

Soft Neurological Signs in Migraine Patients

Clinical Study

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Objective- Migraine is 7th Disabler according to the World Health Organization's recent Global Burden of Disease report, due to its wide range of complications and comorbidities. Pathophysiology of Migraine is not completely understood till this moment and diagnosis is only clinical. Routine Neurological Examination was proved to be normal in migraine patients, So we aim to study soft neurological signs and assure its usefulness in migraine diagnosis and pathophysiology which is rarely addressed in the field of neurology.

Material and Methods- The sample included 80 study participants, 50 cases and 30 healthy control, identified in hospital-based Study recruited from Neurology Outpatient Clinic, Assiut University Hospital. Migraine was ascertained by direct clinical interview using ICHD-III criteria for Migraine. Then they were clinically evaluated for soft neurological signs using the Cambridge Neurological Inventory.

Results- Of the 50 patients, 49 with migraine without aura and only one migraine with aura, mean age 31.78 ± 8.89 , female to male 43:7. In our study we found no affection of Neurological Soft Signs in migraine patients in relation to healthy control.

Conclusion- Our Study revealed the insignificance of SNS in migraine patients.

Index Terms— Migraine, Soft neurological signs.

I. INTRODUCTION (HEADING 1)

Neurological abnormalities include both “hard” signs and “soft” signs. Hard signs refer to impairments in basic motor, sensory, and reflex behaviors. In contrast, “soft” neurological signs (SNS) are described as non-localizing neurological abnormalities that cannot be related to impairment of a specific brain region or are not believed to be part of a well-defined neurological syndrome. This distinction has been argued to be artificial and to reflect the inability to define the brain-behavior relationships that underlie the presence of SNS. Moreover, SNS are frequently clustered in categories attending to their most likely, putative neuroanatomical localization [Igor Bombin et al, 2005]. Neurological soft signs (NSS) are minor semeiotic anomalies not assessed during the standard neurological examination and for a long time postulated to indicate a diffuse dysfunction within the nervous system [Hollander et al, 1990]. A more recent concept assumes the presence of micro-anomalies within more specific brain networks [Cox & Ludwig, 1979-Heinrichs & Buchanan, 1988]. In particular, studies suggest the NSS might predict abnormalities within the cerebellar – thalamo – prefrontal circuitry [Zhao et al, 2014- Mittal et al, 2014] and be viewed as an index of “cognitive dysmetria” [Varambally et al, 2012].

Several authors considered them as a potential marker for endophenotypes of psychotic conditions, being already present before transition to psychosis in at-risk individuals to the same extent as after transition [Tamagni et al, 2013] and even among

non-psychotic relatives in affected pedigrees [Chan et al, 2008].

By contrast, NSS expression has been rarely addressed in the field of neurology.

II. MATERIAL AND METHODS

This study is Hospital based study. We recruited eighty adult persons, Fifty migraine cases forty three females and seven males, their age ranged from fifteen to forty five years, Thirty control twenty four females and six males, their age ranged from fifteen to forty five years The patients and control groups were recruited from Neurology Outpatient clinic at Assiut University Hospital within six months duration.

The protocol of the study was approved by the ethical committee of Assiut University.

III. INCLUSION CRITERIA

Patients aged 18 years and more .

Fulfills Migraine criteria of International Headache Society with normal or corrected-to-normal vision, and normal hearing capability, we excluded Patients who known to have general neurological disease as epilepsy, stroke & brain injuries ,Remarkable dysfunctions in their motor and sensory systems, or deep tendon reflexes or Psychiatric illness as schizophrenia and history of mixed headache types. The socio-economic scoring in this study covered education of the father, work and education of the mother, crowding index and income.

The socioeconomic level was determined based on the scoring system of Fahmy and El-Sherbiny (1983) after modification [Gag & Abd El-Ghany, 2012],which Total socioeconomic score = 23, we scored it as Scores 19+ are considered of high socioeconomic ,Scores 15-<19 are considered of middle socioeconomic standard and Scores <15 are considered of low socioeconomic standard.

The severity of headache attacks and how much it is disabling to the patient we used Headache Disability Index [Jacobson et al, 1994], include Domains: Emotional: 13 items, Functional: 12 items, interpreted as Minimum score: 0 Maximum emotional subscale: 52. Maximal functional subscale: 48 Maximum score: 100

The higher the score the greater the disability caused by the headache.

Due to high comorbidity between migraine and depression we used Hamilton Depression Rating Scale which is a multiple item questionnaire used to provide an indication of depression, and as a guide to evaluate recovery [Hedlund & Viewig ,1979 .] The questionnaire is designed for adults and is used to rate the severity of their depression by probing mood, feelings of guilt, suicide ideation, insomnia, agitation or retardation, anxiety, weight loss, and somatic symptoms. It is initially considered

the "Gold Standard" for rating depression in clinical research. Each item on the questionnaire is scored on a 3 or 5 point scale, depending on the item, and the total score is compared to the corresponding descriptor. Assessment time is estimated at 20 minutes.

Scoring: 0-7: normal, 8-13: mild depression, 14-18: moderate depression, 19-22: severe depression, >22 : very severe depression with Sensitivity:86.4%

Specificity: 92.2%.

In this Study we used Cambridge Neurological Soft Sign Assessment to detect any abnormality in migraine patients which included [Hollander et al,1990].

