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Correlation between Incomplete Hippocampal Inversions (IHI) with Incidence of Seizure Based on MRI Findings: A Systematic Review

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ABSTRACT

Introduction: Incomplete Hippocampal Inversions (IHI) is considered as leading cause of several neurological complications including epilepsy.
This paper provides a systematic literature review about the possible causative role of incomplete hippocampal inversions in patient with epilepsy based on findings of Magnetic Resonance Imaging (MRI).

Materials and Methods: The incomplete inversion of hippocampus with MRI imaging in patient with epilepsy was searched in PubMed and Scopuswith the following search strategy ((incomplete hippocampal inversion or hippocampal malrotations)) and epilepsy) and (magnetic resonance imaging or MRI). Then, data including the number of patients, and concluded results were extracted and compared between the groups.
All types of articles including case series, clinical trials and cohort studies in English language with no time limitation were included.
All searches, selection of articles and the data extraction were performed by two independent reviewers.

Results: Only 11 papers met the inclusion criteria. Data were extracted and compared between two groups of patients and healthy controls. Results of this review showed that among 854 healthy controls and 1402 patients with verified temporal lobe epilepsy or hippocampal abnormalities, 59 cases with Hippocampal Malrotation (HIMAL) were in control groups, and 165 cases were in patients with epilepsy.

Conclusions: The results showed that incomplete hippocampal inversion can be considered as an important cause of seizure. But still, studies with large sample size and equal number of cases and controls should be conducted to strongly confirm this association.

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Introduction

Epilepsy is among the most commonchronicneurological disease and one of the major health problems in developing countries with the incidence of almost (7.5%) (1). Magnetic Resonance Imaging (MRI) is typically used as a noninvasive medical test for the evaluation of patients with epilepsy. After thediagnosisof epilepsy,in order tofind the cause of seizures, prognosisand treatment plans, brain structure shouldbe evaluated with MRI (2).

Previously, the relationship between the hippocampus and epilepsy has been studied. Temporal lobe epilepsy is the most common form of partial epilepsy in which the hippocampal sclerosis is the most common radiologic findings (1). It is suggested that developmental abnormalities of the hippocampus may lead to seizures or may be the main cause of epilepsy (2). Hippocampal folding in temporal lobe occurs at 18 weeks of fetal development, and in week 21, the folding pattern is similar to those in adults (3, 4).

Because hippocampus has many role in cognition and memory processes (5); hence, every malrotation during hippocampal folding may be responsible for most of hippocampus related complications including cardiac and respiratory dysfunction (6), loss of cognitive function, learning and memory impairment (7) and other complications such as incidence of seizure (8). Incomplete Hippocampal Inversion (IHI) which is traditionally known as Hippocampal Malrotation (HIMAL) is the incomplete inversion of the hippocampus to abnormally round shape (9). In other word, the shape of hippocampus in malrotated form is round or pyramidal than oval. Incomplete

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rotation rate of the hippocampus in both healthy subjects and patients with epilepsy are not clear. In addition, there are different estimations on the relationship between incomplete rotation of hippocampus and partial seizures. But, it is not yet clear whether this partial rotation as a structural disorder is the underlying cause for seizure, or it is a common finding in asymptomatic population.

Although the role of hippocampus anomalies in onset of seizures is accepted (6); yet, the exact role of incomplete hippocampus inversion in patients with epilepsy is not fully understood. Hence, finding relationship between incomplete inversion of hippocampus and epilepsy can help to predict the incidence of seizures or other structural abnormalities in the fetus. This study aimed tosystematically review the frequency of reported incomplete rotation ofthe hippocampusinepilepsy patientscompared tohealthy individuals based on MRI findings.

Materials and Methods

Literature search strategy

PubMed and Scopuswere searched for evaluation of incomplete hippocampal inversion with magnetic resonance imaging in patient with epilepsy on words in the title, keywords, and abstract. First these databases searched for incomplete inversion of hippocampus or hippocampal malrotation. Then the search was limited to patients with epilepsy, and finally the results were restricted to those in which MRI has been used for brain structural evaluation. Relevant articles with the following search terms: (incomplete hippocampal inversion or hippocampal malrotations) and epilepsy and MRI were selected and reviewed with the last update on February2015.

Nonrelevant articles were omitted as we reviewed the abstract of the articles. Subsequently, the full text of the relevant papers was studied. To minimize the possibility of missing relevant data, and in order to find further potentially relevant studies, the reference list of related articles was also scanned.

