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BIBLIOGRAPHIC REVIEW ON THE COGNITIVE SYMPTOMATOLOGY OF TYPE I CHIARI MALFORMATION

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Abstract. Chiari malformation (CM) is a rare pathology with low prevalence. CM is within the group of malformations of the craniocervical junction, it is an anatomical alteration of the cranial base. There are considered to be 6 types of CM, being MC type I the most common one. The symptomatology can be very varied, having been reported cases of totally asymptomatic patients and others with serious neurological affections. Furthermore, recent research shows that congenital pathologies of the cerebellum such as CM can be accompanied by neuropsychological deficits. It is difficult to diagnose it due to the complexity of the lesion and the symptoms present in patients. However, the diagnosis is made by neuroimaging techniques, being the most widely used technique the magnetic resonance. Regarding to treatment, surgery is one of the main actions to be carried out after the diagnosis of CM. This review presents an exhaustive analysis of the existing literature on the cognitive functions affected of type I MC. It also describes the effects of surgical treatments on neuropsychological symptoms. The results show the presence of cognitive deficits; however, there is no agreement about exactly what cognitive functions are affected.

Keywords: Chiari malformation; treatment; surgery; cognitive; neuropsychology

REVISIÓN BIBLIOGRÁFICA SOBRE LA SINTOMATOLOGÍA COGNITIVA EN LA MALFORMACIÓN DE CHIARI TIPO I

Resumen. La malformación de Chiari (MC) es una patología rara de baja prevalencia y cuya patogenia actualmente sigue siendo objeto de debate. La MC está dentro del grupo de las malformaciones de la unión craneocervical, es una alteración anatómica de la base craneal. A día de hoy se considera que hay 6 tipos de MC, siendo la MC tipo I la más común. La sintomatología puede ser muy variada habiéndose reportado casos de pacientes totalmente asintomáticos y otros con graves afecciones de tipo neurológicas. Recientes investigaciones manifiestan que las patologías congénitas del cerebelo como la MC, pueden acompañarse de déficits neuropsicológicos. Es de difícil diagnóstico debido a la complejidad de la lesión y sintomatología presente en los pacientes. No obstante, el diagnóstico se realiza mediante técnicas de neuroimagen siendo la técnica más utilizada la resonancia magnética. En cuanto al tratamiento, la cirugía es una de las principales actuaciones a llevar a cabo ante el diagnóstico de MC. Esta revisión presenta un análisis exhaustivo de la literatura existente sobre las funciones cognitivas afectadas de la MC tipo I. Asimismo, realiza una descripción de los efectos de los tratamientos quirúrgicos en la sintomatología neuropsicológica. Los resultados evidencian la presencia de déficits cognitivos; sin embargo, no hay acuerdo sobre cuáles son exactamente las funciones cognitivas afectadas.

Palabras clave: Malformación de Chiari; tratamiento; cirugía; cognitivo; neuropsicología.

Introduction

Chairi Malformation (CM) is a rare disease of low health problem prevalence in populations. According to the European Commission of Public Health, this occurs when 1 of every 5,000 people is affected (Carbajal, 2015). Although the exact prevalence remains unknown ((Aitken, Lindan, Sidney, Gupta, Barkovich, Sorel and Wu, 2009), it is estimated that about one in 1,100 or one among 1,300 individuals present symptoms of CM-I. This data reveals that CM is as prevalent as multiple sclerosis (Mackenzie, Morant, Bloomfield, MacDonald and O'riordan, 2013; Meadows, Kraut, Guarnieri, Haroun and Carson, 2000; Speer et al., 2003). There is an incidence of about 5 cases per 10,000 inhabitants in the world, declining in Spain for up to 4 per 10,000 inhabitants (Orphanet, 2014). However, thanks to the introduction of the nuclear magnetic resonance (NMR) technique as of 1985, its detection has increased. However, its prevalence may appear to be higher than what is believed (Guerra et al., 2015). CM represents between 1% and 4% of all neurosurgical pathologies (Pérez Ortiz, Álvarez Armas, Rodríguez Ramos and Laud Rodríguez, 2017). According to the research carried out by Wilkinson, Johnson, Garton, Muraszko and Maher (2017), there is a greater prevalence of the disease in female adult patients, whereas an equal number of male and female patients are diagnosed in pediatric cases.

