Children with dyscalculia present significantly low performance in all subtests and in the global index, with scores being observed one standard deviation below the control group.

Children with ASD obtain a significantly low score on the global index and the lowest score is observed in the Dog and Cats task, the score being two standard deviations below the control group. On the contrary, its best performance is observed in the Bindig (Figure 1) task.

Children with the lowest performance are those with Borderline Intellectual Disabilities (BID). All their scores are at least 3 standard deviations from the control group. These children belong to a low socioeconomic status unlike the rest of the evaluated children who belong to a medium / medium-high socioeconomic status and their general cognitive performance corresponds to borderline scores.

In summary, the preliminary analyzes show us that the Yellow Red battery allows us to differentiate the different diagnoses of the control group, and the global index is the one that best marks the difference between the groups. Children with dyslexia and ADHD show slightly lower scores compared to the control group in all subtests, not being statistically significant. On the contrary, the diagnoses of dyscalculia, ASD and Borderline Intellectual Disability (BID) are those that obtain scores significantly below the control group. It reveals that they present greater difficulties in the skills that integrate core executive functions: cognitive inhibition, memory of work and flexibility.

Therefore, the scores obtained made it possible to determine neuropsychological profiles within the atypical population according to each diagnosis through the Yellow Red battery assessing different cognitive abilities related to executive functions.

According with several studies where a significant predictive effect of executive functions and academic performance has been proved (Reyes et al., 2015) and the importance of executive functions in learning processes (Fonseca et al., 2016), we highlight the importance of these results confirming that the Yellow Red test is an adequate instrument to assess EF. Yellow Red is suitable to specify different neuropsychological profiles, differentiating them from the typical population, with the aim of designing and executing intervention strategies adjusted for ameliorating these difficulties. Considering that the proper development of these functions is one of many indispensable variables for school success.

The analysis of the data obtained with the TENI battery and its correlation with the Yellow Red and the WISC IV or WISV V scores in the different diagnoses is pending.

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## Original article

# Self-awareness, depression and neurocognitive functions in patients with moderate and severe traumatic brain injury

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*Abstract*

Introduction: Traumatic Brain Injury (TBI) is the most common cause of disability in young patients. In the self-awareness deficits that can arise after TBI, patients experience difficulties in understanding the disabilities resulting from their injury. This is an important problem that affects the rehabilitation processes. Materials and methods: Self-awareness, neurocognitive functions and depressive symptoms were observed in 31 outpatients with a diagnosis of moderate or severe TBI, aged between 16 and 45 years. Instruments: Patient Competency Rating Scale (PCRS), Neurocognitive Assessment and Hamilton Depression Rating Scale (HDRS). Results: Correlations were found between self-awareness and its dimensions with visuospatial skills, executive functions (double task and cognitive inhibition), episodic memory (Rey Auditory-Verbal Learning Test and Montevideo short story) and depressive symptoms. Conclusions: Patients who have suffered a moderate or severe TBI may have impaired self-awareness. Self-awareness is the ability to objectively perceive (perceive our own self), while maintaining a sense of subjectivity, It is a complex function that needs to use executive functions and episodic memory. The relationship found between interpersonal self-awareness and depressive symptoms does not seem to be conclusive, since this association is probably more complex, and involves other variables not considered in this study.
**Keywords**: Depression; neurocognitive functions; self-awareness; traumatic brain injury

## Autoconciencia, depresión y funciones neurocognitivas en pacientes con traumatismo encefálico-cráneo moderado y severo

*Resumen*

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Introducción: Los Traumatismos Craneanos-Encéfalicos (TCE) constituyen la causa más común de discapacidad en pacientes jóvenes. En los déficits de autoconciencia, los pacientes experimentan dificultades para comprender sus discapacidades. Este es un problema clínico que afecta los procesos de rehabilitación. Materiales y Métodos: Se observó la autoconciencia, funciones neurocognitivas y sintomatología depresiva en 31 pacientes con diagnóstico de TCE moderado o severo, con edades 16 y 45 años. Instrumentos: Índice de Competencia del Paciente, evaluación neurocognitiva y Escala de Depresión Hamilton. Resultados: Se encontraron correlaciones entre autoconciencia y sus dimensiones con habilidades visuoespaciales, funciones ejecutivas (doble tarea e inhibición cognitiva), memoria episódica (aprendizaje audioverbal y cuento corto Montevideo ) y sintomatología depresiva. Conclusiones: Los pacientes que han sufrido un TCE moderado o grave pueden tener alteración de la autoconciencia. La autoconciencia es la capacidad de percibirse objetivamente (percibir nuestro propio self), manteniendo al mismo tiempo un sentido de subjetividad, es una función compleja que necesita servirse de funciones ejecutivas y de memoria episódica. La relación entre la autoconciencia interpersonal y sintomatología depresiva, no parece ser concluyente, dicha asociación es más compleja, e involucra otras variables no contempladas en este estudio.
**Palabras clave**: Autoconciencia; depresión; funciones neurocognitivas; traumatismo craneoencefálico

## INTRODUCTION

Traumatic Brain Injury (TBI) represent a major health problem and are one of the leading causes of death and disability worldwide, mainly in young people. People who survive a TBI may suffer a lifelong disability, mainly due to disorders, sensory motor, neurocognitive, self-awareness, psychological and social cognition (Azouvi, Arnould, Dromer & Vallat-Azouvi, 2017; Roozenbeek, Maas & Menon, 2013).

In Impairment Self-Awareness deficits (ISA) that can arise after TBI, patients experience difficulties in understanding the disabilities resulting from their injury and the impact these deficiencies have on their functional capacity, these characteristics make these patients very difficult to treat in rehabilitation plans (Noé et al., 2005; Prigatano, 2005; Prigatano & Sherer, 2020; Vales, 2020). They fail to assess their neurobehavioral competencies, particularly with regard to cognitive and social functioning, they have a reduced ability to adopt the perspective of another person (Bivona et al., 2014; Chesnel et al., 2018).

### Self-awareness from cognitive neuroscience

Self-awareness is commonly affected after a TBI, this is an important clinical problem because it affects and limits the rehabilitation processes. In a meta-analysis carried out on self-referential processing (Northoff et al., 2006), it was found that the structures of the midline of the cerebral cortex that would be a correlate of the "core" of the self, are in turn linked, both with the processing of "reading" one's own mind, as well as that of others. In another meta-analysis of functional neuroimaging studies on the self, on their own or others' judgments, they were associated with a spatial gradient of the activity of the medial prefrontal cortex, which goes from the ventral to the dorsal extension, as well as the common activation of the left temporoparietal junction and posterior cingulate (Denny, Kober, Wager & Ochsner, 2012). In another study of the neural bases in the impairment of self-awareness in TBI patients, she postulates that it was not explained by the location of the focal brain lesion, nor by the amount of traumatic diffuse axonal lesion, but by the breakdown of the functional interactions between the nodes within the fronto-parietal control network (Ham et al., 2014).

Self-awareness can be defined as:

> The capacity to perceive the "self in relatively "objective" terms while maintaining a sense of subjectivity, this will be a natural paradox of human consciousness: on the one hand, it seeks "objectivity", that is, the perception of the situation and at the same time the sense of a private, subjective interpretation of an experience. "Self-awareness or awareness of higher brain functions involves an interaction of thoughts and feelings" (Prigatano & Schacter, 1991, p. 13).

This definition implies that self-awareness is a complex phenomenon that covers cognitive and emotional aspects. Therefore, what would be the relationship with the neurocognitive functions that support self-awareness? As well as what emotional aspects would be involved.

Self-awareness is a complex function, in its alteration there is a lack of subjective experience of the deficiencies due to the lack of integration of "feelings and thoughts", by the underlying neurocognitive and emotional aspects. The emotional reaction in these patients can be greatly diminished or absent altogether, they are often described as "neutral" or "perplexed" when indicated or asked about their neuropsychological de-

ficiencies and associated behavioral disturbances. They appear "insipid", "apathetic" or "indifferent" to a deficiency that is obvious to an observant clinician (Prigatano & Sherer, 2020).

In this sense, it is relevant to study the mood, since it has an important link with the patient's social functioning (Carroll & Coetzer, 2011; Ylvisaker & Feeney, 2000); sadness may appear as a reaction to the loss of their previous identity, their family and social role, and therefore their possible relationship with self-awareness.

In a study on the evaluation of a treatment on self-awareness, it is postulated that the level of self-awareness before treatment was related to the recognition of emotions (Lamberts, Fasotti, Boelen & Spikman, 2017). In another study, the hypothesis is proposed that self-awareness is not usually associated with depression and anxiety, but rather with apathy and cognitive inflexibility (Bivona et al., 2019), as did another study where no association with depression was found (Geytenbeek, Fleming, Doig & Ownsworth, 2017).

Although the research of Bach and David (2006) speaks of a certain independence of self-awareness with executive functions, there are studies that propose its relationship with some of the underlying neurocognitive functions that support or would be related to self-awareness, such as episodic memory and executive functions (such as semantic verbal fluency and cognitive flexibility) (Bivona et al., 2019; Zimmermann, Mograbi, Hermes-Pereira, Fonseca & Prigatano, 2017).

However, in a study conducted four years after TBI, with 90 patient-family pairs, the lack of self-awareness only significantly influenced the burden perceived by the family member, and was not related to the severity of the initial trauma, the sociodemographic data, the severity of impairments (neurocognitive and mood), limitations of activity or participation or quality of life of the patient (Chesnel et al., 2018).

Therefore, it is important to carry out studies on the structures and processes related to self-awareness, in such a way that they allow the construction of models and / or theories that permit a better understanding and treatment of these patients.

## METHODOLOGY

### Objective

Describe and analyze self-awareness and its relationship with neurocognitive functions and depressive symptoms in moderate or severe TBI patients.

### Patients and methods

Outpatients with a diagnosis of moderate or severe TBI according to the Glasgow Scale score, who attended the Neuropsychology Department of the Hospital de Clínicas (Montevideo - Uruguay) between April and December 2016, accepted and signed the informed consent, age between 16 and 45 years, 6 months or more after the TBI, sensory resources (seeing and hearing) that allow you to perform the tests normally, and a valid companion who can provide reliable information.

