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Original

Executive and attentional functions in patients with migraine

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Introduction
Migraine is a disease that affects the overall performance of the patient, especially attention and executive functions (EF), with a direct impact on the person's functionality, highlighting the importance of studies in order to minimize its damage.

Objective
The objective of this study was to evaluate if there is a link between migraine and executive and attentional functions.

Methodology
Observational study (44 subjects; 29 migraineurs and 15 non-migraineurs) on attentional and executive functioning changes in migraine. Subjects over 18 years of age were included in the study, regardless of gender, recruited for convenience at CAM FAME, FAME and Centro AMA, primary recruitment centers, following the criteria of the International Classification of Headache Disorders (ICHD-3). The participants underwent neuropsychological tests that estimated executive and attentional functioning. For attention, the Psychological Attention the Assessment Battery (AAB) was used, and for EF, the Five-Digit Test (FDT) was used. Student's t test, ANOVA, Mann-Whitney and/or Kruskal-Wallis U test were used, whose analyzes fixed the type I error at 0.05.

Results
All AAB subtests pointed to a reduction in the attentional potential in migraineurs when compared to the control group. The FDT showed lowering in the migraineurs group subjects, when compared with the non- migraineurs group. Multivariate analysis identified a relationship between EF, Attention and migraine ($p<0.05$).

Conclusion
migraineurs present a decrease in executive functioning and attentional skills and an increase in execution time when compared to non-migraineurs individuals.

Keywords:
Migraine
Attention and Executive Functions

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Introduction

Migraine tends to lead patients to work incapacity, with losses covering both economic and social aspects, and is one of the most frequently demanded etiologies in primary care medical consultations(1,2).

Given the characteristics of migraines, understanding how it acts on different neurological and neuropsychological mechanisms is crucial for treatment to bring benefits beyond those primarily focused on pain relief or elimination. It should also aim at improving neurocognitive functions and their respective scopes(1,2).

In this sense, identifying factors that trigger migraine, in addition to understanding the impact of pain perception, may contribute to both understanding and treating its different forms of presentation.

Knowing the etiology, therapies, how patients perceive and live with their pain and how their lives are affected by it are basic care measures for a condition that afflicts a large part of the world's population(4,5). However, its deleterious and silent effects, related to neurocognitive deficits, should also be studied, so that management strategies go beyond the curative factor of pain and so that the role of pain can be understood in those skills that, at first, do not call attention to themselves and are not the primary targets of medical interventions. Physical symptoms, those which current strategies and interventions tend to reduce the negative impact of pain on the subject, are often considered the most important in the treatment of the condition given the relative ability to measure pain and its coadjutants. However, in addition to the physical signs, there is the possibility of impairment of noble cognitive variables such as Executive Functions and Attentional Skills, which are not always considered and which, for a long time, have also been underdiagnosed(5).

In this sense, Executive Functions (EF) can be seen as more complex cognitive processes related to the human behavioral repertoire and fundamental to achieving goals, which means that EF are directly related to the selection of objectives, to the choice of effective and efficient strategies and their monitoring. Thus, they can be maintained or refuted as behavior organized in a feedback mechanism. In other words, EF allows the subject to direct behaviors towards goals, evaluate their efficiency and suitability and replace ineffective strategies with efficient and functional ones in order to solve short, medium and long-term problems. To this end, Attention to and management of EF are fundamental for learning and solving problems that range from the everyday to the more complex ones.

Considering that EF is related to the activities of the prefrontal cortex(6,7), understanding how migraine interferes with this mechanism is of fundamental importance for both the doctor and the patient, considering the functional reduction caused by related abilities during periods of crisis.

Allied to EF are Attentional Skills (AS), which can also be influenced by the deleterious effects of migraine, given the involvement of structures that are also noble for them to happen. In this way, the circuitry involved, as well as neurotransmission, can show deficits in patients with migraine, with direct repercussions on the subject's neurocognitive functioning(6,8-10).

Thus, the aim of this study was to assess whether there is a relationship between migraine and EF and AS in subjects from observational and control groups, in order to identify possible impairments that could compromise the quality of life and functionality of patients who have this condition.