CM falls within a group of the so-called malformations of the skull-cervical union. It consists of a neuromuscular deformity, specifically, an anatomical alteration of the skull base, where in some cases, it manifests a herniation of the cerebellum and brainstem through the foramen magnum up to the cervical canal (Jiménez et al., 2015). It is associated with syringomyelia (Tubbs, 2015) where 10% of patients with CM-I may present hydrocephalus due to an obstruction of the left ventricular outflow (Pindrik and Johnston, 2015).

The symptomatology is diverse, with reported cases of asymptomatic patients and others with serious neurological conditions. Symptoms usually begin in adulthood, especially in those cases that do not present syringomyelia. They begin in an acute form

and continue in a progressive manner. The symptomatology tends to fluctuate, with periods of acuteness and remission (Mestres, 2015). The symptoms may be secondary to the alteration of the cerebrospinal fluid (CSF) fluctuation, to the marrow and bulb compression, to the cerebellar impact and, lastly, to those symptoms caused by the involvement of the cranial nerves (Regal, 2011). CM-I is a complex neurological disorder, with the most common clinical presentations including debilitating headaches, pain or pressure in the neck, a burning sensation in the neck, exhaustion, weakness, dizziness, visual disturbances, and scoliosis (Fischbein et al., 2015; Pindrik and Johnston, 2015). Various areas of the central nervous system are affected within the CM-I symptomatology, including the neuro-auditive system, the visual system, the lower cranial nerves, the cerebellum and motor and sensitive pathways (Perez Ortiz et al., 2017). Therefore, the symptomatology is variable, causing otoneurological, optical, respiratory, psychological and cognitive effects (Fischbein et al., 2015). The literature mainly focuses on the neurological symptomatology, but it should be noted that patients affected by cerebellar pathologies present cognitive and emotional symptoms classified under the cerebellar cognitive affective syndrome (CCAS) (Garriga-Grimau, Aznar Lain, Nascimiento and Petrizan Aleman, 2015). Cognitive comorbidities include difficulties in memory and executive functions (decision making), aphasia, psychological disorders and anxiety (Fischbein et al., 2015). As a result, MC-I has a negative impact on the quality of life of those who suffer from it (Mestres et al., 2012).

6 types of CM are thought to currently exist. CM-I is the most common, characterized by the herniation of the cerebellar tonsils that are greater than 5 mm below the foramen magnum level, though a minor tonsillar herniation does not exclude the diagnosis. There may be no symptoms. (Basaran, Efendioglu, Senol, Ozdogan and Isik, 2018). It has also been classified according to its I and II subtype etiology, based on whether it is respectively congenital or acquired, (National Institute of Neurological Disorders and Stroke, 2017).

CM-I is etiologically heterogeneous. The malformation's pathogenesis is unknown and controversial. The possible etiologies include genetic predisposition, congenital anomalies and acquisition by trauma or disease (Heiss, 2013). Given the clinical, genetic and morphological heterogeneity, it is most likely multifactorial with several mechanisms being involved, among them, early craniosynostosis from the skull base, which seems plausible in most cases (Boronat Guerrero, 2017). CM-I is also suggested as being the result of genetic predispositions to an abnormal mesodermal development (Abbott, Brockmeyer, Neklason, Teerlink and Cannon- Albright, 2017). However, four theories have been accepted to explain the congenital forms. The theories can be categorized as those that invoke the hydrodynamic and mechanical factors of the posterior fossa dysgenesis or bone dysplasia (Meadows et al., 2001). The evidence for a genetic basis has been mentioned by several authors (Coria, Quintana, Rebollo, Combarros and Berciano, 1983, Milhorat et al., 1999; Speer et al., 2000 and Szewka, Walsh, Boaz, Carvalho and Golomb, 2006) with the most probable mechanism being autosomal dominant inheritance with variable penetrance (Boronat Guerrero, 2017). Along this same line, it should be noted that CM-I may be associated with known genetic syndromes. A number of Mendelian disorders coexist with this pathology, presenting involvement of the bone and providing support for the mesodermal origin of the malformation, which include velocardiofacial syndrome, type-1 neurofibromatosis, growth hormone deficiency, klippel-Feil, cleidocranial dysplasia, Paget, Williams syndrome and achondroplasia, among others (Coria et al., 1983; Speer et al., 2000).