### Instruments

An initial interview was carried out, where ethical aspects of the research were raised and the pertinent tests began to be carried out in case of acceptance.

*Patient information collected in the initial interview*: age, sex, marital status, years of schooling, manual dominance, Glasgow score, neurosurgery, time of evolution of TBI.

*Neurocognitive functions*: The patients were evaluated with a specific neuropsychological protocol that consisted of the evaluation of the following functions.

· *Attentional processes and executive functions*

• Digits backward (Wechsler, 2002).

• Symbol digit (Lezak, Howieson, Bigler & Daniel, 2012).

• TMA and TMB (Lezak et al., 2012; Tombaugh, 2004).

• Stroop test (Stroop, 1935).

• Verbal fluency task by letter and semantic categories (letter P and Animals) (Marino & Alderete, 2010).

• Complex Figure Rey-Osterrieth (CFRO)-copy strategy (Lezak et al., 2012).

• Similarities (Wechsler, 2002).

· *Working memory*

• Digits Forward (Wechsler, 2002).

· *Episodic memory*

• CFRO evocation.

• Short story Montevideo (MDV) (Dalmás, Fontán & Bocos, 1989).

• Rey Auditory-Verbal Learning Test (AVLT) (Lezak et al., 2012; Rey, 1964).

· *Visuoconstructive skills*

• CFRO.

• Clock drawing test (Lezak et al., 2012).

Patient Competency Rating Scale (PCRS):

It is a 30-question self-report scale, assesses the patient's level of competence and self-awareness after a brain injury.

Each question is answered according to a 5-point Likert type scale: which goes from 1 = "cannot do it" to 5 = "can do it without problem". Both the version for the patient and for the companion are the same, except that the questions change to refer to the patient's attitude (Prigatano & Fordyce, 1986). There is a validated version in Spanish (Ramírez & Ostrosky, 2008).

It has 4 dimensions: Interpersonal Relationships (IntP), Activities of Daily Living (ADL), Cognitive functioning (Cog) and Emotional functioning (Emot).

A PCRS score is obtained for the patient (PCRS-P) and another for the valid relative or companion (PCRS-F), each with its corresponding dimensions. The self-awareness value results from the difference between PCRS-P - PCRS-F, and there is also a self-awareness that corresponds to the differences between each dimension.

This scale has been used in another study very satisfactorily in the TBI population at the Hospital de Clínicas in Montevideo (Diarce, Dansilio & Vales, 2016), and in different studies with TBI patients (Bach & David, 2006; Bivona et al., 2015; Fleming, Strong & Ashton, 1996).

Hamilton Depression Rating Scale (HDRS): It is a scale for the assessment of depressive states - depressive symptomatology, with the aim of quantitatively assessing the severity of symptoms and assessing the changes in the depressed patient. It is valued according to the information obtained in the clinical interview and accepts complementary information from other secondary sources. In this research, information is taken from the companion, for this reason this scale is used and not the Beck self-administered depression inventory, be-

cause many TBI patients may have deficits in their self-awareness and / or have anosognosia of their current state.

Its original version consisted of 21 items, but the 17-item version is the most used, each item has between three and five responses, with a score of 0-2 or 0-4 respectively. The total score ranges from 0 to 52 (Hamilton, 1960).

In turn, the Spanish version of this scale has been validated (Ramos-Brieva & Cordero-Villafafila, 1988), and has been used with patients with acquired brain injury (Mauri, Paletta, Colasanti, Miserocchi & Altamura, 2014).

### · Statistic analysis

Shapiro Wilk Test is applied to examine the normality of the variables. Student's t test is used to compare groups with normal distribution, and Wilcoxon test for non-normal distribution. Pearson's correlation coefficient is used to correlate variables with normal distribution, and Spearman's coefficient for non-normal distributions.

### Ethics

The present study and its corresponding informed consent were approved by the Ethics Committee of the Hospital de Clínicas belonging to the University of the Republic, in the city of Montevideo (Uruguay) on April 6, 2016.

### Results

31 patients (20 men and 11 women) participated in this study, with an average age of 30.87 years, 23 of them single, 4 with a partner and 4 divorced, the years of schooling ranged between 2 and 16

years, the average being 8, 19 years old, 26 were unemployed, 3 with a pension, one with a medical license, only one was employed, 29 were right-handed, 2 were left-handed.

Regarding data related to TBI, the mean score of the Glasgow scale was 6.59 + - 2.91 (21 severe, 10 moderate), 19 patients underwent neurosurgery, the mean evolution time was 48 months, 27 they were due to traffic accidents, 3 due to a gunshot wound and another due to domestic violence.

TABLE 1.
*Results of the neurocognitive evaluation*

| Test or scale | Mean (SD) | Median |
|---|---|---|
| Digits Backward | 3.2 (0.89) | 3 |
| Trail Making A (TMA) | 110 (53.26) | 101 |
| Trail Making B (TMB) | 212.6 (65.48) | 210 |
| Stroop test | 48.26 (14.85) | 50 |
| Verbal fluency task (animals) | 12.03 (4.37) | 11 |
| Symbol digit | 19.82 (6.63) | 19 |
| Clock post interference evocation test | 6.812 (2.99) | 8.5 |
| Similarities (Wechsler) | 13.16 (4.62) | 13 |
| Digits Forward | 5 (1.08) | 5 |
| Short story Montevideo immediate evocation | 6.86 (3.98) | 6 |
| Short story Montevideo deferred evocation | 4.63 (4.29) | 3.5 |
| Rey Auditory-Verbal Learning Test post interference evocation | 34.14 (9.52) | 34 |
| Rey Auditory-Verbal Learning Test total score | 34.14 (9.52) | 34 |

Source: Authors.

TABLE 2.
*Competence according to the patient and the family member, self-awareness and its dimensions*

| Test o scale | Mean (SD) | Median |
|---|---|---|
| Patient competence reported by the patient (PCRS-P) | 116.19 (25.60) | 126 |
| Patient competence reported by the family member (PCRS-F) | 110.26 (24.82) | 115 |
| Self-awareness (SA) | 5,94 (25.83) | 5 |
| Self-awareness of activities of daily living (SAdla) | 2.36 (11.73) | 2 |
| Interpersonal Self-awareness (SAi) | 2.16 (8.68) | 1 |
| Cognitive Self-awareness (SAc) | 0 (5.42) | 0 |
| Emotional self-awareness (SAe) | 1.42 (7.05) | 2 |

Source: Authors.

TABLE 3.
*Significant correlations between self-awareness, neurocognitive functions and depressive symptoms*

| Correlations | r | p |
|---|---|---|
| SA - Clock drawing test | +0.52 | 0.04 |
| SAi - TMB | -0.57 | 0.02 |
| SAi – Rey Auditory-Verbal Learning Test - total score (AVT) | +0.43 | 0.05 |
| SAc – Stroop test | -0.53 | 0.01 |
| SAc - Short story Montevideo - immediate evocation (MVDI) | +0.41 | 0.03 |
| Depressive symptoms (HDRS) – PCRS-P | -0.43 | 0.02 |
| Depressive symptoms (HDRS) – PCRS-F | -0.48 | 0.01 |
| Depressive symptoms (HDRS) – SAi | +0.38 | 0.03 |

Source: Authors.

Regarding depressive symptoms according to the Hamilton depression rating scale (HDRS), the average value was 10.39 with a standard deviation of 7.2 and a median of 9 (Tabla 1, Tabla 2, Tabla 3).

*Associations with low and high levels of impairment self-awareness*

With the absolute value of self-awareness and its dimensions, the median was taken, and two groups were differentiated: a group with low Impairment Self-Awareness (ISA) (values lower than the median) and a group with high ISA. (values greater than and equal to the median). Student's t or Wilcoxon tests were performed for low and high levels of ISA - with neurocognitive functions and depressive symptoms.

A significant difference was found ($p = 0.02$), the group with low ISA had a higher value in post-interference Rey Auditory-Verbal Learning Test (AVPI) (mean = 7.63 $SD$ = 4.31) compared to the group with high ISA (mean = 3.92 SD = 2.43).

In turn, a significant difference was found ($p = 0.04$), the group with low ISA had a lower value in the trail making A (TMA) (mean = 89.64 $SD$ = 32.80) compared to the group with high ISA (mean = 129.00 $SD$ = 62.24).

## DISCUSSION

In the present study, 52% of the patients studied presented an impairment self-awareness (Ramírez & Ostrosky, 2008), these difficulties are related to what was described by other authors when studying self-awareness in patients with TBI (Bach & David, 2006; Bivona et al., 2015; Fleming et al., 1996).

According to the results, when evaluating the neurocognitive functions, some outstanding results could be observed. In reference to visuoconstruction, the clock drawing test was used, which has been a test originally used to explore the unilateral visuospatial inattention most commonly associated with right parietal dysfunction, however it is also a complex task that is sensitive to a variety of injuries, incorporating not only visuo-perceptual and visuospatial skills, but also receptive language, numerical knowledge, working memory and executive functions (Lezak et al., 2012). There have been studies with the clock drawing test with TBI patients, finding that there are deteriorations in the performance of said test (De Guise et al., 2010, 2011). It should be noted that in this study, the quantitative value is taken into account, which is often less useful to identify the location of focal lesions (for example, right versus left, anterior versus posterior, or cortical versus subcortical), not thus the qualitative ones (Lezak et al., 2012). The association of self-awareness with the clock drawing test may not only have to do with visuospatial functions, but also with the different functions that the clock assesses previously described.

An association was found between the interpersonal dimension of self-awareness and tests of an executive functions (double task and cognitive inhibition), low and high levels of self-awareness deficit are associated with processing speed, as well as tests of episodic memory and learning audioverbal and memory of the short story of Montevideo. The analysis of these associations is linked to the previous section, although there are also studies that have found deficits in these neurocognitive functions with patients with low levels of self-awareness (Bivona et al., 2014).