Study selection

There was no time limitation for the included articles, but we excluded the articles to those in English language. All types of the articles including the case series, clinical trials and cohort studies in which the study has been conducted on at least two patients were selected. But, we did not include review articles,meta-analysis and book chapters. Inclusion criteria for study selection were patients with verified hippocampal malrotation with or without epilepsy. Those papers with duplicated data were omitted. Exclusion criteria for this review were articles in which the patients with epilepsy had not been studied for incomplete inversion of hippocampus, or studies in which the incidence of seizure was due to hippocampal sclerosis or neuropathology of the temporal lobe. In order to avoid selection bias, we included all studies in which the incomplete hippocampal inversion had been investigated in patients with or without epilepsy, or studies in which the patients with epilepsy were studied for the presence of hippocampal abnormalities.

Data extraction

Data about authors, country of origin, publication date, study design and the concluded results were extracted. The data regarding hippocampal malrotation obtained in each study were compared. Total number of patients and controls were identified and structural features of hippocampus were compared between the groups. All information from included articles were tabulated. Results were organized based on the association between hippocampal abnormalities, specifically incomplete hippocampal inversion with the incidence of epilepsy. The quality assessment of selected papers was performed based on recommendations of CONSORT checklist 2010 by two independent reviewers (10).

Results

From overall 645 article found in PubMed and 12 in Scopus, only 33 articles seemed to be relevant to the purpose of this study in the first step. After carefully reviewing the articles, only 11 papers met the inclusion criteria for further assessment. Therefore, full texts of these articles were collected and the data were extracted based on the main purpose of this study.

Figure 1 shows step by step selection process of articles.

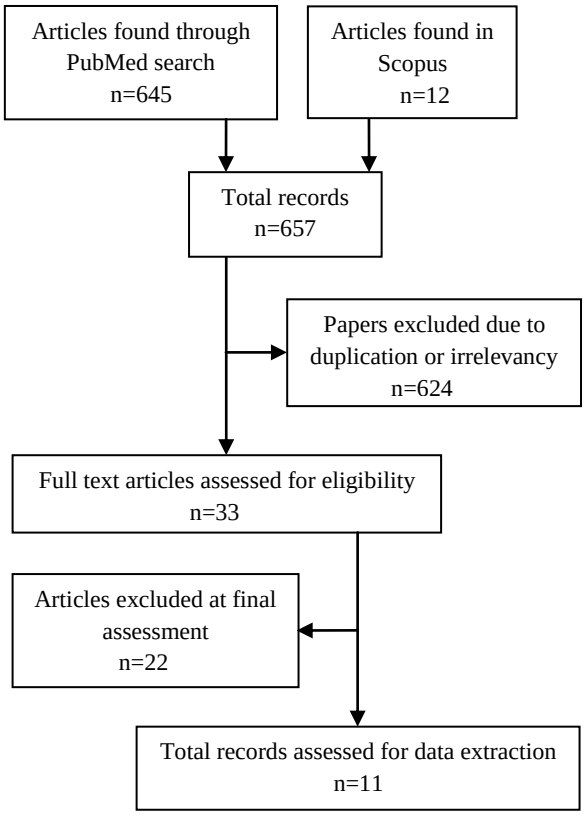

Figure1: Flowchart for selection of studies.

The number of patients and healthy individuals studied for evaluation the relationship between incomplete hippocampal inversion with the incidence of seizure varied from 2 patients in a case report to 527 participants among the studies. The age of studied patients or healthy controls also varied from one month old neonates (11) to a patient with 101 year old (12) among the included studies. Among all the individuals, 854 people were healthy controls and 1402 were patients with verified temporal lobe epilepsy or hippocampal abnormalities. Of these cases, 59 hippocampal malrotation had been reported in control groups, while 165 had been observed in patients with epilepsy. The findings show that the rate of incomplete hippocampal inversion is almost double in patients with epilepsy compared to controls. Analysis of extracted data showed that incomplete hippocampal inversion occurs with high frequency unilaterally on the left side. According to documented data reported in reviewed papers, only minority of hippocampus malrotations with almost (20%) are bilaterally, while the frequency for left and right sided malrotations are (71% and 9%), respectively. Although the data regarding demographic information including sex and age were limited, but most of the included papers have concluded that HIMAL is more frequent in men than in women.

Table1: Characteristics of literatures included in this review.