Early diagnosis is essential for the favorable evolution of the disease and to prevent damage progression of the central nervous system. However, this is difficult to diagnose due to the injury's complexity and the symptomatology present in patients, with their symptoms considered as unspecified in many occasions (Loved et al., 2009). CM-I is usually diagnosed in adulthood. The diagnosis can be discovered accidentally at around 15-37% of the cases, without the patient presenting a specific symptomatology, or in those patients evaluated by nonspecific symptoms, such as a headaches or dizziness. The average time for the diagnosis as of first visiting the physician is approximately 3 or 4 years, with only 8.46% of the patients having prior knowledge of the disease (Fischbein et al., 2015; Pindrik and Johnston, 2015). In addition, the symptoms often overlap with other disorders such as fibromyalgia and chronic fatigue, hindering the performance of the differential diagnosis (Ellenbogen and Bauer, 2013). Within this same line, it is important to mention the study carried out by Milhorat et al. (1999) in which 59% of the subjects reported having been diagnosed erroneously for mental problems.

The diagnosis is carried out by means of neuroimaging techniques (Pérez Ortiz, Álvarez Armas, Rodríguez Ramos and Laud Rodríguez, 2017). Advanced imaging aims to improve the accurate assessments of the malformation's seriousness and its effects on the dynamics of the cerebrospinal fluid (CSF) (Fakhri, Shah and Goyal, 2015). The degree to which the CSF flow is alternated has been seen to correlate with the severity and the development of clinical symptoms (McGirt, Nimjee, Fuchs and George, 2006). The combination of magnetic resonance imaging, and computed tomography (CT) for cranial scan, provide precise anatomical information. X-ray is also used to identify bony irregularities related to CM (Choudhury et al., Sarda, Baruah and Singh, 2013; National Institute of Neurological Disorders and Stroke, 2017).

Surgery is one of the main actions to be carried out when CM is diagnosed, as long as it is valued as a valid option for decreasing the symptoms and/or preventing the occurrence of future problems associated with it. However, with or without surgery, it is necessary to work together with the patient during their rehabilitation and physical and cognitive improvement (Cesmebasi et al., 2014). The most common treatment is surgery for the posterior fossa decompression. In the case of those patients diagnosed with asymptomatic CM-I, surgical intervention of any kind is generally not carried out. However, there is some controversy among neurosurgeons on the desirability of this. In this sense, it is important to note that between 15% and 30% of adult patients with CM-I are asymptomatic. In contrast, patients with neurological deficits or evolutionary symptomatology are candidates for surgical treatment. Because, although a cranial intervention always entails risks, it has been shown to have multiple benefits. The aim with surgery is to eliminate the pressure generated at the foramen magnum level (Arnautovic, Splavski, Boop and Arnautovic, 2015; Sahuquillo and Poca, 2014). However, with or without surgery, it is necessary to work together with the patient during their rehabilitation and physical and cognitive improvement.

This review includes an analysis of the existing evidence in the cognitive symptoms of patients with CM-I and the effects of surgical treatments in neuropsychological and cognitive symptomatology.

Methodology

To achieve the research objective, a bibliographic review of the currently existing scientific evidence has been conducted. The search was carried out between February and May 2018. We reviewed the following electronic databases: *Pubmed, Medline, EBSCOhost and Google Schoolar.*

Several search strategies were created that combined different descriptors using the controlled medical terminology MeSH (*Medical Subject Headings*) in English and DeCS (*Descriptores en Ciencias de la Salud*) in Spanish, and the Boolean operators AND, OR and NOT. Several filters were also applied (language, time periods, etc.) to narrow down the search based on the main objective. An inverse search was likewise carried out based on the bibliographic references of selected articles within the previously mentioned databases. The search terms used were "Chiari malformation AND treatment AND surgery AND cognitive AND neuropsychology". The inclusion criteria were the following: research written in English or Spanish, published in the year 2000, in a population diagnosed with CM-I. Single case studies were ruled out in terms of the exclusion criteria.