Self-awareness, as mentioned above, can be defined as the ability to objectively perceive (perceive our own self), while maintaining a sense of subjectivity (Prigatano & Schacter, 1991). This ability to perceive oneself is linked to consciousness, as a process that fluctuates between two variants. For Damasio (2010) there would be a consciousness centered on the here and now, it is the feeling of being and being in a moment, and Another consciousness of consciousness, that is, a consciousness that evaluates that central or nuclear consciousness (called expanded, extended or autobiographical consciousness), for this it accesses the past to our memory and projects and tries to anticipate the future, providing an elaborate the feeling of what happens, linked to their identity and personality (Damasio, 2010). By accessing the past, it takes the memories, links them and relates them to the central consciousness, that is, to what is happening at this moment. Without these memories we would not have a sense of the past or future, and there would be no historical continuity, there would be no self-awareness (Damasio, 2010; Tirapu-Ustárroz & Goñi-Sáez, 2016).

The development and concept of self-awareness described above would imply that it would need to use neurocognitive functions for its functioning, as shown in this study, as well as others already mentioned (Bivona et al., 2019; Zimmermann et al., 2017).

In this study, depressive symptoms were also evaluated using the Hamilton Depression Rating Scale (HDRS). The mean HDRS was not very high (mean = 10.39 SD = 7.20), registering 61% of patients without depressive symptoms, 30% with mild symptoms and 9% with moderate symptoms. These data differ from some studies where they have found a higher prevalence of depressive symptoms in TBI patients (Carroll & Coetzer, 2011; Malec, Testa, Rush, Brown

& Moessner, 2007). In turn, no associations were found with neurocognitive functions.

According to the literature reviewed, there is controversy among the authors whether depressive symptoms are associated with difficulty in self-awareness. In a study with TBI patients, where identity changes and self-awareness are exploited after a TBI, an association has been found between self-awareness and depressive symptoms (Carroll & Coetzer, 2011). However, other authors do not associate self-awareness difficulties with depressive symptoms (Bivona et al., 2019), but with the apathy produced by the same TBI (Prigatano & Sherer, 2020).

In the present study, an association between depressive symptoms and ISA was evidenced in interpersonal relationships. In other words, the higher the interpersonal ISA the patient would have more depression. This finding could be contradictory, since an inverse association between both concepts would be expected, that is to say that the patient when making contact with their interpersonal difficulties (interpersonal self-awareness) would have higher levels of depression.

On the other hand, the patient's depression was negatively associated with the patient's competence both perceived by the patient and by the family member, showing the importance of interpersonal relationships for the patient. This last result is in line with the study of impairment of self-awareness that occurs four years after TBI, which is related only to the burden of the family member and not to other variables (Chesnel et al., 2018).

This data probably implies that the relationship between self-awareness and depression is more complex, involving elements not explored in this study.

## CONCLUSIONS

Self-awareness " or awareness of higher cerebral functions thus involves an interaction of "thoughts" and "feelings ... that it is the highest of all integrated functions" (Prigatano & Schacter, 1991). For this, self-awareness needs to be used for neurocognitive functions for their functioning. This study shows a possible link with visuo-perceptual and visuospatial skills (clock drawing test), executive functions (double task and cognitive inhibition) and episodic memory (Rey Auditory-Verbal Learning Test and Short story of Montevideo), as in other studies (Bivona et al., 2019; Zimmermann et al., 2017).

Although our analysis reveals an association of interpersonal self-awareness with depression, contradicting other research (Bivona et al., 2019; Geytenbeek et al., 2017). This finding does not seem to be conclusive, since the aforementioned association is probably more complex, and involves difficulties linked to the subjective experience that self-awareness implies, resulting in a person making decisions and behaviors experiencing reactions that negatively impact their functioning in daily life (Prigatano & Sherer, 2020) or as other research suggests, that self-awareness is related to apathy and executive functions and not to depression (Bivona et al., 2019).

Given the relationship between depression and the patient's competence, congruent with the study that relates self-awareness with the overload of the family member with TBI (Chesnel et al., 2018), it is important to have therapeutic strategies that allow the impairment self-awareness of patient as well as involved aspects of the family member or caregiver.

Deepening the study of neurocognitive functions and their relationship with self-awareness would allow the design of intervention strategies that benefit patients with TBI.

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# Original article

JOURNAL OF APPLIED COGNITIVE NEUROSCIENCE

# Predictors of favorable response to implanted of ventriculoperitoneal shunt in patients with idiopathic normal pressure hydrocephalus

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*Abstract*

Introduction: The indication of a ventriculoperitoneal shunt (VPS) is discussed in patients with idiopathic normal pressure hydrocephalus (iNPH), due to the heterogeneity of the response to treatment and the risks involved in neurosurgery. Objective: To search for clinical factors and complementary studies in order to determine predictors of a favorable response to the VPS placement in patients with iNPH. Methodology: A retrospective study of patients with probable iNPH (according to international guidelines) treated with VPS assisted in a neurological clinic from January 2014 to January 2017 was conducted. A univariate statistical analysis of the variables considered as possible prognostic factors was performed. Results: 58 patients were included. Women presented 3.68 times more chances of improvement after the VPS (p=0.019). Good response to the gait test was associated with better response to the VPS (p=0.024). Conclusions: Female sex and good response to the gait test could be considered as predictors of a favorable response to the VPS placement in patients with iNPH. A prospective study is necessary to achieve a homogeneous diagnostic evaluation and a more extensive longitudinal follow-up to evaluate the clinical evolution in this group of patients.
**Keywords**: Idiopathic normal pressure hydrocephalus; ventriculoperitoneal shunt; cognitive impairment; gait disorder; neurosurgery

## Predictores de respuesta favorable a la colocación de derivación ventriculoperitoneal en pacientes con hidrocefalia normotensiva idiopática

*Resumen*

Introducción: La indicación de la derivación ventriculoperitoneal (DVP) se discute en pacientes con hidrocefalia normotensiva idiopática (HNTi), debido a la heterogeneidad de la respuesta al tratamiento y los riesgos que conlleva la neurocirugía. Objetivo: Búsqueda de factores clínicos y estudios complementarios, para determinar predictores de respuesta favorable a la colocación de DVP en pacientes con HNTi. Metodología: Estudio retrospectivo de pacientes con probable HNTi (según guías internacionales) tratados con DVP asistidos en una clnica neurológica desde enero de 2014 hasta enero de 2017. Se realizó un análisis estadístico univariado de las variables consideradas como posibles factores pronósticos. Resultados: se incluyeron 58 pacientes. Las mujeres presentaron 3,68 veces más posibilidades de mejora tras la DVP (p=0,019). La buena respuesta a la prueba de la marcha se asoció con una mejor respuesta a la DVP (p=0,024). Conclusiones: el sexo femenino y la buena respuesta a la prueba de la marcha podrían considerarse predictores de una respuesta favorable a la colocación de la DVP en pacientes con HNTi. Es necesario un estudio prospectivo para lograr una evaluación diagnóstica homogénea y un seguimiento longitudinal más extenso para evaluar la evolución clínica en este grupo de pacientes.
**Palabras clave**: Hidrocefalia normotensiva idiopática; derivación ventriculoperitoneal; deterioro cognitivo; trastorno de la marcha; neurocirugía

## Introduction

In 1965, Hakim and Adams first described Normotensive Hydrocephalus (NPH) as a condition characterized by the clinical triad of gait disorder, urinary incontinence, and memory impairment, associated with the presence of normal Cerebrospinal Fluid (CSF) pressure in Lumbar Puncture (LP), enlarged cerebral ventricles and improvement after ventricular shunt surgery (Adams, Fisher, Hakim, Ojemann & Sweet, 1965; Halperin et al., 2015). This triad is present in less than 60% of patients and its individual components are not specific: gait disturbances due to many other etiologies occur in 20% of people over 75 years of age; there is urinary incontinence in 18% of men and 38% of women older than 60 years; the prevalence of mild cognitive impairment and dementia is approximately 35% in people older than 70 years; and the ventricles tend to enlarge with age and in patients with neurodegenerative disorders (Espay et al., 2017).

NPH was described as a potentially reversible cause of gait disorder and dementia and NPH is now separated into idiopathic NPH (iNPH) and secondary NPH (sNPH) (Halperin et al., 2015). Ventriculoperitoneal Shunt (VPS) surgery is considered the standard of care for patients with sNPH, but in iNPH, its response is variable (Halperin et al., 2015; Relkin, Marmarou, Klinge, Bergsneider & Black, 2005; Mori et al, 2012; Andersson, Rosell, Kockum, Söderström & Laurell, 2017; Toma, Papadopoulos, Stapleton, Kitchen & Watkins, 2013; Vanneste, Augustijn, Dirven, Tan & Goedhart, 1992). Post VPS benefits in patients with an initial diagnosis of iNPH persist in only one-third of patients, with a known revised diagnosis in more than 25% of patients (Alzheimer's disease, Lewy body dementia, and Progressive supranuclear palsy). Previously reported cases of NPH with "dual" pathology (that is, developing a "second" disorder) likely represent ventriculomegalic presentations of selected neurodegenerative disorders in which the benefits of VPS may be short-lived, with consequent unfavorable risk-benefit ratio (Espay et al., 2017; Saper, 2017). In addition to this, the pathophysiology of iNPH is controversial. There are new considerations in this regard, like alterations in cerebral blood flow with ischemia secondary to a phenomenon of the last meadow at the subependymal/periventricular level, irreversible compression of the projection fibers of the frontal regions and reduced clearance of CSF with an accumulation of toxic degradation products that leads to neurotoxicity (Bräutigam, Vakis & Tsitsipanis, 2017; Martín-Láez et al, 2018; Ringstad, Vatnehol & Eide, 2018). It is proposed that once a point of no return has been reached in any of these pathophysiological mechanisms, the therapeutic intervention may not have a modifying effect of the disease's course or not represent a solution for all of them. Then, the problem no longer lies only in achieving an accurate diagnosis, but also in its timing.

In this context, searching for clinical factors and complementary studies in order to determine the predictors of a favorable and sustained response to the VPS placement in patients with iNPH is substantially important (Halperin et al., 2015; De Mol, 1985) This is the main objective of this study.

