Memory impairments and mental status in patients with migraine

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Abstract

Migraine is the second most common type of primary headache having a worldwide prevalence of 10-12% in the adult population. The disease is principally characterized by recurrent attacks of unilateral headache that typically last 4 to 72 hours, associated with other neurological symptoms in addition to pain, such as nausea, photophobia and fatigue as well as numerous disturbances in autonomic, mental, sensory and motor functions. Patients with migraine consistently show performance deficit on memory task, whether the material in question is verbal or non-verbal, recently learned item or older material. ***Aim:*** *The study has been design to assess the memory deficit in migraine patients and it's comparison to normal control group.* ***Methods:*** *The sample consists of 100 subjects, out of which 50 migraine patients diagnosed by neurologist and 50 normal controls without a history of headache have been included in the study. Mini Mental Status Examination and Wechsler memory scale (WMS III) have been used in the study.* ***Results:*** *Migraine patients performed poor in comparison to normal control on MMSE and subtest of WMS III. It has further been found that patients with migraine were having problems of immediate, recent and remote memory. They were having impaired logical memory in terms of conceptualizing theme of the story and had difficulty in learning and remembering the information.* ***Conclusion:*** *The present study suggests that patients with migraine might present higher risk of cognitive impairments, especially in certain neuropsychological domains such as orientation, logical memory and conceptualization.*

Key words: Migraine, Memory impairments, Orientation

Introduction

A migraine is usually a moderate or severe headache felt as a throbbing pain on one side of the head. Many people also have symptoms such as nausea, vomiting and increased sensitivity to light or sound. Migraine is a common health condition, affecting around one in every five women and around one in every 15 men. They usually begin in early adulthood. It is a common neurological disorder with a prevalence of approximately 12%, and a cause of significant disability for many patients. As a result, the World Health Organization has listed migraine as a significant public health concern and a major cause of years of life lived with disability (Leonardi et al. 2005, O'Brien et al. 1994 and Jelinski et al. 2006).

Migraines often begin in childhood, adolescence or early adulthood. It may progress through four stages:

1. prodrome- One or two days before a migraine, warn of an upcoming migraine, including: Constipation, Mood changes, Food cravings, Neck stiffness, increased thirst

2. Aura--It may occur during migraines, Auras are symptoms of the nervous system. They are usually visual disturbances, such as flashes of light or wavy, zigzag vision.

3. headache-- It may occur during a migraine, Pain on one side of head, Pain that feels throbbing, Sensitivity to light, sounds, and sometimes smells and touch, Nausea.

4. post-drome-- occurs after a migraine attack. Confusion Moodiness, Dizziness, Weakness.

Due to the high life time prevalence of migraine in the general population and an increasing life expectancy, a causal association between migraine and cognitive impairment would have major public health consequences. These consequences would be especially important among women who have a higher prevalence of migraine and dementia compared to men (Bigal et al, 2009, Ott et al 1998, Le Pira et al.2000). One cross-sectional study looked at cognitive performance just among migraineurs and found that attack frequency was not related to cognitive performance. However, there was some evidence that the location of pain (right side, left side or bilateral) may impact immediate and delayed recall on the Rey Complex Figure Test. Some studies did not find any cognitive difference between migraine patients and non-migraine subjects. Conversely, other studies revealed that migraine patients are characterized by a poorer cognitive performance. The discrepancies among studies assessing cognitive functions in migraine may be ascribed to several reasons, possibly related to differences in patients' characteristics (some studies enrolled both patients with or without aura), sample sizes or neuropsychological assessments.

Rationale of the study

Among migraineurs with aura, those with right-sided and bilateral pain exhibited the worst recall (Gaist et al. 2005, Gaist M and van Boxtel, 2000) but some studies did not find any cognitive difference between migraine patients and non-migraine subjects. However, no general consensus has yet been established regarding the cognitive performance of these patients. Cognitive defects in migraine have been reported by several authors but these findings however, are controversial so the present study was designed to examine cognitive functioning (Memory and orientation) in patients with migraine and normal controls.

Objectives

The present study has been undertaken with the following aims

1. To assess the memory deficits in migraine patients as compared to normal control
2. To examine the gender differences of cognitive functions in migraine patients
3. To determine the relationship of disease status and gender along with MMSE and domains of WMS-III
4. To find out the role of WMS-III (all domains) as a predictors of MMSE

Methods

The sample consisted of 100 subjects, out of which 50 were patients with migraine selected by neurologists from Department of neurology, S.S. Hospital, B.H.U. Varanasi and 50 were normal controls. Both female and male participants were included in each group. For both groups GHQ-12 (Goldberg and Williams, 1988) was used to assess any psychiatric problems and subjects having cut off score more than 2 were excluded. Inclusion criteria for the registered patients were in the age group of 20-45 years and having recurrent attacks of unilateral headache. Patient's history of headache was taken in detail. Purposive sampling technique was used for selecting the sample.