No	First author	Year	Country	Study design#	Number of participants	Study population*	Inversion of the hippocampus	
1	Bajic D, (13)	2008	Sweden	PS	100	HI	19**	10 men 9 women
2	Barsi P, (14)	2000	Hungary	C-S	527	EP	32	20 men 12 women
3	Henry T.R, (15)	2011	USA	CC	19	Case-Control	3.8 (37.5%) patient and 4/11 (36.6%) controls	
4	Kuchukhidze G, (16)	2010	Austria	C-S	220	EP	15	
5	Gamss R.P, (12)	2009	USA	C-S	497	HI	6	
6	Ramantani G, (17)	2013	Germany	C-S	4	EP	3	
7	Shinnar SH, (11)	2012	USA	PS	295	Case-Control	15.199 patients and 2.96 controls	
8	Bajic D, (18)	2009	Sweden	PS	350	Case-Control	60.201 patient and 28.150 controls	
9	Yeghiazaryan N.S, (19)	2010	Italy	Cs	2	Case Report	2	
10	Baulac M(20)	1998	France	PS	19	EP	19	
11	Lehericy S (21)	1995	France	C-S	222	EP	16	

* HI: Healthy individuals, EP: Epileptic patients,

** Information about gender has only been reported in some studies.

PS: Prospective study, CC: Case-Control, C-S: Cross-sectional, Cs: Case series

Some limitations in this study include the small number of enrolled patients in some studies, which could lead to insignificancy of the differences. Also in some studies, there was no distinction between morphological changes in the hippocampus and incomplete rotation, and may be incomplete rotation had been considered as part of the changes in the hippocampus.

Discussion

Association between IHI and onset of epilepsy is a controversial issue. The results show that developmental abnormalities of the hippocampus on epileptic side are a common disorder in patients with epilepsy; moreover, there is sufficient data to support the role of incomplete hippocampal inversion in the incidence of seizure. But, some studies propose that temporal lobe epilepsy may be due to disturbance in hippocampal development, which may subsequently affect other parts of the brain leading to epilepsy.

Despite these conflicting results, data which suggest association between HIMAL and incidence of seizure are not negligible, and almost (11.3%) of temporal lobe epilepsy is due to HIMAL. Hence, it is suggested that incomplete inversion of hippocampus at least in some circumstances may be the most important cause of epilepsy. Hippocampal malrotation is also suggested to be associated with agenesis of the corpus callosum and complex prefrontal dysfunction leading to limbic system malformations (22) and attention and memory impairmentand also unipolar depression (23, 24), respectively. As well, several studies have demonstrated the association between the changes in hippocampal shape and positioning and incidence of seizure (25).

On the other hand, the frequency of HIMAL in epileptic patients and non-epileptic population is also doubtful, and results do not firmly support any of the hypothesis. For example, the results of some studies show that IHI is a rare finding in non-epileptic population (12), while others show that it is a usual morphologic change in healthy people (13). In this systematic review, and based on extracted data, an association was found between incomplete inversion of hippocampus and incidence of seizure (11.3% compared to 6.9%). But, it should be noted that the number of patients and controls varied in different studies. Nonetheless, this association was significant in some results. Therefore, increasing sample size with

equal number of participants in case and control groups may help to clarify this association.

Conclusion

According to the results obtained in this study, incomplete hippocampal inversion can be considered as an important cause of seizure. And, many studies strongly support this association.