## Methodology

A retrospective review of medical records of patients with probable iNPH (according to international guidelines) treated with VPS assisted in a neurological clinic from January 2014 to January 2017 (Relkin et

al., 2005; Mori et al., 2012; Andersson et al., 2017). Clinical data and complementary studies were recorded (brain MRI and CT, gait test post-lumbar puncture) (Gallagher, Marquez & Osmotherly, 2019). Clinical response was evaluated with the Modified Rankin Scale (mRS) at baseline and 12 months follow-up, dichotomously: equal or better than the previous mRS (Bruno et al., 2010). For MRI evaluation, clinical signs were dichotomized: Positivity was defined as an abnormal Evans index (greater than 0,3), an acute callosal angle (less than 90º), the presence of at least one DESH (disproportionately enlarged subarachnoid space) (Relkin et al., 2005; Mori et al., 2012; Andersson et al., 2017). Positive lumbar puncture was defined as a more than 20% change in walking speed or the number of steps before and after the puncture) (Gallagher et al., 2019). A univariate statistical analysis of the variables considered as possible prognostic factors was performed.

## RESULTS

58 patients were included, 33 men and 25 women (M:W 1,3:1). The mean age was 73,2 (SD 7,5). All patients presented with a gait disorder and 46.5% of them had a history of falls. 84.5% had some degree of associated cognitive impairment and 87.9% had urinary disorders, urination urgency being the most frequent.

TABLE 1.

*Analysis of clinical factors and complementary studies evaluated in relation to mRS at 12 months of follow-up from VPS placement*

| Clinical factors | | |
|---|---|---|
| Sex (N = ?) | Women 3.68 times more chances to improve | p = 0.019 |
| Age | Without statistical correlation | p = 0.2 |
| Time of evolution from the onset of symptoms | | p = 0.9-0.7 |
| Gait dysfunction | No statistical correlation at 3 and 12 months of follow-up. | p = 0.5-0.7 |
| Urinary disorder | | p = 0.4-0.8 |
| Cognitive impairment | | p = 0.8-0.7 |
| MMSE | Without statistical correlation | OR 1.13 |
| Complementary studies | | |
| Evans Index | Without statistical correlation | p = 0.09 |
| Callosal angle | Each degree of increase in the angle of the callus was associated with a 5% reduction in the possibility of improvement, although this effect was not significant. | p = 0.08 |
| DESH | The presence of DESH was associated with the reduction of 1 in mRS in 56.25% of the patients, without reaching statistical significance. | p = 0.2 |
| Fazekas score | Without statistical correlation | p = 0.75 |
| Gait test (with LP) | Patients with good response to the gait test had a better response to the VP shunt. | p = 0.024 |

MMSE: Mini-mental state examination. DESH: disproportionately enlarged subarachnoid space hydrocephalus. LP: lumbar puncture.

Among the clinical factors: women presented 3.68 times more chances of improvement after the VPS (p = 0.019), while age, time of evolution of the clinical manifestations and MMSE had no correlation (Table 1). Regarding the complementary studies: good response to the gait test was associated with better response to the VPS (p = 0.024) and each degree of increase in the angle of the callosum was associated with a 5% reduction in the possibility of improvement, although this effect was not significant (p = 0.08); the Evans index had no prognostic correlation (Table 1). In 19 of 58 patients, Disproportionately Enlarged Subarachnoid Space Hydrocephalus (DESH) data was available: in 3 it was negative and in 16 positive. Of the 3 negatives, one year of follow-up (after VPS) were unchanged (according to mRS); of the 16 positives: 9 had improved 1 point in mRS at one year of follow-up (56.25%) and 6 were unchanged (43.75%) and none got worse. However, none of these findings were statistically significant.

In this group of patients, we observed that of the 41 patients who improved after 3 months, only 24 (59%) maintained it at 1 year (p = 0.043) (Figure 1).
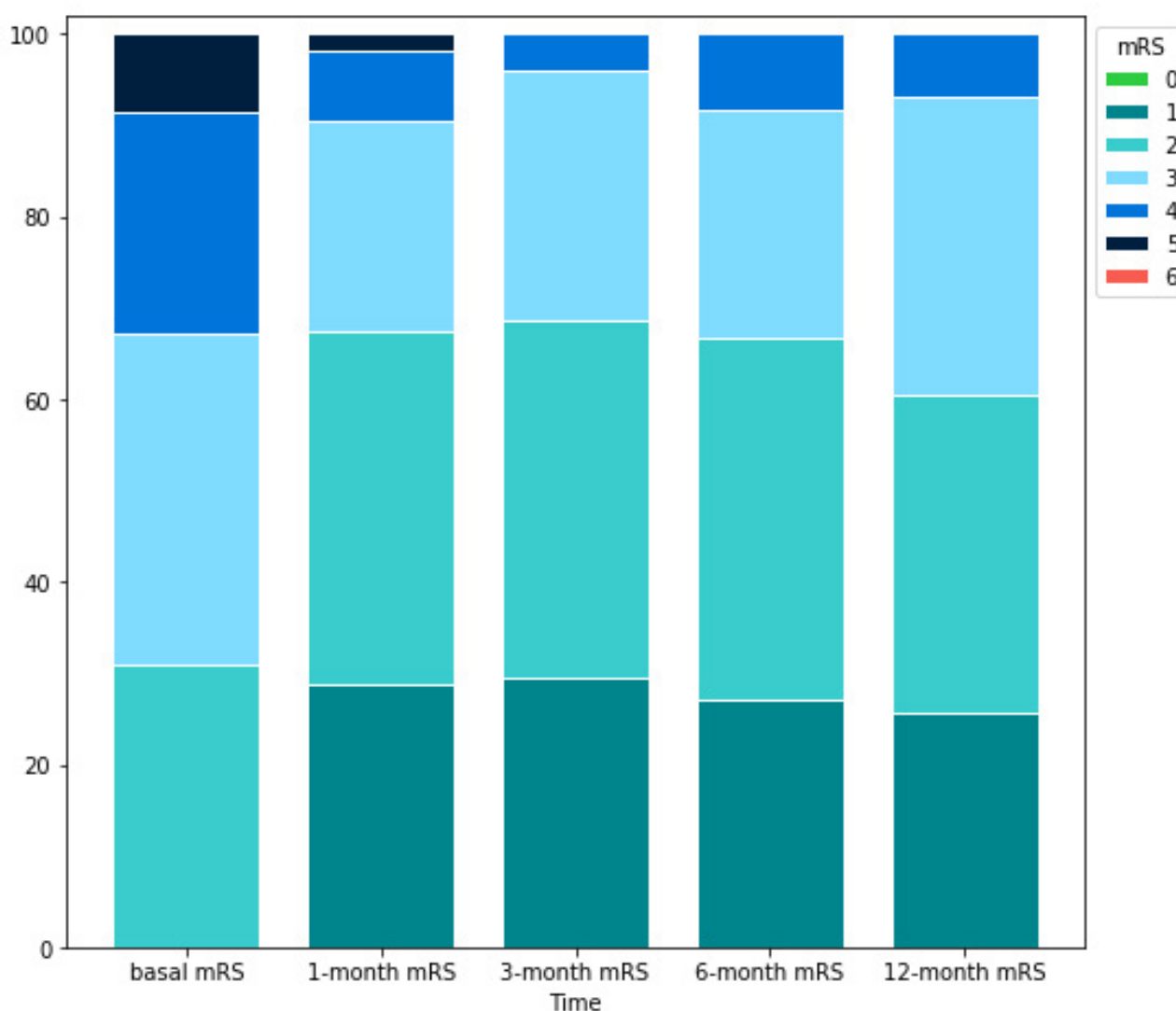


**Figure 1.** Follow-up of the patients (expressed as a percentage) from the VPS placement to 1, 3, 6 and 12 months, evaluated according mRS (0-6).
Source: Authors.

This research study has the following limitations: data collection was carried out retrospectively and, in some patients,, all the necessary clinical data and complementary studies were not available. The sequence of complementary studies carried out was not completely the same for all patients; this reveals the need for a homogeneous diagnostic evaluation appropriate to international guidelines. Also, it is important to consider that mRS was calculated indirectly by recording clinical evaluations.

## Conclusions

Female sex and good response to the gait test could be considered as predictors of a favorable response to the VPS placement in patients with iNPH. A prospective study is necessary to achieve a homogeneous diagnostic evaluation and a more extensive longitudinal follow-up to evaluate the clinical evolution in this group of patients.

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## Short Article

JOURNAL OF APPLIED COGNITIVE NEUROSCIENCE

# Utility of a Screening Test (MoCa) to Predict Amyloid Physiopathology in Mild Cognitive Impairment

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*Abstract*

Introduction: The MoCa (Montreal Cognitive Assessment) Screening test has become relevant in recent years in the screening of patients with Mild Cognitive Impairment (MCI). It is important to seek and study simple and reliable tools in clinical practices that correlate with biological markers that have been used to predict conversion from MCI to AD. Objective: To analyze the MOCA and its cognitive sub-scores and the relationship with Amyloid pathophysiology in Alzheimer's Disease. Methodology: 32 patients with MCI were studied, they were separated according positive (n: 20) and negative (n: 12) underlying amyloid pathology. The patients performed a extensive cognitive assessment that included MoCa Test. Results: MoCa Total Scores showed significantly different results between groups ($p < 0.001$) as well as the Memory Score (MoCa MIS), the Executive (MoCa EIS), the Attentional Score (MoCa AIS)) ($p < 0.001$) and the Orientation Score (MoCa OIS)) ($p < 0.05$) with worse performance of patients with amyloid pathophysiology. Score of MoCa a cut-off point of $< 24$ was established, since the diagnostic sensitivity at this point was 83% and the specificity 70%. Conclusions: The MoCa is a useful tool to differentiate biomarker status in MCI. Future studies should study this tool in the prodromal phases of the disease.
**Keywords**: Neuropsychology; dementia; mild cognitive impairment; Alzheimer's disease; amyloid