The study followed the ethical precepts of the National Health Council (CNS), Resolution 466/2012 and was approved by the Ethics and Research Committee of the Barbacena Medical School - FUNJOB, under CEP substantiated opinion number 5.331.909.

Methods

This was a cross-sectional study to assess whether there are changes in attention and executive functioning in migraineurs and non-migraineurs. Patients over the age of eighteen (18) were included, regardless of gender, and recruited consecutively for convenience at the Dr. Agostinho Paolucci Multiprofessional Academic Center of the Barbacena Faculty of Medicine - CAM FAME, the Barbacena Faculty of Medicine and the AMA Development Center - Barbacena/MG, between May and August 2022. Patients with cognitive impairment (difficulties in understanding and communicating) were excluded, as this would make it impossible to respond to the protocols, as were those who did not agree to take part in the study.

Migraineurs were diagnosed by the neurologist in charge of the research and by the students, according to the criteria of the International Classification of Headache Disorders(1), were invited to take part in the research. Thus, in an initial approach, patients who showed interest in complaining of migraine and patients diagnosed with migraine signed an informed consent form (ICF). The control group was recruited by randomly inviting people to the collection sites to answer the following questions: 1) Do you have migraines? 2) If not, would you like to take part in the study?

During the study period, all patients diagnosed with migraine who underwent neuropsychological assessment were included. The Psychological Battery for the Evaluation

of Attention was used for the AS test (AAB)(10) and the Five Digits Test was used for the Executive Function test (FDT)(11).

The AAB(10) measures, at different stages of life, attentional performance in 3 (three) distinct types of attention, related to 1) the ability to maintain the focus of attention on a given stimulus for a prolonged period; 2) the ability to distribute attention resources for the simultaneous execution of multiple tasks; 3) the ability to alternate attention resources between different stimuli. It assesses Concentrated Attention (CA), Divided Attention (DA), Alternate Attention (AA) and General Attention (GA) and has been validated to assess adults, with an average application time of around 20 minutes.

In turn, the FDT(11) can also be used as a measure of attentional processes and their accuracy, as well as assessing the speed and mental efficiency of individuals, with an average application time of 20 minutes.

After the tests were administered in accordance with the regulations of the Federal Psychology Council (CFP) by a psychologist registered with the Regional Psychology Council (CRP), they were corrected by a qualified neuropsychologist.

The tests estimated executive and attentional functioning as a result of the presence of migraine in the related patients, whose analyses set the type I error at 0.05.

Participants

A total of 44 people took part in the study, of both genders (74% women and 26% men), aged between 19 and 58, with a mean age of 31 years old (standard deviation - SD=12.99), with schooling ranging from incomplete elementary school to complete higher education. They were divided into 2 (two) groups: observational (migraineurs) made up of 29 people and control (non-migraineurs) made up of 15 people.

For both groups, short interviews were carried out and the following batteries were applied AAB(10) and FDT(11).

Materials

- Psychological Battery for the Attention Assessment (AAB)(10): Psychological Battery for the Attention Assessment (AAB)(10) measures, at different stages of life, attentional performance in 3 (three) distinct types of attention, related to the ability to maintain the focus of attention on a given stimulus for a prolonged period of time; the ability to distribute attention resources for the simultaneous execution of multiple tasks; the ability to alternate attention resources between different stimuli. It assesses concentrated attention, divided attention, alternating attention and general attention and has been validated to assess adults, with an average application time of around twenty minutes.
- Five Digit Test (FDT)(11): The FDT checks the speed of reasoning and response, as well as its accuracy and assertiveness. It can also be used as a measure of attentional processes and their accuracy. It assesses the speed and mental efficiency of individuals, with an average application time of 10 minutes.
- Structured abbreviated anamnesis.

