ISSN 0970-938X
www.biomedres.info

Executive functions in patients with different types of headaches.

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Abstract

Patients suffering from headache complain of the appearance of cognitive symptoms, although there is not much research in this regard, so the objective of the study was to analyze the deterioration in executive functions in patients with different types of headaches. The executive functions are processes related to the planning of the behaviour oriented to the achievement of a goal. A cross-sectional study was carried out, with a sample of 48 participants; 18 with vascular headache, 14 with tension headache, 16 with migraine. Significant differences have been found in the capacity for abstraction, which has discriminated between patients with vascular headache and tension headache, as well as between these and patients with migraine. Similarly, overall cognitive performance is different in patients with migraine compared with patients with vascular headache and tension headache. The type of headache and global cognitive impairment moderately affect the variability of abstraction capacity. Finally, the existence of a directly proportional relation of positive nature that indicates a dependent between the variables has been evidenced. It can be concluded that global cognitive deterioration affects the performance of abstraction capacity.

Keywords: Cognitive Impairment, Executive Functions, Headache.

Accepted April 05, 2021

Introduction

The most frequent neurological etiologies in headaches usually are Cerebrovascular Accidents (CVA), traumatic brain injury (TBI), epileptic disorders, brain tumors, as well as infections and organic clinical pictures of dementia. The CVA accounts for 24.5% of emergency health care [1]. Second in frequency is the epilepsy, which accounts for 10%-15% of cases [2]. According to a previous study [3], the third most frequent pathology is headache (8%), and other pathologies with less prevalence such as central nervous system tumors, dementia, or TBI are the reason for ED consultation in less than 5% of cases [4].

Headache is a symptom that can be of mild, moderate or severe intensity; it has a frequency of one or several episodes weekly; the pain can be pulsing, accompanied by nausea, and discomfort such photophobia or phonophobia; and are located in one or more regions of the brain (frontal, occipital, hemicranial). There are different types of headache pain, some are primary (90%), including migraine, tension headache, and others are secondary (10%), caused by another pathology, such as vascular headache [5].

Migraine is a disabling primary headache whose prevalence is 20.2% in women and 9.4% in men [6], while the tension headache has a higher prevalence ranging from 30% to 78% compared to headache of vascular origin [5]. Has been demonstrated that severe headache causes an increase in cerebral white matter hyperintensity and that migraine with aura is associated with cerebral strokes [7].

Any neurological pathology results in the appearance of a variety of clinical manifestations, like behavioral, emotional, functional and neuropsychological alterations. These are mainly related to an alteration of cognitive functions (orientation, attention, memory and learning, calculation, language and executive functions).

Executive Functions (EF) consist of a constellation of higher order cognitive functions related to the planning of goal-oriented behavior. Muriel Lezak [8] defines them as "mental capacities necessary for formulating goals, planning how to achieve them, and carrying out the plans effectively". The latter include a number of cognitive processes such as motor programming, language, and abstract reasoning. Generally, a lesion in the prefrontal cortex implies the presence of a dysexecutive syndrome characterized by behavioral disorganization and control [9].

Prospective studies that addressed the symptomatology presented by patients with CVA, have shown an impairment of verbal memory, as well as visual skills and other areas such as attention and EFs [10]. In subjects with epilepsy, some studies demonstrate that there are cognitive deficits focused on attentional processes and so-called EFs [11]. In patients with TBI, the existence of cognitive impairment in attentional capacity has been manifested, as well as in cognitive flexibility, inhibition capacity and resistance to interference, processes that are part of the EFs [12].

However, in patients with headache, few studies have investigated in detail the cognitive performance and to a lesser extent the EF.

Recent studies have shown that cognitive impairment and its impact can be magnified by the presence of headache symptoms [13]. Other authors assert that EFs, working memory, and attentional capacity are impaired in patients with headache [14].

Most of the patients that suffer from some type of headache complain of the appearance of cognitive symptoms, although it is still a relatively unexplored topic in this type of pathologies [15]. From previous studies, the absence of empirical evidence demonstrating the type of specific affectation in EFs is noted, so the aim of this research work is to analyze EFs in patients with different types of headache and their possible relationship with cognitive impairment.