The bibliographic search recovered a total of 458 articles. Some were found to be duplicates from the different databases, and after ruling these out, the figure of recovered articles for the analysis numbered a total of 416 articles. After reading all their titles, 329 articles were ruled out, which did not meet the criteria. The articles that were ruled out were those in which the title did not coincide with the proposed study's objective. In addition, articles that only focused on a surgical perspective without addressing the involvement of the cognitive functions' intervention, were likewise ruled out. 87 were chosen, proceeding with a critical reading based on the titles and summaries, discarding 45 by not adapting to the study's objectives. We fully reviewed 42 bodies of texts from the following databases: *Pubmed* (22 articles), *Medline* (7 articles), *Google Académico* (5 articles) *and EBSCOhost* (8 articles), of which 35 were discarded because they did not meet the inclusion criteria. Those articles that did not analyze the neuropsychological effects of CM were also discarded. In the same way, articles from single case designs were ruled out. CM is a rarely researched disease, by which, due to the scarcity of research, no articles before the year 2000 were found that addressed the neuropsychological aspects nor the possible causes or effects of the disease. Lastly, 7 articles were analyzed from selected scientific journals in the field of neuroscience. At least one standardized instrument was selected in all the articles to measure specific domains or neuropsychological functions.

Results

The entire sample included a total of 862 subjects, divided into two groups from between 5 and 74 years of age. The clinical group was composed of 799 participants diagnosed with CM-I, and the control group by 63 healthy controls, matched by age and years of education (Allen et al., 2014; Garcia et al., 2018). In this sense, we should point out that several studies were characterized by the absence of the control group (Allen et al., 2017; Novegno et al., 2008, Grosso et al., 2001; Lacy et al., 2011 and Riva et al., 2011), and that a study contributed with 638 cases of patients diagnosed with CM-I.

The clinical sample in the studies analyzed is composed of 96 women and 55 men. It should be noted that in the study carried out by Allen et al. (2017) and Novegno

et al. (2008), they make no reference as to the participants' sex, therefore, the participants' gender is unknown in 81.10% of the clinical sample. The control group is formed by 47 women and 16 men. The data obtained is consistent with those provided by Amado et al. (2009) in which he asserts that CM affects both sexes, with a slight predominance in women.

On the other hand, we should mention that 664 of the patients diagnosed with CM-I had undergone decompression surgery (Allen et al., 2014; Allen et al., 2017; Riva et al., 2011). In contrast, 49 subjects were not subjected to surgical intervention (Garcia et al., 2018; Novegno et al., 2008). Within this same line, it should be noted that those studies carried out by Lacy et al. (2011) and Grosso et al. (2001) do not mention whether or not the patients had undergone intervention by posterior fossa decompression.

The following are the studies that analyze those neuropsychological aspects related to CM-I (Table 1).

CM-I correlates with an anxious-depressive symptomatology and pain (Allen et al., 2014; Allen et al., 2017; Garcia et al., 2018).

Garcia et al., (2018). They mostly found deficits in those tasks that involve a complex network of brain structures, in which the frontal lobe plays a key role, together with the connections it has with the cerebellum as, for example, Happe's Strange Stories, which is used to evaluate the theory of mind. The results support the presence of a cerebellar cognitive affective syndrome (CCAS) in patients with CM-I, since they display deficits in executive functioning, verbal fluency, spatial cognition and recall. Within this line, Allen et al. (2017) suggests that future research should distinguish between the cognitive effects resulting from damage to the fiber tract in the cerebellum (CCAS), with the effects of pain (distraction) in cognition. It should be noted that recent studies address the relationship between pain, attention and memory based on the hypothesis that the clinical experience of pain, combined with individual differences in focusing attention, has an impact on memory. Allen et al. (2017) concludes that chronic pain in CM diverts the attention focused on memory processes, or that pain pushes away the ability to focus on memory recovery.

In the study carried out by García et al. (2018), no participant received surgical intervention, or presented hydrocephalus or other specific craneo-cervical malformations. In contrast, participants from the study carried out by Allen et al. (2014) underwent posterior fossa decompression (PFD). They are based on the hypothesis that the herniation descending from the cerebellar tonsils causes structural damage directly related with the pressure from the regional neural circuit, causing dysfunction when generating chronic disorders such as pain. In addition, they pose the hypothesis that such damage in the cerebellum and its efferent/afferent circuits may give rise to cognitive deficits in executive function and episodic memory. Their study found that patients with CM-I showed worse cognitive performance for those tasks requiring reaction time (working memory, inhibitory control and processing speed), but did not observe differences in episodic memory. However, after control of the anxiety and depression effects, the effect of the response to inhibition remained statistically significant, while other tasks known for executive function, such as working memory and processing speed, were not.