## Utilidad de un test de Screening (MoCa) para predecir Fisiopatología Amiloide en Deterioro Cognitivo Leve

*Resumen*

Introducción: El MoCa (Montreal Cognitive Assesment) ha cobrado relevancia en los últimos años en el cribaje de pacientes con Deterioro Cognitivo Leve (DCL). El uso de herramientas clinicas simples y confiables con alta capacidad de predicción de la conversion del DCL a Enfermedad de Alzheimer (EA) es de gran importancia. Objetivo: Analizar la capacidad del MoCa y sus sub-scores cognitivos para la detección de fisiopatología amiloide en un grupo de pacientes con DCL. Metodología: Se estudiaron 32 pacientes con DCL, se los separó según fisiopatología amiloide subyacente positiva (n:20) y negativa (n:12). Los pacientes realizaron una extensa evaluación cognitiva que incluyó en MoCA. Resultados: El Score Total del MoCa arrojó resultados significativamente diferentes entre grupos ($p < 0.001$) así como el Score de Memoria (MoCa MIS), el Ejecutivo (MoCa EIS), el Score Atencional (MoCa AIS) ) ($p < 0.001$) y el de Orientación (MoCa OIS) ) ($p < 0.05$) obteniendo un peor desempeño los pacientes con fisiopatología amiloide. Se establecio un punto de corte de $< 24$ para el Score Total del MoCa, ya que la sensibilidad en este punto fue de 83% y la especificidad de 70%. Conclusiones: El MoCa es una herramienta útil para utilizar en pacientes con Deterioro Cognitivo Leve debido a Enfermedad de Alzheimer. Futuros estudios deberían estudiar esta herramienta en las fases prodrómicas de la enfermedad.
**Palabras clave**: Neuropsicología; demencia; deterioro cognitivo leve; enfermedad de Alzheimer; amiloide

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## INTRODUCTION

Mild Cognitive Impairment (MCI) (Petersen et al, 1999) is a stage between normal aging and early dementia. The identification of subjects with MCI at risk of conversion to Alzheimer's Disease (AD) is very important not only for clinicians, but for patients and their families. The MoCa Screening Test (Montreal Cognitive Assessment) is a very well-known 10-minute cognitive screening test for detection of MCI. It is widely known to have a high sensitivity (90%) and specificity (87%) in the detection of MCI and the distinction from normal cognition (Nasreddine et al, 2005). In 2017, the UDS 3 (Uniform Data Set) (Weintraub et al., 2018) of the ADC program (Alzheimer's Disease Centers) of the National Institute of Aging included it as part of its neuropsychological evaluation as a screening test (Besser et al., 2018). It has been translated into more than 37 languages, and is a simple, fast and economic tool that is being used to detect cognitive changes in prodromal stages of neurodenegerative diseases. It is important to provide simple and reliable tools in clinical practices, besides biological markers that have been used to predict conversion from MCI to AD.

Sub scores from MoCa have already been used to predict conversion to AD in individuals with MCI , establishing cut off scores from MoCa Total Score and MoCa Memory Index (MIS) (Julayanont, Brousseau, Chertkow, Phillips & Nasreddine, 2014). The MoCa MIS is calculated by adding the number of words remembered in free delayed recall, category-cued recall, and multiple choice–cued recall multiplied by 3, 2 and 1, respectively, with a score ranging from 0 to 15 to get better information from a probable memory deficit. The Executive Index Score (EIS) is calculated by adding raw scores for the modified Trail-Making Test Part B, clock drawing, digit span forward and backward, letter A tap- ping, serial-7 subtraction, letter fluency, and abstraction, with a score ranging from 0 to 13. The Visuospatial Index Score (VIS) is determined by adding the raw scores of the cube copy, clock drawing, and naming, with a score from 0 to 7. The Language Index Score (LIS) is obtained by adding the raw scores for naming, sentence repetition, and letter fluency, with a score ranging from of 0 to 6. The Attention Index Score (AIS) is obtained by adding the raw scores for digit span forward and backward, letter A tapping, serial-7 subtraction, sentence repetition, and the words recalled in both immediate recall trials, with a score ranging from 0 to 18. The Orientation Index Score (OIS) is the sum of points for the orientation section, with a score ranging from 0 to 6.

The objective of this study is to analyze the MoCa and its cognitive sub-scores and its accuracy to identify amyloid physiopathology underlying AD in a South American cohort of MCI patients.

## METHODS

32 patients with MCI were studied. Inclusion criteria for this study were those included in the Alzheimer's Disease Neuroimaging Initiative (ADNI) criteria: presence of a subjective memory concern reported by the study subject, a partner, or their attending clinician; age between 55 and 85 years, at least 6 years of formal education and at least one study companion spending 10 or more hours a week with the participant; absence of visual or auditory deficits which could affect cognitive test performance; Hachinski Ischemic Score (HIS) (Hachinsk et al., 1975) less than or equal to 4; score of 6 points or less on the Geriatric Depression Scale (GDS); no concomitant neurological

or psychiatric diseases, or contraindications for lumbar puncture, brain MRI, or PET brain imaging. Furthermore, for MCI criteria, following specific criteria were used: MMSE (Folstein, Folstein & McHugh, 1975) scores between 24–30 (inclusive), a Clinical Dementia Rating (CDR) (Hugues, Romey, Duval, Vincent & Lazdunski, 1982) of 0.5, absence of significant levels of impairment in other cognitive domains, essentially preserved activities of daily living, and an absence of dementia.

Patients were assessed with an extensive cognitive evaluation that included MoCa test. For the purpose of this study, MMSE test was the only test analyzed with the MoCa, in order to study the relationship of another screening measure to amyloid pathology. All study subjects with MCI were grouped according to Aβ biomarker results (i.e. positive or negative). Aβ biomarker results were studied through Amyloid PET scans (11C-Pittsburgh compound B) using fluorodeoxyglucose (FDG) and 11C-Pitts-

burgh compound-B (PIB-PET) or Cerebrospinal fluid (CSF) samples using enzyme-linked immunosorbent assay (ELISA) kits (Innogenetics; Ghent, Belgium) following ADNI Quality Control Program guidelines.

## RESULTS

Table 1 shows the comparison between the groups of patients with MCI separated according to the presence of amyloid physiopathology identified with a positive PET PIB biomarker or low level of Aβ42 in the CSF.

MoCa Total Score yielded significantly different results between groups ($p < 0.001$) as well as the Memory Score (MoCa MIS), the Executive (MoCa EIS), the Attention Score (MoCa AIS) ($p < 0.001$) and the Orientation score. (MoCa OIS) ($p < 0.05$). Patients with amyloid physiopathology had worse performance in these scores (Table 1). MMSE (Mini mental State Examination) showed significant differences between groups as well.

TABLE 1.
*Demographic and Neuropsychological Characteristics*

|  | MCI amyloid negative | MCI amyloid negative | p |
|---|---|---|---|
| Age | 69,2 ± 8 | 71,4 ± 4,8 | ns |
| MMSE | 28 ± 3,3 | 24,7 ± 4,2 | p < 0.01 |
|  |  |  |  |
| Moce Subscores |  |  |  |
| Total Score Moca | 25,2 ± 3 | 2,0 ± 4,3 | p < 0.001 |
| MocCa MIS | 8,3 ± 3,6 | 4,3 ± 3,6 | p < 0.001 |
| MoCa EIS | 11,8 ± 1,6 | 9,6 ± 2,2 | p < 0.001 |
| Moca VIS | 6,3 ± 0,9 | 5,7 ± 1,3 | ns |
| MoCa LIS | 5,6 ± 0,7 | 5,1 ± 1 | ns |
| MoCa AIS | 17,2 ± 1,1 | 13,4 ± 3,6 | p < 0.001 |
| MoCa OIS | 6 ± 0 | 5,2 ± 1,2 | p < 0.5 |

Note: Results described in Mean and Standard Desviation. MMSE: Mini Mental State Examination. MoCa MIS: MoCa Memory Index Score, MoCa EIS: MoCa Executive Index Score, MoCa VIS: Visuoespatial Index Score, MoCa LIS: MoCa Language Index Score, MoCA AIS: MoCA Attentional Index Score, MoCa OIS: MoCa Orientation Index Score. Ns: non significant.
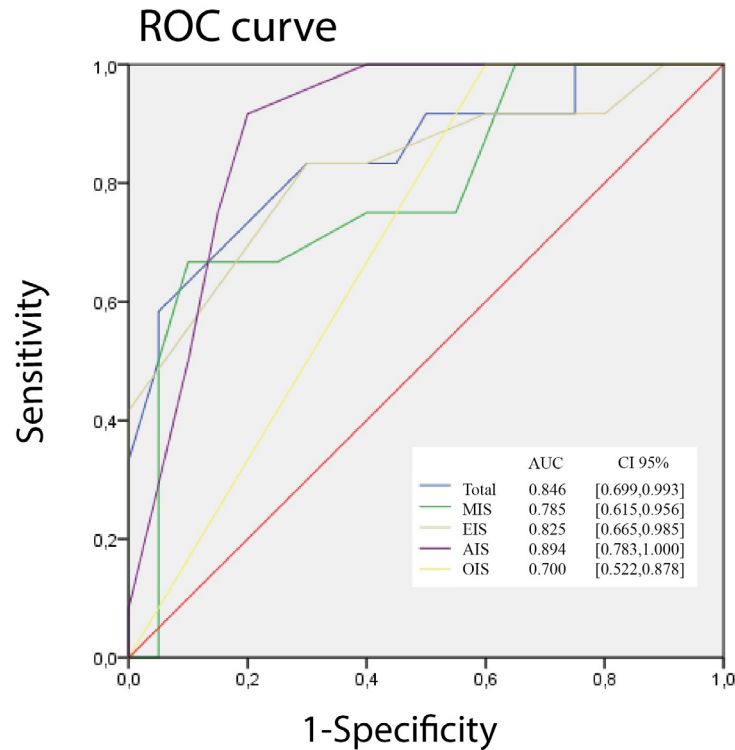
**Figure 1.** ROC Curves for MMSE and MoCa Sub scores.
Source: Authors.

ROC analysis was performed to calculate the cutoff score and diagnostic value to detect amyloid physiopathology. ROC CURVES were made for each of these scores. MMSE, MoCa AIS, MoCa EIS and MoCa Total Score presented the largest area under the curve (Figure 1). For the total Score of MoCa a cut-off point of < 24 was established, since the diagnostic sensitivity at this point was 83% and the specificity 70%.

#### DISCUSSION AND CONCLUSIONS

This study was designed to test the capacity of the MoCA to differentiate groups of patients with MCI according to their biomarker status. Results showed that MoCa Total Score and subscores (MoCa Ais, EIS) showed greater sensitivity and specificity than a commonly used screening test as MMSE, to differentiate groups of patients with MCI with and without amyloid physiopathology.