Methods

The methodology used is correlational, the study design was observational-cross-sectional, and the whole study has been conducted between April-2018 and April-2019. The study was methodologically approved by the Bioethics Committee of the Universidad Central del Ecuador. The 48 participants were patients who attended to the Neurology Outpatient Clinic of the General Teaching Hospital of Riobamba and who met the following criteria:

• A neurological diagnosis of headache made by a neurologist according to the criteria of the International Classification of Headache Disorders (ICHD-3).

• Meet diagnostic criteria according to DSM-V and ICD-10 [16,17].

• Having a neurological picture of acute headache or having suffered it in the last 3 months.

• Not to have more than 9 months of evolution of the neurological symptoms.

• Not to have clinically relevant and demonstrable neurological, psychopathological or substance abuse history.

• Accomplish with the norms of the Declaration of Helsinki and show informed consent to participate in the study.

• Do not present any type of sensory disability that prevents or hinders the evaluation.

• Not to have other concomitant neurological symptoms.

All patients received a clinical examination of the cranial nerves by a neurologist. After diagnosing the type of headache (migraine, tension, vascular) based on the parameters of the ICHD-3, the clinical history has been reviewed and, in accordance with the inclusion criteria, the sample was selected. Subsequently, after complying with the norms of the Declaration of Helsinki, informed consent was requested and the Brief Neuropsychological Battery in Spanish "NEUROPSY" was applied [18].

Materials

The instrument used consists of a test battery for different specific domains such as attention, language, memory, EF and calculation. It allows obtaining a total score of cognitive functions, in which the patient's performance can be classified using the subject's schooling and age, into normal, mildly impaired, moderately impaired and severely impaired. In accordance to Ramos-Galarzaa [18] the overall test-retest reliability is $\alpha = 0.87$, and as for the sensitivity and specificity rates, these allow discrimination between groups of patients with dementia and incipient cognitive impairment in both Mexico and Brazil. The discriminant validity in the correct classification of patients with mild and moderate dementia in comparison with a control group, was with an accuracy greater than 91.5% and in subjects with brain damage measured 95%.

The variables that have been selected from the Neuropsy test as indicators of cognitive performance, have been the Neuropsy total score and a set of variables that are part of the EF, and are shown below:

Total Neuropsy Score: Consists of the sum of all the tests once the pertinent scores and corrections have been made according to the patient's performance. This score reflects the level of global cognitive impairment. The levels of impairment that can be obtained are normal, mild, moderate and severe. Although the maximum score ranges around 124 in patients with schooling from 1 to 4 years and 130 in the subsequent cases [18].

Regression digit span test: A task consisting in a repetition in reverse order of a series of numbers with increasing amplitude, being an indicator of working memory, an aspect related to EF [19]. The maximum score is 6 points.

Phonetic verbal fluency: Is a test in which the subject is asked to be able to mention during one minute all the elements or words beginning with the letter "F" under the phonemic slogan of the same letter. Once the number of correct answers has been counted, these have to be coded according to the following scale; 0-6 (1), 7-13 (2), 14-18 (3), 19-50 (4), so the maximum score that can be obtained is 4 points.

Similarity: Refers to the subject's capacity of abstraction to determine the similarity between pairs of concepts without any apparent relationship. The maximum score is 6 points.

Calculation: Consists of performing a series of arithmetic operations, in which the subject has to perform a calculation for three problems of low level complexity. Maximum score = 3 points.

Sequence learning: It is defined as the inability to program, follow, remember or learn a sequence, whether motor, verbal or graphic. The task consists of continuing with the reproduction of a model formed by a sequence of geometric characters. Has been shown that the impossibility of sequencing is due to a prefrontal cortex involvement [20].

A score of 1 is given in case of correct execution.

Change of hand position: The examiner performs 3 sequential hand movements and waits for the subject's execution. The maximum score is 4 points.

Alternating movements of both hands: The task consists of the execution of alternating and simultaneous movements. The maximum score is 2 points.

Opposite reactions: Consists of the execution of an intransitive gesture in contraposition to the one performed by the examiner. The maximum score is 2 points.

According to Liepmann [21], the alteration of the execution of a motor act like those described above, previously learned and not caused by paralysis or movement disorder, nor sensory or perceptual alterations, may be due to an executive alteration of the frontal lobe.