Table 1
Neuropsychological Alterations in CM- I

Authors	Sample	Neurological Signal	Neuropsychological Instruments	Neuropsychological Profile	Findings
Allen et al., 2014.	n total: 48 n control: 24 Ages: 15 to 59	Headache, dizziness, and balance problems.	RAVLT; STROOP; Ospan Test and the task of substituting digital signals.	Deficits in inhibition response and processing speed.	Patients with posterior fossa decompression (PFD) present general cognitive dysfunction, persisting even after anxiety control.
Allen et al., 2017.	n: 638 n control: 0 Ages: 18 to 74	Chronic pain.	SF-MPQ-2 (McGill Pain-Short Form-Revised). RAVLT: Rey-Osterrieth verbal learning essay. RRQ: rumination and reflection questionnaire .	Deficits in memory (immediate recall).	Chronic pain is involved in focused attention, affecting cognition. Increases in reflection facilitate memory.
García et al., 2018.	n total:78 n control: 39 Mean: 45.59	Headache, dizziness, muscle pain, muscle weakness and difficulty sleeping.	Zoo map; inverse digits; STROOP; F-A-S; BNT (Boston naming test); TAVEC (Spain-Complutense Verbal Learning Test); SDMT (Symbols and digits tests); Benton Facial Recognition Test; FEEL (Facially expressed emotion labelling test), Happe's Strange Stories.	Lower performance in executive functioning, verbal fluency, recall accuracy, visual and verbal memory, remembrance, processing speed, facial recognition and theory of mind	Cognitive profile associated with cerebellar diseases.
Grosso et al., 2001	n total: 9 n control: 0 Ages: 6 to 13.	Abnormal EEG, seizure and epilepsy disorders.	-Wechsler children's intelligence scale. -Goodenough Test. -Bender visual motor skills.	Intellectual disabilities, speech impairment, visuoperceptual disability.	There is no correlation between the degree of ectopia and its clinical manifestation.

Lacy et al., 2016.	n total: 77 n control:0 Ages: 6 to 17	Headaches, swallowing problems, problems walking, seizures.	Questionnaire for parents BRIEF (The Brief Rating Inventory of Executive Functioning).	Deficits in executive and metacognitive functions, (working memory and difficulties in its induction).	Depression, sex, age, and posterior fossa decompression are not related to executive dysfunction.
Novegno et al., 2008.	n total: 10 n control: 0 Ages:1 to 16	Pain in the upper limbs, vertigo, papilledema, seizure and walking disorders.	Griffith mental development test or the Uzgiris-Hunt scales; Wechsler children's intelligence scale; Rey- Osterrieth Complex Figure Test; Gauthier Test.	Deficits in planning and troubleshooting, verbal fluency and recall, visual attention disorders, dyspraxia. Deficits in visual memory hyperactivity disorder.	Deficits in executive functioning, similar to patients with injuries to the dorsolateral prefrontal cortex and/or cerebellar injury.
Riva, Usilla, Saletti, Esposito y Bulgheroni, 2011.	n total: 2 n control: 0 Ages: 5 to 15	Neurological signs not reported.	Griffith mental development scale; other non-reported instruments that measure intelligence, language and behavior.	Case 1: Deficits in lexical comprehension and production, executive functions and pathological behavior. Case 2: Semantic fluency and phonological deficiency, hyperactivity and distractibility.	The cerebellum's impact on mental functioning is not exclusive, with such influencing factors as genetics and individual characteristics.

Novegno et al. (2008) described 10 children (20% with a borderline intelligence quotient). In contrast, Grosso et al. (2011) detected intellectual disability in all participants. Analogously, the displacement tonsillar fossa displacement was 10.1mm in both studies.

Behavior disorders can also be detected in children (Novegno et al., 2008). It should be noted that those who have headaches, difficulties swallowing and walking disorders as their main symptoms may have a higher risk of cognitive impairment and emotional dysregulation (Lacy et al., 2016).

Although all authors agree in the presence of cognitive deficits, there is no agreement on which of the cognitive functions are the ones exactly to be affected (Table 2).