Cost effectiveness and accessibility of neuropsychological tests in the primary care setting, compared to neuroimaging studies or other biomarker assays, make them an appealing and useful tool for AD detection, particularly in developing countries were biomarkers technology is not available and resources are scarce. The results from this study add to previous results obtained from a South American Cohort were cut off scores from a memory test, the AVLT (Auditory Verbal Learning Test) were provided to predict AD presence (Clarens et al., 2020).

The MoCa total score and the subsequent analysis of its subscores is a useful tool to be used in the detection of patients with MCI due to Alzheimer's disease.

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# Neuroimage

# A look back into a typical patient with memory complains

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*Aim*: The purpose of these images is to extol the biological perspective from the clinical setting perspective of a typical AD case. This participant was profoundly studied and also followed-up for five years in the study ADNI- Argentina.

*Clinical setting*: The participant was 72 years old woman with an amnestic Mild Cognitive Impairment (MCI). She was enrolled in 2013, following the ADNI2 criteria as Late MCI. Her APOE status was 3/4, and scored 27/30 in the MMSE and 0.5 in CDR at baseline.

*Biological Findings in CSF at Baseline*: Aβ42 447 pg/ml; T-tau 599 pg/ml; P-tau 103 pg/ml; Nfl 1124 pg/ml.

*MRI at baseline*: MTA 3/2, Fazekas 0, Koedam 1, Hippocampus volumes: L 2691, R 2318.

*Conclusion*: The molecular imaging revealed, beyond the clinician´s eye, all the phenomena that had preceded the first clinical symptom. According to the new ATN scheme, the participant was positive in every aspect, and most probably, the whole process could have lasted around 15 years before its enrollment. After 60 months of follow-up the participant´s MMSE was 15 and de CDR was 1. Sometimes an image can say a thousand words about the time that had elapsed when the physician first met the patient.
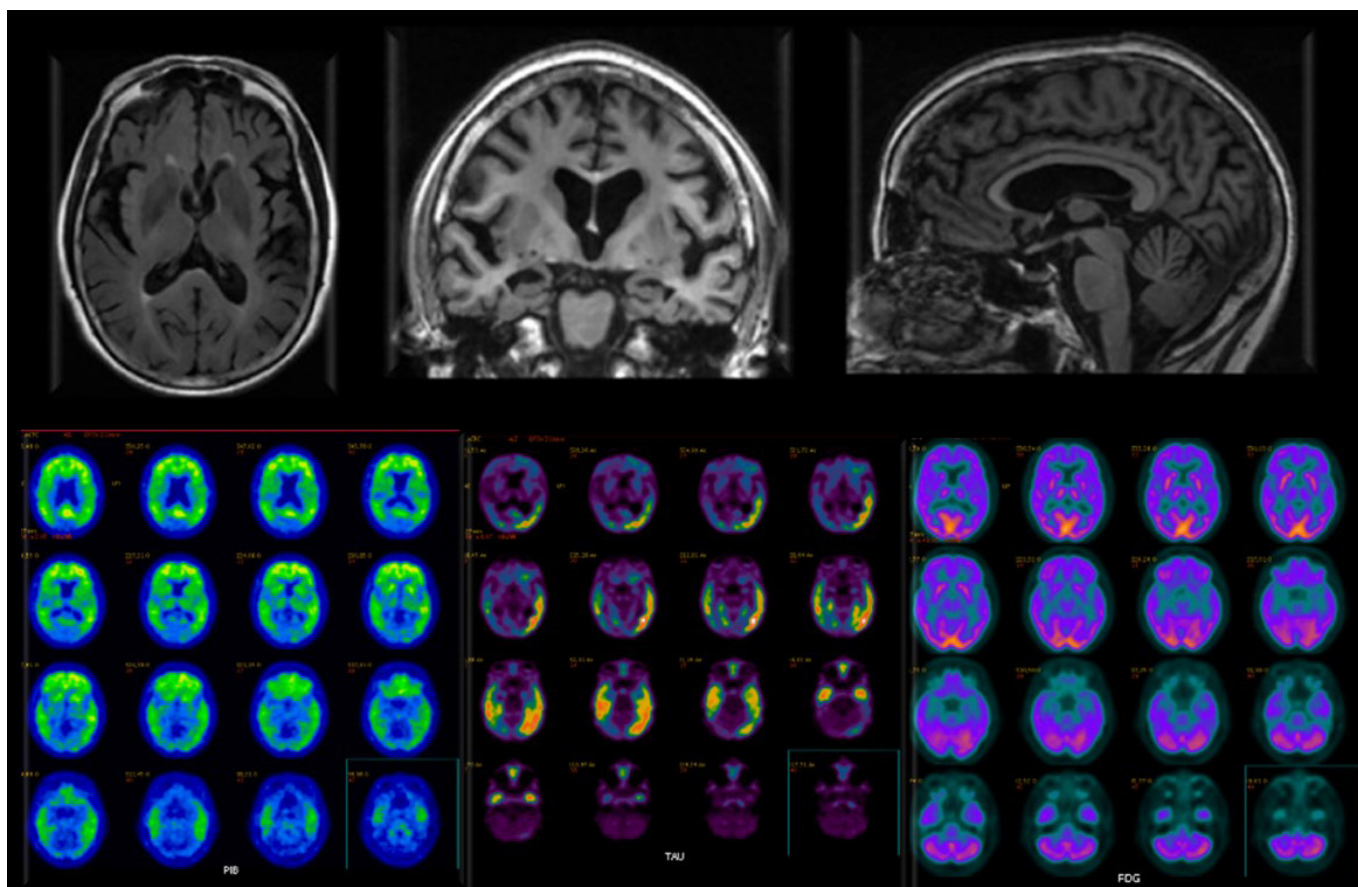
**Figura 1.** PET-PiB: A+, Tau-PET: T+, PET-FDG: N+
Source: Authors.

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# Neuroimage

# Anti-Ma2-associated encephalitis

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A 30 year old male with no relevant previous medical history, consulted in the Emergency Room with a 1-month history of a sleep disorder with daily somnolence, adding 3 days before consultation temporal and spatial disorientation. Family members also referred hyperphagia. The patient didn't present headache, fever, behavioral manifestations, or any other systemic or neurological signs or symptoms. He denied recent trips or vaccination.

Neurological examination was normal.

A contrast enhanced brain MRI was performed, revealing in T2/FLAIR weighted images a diffuse hyperintense hypothalamic and interpeduncular lesion with homogeneous contrast enhancement (Figure 1, A-B). General laboratory tests were normal, with negative HIV and VDRL results and normal B12 and thyroid function values. A lumbar puncture was performed, showing mononuclear pleocytosis and high protein levels, with a negative citologic test. Full body CT scan showed no alterations, and testicular ecography revealed hypoechoic lesions and macrocalcifications suggestive of testicular cancer.

Testicular exeresis was performed, with anatomy pathology findings of seminoma. Paraneoplastic and autoimmune antibodies in CSF showed positive results for anti-Ma2 antibodies.

It was concluded that the patient had an Anti-Ma2-associated encephalitis.

Chemotherapy was started and the patient received five pulses of methylprednisolone 1g, maintaining long term treatment with high doses of prednisone. The patient had subtle clinical improvement.

3 months later, the patient consulted in the emergency room for anterograde amnesia. A new brain MRI was done, showing improvement of the hypothalamic lesion but with bilateral hippocampal hyperintensity without contrast enhancement (Figure 1, C-D). It was interpreted that the patient had now added an anti-Ma2-associated limbic encephalitis. A new full body CT scan was done, showing new retroperitoneal adenopathies despite chemotherapy. The patient received immunoglobulin 2g/kg and started a new oncologic treatment, with modest clinical improvement in the following months.

A new brain MRI was performed a year later, showing only slight hyperintensity in the right wall of the third ventricle in T2/FLAIR sequences and no contrast enhancement (Figure 1, E-F).

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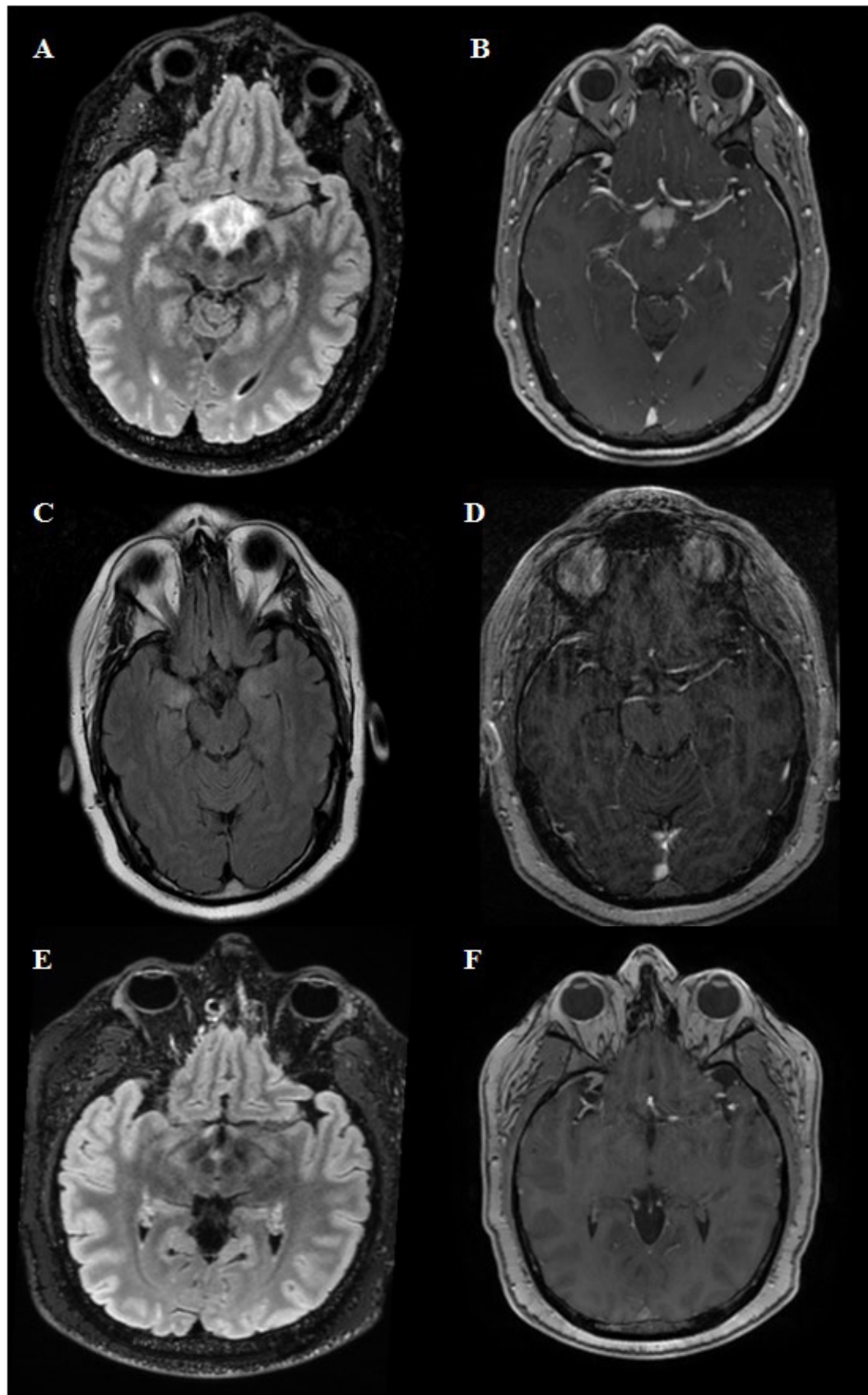Email:
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**Figure 1.** T2/FLAIR sequence (A) shows a diffuse hyperintense hypothalamic and interpeduncular lesion that is contrast enhancing (B). 3 months later, a new brain MRI was performed showing bilateral hippocampal hyperintensity (C) without contrast enhancement (D). Control brain MRI completed a year later shows remaining hyperintensity in the right wall of the third ventricle in T2/FLAIR sequence (E) and no contrast enhancement (F).
Source: Author.