Data analysis

The statistical processing of the data was carried out using IBM SPSS Statistics software, version 22. Descriptive statistical techniques used were: mean, mode, median, standard deviation, frequency analysis (absolute and relative); in addition to inferential tests such as one-factor Anova and Chi2 (for the establishment of differences in means) and analysis of covariance, Pearson's correlation coefficient and linear regression model (to determine the relationship between variables).

Discussion and Conclusion

The 48 patients with the diagnosis of headache were distributed as follows: 18 with vascular headache, 16 with migraine and 14 with tension headache.

The minimum age value was 16 years and the maximum 62 years, with a median of 37 and a mode of 39, which were similar to the central tendency measure of the mean. Around 70% of the participants were female and approximately 60% had studies compatible with the 10-24 years of schooling interval, which corresponds to the category of higher education. Practically the entire sample showed a right-handed manual dominance.

Respectively to the socio demographic characteristics according to the different types of headache, it was found that in both tension-type headache and migraine, more than 75% of the sample was female. The highest average age is related to tension headache, and the variability of scores between the 3 groups is usually very similar. Most of the distribution has high levels of schooling, irrespectively of headache type, additionally were found a few cases of education levels between 1-4 years. Most of the participants are married and most of them have a right-handed laterality (Table 1).

Table 1. *Descriptive analysis. Sociodemographic features in function of headache diagnostic.*

Variable		Vascular headache N (%)	Tension headache N (%)	Migraine N (%)	X^2
Gender	Male	4 (22,2%)	8 (57,1%)	4 (25%)	,079 Ns
	Female	14 (77,8%)	6 (42,9%)	12 (75%)	
Age M (SD)		41,83 ± 14,07	30,21 ± 11,33	31,50 ± 13,81	,028 *
Schooling	0-4 years	1 (5,6%)	1 (7,1%)	2 (12,5%)	,088 Ns
	5-9 years	8 (44,4%)	7 (50%)	1 (6,3%)	
	10-24 years	9 (50%)	6 (42,9%)	13 (81,3%)	
Civil status	Single	4 (22,2%)	7 (50%)	6 (37,5%)	,259 Ns
	Married	14 (77,8%)	7 (50%)	10 (62,5%)	
	Divorced	--	--	--	
	Widower	--	--	--	
Laterality	Right handed	18 (100%)	13 (92,9%)	15 (93,8%)	,531 Ns
	Left handed	--	1 (7,1%)	1 (6,3%)	
	Ambidextrous	--	--	--	

Abbreviation: SD, Standard Deviation; M, Mean; N, Sample; Ns, No significance; X2, Chi2.
*=statistically significant relationship, p=o<0.05

When the Chi2 test was applied to determine if there were differences in the sociodemographic variables in relation to the different types of headache, it was found that there were not statistically significant relationships (P>0.05), indicating that the groups were relatively equal regarding these variables, except the "age" variable, in which the one-factor Anova showed statistically significant differences (P=0.28).

Analyzing the main EFs in patients with different headache conditions, it is evident that in the variables: working memory, sequencing, calculation, phonetic fluency, manual position change, manual alternating movements and opposite reactions; there is no significant association (P>0.05) (Table 2). However, previous studies with a similar sample of participants with a type of episodic and migraine headache, have concluded that there is executive dysfunction, thus the difference may be the type of headache [14] or the age of the sample [22].

In the total score of the Neuropsy test, which is an indicator of the level of cognitive impairment, has been found that there are significant differences when it is analyzed according to the type of headache (F=7.80; P>0.001), which indicates as observed in the average values, that the group with migraine has a higher score. Previous studies confirm the presence of cognitive dysfunction in this type of patient [15].

Similarly, the only EF that is compromised in relation to headache types is the abstraction capacity (F=8.28; P>0.001), an aspect that suggests that patients with tension headache (who obtained the worst average), may have problems in performing tasks involving abstract reasoning capacity. Other authors found that patients with chronic headache and those with migraine presented worse performance in executive tests, unlike patients with episodic headache and subjects without any neurological involvement [23]. Likewise, a possible cause of the appearance of this type of pathology, as well as the explanation of the executive deficit, represents the presence of brain alterations occurring in the frontal cortex and anterior cingulate cortex [24].