Measures

1. **Hindi version of Mini-Mental Status Examination (HMMS): (**Folstein, Folstein & Mc Hugh's (1975) The HMMS (Dwivedi, Pandey & Gopal jee, 1996), was used to assess the orientation and other cognitive capabilities in migraine patients. This test has 11 contextual areas with time orientation, place orientation, registration, attention and calculation, recall of previously registered 3 items, naming of two objects, and repetition of 5 words in a row, following the 3 stage command, reading and writing of a sentence, and copying of a figure showing 2 pentagons crossing each other. Thus, the total score range from 0 to 30 with a score below 24 indicating cognitive impairment.

2. **Wechsler Memory Scale (WMS-III**) Wechsler, D. (1997a). The WMS-III consists of 11 subtests, with six primary subtests required to derive index scores and 5 optional subtests required to drive supplementary information. Logical Memory I and Logical Memory II assess immediate and delayed auditory verbal memory that is semantically organized. Two different stories (A and B) were read to the subject, and immediately afterwards the subject was asked to retell the story from memory. After an interval of ~25 min, the participant was again asked to recall as many details as possible from both stories A and B. For recognition memory, the participant was required to give "Yes" or "No" answers to a set of 30 questions relating to stories A and B, which includes a mixture of correct and incorrect statements about the story content. Participants were scored on the accuracy of the story recall ("story" and "theme" units) and number of correct responses to recognition questions. Raw scores were the cognitive variables in this study.

Results

Obtained data has been analyzed by Mean, SD and t test for the comparison of Migraine patients and normal control on MMSE and WMS-II scale.

Table-1: Mean, SD and t ratio of Migraine and Normal controls on MMSE and information and orientation domain of WMS-III

Measures	Sample	N	Mean	SD	SEM	t ratio
MMSE	Migraine	50	20.1200	5.14	.72	
	Normal	50	25.58	3.93	.55	5.96**
Information and orientation-I Total recall	Migraine	50	58.64	4.84	.68	
	Normal	50	67.78	5.69	.80	8.64**

**P<0.01

It has been found that Migraine patients had poor score on MMSE and information orientation in comparison to normal control and differences was found to be significant at 0.01 level (MMSE, Migraine., M= 20.12, SD=5.14, Normal., M=25.58,SD=3.93, t=5.96,p<0.01, Information orientation, Migraine, M=58.64,SD=4.84, Normal., M=67.78,SD=5.69, t=8.64,p<0.01). It was found that majority of migraineurs were unable to give information regarding three stages command, copying of figure, time and place orientation. Some patients were unable to even tell the days of week. These findings suggest the existence of a reversible brain dysfunction during attacks of migraine.

Table-2: Mean, SD and t test of migraine patients and normal control on Logical memory domain of WMS-III.

Subtests of WMS-III	Migraine (N=50)		Normal (N=50)		t ratio
	Mean	SD	Mean	SD	
Logical memory-I Recall total scale	9.20	2.32	12.76	2.08	8.05**
Logical memory-I Thematic total scale	8.14	1.80	13.02	1.92	13.08**
Logical memory-II Recall total scale	7.36	1.32	12.62	1.93	15.86**
Logical memory-II Thematic total scale	7.40	1.56	11.12	2.09	10.05**
Logical memory-II% Retention	8.06	1.05	12.30	1.63	15.41**

****P<0.01**

It has been observed that Migraine patients performed significantly poor on logical memory-I (Migraine: Mean= 9.20, SD=2.32, Normal: Mean=12.76, SD=2.08, t=8.05, P<0.01) indicating inability to recall the stories as well themes of the stories in the migraine patients. Similar trend impairments have been observed in this group while assessing the thematic memory. When migraine patients were assessed on logical memory-II of Wechsler memory scale, it has been found that patients with Migraine performed poorly as compared to normal controls and difference between these two groups has been found to be significant at 0.01 level.

It has further been visualized that Migraine patients performed poorly on logical memory-II and thematic total score, which indicating that Migraine patients performed significantly worse than normal control on all sub tests of WMS-III. These show that Migraine patients were having problem in conceptualizing theme of the story.

Table-3 Mean, SD and t test of male and female subjects on MMSE and Logical memory domain of WMS-III

Subtests of WMS-III	Female (N=50)		Male (N=50)		t ratio
	Mean	SD	Mean	SD	
MMSE	21.72	5.09	23.98	5.34	2.16*
Information and orientation-I	61.32	7.51	65.10	5.89	2.79**
Logical memory-I Recall total scale	10.46	2.97	11.50	2.62	1.85*
Logical memory-I Thematic total scale	10.70	9.63	10.46	3.48	0.39 NS
Logical memory-II Recall total scale	9.76	2.83	10.22	3.38	0.73 NS
Logical memory-II Thematic total scale	9.00	2.46	9.52	2.77	0.99 NS
Logical memory-II% Retention	9.70	2.62	10.66	2.36	0.57 NS

*P<0.05, **P<0.01

When male and female were assessed on Mini mental status examination and all subtests of WMS-II, it has been found that female participants performed poorly on MMSE, information and orientation-I and logical memory-I as compared to male counterparts and differences has been also found to be significant but there is no significant difference on all domains of WMS-III which indicates that females were not

having problems in conceptualizing theme of story they have basically orientation and information conveying problems.