Proceedings

The study was approved by the Research Ethics Committee of the Faculty of Medicine of the University of São Paulo, Barbacena(7) All participants were assessed individually and in accordance with the specific instructions for each instrument, as well as in accordance with the regulations of the Federal Council of Psychology (CFP) regarding neuropsychological assessment. Each assessment was carried out in a single session and the instruments were used in the following order: 1) Structured abbreviated anamnesis,2) AAB(10) and 3) FDT(11). The evaluations were carried out at the Dr. M. M. Multiprofessional Academic Center Agostinho Paolucci of the School of Medicine of Barbacena – CAM FAME, at the Barbacena Medical School Campus and at the AMA Development Center - Barbacena, by an accredited psychologist. The data from the questionnaires (anamnesis, AAB(10) and FDT(11)) were transcribed into a spreadsheet and processed using STATA v 9.2 statistical software. The relative and absolute distribution of the qualitative variables was calculated, as were the measures of central tendency of position and dispersion of the quantitative variables. The existence of a relationship between the variables studied was measured using the Chi-square and Fischer's exact tests. The existence of a relationship between qualitative and quantitative variables was measured using Student's T-test, ANOVA, Mann-Whitney U-test or Kruskal-Wallis as indicated. Statistically significant differences were those whose p-value was less than 0.05.

Results

The study included 44 people of varying ages and years of schooling of both sexes. The subjects were divided into two groups.

Figure 1 shows the average performance in the General Attention (GA) assessment between migraineurs (experimental group) and non-migraineurs (control group), showing the significant difference between them in terms of attentional skills. Of the 44 subjects, 29 were migraineurs and 15 were non-migraineurs. With regard

to General Attention, the migraineurs group showed lower results compared to the non-migraineurs group, showing worse performance compared to the control group, maintaining the same pattern of decrease in the AC, AD and AA variables, also compared by age group, schooling and raw score, with a mean of 220.0 for migraineurs and 292.7 for non-migraineurs($p = 0.0001$; CI 0.0008-0.1) showing a better positive relationship between time, absence of migraine and performance.

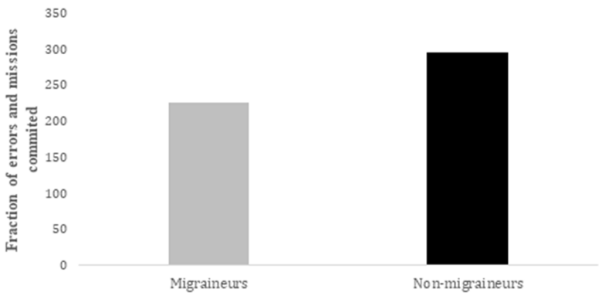

Figure 1. Average performance in General Care between Migraineurs and Non-migraineurs

Figure 2 shows the average performance in the evaluation of Concentrated Attention (CA) between migraineurs (experimental group) and migraineurs (control group). The migraineurs group had lower average performance ($M = 102.7$), taking longer to perform the tasks compared to the experimental group ($M = 87.8$), ($p = 0.010$; CI 0.03-0.9), which showed a better positive relationship between time, absence of migraine and performance. The migraineurs group made more mistakes and omissions during testing.

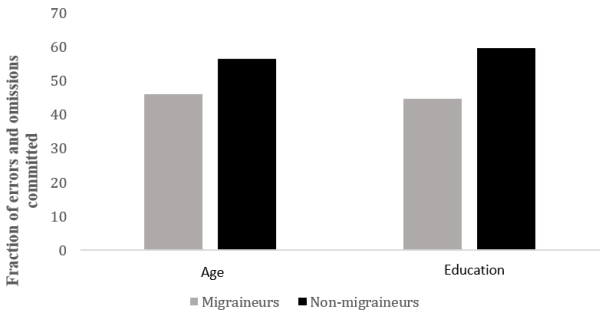

Figure 2. Average performance in Focused Care between migraineurs and non-migraneurs comparing age group and education

Figure 3 shows the average performance in the Divided Attention (DA) assessment between migraineurs and non-migraineurs. The migraineurs group had lower average performance ($M = 83.4$), taking longer to perform the tasks compared to the experimental group ($M = 51.1$) ($p = 0.002$; CI 0.0-0.9), which showed a better positive relationship between time, absence of migraine and performance. When comparing migraineurs vs. non-migraineurs in terms of age group and schooling, the pattern of more errors, more omissions and more time performing the tasks was maintained, with a significant difference between the groups.