To determine the exact relationship between EF, Neuropsy total score, and headache types, a multiple comparisons analysis was performed using Tukey's post hoc test. The results obtained showed that performance on the abstraction tests (similarities) significantly differentiated patients with vascular vs. tension headache (P=0.006). Similarly, when comparing such performance in patients with tension headache vs. migraine, a highly significant relationship is evident (P<0.01), in contrast to the other groups (Table 3). Other studies conducted to measure executive functioning in migraine patients have suggested that visual reasoning and cognitive flexibility, both components of EF related to the level of abstraction, were affected in contrast to control groups [25].

In contrast, when the Neuropsy total score is analyzed, the data point to highly significant differences between the migraine group relative to vascular headache patients (P=,006) and tension headache patients (P=,003), results that indicate that migraine patients may have cognitive performance associated with a higher level of impairment (Table 3). Other studies that have compared performance on different neurocognitive measures, including tests assessing sensorimotor functioning, attention processing, language and memory have concluded that patients with migraine have significantly lower performance than, in other types of headache [26].

Table 2. *Mean difference test: One factor Anova. EFs (Neuropsy) in function of headache diagnostic.*

		N	Mean+SD	One factor Anova		
				F value	Df	P
Neuropsy total score	Vascular headache	18	94,26 ± 7,98	7,80	45;47	,001**
	Tension headache	14	92,35 ± 14,94			
	Migraine	16	108,63 ±13,65			
Operative memory	Vascular headache	18	3,16 ± 1,24	1,27	45;47	,290NS
	Tension headache	14	3,42 ± ,85			
	Migraine	16	3,75 ± 1			
Phonetic fluency	Vascular headache	18	1,72 + ,82	2,00	45;47	,147NS
	Tension headache	14	1,85 ± ,86			
	Migraine	16	2,43 ± 1,45			
Calculation	Vascular headache	18	1,61 ± ,97	,44	45;47	,645NS
	Tension headache	14	1,57 ± ,93			
	Migraine	16	1,87 ± 1,02			
Sequence learning	Vascular headache	18	,55 ± ,51	,676	45;47	,514NS
	Tension headache	14	,64 ± ,99			
	Migraine	16	,75 ± ,44			
Manual position change	Vascular headache	18	3,11 ± 1,13	,589	45;47	,559NS
	Tension headache	14	3,07 ± 1,14			
	Migraine	16	3,43 ± ,81			

Alternating manual movements	Vascular headache	18	1,66 ± ,59	1,80	45;47	,176NS
	Tension headache	14	1,50 ± ,65			
	Migraine	16	1,93 ± ,68			
Opposite reactions	Vascular headache	18	1,72 ± ,46			
	Tension headache	14	1,64 ± ,49	1,11	45;47	.317NS
	Migraine	16	1,87 ± ,34			
Similarity	Vascular headache	18	5,27 ± ,82			
	Tension headache	14	4 ± 1,66	8,28	45;47	,001**
	Migraine	16	5,56 ± ,72			

Abbreviations: SD: Standard Deviation; F: Snechdecor's F; EF: Executive Functions; Df: Degrees of freedom; N: Sample; Ns: No significance; P: statistical significance value.
** High statistical significance value = o<de ,01.

Table 3. *Multiple binary combinations: Post hoc test. Tukey's range test. Similarity and total score (Neuropsy) in function of headache diagnostic.*

Variable/Diagnostic		**Diagnostic**	**Mean difference (SE)**	**P**
Similarity	Vascular headache	Tension Headache	1,27 (,39)	,006**
		Migraine	-,28 (,38)	,738 NS
	Tension headache	Vascular Headache	1,27 (,39)	,006 **
		Migraine	-,156 (,40)	,001*
	Migraine	Vascular Headache	-,28 (,38)	,738 NS
		Tension Headache	-,156 (,40)	,001*
Neuropsy total score	Vascular headache	Tension Headache	1,90 (4,44)	,904NS
		Migraine	-14,36 (4,36)	,006**
	Tension headache	Vascular Headache	1,90 (4,44)	,904NS
		Migraine	-16,27(4,58)	,003**
	Migraine	Cefalea vascular	-14,36 (4,36)	,006**
		Cefalea tensional	-16,27(4,58)	,003** -

Abbreviation: SE: Standard Error; EF: Executive Functions; Ns: No significance; P: Statistical significance value
* Significance level = o<de ,05.
** Significance level = o<de ,01.