- Coordination: finger to finger ,finger to nose ,heel to shin, finger to thumb, Rapid alternating movements, mirror movements, hopping ,toe walking, heel walking, two tongue twisters.

- Involuntary Movements: in Romberg position.
- Sensory Functions: astereognosis, agraphesthesia, position sense, direction of cutaneous kinesthesia.
- Visuospatial Station: face – hand test, right – left confusion on self and on examiner, cube drawing.

IV. STATISTICAL ANALYSIS

- The data were coded, entered and analyzed using SPSS (version 16) software program
- Mean and standard deviation, sample t-test, Pearson chi-squared test, ANOVA, Post Hoc (LSD) Tests, Multiple Linear Regression Test were applied in this study.
- P value was considered significant <0.05.

V. RESULTS

Demographic and Clinical data of cases and controls, 50 cases with mean age 31.78 ± 8.89 and 30 control with mean age 28.10 ± 7.73 , with male ratio 7:6 (14% : 20%),female ratio 43:24 (86% : 80%),Social scale of cases is 12.74 ± 5.12 and of control is 14.93 ± 4.49 ,with no significant difference between them also no affection of neurological examination among both cases and controls ,in cases 49 with migraine without aura and only one migraine with aura, there is significant difference between them according to depression 41: :12 (82%: 40%).

Table (1): Demographic & Clinical data of migraine cases and controls

	Case (n=50)	Control (n=30)	p- value
Age(Mean \pm SD)	31.78 ± 8.89	28.10 ± 7.73	0.064
Sex (n & %)			
Male	7	6	0.539
Female	43	24	
	86%	80%	

Social Scale(Mean \pm SD)	12.74 ± 5.12	14.93 ± 4.49	0.056
Migraine(n & %)			
MO	49	0	0.0001
MA	98%	0%	
	1	2%	
Soft Neurological Signs	0	0	
Neurological Examination	0	0	
Depression	41	12	0.0001
	82%	40%	

MO: Migraine without aura MA : Migraine with aura

In our study we found no affection of Soft Neurological Signs in migraine patients, in comparison between cases and healthy control even in those who have comorbid migraine and depression, even in sever migraine attacks although we found that there is positive correlation Between Headache Disability Index and total Hamilton Depression Rating Scale of Migraineurs.

HDRS	HDI SCORE	
	r-value	p-value
	0.518	0.000

Which means that the more disability the more sever depression comorbid.

Also although, Multiple Linear Regression Test Analysis of Hamilton Depression Rating Scale& Related Factors showed significance between HDRS and age, we also didn't find any abnormality in old migraineurs with comorbid depression.

Multiple Linear Regression Test Analysis of Hamilton Depression Rating Scale& Related Factors.

Variable	R	B	β	T	Significance
HDRS	0.496				
Age		-.476	-.483	- 2.802	.008

HDRS : Hamilton Depression Rating Scale.

a) DISCUSSION

Few studies were done in this field as NSS expression has been rarely addressed in the field of neurology, possibly because the concept of a neurological semeiotics failing to localize lesions is in dramatic contrast with its founding principles[Tremolizzo et al,2011**Error! Reference source not found.**],the only notable exceptions relate to NSS correlations with specific cognitive functions and impairments ,mainly of the executive type [Arabzadeh et al,2014- Li et al,2012- Chan

et al,2009] So further research is needed in the future with larger sample size for more accurate results.

Only one study done by Tremolizzo et al (2015), studied neurological soft signs in primary headaches using 16-items Heidelberg scale, found that NSS were increased by ~70 and ~90% in tension-type headache and migraine headache, and remained significant even after controlling for age and education. Headache type and characteristics did not influence NSS presentation, while headache patients with white matter hyperintensities (WMH) at brain MRI had higher NSS scores compared both to normal controls and patients without WMH. NSS identify a subset of primary headache patients sharing the same comorbidities or minimal brain anomalies, suggesting that tailored prophylactic options might apply [Tremolizzo et al,2015].

Many of soft neurological signs studies were done in the field of psychiatry specially schizophrenia and obsessive compulsive disorder, but only one recent was done bipolar disorders which used the NSS scale validated by Krebs et al., Bech-Rafaelsen Mania Scale, the Hamilton Depression Rating Scale and found that total score of NSS were significantly higher in bipolar I patients compared to their healthy siblings and controls [Mrad et al, 2016].

Against these findings we found negative results regarding soft neurological signs in those with migraine or comorbid migraine and depression regardless severity of each which may be related to the different tools of assessing the soft neurological signs and the timing within the migraine cycle when the assessment was done.

But this does not mean that there is no abnormality in migraine patients, we recommend further studies with larger sample size using more than one tool for assessment and at different phases of the cycle, so we may be able to detect migraine specific abnormalities that help in objective diagnosis of migraine mystery.

VI. CONCLUSION

SNS in patients with migraine have no diagnostic significance.

VII. LIMITATIONS

The sample size used in the study was 50 cases and 30 controls. A larger sample could have given more information about the correlation between specific categories of soft neurological signs and the various migraine types.

VIII. FINANCIAL SUPPORT AND SPONSORSHIP

Nil.

IX. CONFLICTS OF INTEREST

There are no conflicts of interest

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