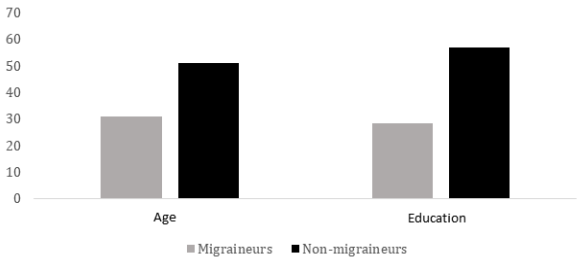

Figure 3. Average performance in Divided Care between Migraineurs and Non-Migraines comparing age group and education

Figure 4 shows the average performance in the Alternate Attention (AA) assessment between migraineurs and non-migraineurs. The migraineurs group had a lower average performance ($M = 106.6$), taking longer to perform the tasks compared to the experimental group ($M = 81.0$) ($p = 0.0001$; CI 0.01-0.9) which showed a better positive relationship between time, absence of migraine and performance. The decrease in the skills assessed was maintained when comparing migraineurs and migraineurs in terms of age and schooling, which shows the deleterious effect of migraine on neurocognitive functions. The way in which migraineurs organize themselves cognitively to carry out tasks seems to have a direct link with the reduced attentional ability in this group, causing them to take longer to perform them, with delays in the process of understanding them, attempts to reduce and/or correct errors made, although this has a negative impact on their performance.

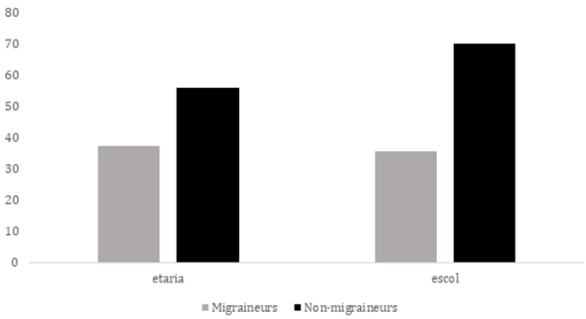

Figure 4. Average performance in Alternate Care between migraineurs and non-migraneurs comparing age group and education

In Figure 5, the Inhibition and cognitive flexibility skills measured in the FTD showed no statistically

significant differences between the groups (p = 0.524 and p = 0.377, respectively; CI 0.3-0.6), although the execution of the tasks was different between the groups (comprehension and execution of the task), important variables in neuropsychological clinical practice. In the EF tests, the migraineur group maintained the pattern of taking longer to perform the tests, although this was not statistically significant. The non-migraineur group, on the other hand, had a shorter execution time, greater accuracy and fewer mistakes and omissions in the task. Cognitive flexibility seems to play a fundamental role in the processes of understanding and performing tasks, favoring better performance. In this sense, migraine seems to have a negative impact when related to neurocognitive processes.

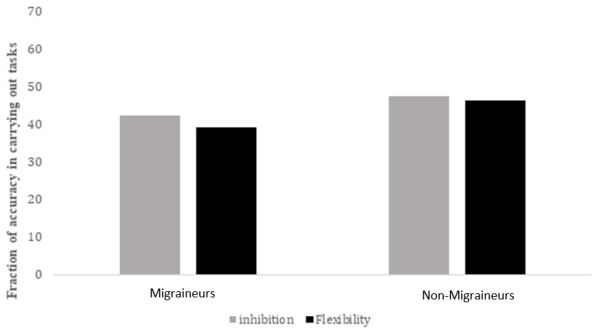

Figure 5. Executive Functions between Migraineurs and Non-migraines

Discussion

The aim of this study was to assess whether there is a relationship between migraine and executive functioning and attentional skills.

The data found point to a reduction in the attentional skills of people with migraine, which may suggest impaired performance in activities that require attention and concentration, whether academic and/or professional. In 2003, studies had already shown that migraineurs performed worse in memory and attention tests(12) and, more recently, we have seen migraine interfere with many other neurocognitive abilities, resulting in a considerable reduction in the subject's functionality(13).