Anti-Ma2 antibodies are usually present in men with testicular tumors, and they may be accompanied by a paraneoplastic syndrome including limbic, diencephalic or brainstem encephalitis (Ortega, Sola-Valls, Escudero, Saiz & Graus, 2018). Brain MRI shows hyperintensity in the midbrain, diencephalon (thalamus/hypothalamus) or temporal lobes in T2/FLAIR weighted images, with almost half of these lesions presenting with contrast enhancement. CSF regularly has inflammatory changes (Ortega et al., 2018; Dalmau et al., 2004).

Clinical presentation usually varies according to the region affected, and these patients tend to have a good response to oncologic and immunologic treatment, with stabilization or even clinical improvement (Hoffmann et al., 2008).

Even though this is a rare entity, it is important to consider it as a differential diagnosis in cases of young men with midbrain or diencephalic lesions, since its early diagnosis and treatment could hinder its progression.

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# Neuroimage

# Cytotoxic Lesion of the Corpus Callosum in a patient with Aphasic Status Epilepticus

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A 47-year-old man with a history of aphasic seizures presented to the emergency room with a 12-hour global aphasia. Upon admission, brain MRI did not reveal acute lesions, and EEG showed sharp waves in the left frontal-temporal region. An Aphasic Status Epilepticus was diagnosed and antiepileptic treatment was initiated with adequate response.

A week after the episode, a new brain MRI showed a high-signal ovoid lesion on T2-weighted and FLAIR sequences in the central part of the splenium of the corpus callosum (Figure 1). On Diffusion-Weighted Images (DWI) the lesion was hyperintense with decreased Apparent Diffusion Coefficient (ADC) values, indicating restricted diffusion consistent with a Cytotoxic Lesion of the Corpus Callosum (CLOCC) (Takayama, Kobayashi, Sugishita & Mihara, 2000; Conti et al., 2007). Follow-up MRI one month later showed complete image resolution (Figure 2).

CLOCCs are secondary lesions associated with various entities in which high levels of cytokines and extracellular glutamate cause intracellular edema and reduced diffusion, a condition called cytotoxic edema, which affects vulnerable brain regions such as the splenium of the corpus callosum (Starkey, Kobayashi, Numaguchi & Moritani, 2017; Tetsuka, 2019).

In epileptic patients, CLOCCs may be due to the effect of seizures, especially prolonged ones, as well as antiepileptic treatment itself (Prilipko, Delavelle, Lazeyras & Seeck, 2005; Polster, Hoppe & Ebner, 2001). CLOCCs are rare radiological findings and must be recognized to avoid misdiagnosis.
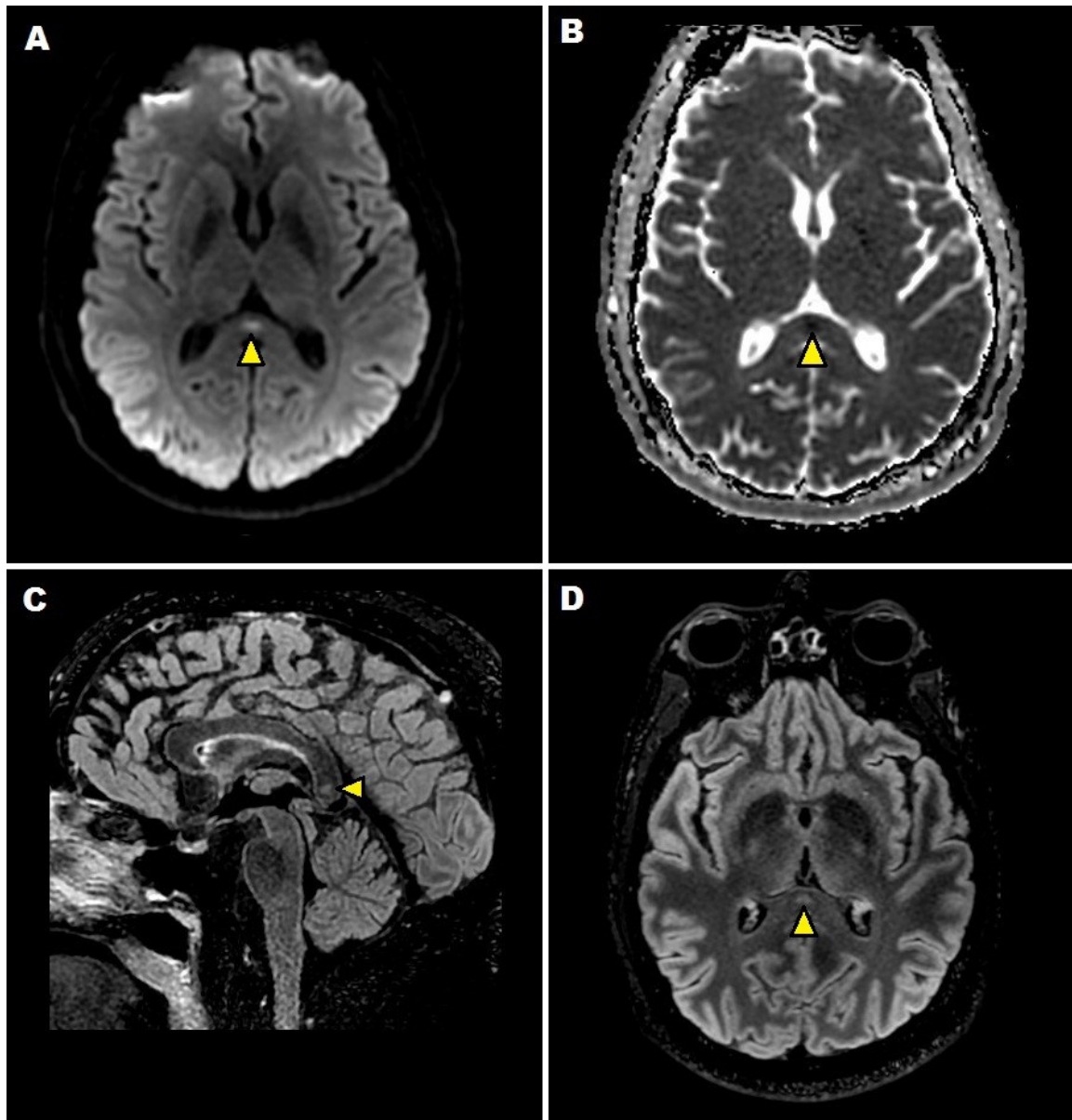
**Figure 1.** A-B. Axial DWI MRI image (A), and ADC map (B) show an ovoid focal lesion in the splenium. C-D. Sagital (C) and axial (D) FLAIR images revealed a slight hyperintense signal at the same location. Source: Authors.
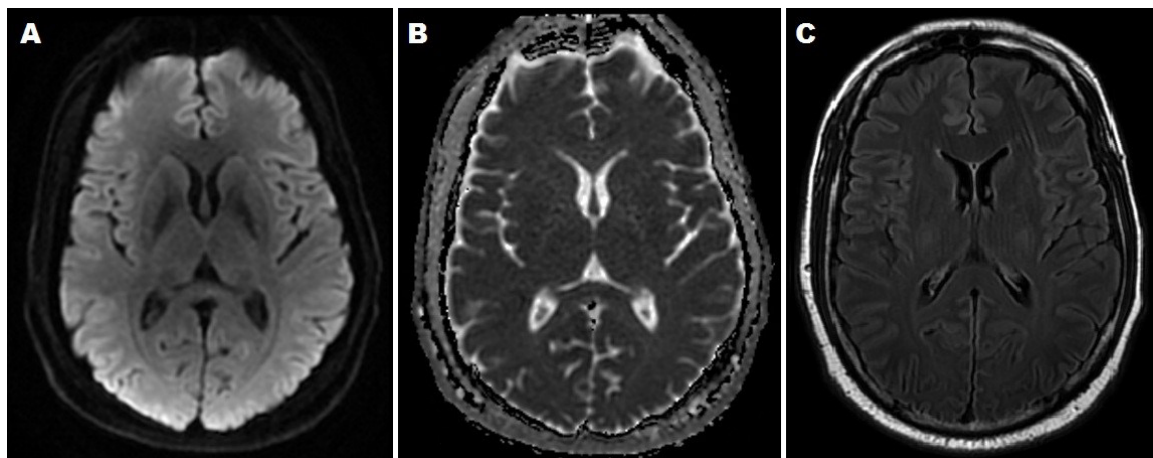


**Figure 2.** A-C. Follow-up MRI one month later shows complete resolution of the lesion in both DWI (A), ADC map (B) and FLAIR (C) images. Source: Authors.