Table 2
Cognitive Functions Affected by CM-I

Cognitive function	Altered area.
Executive functions	Working memory (Lacy et al., 2016). Initiating a response (Allen et al., 2014; Lacy et al., 2016). Planning and problem solving (Novegno et al., 2008). García et al., 2018.
Memory	Immediate recall (Allen et al., 2017). Visual memory (Novegno et al., 2008; García et al., 2018). Verbal memory (García et al., 2018).
Language	Verbal fluidity (Novegno et al., 2008; García et al., 2018). Recall (Novegno et al., 2008; Grosso et al., 2001). Speech impairment (Grosso et al., 2001). Lexical comprehension and production deficit (Riva et al., 2011).
Attention deficits	Visual attention disorder (Novegno et al., 2008). Hyperactivity and distractibility (Riva et al., 2012).
Processing speed	Allen et al., 2014; Allen et al., 2017; García et al., 2018.
Others	Dyspraxia (Novegno et al., 2008). Hyperkinesia (Novegno et al., 2008). Recall accuracy (García et al., 2018). Facial recognition (García et al., 2018). Theory of mind (García et al., 2018). Intellectual disability (Grosso et al., 2001; Novegno et al., 2008). Visuoperceptual deficits (Grosso et al., 2001). Pathological behaviour (Riva et al., 2012).

Discussion

This review examines the neuropsychological profile of patients with CM-I and carries out a compilation of the benefits found in the various treatments at the cognitive level.

CM is a controversial issue in contemporary literature, which currently continues the debate on pathogenesis, cognitive deficits and the most optimal treatment.

Approximately 80% of patients experience intense headaches, with analgesics used for reducing such pains, some based on opiates, which may have a negative effect on cognition (Allen et al., 2014). In addition, more than 40% of patients with CM-I state as having cognitive symptoms (Fischbein et al., 2015). Mahgoub, Avari and Francois. (2012) assert that there is a high risk of neuropathological processes of dementia in adults with CM-I. However, despite advances in our understanding of CM-I, studies including cognitive symptoms are scarce, with limited evidence being published.

Surgery is the only treatment available for correcting functional anomalies or halting the progression of damage in the central nervous system (Mestres, 2015). However, in spite of the evidence of cognitive alterations, such as in memory (Tavano et al., 2007), executive functions (Koziol and Barker, 2013) or alterations in the language (Fabbro et al., 2004) only four articles addressed cognitive functions after intervention (Allen et al., 2014; Allen et al., 2017; Lacy et al., 2016; Riva et al., 2011). Lacy et al. (2016) indicated that the executive functioning reported by parents was not affected by surgery or depression. Within this same line, Allen et al. (2017) were not able to identify group differences in the memory performance between those subjected to posterior fossa decompression and those who were not. This data could coincide with the study carried out by Kumar et al. (2011), who mention that memory impairment is due to a possible alteration of the tract's integrity. Cognitive disorders are due to the abnormal development of the cerebral white matter and the myelin's integrity. On the other hand, Riva et al. (2011) obtained contradictory results; the language of a child improved considerably but his behavior continued to deteriorate, as opposed to another case where the language worsened after surgery while the attentional deficits improved. The study carried out by Riva et al. (2011) is the only one that made a comparison of cognitive functions before and after surgery.

Schmahmann (2013) asserts that congenital malformations of the cerebellum such as CM, may be accompanied by brain damage that justifies limited cognitive functioning. The cerebellum plays a key role in the control of movement, with extensive cortical connections that are involved in several cognitive processes (Rogers, Savage and Stoodley, 2018). Although, the cerebellum, from a traditional point of view, does not exert a role in cognition, there is currently evidence regarding the cerebellum's participation in various processes and cognitive functions such as in attention, memory, learning, executive functions, language and visuoconstructional skills (Tirapu-Ustárroz, Iglesias Fernández and Hernandez-Goñi, 2011).