Although the data on EF was not statistically significant, the bias of the attentional training (caused by the AAB battery)(10) may have masked results that were also lower, given previous studies(14).

Even though this study did not consider the drugs used by patients with migraine, nor their relationship with performance in the related tests, pain can be seen as a detrimental factor in cognitive functions, which can also lead to a reduction in academic and/or work activities. Here it is also worth mentioning the adverse effect of medication on neurocognitive functions that goes unnoticed due to the omission of the fact, absence and/or abandonment of therapy or even the presence of more prominent comorbidities (15-17).

The way in which the neuropsychological skills of attention and executive functions are interrelated with productivity at work are important factors to study, given that the study population, which is most affected, is part of an economically active group for the country.

Since EFs are cognitive control processes, necessary in activities that require concentration, impulse control and reasoning, (14) pain can become a distraction, impairing efficiency in the tests, increasing the time needed to perform them, as well as the number of mistakes. In addition, depending on the severity and intensity of the pain, it can become disabling, causing significant damage to patients.

EF is generally compromised in various acquired neurological disorders, as well as in neurodevelopmental disorders related to defects in the frontal-striatal circuitry, disorders such as Depression, Attention Deficit Hyperactivity Disorder (ADHD), dementia and schizophrenia will show a significant decrease in working memory skills, categorization, cognitive flexibility, inhibitory control, planning and problem-solving, decision-making, fluency and self-regulation or self-monitoring, which are important indicators of functionality and quality of life(6, 18).

It is worth remembering that EF is subject to the individual's maturational development, reaching its peak in late adolescence and early adulthood, with a decline from the 5th decade of life onwards, (6) which can also be influenced by clinical conditions such as migraine. In this sense, the treatment of this clinical condition, in addition to the obvious benefits of stopping the painful process, could also bring benefits in terms of the maintenance and quality of EF, which justifies the importance of early identification and appropriate treatment of related conditions(15).

Furthermore, when it comes to the relationship between EF, namely productivity and quality of life, the occurrence of comorbidities, especially psychiatric ones, can be a crucial factor, both for differential diagnosis and for effective treatment of the diseases involved(16, 17, 19).

In the same sense, attentional skills also have a direct correlation with the subject's neurobiological maturation process, with the integrity of the neuronal circuitry involved, with environmental elements of exposure, among others.

Attention, a highly complex ability, requires the control of intrinsic and extrinsic factors since memory and learning depend on its full activity.

Among the hierarchical relationships are alertness, attention, and selective attention, which also have their own neuroarchitecture and act in conjunction with other cognitive functions(20). Attention and EF are complementary elements acting in concert in the CNS. In addition, we must consider the pathophysiological issues involved in migraine and how they affect the subject(21).

In the context of this study, attentional skills remained lower in the group of subjects with migraine, which may indicate a close relationship between neuropsychological skills, neurological functioning, and intervening factors (e.g. pain). The longer it takes to concentrate, a process that depends on attention, the longer it takes to complete reasoning and tasks (mental and/or motor), thereby contributing to the length of time needed and greater possibility of error, considering the characteristics of each attentional entity, whether concentrated, divided or alternating(22).

The way in which the subject establishes concentration strategies that favor attention is decisive for the learning process. Faults in cognitive mechanisms, which begin with concentration, have a detrimental effect on the subject in connected spheres, whether academic or professional. In addition, the way in which semiological conditions (e.g. migraine, anxiety, ADHD, etc.) interfere with cognitive processes is also of interest, since the neural circuitry works together, and it is impossible to dissociate it from separate understandings. (23)

Conclusion

Given the results found, we can infer that migraine negatively interferes with attentional abilities and executive functions(6,18). Since attention and EF are important parts of cognition, any alterations can compromise the functioning of the whole, varying in severity according to the injury and/or dysfunction. Thus, the longer time taken to perform the tasks, both in the AAB(10) and FTD(11), showed slowness and low accuracy when compared to the migraineur group, which corroborates the hypothesis that migraine can impair efficiency in cognitive activities.