Table-4 correlation analysis between disease status, Gender, MMSE along with domains of WMS-III

Measures Demogra	MMSE	Informon &orientation-I	Logi-I Recall scale	Logi-I Thematic scale	Logi-II Recall scale	Logi-II Thematic scale	Logi-II %
Disease status	0.52**	0.66**	0.63**	0.79**	0.85**	0.71**	0.84**
Gender	-0.21*	-0.27**	-0.18	-0.03	-0.07	-0.10	-0.19
MMSE	--	0.39**	0.38**	0.38**	0.43**	0.47**	0.96**

*P<.05, **P<0.01

Results reveal that disease status (Migraine/normal) was positively significantly associated with MMSE and all domains of WMS-III, whereas gender was negatively significantly associated with only MMSE and information-orientation unit of WMS. Trends of relationship of remaining domain shows negative and non significant with gender.

Table 5: Step wise multiple regression analysis using Mini mental examination as a criterion and different domains of Wechsler memory-III as a predictors

Criterion (MMSE)							
Predictors	**R**	**R^2**	**R^2 change**	**B**	**Beta (β)**	**t**	**F**
Logical memory-II (Thematic)	0.47	0.22	0.27	0.75	0.37	3.91**	26.99**
Logical memory-I	0.51	0.26	0.05	0.44	0.24	2.49**	17.29

**P<0.01

It is clear that Logical memory-II thematic portion is concern with deep cognition emerged as the best predictor of mental status examination in patients which is contributing 27% in the total variance followed by Logical memory-I that contributing 5% of total variance. Examination of β reveals that the Logical memory-II (Thematic) and Logical memory-I predictors contributed positively (β =0.37 & 0.24 respectively) to MMSE. The above patterns of findings suggest that Logical memory-II (Thematic) and Logical memory-I influence the Mental status of the Migraine patients.

Discussion

In this study assessments of orientation and memory dysfunction of migraine patients have been done along with its comparison with normal controls. The obtained results demonstrate significant deficits in the group of migraine patients as compared to normal controls in memory as assessed by Wechsler Memory-III and mental status examination assessed by MMSE (Table-1). Similar results were found by (Gaist et al. 2005) who conducted a study on migraine patients. Among migraineurs with aura, those with right-sided and bilateral pain exhibited the worst recall in memory test. Cognitive performance decreases during migraine attacks, especially in reading and processing speed, verbal memory and learning, supporting patients' subjective complaints (Gil-Gouveia 2015(. These findings suggest the existence of a reversible brain dysfunction during attacks of migraine without aura, which can relate specifically to migraine or be a consequence of acute pain processing by the brain.

In logical memory-I and II Migraine patients performed poorly which indicates the impairments in ability to remember information immediately after orally presented. They are also unable to sustain the

information after 25-30 minutes. Results are consistent with previous finding. During Migraine attacks, patients are sensitive to all sensory stimuli and experience cognitive symptoms, often beginning before the headache itself (Hadjikhani et al. 2001). They feel distracted, unable to concentrate and have difficulty performing mental tasks and retrieving names (Rossi et al. 2003, Martins et al. 1988) symptoms that might suggest a de-executive disorder. These manifestations may contribute to the impairment associated to the attacks and influence patients' quality of life (Ardila et al. 1988, Downson,A.J.,2001). Chronic pain is a debilitating condition associated with biopsychosocial consequences. Something that's debilitating seriously affects someone or something's strength or ability to carry on with regular activities, like a debilitating illness. Subjective reports by chronic pain patients and objective empirical research have demonstrated that chronic pain is associated with cognitive deficits in various domains of functioning including, attention, working memory, and executive function (Moriarty et al., 2011; Berryman et al., 2013; Moriarty and Finn, 2014).

In Mini mental examination test migraine patients perform poorly than normal controls especially in time orientation and delayed recall of previous words which indicates that Patients with migraine may experience a significant decline in cognitive function at the onset of a headache attack. These results are consistent with previous study in which Edward (2011) found that Cognitive dysfunction with migraine may be an under-recognized disability associated with migraine, especially when considered independently from the headache intensity. Some previous studies found that patients with migraine showed normal range of performance on MMSE (Wen et al.2016). In this study female patients with migraine exhibited impaired orientation, recall, and disturbed logical memory which also extend that gender plays an important role in the prevalence of migraine. Previous studies about gender differences in migraineurs found that the influences of migraines on the structures and functions of brain are different for males and females (Maleki et al 2012). One recent neuroimaging study showed dysfunctional organization in the resting functional network of the brain that was more evident in female migraine patients (Liu J et al. 2011). To date, converging evidence shows that the incidence of migraine in females is about three times as high as in males, and that estrogen could be the main cause of this gender difference (Brandes JL 2006).

Conclusion

In conclusion, cognitive impairments seem relatively common in female migraineurs. Their orientation, delayed recall and logical memory are disturbed. They had problems in conceptualizing the themes. Patients with migraine might present higher risk of cognitive impairment, especially in certain neuropsychological domains such as visual memory, verbal memory, and information processing speed, attention, and executive functions. It is uncertain, however, whether this cognitive profile is associated with an underlying migraine pathophysiological process or with the presence of confounding factors.

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