There is currently no standard protocol for cognitive assessment in CM-I (Rogers et al., 2018). In this sense, it is important to point out the importance of conducting a neuropsychological evaluation in order to use it as a base line at the beginning of rehabilitation and/or treatment with the aim of decreasing neuropsychological alterations in patients. The results obtained by Allen et al. (2014), García et al. (2018), Novegno et al. (2008) and Riva et al. (2014) reveal that patients with CM-I have a cognitive profile associated with cerebellar diseases. In this sense,

García et al. (2018) provides evidence about the cerebellum's implication in cognitive functioning, and the importance of the cerebellar cortical connectivity. In addition, they also suggest that verbal memory, processing speed, facial recognition and the theory of mind are domains that could be included as areas that are likewise involved in the cerebellar cognitive profile. However, Allen et al. (2014) suggests that working memory and processing speed are not closely related to the role of the cerebellum or brainstem as is the response inhibition (O'Halloran, Kinsella and Storey, 2012). With regard to the possible causes of cognitive dysfunctions, Allen et al. (2014) suggest that cognitive disorders are the result of an injury to the cerebellar tonsils. On the other hand, they pose the hypothesis that damage to the brainstem, in place of injury to the cerebellum, is what causes damage to the fiber tract, affecting the connections between the brainstem and the prefrontal cortex, and causing cognitive deficits, specifically executive dysfunction or more diffused cognitive deficits. The duration (Riva et al., 2011) and the scope (Del Casale et al., 2012) for the understanding of the brainstem is involved when manifesting the cognitive deficits. Grosso et al. (2001) found no correlation between the degree of ectopy and clinical manifestation. Although, the cerebellum's implication in cognitive functioning is unquestionable, there is still controversy regarding what the cerebellum's role is.

Recent publications, such as the review conducted by Rogers, Savage and Stoodley (2018) on cognition in CM-I, agree with the results of Allen et al. (2014), García et al. (2018), Lacy et al. (2016), Novegno et al. (2008), and Riva et al., (2011), in which they confirm that CM will probably incur cognitive deficits. However, there is insufficient evidence to describe a valid cognitive deterioration profile in CM-I. It would be necessary to conduct more research in this field in order to confirm these results and to integrate them with the pathophysiological model. The negative day-to-day impact that CM incurs should also be noted. Within this same line, Mestres et al. (2012) reveal that CM adversely affects the quality of life, especially in the work environment.

With regards to limitations, the scarcity of studies that analyze neuropsychological consequences after surgical intervention in people with CM-I is worth noting. It is necessary to continue building over the neuropsychological alterations with or without surgical intervention. Secondly, those articles in which the patients had comorbid neuropathology, such as spina bifida, basilar imprint, hydrocephalus or syringomyelia, were not excluded (Lacy et al., 2016; Novegno et al., 2008; Riva et al, 2011). The heterogeneity in the analyzed neuropsychological functions, along with the diversity of the neuropsychological instruments used in the various articles to measure an equal cognitive function, makes it difficult to compare results between studies. On the other hand, the sample size for most of the articles is characterized as being small. This may be due to the low prevalence of the disease in the population.

CM is a rare disease that has not reached the highest organizational level required to be carried out in multicenter studies, by which there is a lack of high evidence studies (De Oliveira Sousa et al., 2018). For a complete assessment of its impact on neurocognitive functioning and behavior, prospective and longitudinal studies must be designed in series (Riva et al., 2011).

In short, this review demonstrates the paucity of studies related to CM outside the clinical and surgical context, ignoring the neuropsychological aspects and emotional deficits. In relation to the overall objective of this work, it concludes that surgical treatments reduce the physical symptoms associated with CM, yet, few articles were found addressing the benefits of treatment based on cognition. The purpose of this study

was to undertake a comprehensive review of the literature to evidence the generalized cognitive impairment or specifically damaged neuropsychological functions in patients with CM. The possible day-to-day negative impact of cognitive impairment in patients, makes the detection and control of CM an important one. Ryan and Pealmen. (2004) reported that the quicker and more accurate that a patient receives their diagnosis and treatment, the better they will control their symptoms and return to a normal lifestyle. It is important to note, in this connection, the importance of the clinician to recognize the early signs of both the physical and neuropsychological disorders of CM-I. As such, extensive tests should be carried out on the patient's physical, neurological, cognitive and affective state. Early identification will assist in developing a treatment, as well as the appropriate referrals for more profound neuropsychological evaluations. Even though neuroimaging technologies have led to improved anatomical diagnoses, little is known about the cognitive symptom's incidence, since there are few articles that examine its neuropsychological, evolutionary and behavioral impact in patients with CM. Therefore, it is necessary for future research to not only focus on the surgical treatment or the neurological symptomatology, but also the cognitive consequences through an interdisciplinary perspective.

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