To determine whether age and Neuropsy total score affect the variability of the similarity test, was performed an analysis of covariance which showed that the controlling of the age has no distorting effect on the similarity variable (P>0.05). In contrast, a highly significant relationship (P<0.01) was evident for the Neuropsy total score, suggesting that it is an effect modulating variable. Similarly, headache types also constitute a variable that affects the performance on the resemblance tasks (P=0.027). The effect size is moderate (0.441), consequently a part of the variability of the tasks that demand an abstraction level is modulated by the headache type and the global impairment level (Table 4).

To quantify the existence of a relationship between the similarity and the Neuropsy total score, has been applied the Spearman correlation coefficient. The results obtained point to the existence of a positive-directly proportional relationship of moderate intensity, between both variables, the results were in vascular headache (r Spearman=0.50; P<0.05); while in tension headache has been demonstrated a statistically significant relationship(r Spearman=0.59; P=0.25); and in migraine there was an absence of association (P>0.05) (Table 5).

A possible explanation for the absence of a relationship between these variables in migraine may be since the fact that the decrease in cognitive impairment and EFs are correlated with variables such as duration and frequency of headaches [26]. For this reason, some researchers claim that the increased frequency and severity of migraine episodes are associated with certain EFs such as inhibitory control [27]. These data suggest that migraine patients who tend to a greater severity, exhibit an altered brain connectivity related to executive alterations [28].

In order to test a possible causal relationship between the variables aforementioned, the linear regression model was applied and obtained R2=0,298, thus, the 29% variation in performance on the similarities subitem is explained by the Neuropsy total score. The One Factor Anova (P=0,00) indicates that the variables are linearly related and that the regression line equation predicts that performance on the similarities is = 0.48 + 0.50 of the Neuropsy total score (Table 6). These data suggest that global cognitive performance can mildly-moderately predict performance on abstraction ability. Previous studies on pathologies such Alzheimer's disease, have shown that executive deficits do not appear in isolation, but are part of global cognitive performance [29-31].

Table 4. *Analysis of Covariance. Similarities in different headache types, controlling for the effect of Age and Neuropsy total score.*

Variable	Factor	RMSE	F	g.l	P	Partial Beta²
Similarities	Headache types	8,11	3.96	2; 45	.027*	8,28
	Covariables: Age Total score Neuropsy	,178 12,55	.174 12.27	1; 45 1; 45	679 NS .001**	--
Abbreviations: RMSE: Root Mean Square Error; F: Snechdecor's F; g.l: degrees of freedom; P: Probability or statistical significance.; Ns=NO significance (P>.05) *= significance 5% (P<.05) **=High statistical significance value 1% (P<0.01)						

Table 5. *Bivariate correlation analysis using Spearman's correlation coefficient: Similarities and their relationship with the Neuropsy total score in patients with different headache types.*

Association	Method	Vascular headache		Tension headache		Migraine	
		R	P	R	P	R	P
EF/ Total score Neuropsy	Spearman	.076	.048*	.59	.025*	.425	.11NS
Abbreviations: EF: Executive Functions; Ns; No significance; P: Value of statistical significance; R; value of the Correlation coefficient, *High statistical significance value = or<of ,05.							

Table 6. *Linear regression. Similarities and their relationship with Neuropsy total score.*

R	R2	one-way ANOVA		Unstandardized coefficient	
		R	P	R	P
EF/ Total score Neuropsy	Spearman	.076	.048*	.59	.025*
Abreviaciones: F; Snechdecor's F; P; Value of statistical significance; R; Value of the. correlation coefficient; R2; Coefficient of determination. **High statistical significance value = o<de ,01.					

Conclusion

The Performance in certain executive functions (abstraction) differed between patients with vascular vs. tension headache and between patients with tension headache migraine.

Global cognitive performance discriminates between migraine patients compared to vascular headache patients and tension headache patients.

Both global cognitive impairment and the different types of headache moderately affect the variability of the similarity variable.

There is a directly proportional positive relationship of moderate intensity between tasks that assess abstraction and total cognitive performance, so that the total cognitive performance allows prediction of performance in abstraction tasks.

The study has a number of limitations regard the small sample size, which forms part of each type of cephalic pathology, so the results should be taken with some caution. Likewise, the incorporation of an asymptomatic control group that would allow a comparative difference.

Future lines of investigation could include neuropsychological assessment tests specifically designed to measure executive functions in function of the headache type, to determine which components would be most affected.

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