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# Neuroimage

# Optic tract and internal capsule lesion in a patient with Wernicke-Korsakoff syndrome

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A 72-year-old man, presented with a one-week history of confusion and an anterograde amnesic disorder accompanied by confabulation, with lack of insight to his symptoms.

Medical history included alcohol abuse and admitted twenty-years of alcohol ingestion (approximately 186 gr/day).

Neurologic examination was notable for slightly decreased consciousness, disorientation to time, severe anterograde amnesia and unsteadiness of stance and gait with four limb ataxia.

A metabolic blood panel including liver profile showed alanine aminotransferase mildly elevated (66 UI/L) with elevated gamma-glutamyl-transpeptidase (gGT: 426 UI/L). Tests for HIV, syphilis and vitamin B12 levels were negative.

Review of initial brain MRI showed a symmetrical, increased fluid-attenuated inversion recovery (FLAIR) signal lesion extending through the hypothalamus, periaqueductal area, mamillary bodies, bilateral anterior thalami, chiasm, both optic tracts and posterior limbs of both internal capsules with restricted diffusion and patchy contrast enhancement (Figure 1, 1a–1b).

A possible Wernicke-Korsakoff syndrome diagnosis was achived. Following the initial examination, the patient was initiated on prophylactic parenteral thiamine reposition.

CSF analysis showed elevated proteins (174 mg/dl) and lactate concentration (2.9 mmol/L). Cytologic and immunocytochemical study showed no neoplastic processes. Screening of autoimmune antibodies in CSF and paraneoplastic antibodies in serum were negative. EEG and full-body CT scans were unremarkable.

Thiamine serum levels were normal (16,5 ug/L) (blood sample collected previous to reposition).

Finally, a neurocognitive test indicated malperformance in tasks related to immediate and delayed recall and disturbances in recent and remote memory with confabulation.

A new brain MRI after supplementation showed regression of the previous lesion (Figure 1, 2a-2b).

He was discharged one month later with residual anterograde amnesia and gait instability that are still present eleven months later, at the last follow up.
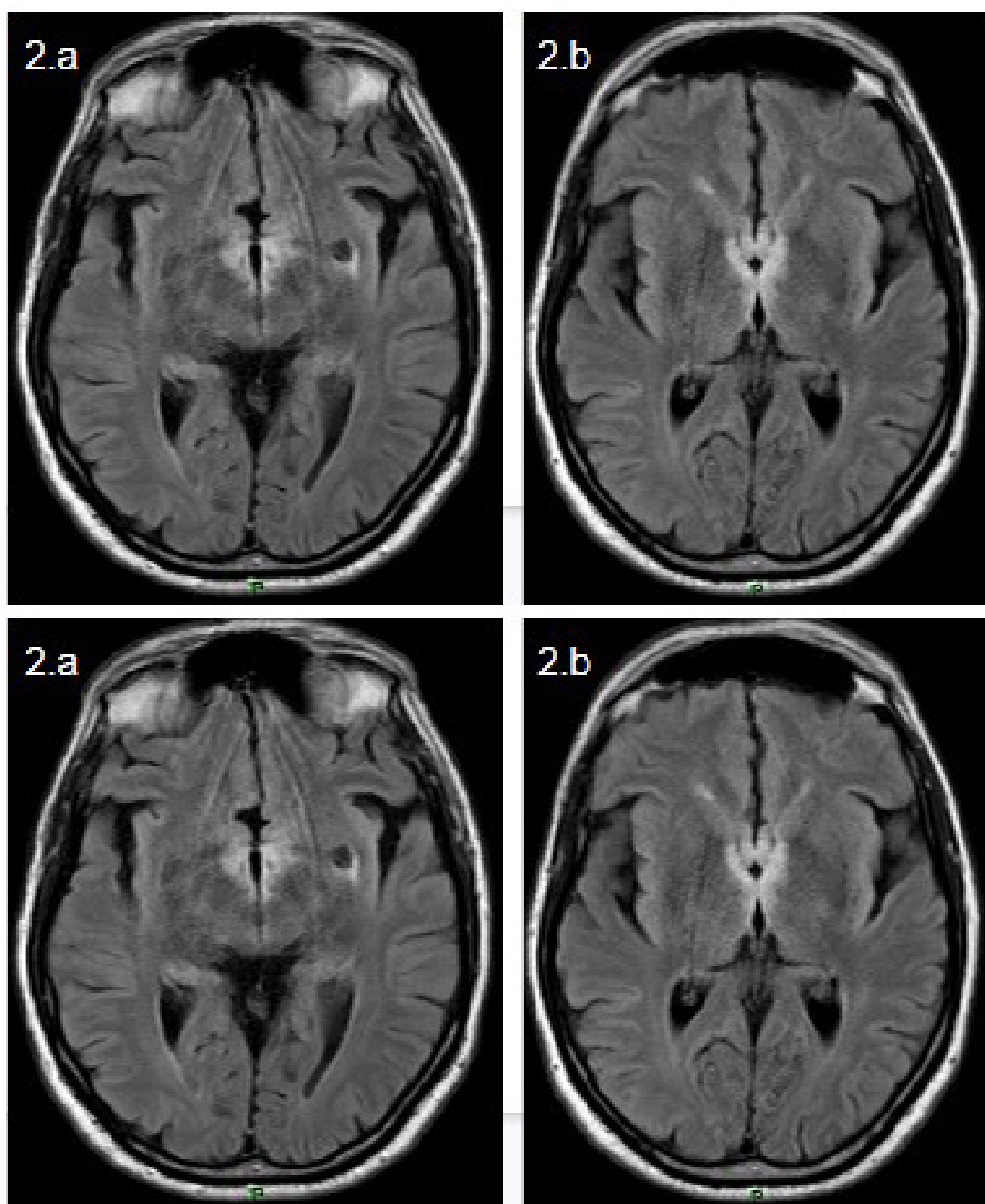
**Figure 1.** (1) Axial FLAIR MRI sequence showing extensive, symmetrical, hyperintense lesion in chiasm and both optic tracts (1.a) and periaqueductal area, hypothalamus and posterior limb of internal capsules (1.b). (2) Axial FLAIR MRI sequence showing regression of the hyperintense lesion one month after thiamine reposition in chiasm and both optic tracts (2.a) and periaqueductal area, hypothalamus and posterior limb of internal capsules (2.b)
Source: Authors.

Wernicke's encephalopathy (WE) prototypical clinical triad consists of motor problems such as ataxia or gait incoordination, ocular signs (commonly ophthalmoparesis and nystagmus) and mental status changes (Wicklund & Knopman, 2013; Isenberg-Grzeda, Rahane, DeRosa, Ellis & Nicolson, 2016). Thiamine (vitamin B1) deficiency secondary to alcoholism is the most common etiologic factor (Isenberg et al., 2016). If left untreated or undertreated, there is an increased risk of developing a chronic sequelae: the Korsakoff's Syndrome (KS), characterized with loss of working memory

and confabulation with sparing of remote memories (Sullivan & Pfefferbaum, 2009; Sinha, Kataria, Kolla, Thusius & Loukianova, 2019). Both syndromes together are termed Wernicke-Korsakoff syndrome (WKS).

Even though diagnosis of WKS remains primarily clinical3, brain MRI findings in previously reported typical locations (Wicklund & Knopman, 2013; Isenberg, et al., 2016) are highly specific of this syndrome, suggesting MRI is a valuable confirmation tool.

Normal thiamine serum levels shouldn't dismiss the initial suspicion, as its blood concentration does not necessarily reflect brain tissue's concentration (Sinha et al., 2019).

Our case suggests that, even when MRI lesions are not characteristic, intravenous thiamine reposition should be immediately initiated if WKS is suspected, considering the patient's outcome depends on prompt diagnosis and adequate treatment.

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# Comments on Books:

## Complex clinical presentations of depression and its best therapeutic responses

Pablo Miguel Bagnati · Andrea Márquez Lopez Mato · Marcelo Cetkovich Bakmas · Gustavo Vázquez

**Janus Kremer**

Book in Spanish, 85 pages.
Editorial Vision y Formación medica (Buenos Aires, Argentina), June 2020.

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I have gratefully read this book. I had the pleasure and honor of sharing more than 30 years of working together with the authors.

Each one of them, are leaders in their fields, and hallmarks of the Argentinean Psychiatry.

This book is extremely well written. It covers aspects of everyday practice with simplicity to be easily understood by young doctors as well as provides high quality of updated concepts that were be of enormous utility to senior neuropsychiatric staff involved in the care of patients with depression and its resistant to treatment form of presentation.

Andrea Lopez Mato excels in a didactyly approaching the neurobiological and neuroendocrine pathways leading to depression. Her approach is one way, easily understandable, but on the other hand, specially with the graphics and figures gives a deep understanding of such a complex aspect of mental illness.

Pablo Miguel Bagnati's chapter focusses on depression in neurological disorders. It is clear to me when I read this chapter, that the author has an enormous experience dealing with this population in everyday of his clinical practice. His graphics are absolutely appropriate and very didactive.

Marcelo Cetkovich Bakmas approaches with an exquisite precision an extremely complex such as Psychotic depression is. In this chapter is discussed the definition of the concept, its difficulties in the differential diagnosis, the widely aspects of how can it clinically present and the different potential treatments, As well, regarding the etiology of the psychotic depression, the author gets into neurobiological hypothesis, sharing with the reading public a complete scope of this challenging and frequent clinical presentation.

Gustavo Vazquez gets into one of the one most challenging aspects of modern psychiatry: the bipolar depression. The field is faced with excellence, avoiding simplification and getting into the labyrinths of such an intricate chapter of neuropsychatric clinic. The author discusses the etiology, differential diagnosis, clinical classifications and potential treatment strategies.

In conclusion, I found this book easy to read in one hand, and rich, complete and complex in the other. In my humbled opinion, this book will be of enormous aid to junior and senior staff involved in the rich world of modern neuropsychiatry.