Further studies could contribute to understanding how migraine specifically affects each ability, favoring better therapies and, consequently, improving patients' quality of life and functionality.

Authors contributions: Valeska Magierek: Contribuições substanciais para a concepção, análise e interpretação de dados para o trabalho; elaboração e revisão do trabalho; aprovação final da versão a ser publicada; concordância para ser responsável por todos os aspectos técnicos do trabalho e auxílio na estatística. Responsável pela aplicação, correção e análise dos testes utilizados para a coleta de dados, uma vez que os testes neuropsicológicos necessitam de registro no Conselho Regional de Psicologia por parte do aplicador. A autora é neuropsicóloga (CRP 15389/04).

Letícia Silva Gomes de Carvalho: Contribuições para a concepção, análise e interpretação de dados para o trabalho; auxílio na revisão; aprovação final da versão a ser publicada; concordância em ser responsável por todos os aspectos do trabalho.

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Mauro Eduardo Jurno: Contribuições substanciais para a concepção, análise e interpretação de dados para o trabalho; elaborar o trabalho e revisá-lo; aprovação final da versão a ser publicada; concordância em ser responsável por todos os aspectos do trabalho. O autor foi o Professor orientador do Trabalho de Conclusão de Curso (TCC) que originou este artigo.

Conflict of interest: Declaramos não estar submetido a qualquer tipo de conflito de interesse junto aos participantes ou a qualquer outro colaborador, direto ou indireto, para o desenvolvimento do Projeto de Pesquisa intitulado "Funções executivas e atencionais no paciente com enxaqueca", cujos pesquisadores envolvidos são: Valeska Magierek, Letícia Silva Gomes de Carvalho, Camila Gualberto Bernardes de Assis, Mauro Eduardo Jurno.

Financing: Declaro ainda que nossa atuação como pesquisadores é independente, autônomo e comprometida com o interesse precípuo de defesa de direitos e a segurança do(s) participante(s) de pesquisa nos termos da Resolução 466/12 e demais diretrizes éticas em pesquisas envolvendo seres humanos, sem quaisquer envolvimento financeiro, tendo sido os custos relacionados à execução do projeto arcados pelos pesquisadores relacionados.

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References

1. The International Classification of Headache Disorders, 3rd edition (beta version). Cephalalgia. 2013;33(9):629-808.Doi