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References

1- Rodenburg R, Meijer AM, Dekovic M, Aldenkamp AP. Family factors and psychopathology in children with epilepsy: a literature review. Epilepsy & behavior: E&B. 2005 Jun;6(4):488-503.
2- Bernasconi A, Bernasconi N. Unveiling epileptogenic lesions: the contribution of image processing. Epilepsia. 2011;52(s4):20-4.
3- Kier EL, Kim JH, Fulbright RK, Bronen RA. Embryology of the human fetal hippocampus: MR imaging, anatomy, and histology. AJNR American journal of neuroradiology. 1997 Mar;18(3):525-32.
4- Kier EL, Fulbright RK, Bronen RA. Limbic lobe embryology and anatomy: dissection and MR of the medial surface of the fetal cerebral hemisphere. AJNR American journal of neuroradiology. 1995 Oct;16(9):1847-53.
5- Smith DM, Mizumori SJ. Hippocampal place cells, context, and episodic memory. Hippocampus. 2006;16(9):716-29.
6- Nickels KC, Wong-Kisiel LC, Moseley BD, Wirrell EC. Temporal lobe epilepsy in children. Epilepsy research and treatment. 2012;2012:849540.
7- Bohbot VD, Allen JJ, Nadel L. Memory deficits characterized by patterns of lesions to the hippocampus and parahippocampal cortex. Annals of the New York Academy of Sciences. 2000 Jun;911:355-68.
8- Jacob FD, Habas PA, Kim K, Corbett-Detig J, Xu D, Studholme C, et al. Fetal hippocampal development: analysis by magnetic resonance imaging volumetry. Pediatric research. 2011 May;69(5 Pt 1):425-9.
9- Raininko R, Bajic D. "Hippocampal malrotation": no real malrotation and not rare. AJNR American journal of neuroradiology. 2010 Apr;31(4):E39; author reply E40.
10- Lee JS, Ahn S, Lee KH, Kim JH, Schulz KF, Altman DG, et al. CONSORT 2010 Statement: Updated guidelines for reporting parallel group randomised trials. Epidemiology and health. 2014 Nov 8.
11- Shinnar S, Bello JA, Chan S, Hesdorffer DC, Lewis DV, Macfall J, et al. MRI abnormalities following febrile status epilepticus in children: the FEBSTAT study. Neurology. 2012 Aug 28;79(9):871-7.
12- Gamss RP, Slasky SE, Bello JA, Miller TS, Shinnar S. Prevalence of hippocampal malrotation in a population without seizures. AJNR American journal of neuroradiology. 2009 Sep;30(8):1571-3.
13- Bajic D, Wang C, Kumlien E, Mattsson P, Lundberg S, Eeg-Olofsson O, et al. Incomplete inversion of the hippocampus--a common developmental anomaly. European radiology. 2008 Jan;18(1):138-42.
14- Barsi P, Kenez J, Solymosi D, Kulin A, Halasz P, Rasonyi G, et al. Hippocampal malrotation with normal corpus callosum: a new entity? Neuroradiology. 2000 May;42(5):339-45.
15- Henry TR, Chupin M, Lehericy S, Strupp JP, Sikora MA, Sha ZY, et al. Hippocampal sclerosis in temporal lobe epilepsy: findings at 7 T(1). Radiology. 2011 Oct;261(1):199-209.
16- Kuchukhidze G, Koppelstaetter F, Unterberger I, Dobesberger J, Walser G, Zamarian L, et al. Hippocampal abnormalities in malformations of cortical development: MRI study. Neurology. 2010 May 18;74(20):1575-82.
17- Ramantani G, Koessler L, Colnat-Coulbois S, Vignal JP, Isnard J, Catenoix H, et al. Intracranial evaluation of the epileptogenic zone in regional infrasylvian polymicrogyria. Epilepsia. 2013 Feb;54(2):296-304.
18- Bajic D, Kumlien E, Mattsson P, Lundberg S, Wang C, Raininko R. Incomplete hippocampal inversion-is there a relation to epilepsy? European radiology. 2009 Oct;19(10):2544-50.
19- Yeghiazaryan NS, Morana G, Rossi A, Veggiotti P, Savino G, Giordano L, et al. Temporal lobe epilepsy and hippocampal malrotation: is there a causal association? Epilepsy & behavior: E&B. 2010 Aug;18(4):502-4.
20- Baulac M, De Grissac N, Hasboun D, Oppenheim C, Adam C, Arzimanoglou A, et al. Hippocampal developmental changes in patients with partial epilepsy: magnetic resonance imaging and clinical aspects. Annals of neurology. 1998 Aug;44(2):223-33.
21- Lehericy S, Dormont D, Semah F, Clemenceau S, Granat O, Marsault C, et al. Developmental abnormalities of the medial temporal lobe in patients with temporal lobe epilepsy. AJNR American journal of neuroradiology. 1995 Apr;16(4):617-26.
22- Sato N, Hatakeyama S, Shimizu N, Hikima A, Aoki J, Endo K. MR evaluation of the hippocampus in patients with congenital malformations of the brain. AJNR American journal of neuroradiology. 2001 Feb;22(2):389-93.
23- Stiers P, Fonteyne A, Wouters H, D'Agostino E, Sunaert S, Lagae L. Hippocampal malrotation in pediatric patients with epilepsy associated with complex prefrontal dysfunction. Epilepsia. 2010 Apr;51(4):546-55.

24- Rogers MA, Kasai K, Koji M, Fukuda R, IwanamiA, Nakagome K, et al. Executive and prefrontaldysfunction in unipolar depression: a review of neuropsychological and imaging evidence. Neuroscience research. 2004 Sep;50(1):1-11.

25- Bernasconi N, Kinay D, Andermann F, Antel S, Bernasconi A. Analysis of shape and positioning of the hippocampal formation: an MRI study in patients with partial epilepsy and healthy controls. Brain: a journal of neurology. 2005 Oct;128(Pt 10):2442-52.