10.1177/0333102413485658
2. Steiner TJ, Stovner LJ, Vos T, Jensen R, Katsarava Z. Migraine is first cause of disability in under 50s: will health politicians now take notice? *The Journal of Headache and Pain*. 2018;19(1). Doi 10.1186/s10194-018-0846-2
3. Araújo CMd, Barbosa IG, Lemos SMA, Domingues RB, Teixeira AL. Cognitive impairment in migraine:A systematic review. *Dementia & Neuropsychologia*. 2012;6(2):74-9. Doi 10.1590/s1980-57642012dn06020002
4. Su M, Wang R, Dong Z, Zhao D, Yu S. Decline in attentional inhibition among migraine patients: an event-related potential study using the Stroop task. *The Journal of Headache and Pain*. 2021;22(1).Doi *10.1186/s10194-021-01242-6*
5. Diamond A. Executive Functions. *Annual Review of Psychology*. 2013;64(1):135-68. Doi 10.1146/annurev-psych-113011-143750
6. Rist PM, Kurth T. Migraine and Cognitive Decline: A Topical Review. *Headache: The Journal of Head and Face Pain*. 2013;53(4):589-98. Doi 10.1111/head.12046
7. Speciali JG. Migrânea: mudanças de paradigmas. *Revista Dor*. 2012;13(2):102-3. Doi 10.1590/s1806-00132012000200001
8. Vincent MB. Fisiopatologia da enxaqueca. *Arquivos de Neuro-Psiquiatria*. 1998;56(4):841-51. Doi 10.1590/s0004-282x1998000500024
9. Liguori BEV, Senna CEdO, Grateki GG, Fonseca ICRd, Pereira PF, Jurno ME. Cognitive deficit in migrainous patients: evaluation trough Addenbrooke's Cognitive Examination. *Revista Médica de Minas Gerais*. 2018;28.Doi 10.5935/2238-3182.20180022
10. Schmitz N, Arkink EB, Mulder M, Rubia K, Admiraal-Behloul F, Schoonmann GG, et al. Frontal lobe structure and executive function in migraine patients. *Neuroscience Letters*. 2008;440(2):92-6.Doi 10.1016/j.neulet.2008.05.033
11. Swartz RH, Kern RZ. Migraine Is Associated With Magnetic Resonance Imaging White Matter *Abnormalities. Archives of Neurology*. 2004;61(9). Doi 10.1001/archneur.61.9.1366
12. Campos MC, Silva MLd, Florêncio NC, Paula JJd. Confiabilidade do Teste dos Cinco Dígitos em adultos brasileiros. *Jornal Brasileiro de Psiquiatria*. 2016;65(2):135-9.Doi 10.1590/0047-2085000000114
13. Vuralli D, Ayata C, Bolay H. Cognitive dysfunction and migraine. *The Journal of Headache and Pain*. 2018;19(1).Doi 10.1186/s10194-018-0933-4
14. Kaiser Pinotti L, Castro AdS, de Oliveira Garcia GH, Alvim PHP, Roza TH, Andrade FA, et al. Executive functions in migraine patients: a systematic review with meta-analysis. *Cognitive Neuropsychiatry*. 2022;28(1):52-66.Doi 10.1080/13546805.2022.2149390
15. Santos KALdM, Martins HAdL, Ribas VR, Lima LCS, Santos CCd, Oliveira DdA, et al. Topiramate and cognitive function: review. *Headache Medicine*. 2015;6(1):12-8.Doi 10.48208/HeadacheMed.2015.3
16. Beltramini GC, Cendes F, Yasuda CL. The effects of antiepileptic drugs on cognitive functional magnetic resonance imaging. *Quant Imaging Med Surg*. 2015;5(2):238-46. Doi 10.3978/j.issn.2223-4292.2015.01.04
17. Stefane T, Napoleão AA, Sousa FAEF, Hortense P. Influência de tratamentos para enxaqueca na qualidade de vida: revisão integrativa de literatura. *Revista Brasileira de Enfermagem*. 2012;65(2):353-60.Doi 10.1590/s0034-71672012000200023
18. Dajani DR, Uddin LQ. Demystifying cognitive flexibility: Implications for clinical and developmental neuroscience. *Trends in Neurosciences*. 2015;38(9):571-8.Doi 10.1016/j.tins.2015.07.003
19. Lipton RB, Hamelsky SW, Kolodner KB, Steiner TJ, Stewart WF. *Migraine, quality of life, and depression. Neurology*. 2000;55(5):629-35. Doi 10.1212/wnl.55.5.629
20. Kowacs F, Roesler CAdP, Piovesan ÉJ, Sarmento EM, Campos HCd, Maciel Jr JA, et al. Consensus of the Brazilian Headache Society on the treatment of chronic migraine. *Arquivos de Neuro-Psiquiatria*. 2019;77(7):509-20. Doi 10.1590/0004-282x20190078
21. Ong JJY, Wei DY-T, Goadsby PJ. Recent Advances in Pharmacotherapy for Migraine Prevention: From Pathophysiology to New Drugs. *Drugs*. 2018;78(4):411-37. Doi 10.1007/s40265-018-0865-y
22. Peres MFP, Valença MM, Silva-Neto RP. Management of psychiatric comorbidities in migraine. *Headache Medicine*. 2018:61-7. Doi 10.48208/HeadacheMed.2018.13
23. Silva D and Santos MTG. GAZZANIGA, M. S.; HEATHERTON, T. F. Memória. In. GAZZANIGA, M. S.; HEATHERTON, T. F. Ciência Psicológica: Mente, Cérebro e Comportamento. Porto Alegre: Artmed, 2005. *Faculdade Sant'Ana em Revista* 2017;1(2):228-231