Research Article ISSN 2641-4333

Neurology - Research & Surgery

Cognitive Functions and Brain Volumetric Changes in A Sample of Epileptic Patients

Aya Ahmed Ashour[1], Prof. Dr. Ayman Mohamed Ahmed Nassef[2], Prof. Dr. Eman Mahmoud Awad[2], Asst. Prof. Dr. Ahmed Mohamed Hazzou[3], Asst. Prof. Dr. Maha Ali Nada[3*], and Asst. Prof. Dr. Yosra Abdel-Zaher Abdullah[4]

[1]Assistant lecturer of Neurology, Faculty of medicine, Ain shams university, Cairo, Egypt.

[2]Professor of Neurology and Psychiatry, Faculty of medicine, Ain Shams university, Cairo, Egypt.

[3]Assistant Professor of Neurology and Psychiatry, Faculty of medicine, Ain Shams university, Cairo, Egypt.

[4]Assistant Professor of Diagnostic Radiology, Faculty of medicine, Ain Shams university, Cairo, Egypt.

[*]Correspondence:
Asst. Prof. Dr. Maha Ali Nada, Assistant Professor of Neurology and Psychiatry, Faculty of medicine, Ain Shams university, Cairo, Egypt.

Received: 14 September 2019; **Accepted:** 15 October 2019

Citation: Aya Ahmed Ashour, Ayman Mohamed Ahmed Nassef, Eman Mahmoud Awad, et al. Cognitive Functions and Brain Volumetric Changes in A Sample of Epileptic Patients. Neurol Res Surg. 2019; 2(2): 1-7.

ABSTRACT

Background: *Epilepsy is a serious common neurological disorder that can affect any age. Cognitive dysfunctions are highly prevalent in patients with epilepsy and are more likely to occur in patients with idiopathic generalized epilepsy (IGE). Associations were found between cognitive functions and brain volume loss in patients with epilepsy.*

Objective: *This work was carried out to assess the cognitive, volumetric changes in brain of epileptic patients in adult and adolescent patients with epilepsy.*

Patients and Methods: *A case control study was conducted to include 61 patients, 20 of them with idiopathic generalized epilepsy (IGE), 21 with temporal lobe epilepsy (TLE) and 20 with frontal lobe epilepsy (FLE). Patients were selected from the Epilepsy Outpatient Clinic in Ain Shams University Hospitals. Along with 23, age and sex matched healthy controls. Both cases and control groups were subjected to Magnetic resonance imaging MRI brain volumetry and detailed cognitive testing.*

Ethical issues: *An informed consent was taken from each adult patient, guardian of adolescent patient and healthy control.*

Results: *Statistically significant difference was found in comprehension subcategory of the Wechsler adult intelligence scale (WAIS) between patients with IGE and healthy controls, denoting poorer social judgment in the IGE group. The IGE group also showed poorer performance in digit symbol subcategory of the same test denoting worse psychomotor speed and sustained attention. Also, significant difference in similarities subcategory was found between TLE group and control group denoting poorer abstract thinking among the TLE group. The IGE and TLE groups also showed lower attention and concentration than control group in the mental control subcategory of the Wechsler memory scale (WMS) yet failed to show superiority over each other.*

No statistically significant difference was found on comparing the whole brain volume between cases and control groups. A statistically significant direct relationship was found between the arithmetic subcategory of WAIS and the decrease in the whole brain volume of the patients with FLE.

Conclusion: *Patients with IGE had worse psychomotor speed, sustained attention and concentration in addition to poorer social judgment. Also, patients with TLE showed lower attention and concentration together with poorer abstract thinking despite normal IQ. The study also concluded that relative increase in the whole brain volume in patients with frontal lobe epilepsy was associated with better mathematical problem solving.*

Keywords
Epilepsy, Cognition, Brain volume.

Introduction
Epilepsy is the commonest serious neurological condition, with a prevalence of 0.5-1%. It can occur at any age, but is particularly likely to develop in the very young and the elderly [1].

There is a high prevalence of cognitive dysfunction in patients with epilepsy. Approximately 30% of patients with epilepsy have intellectual disability, and up to 50% of patients with focal epilepsies experience specific cognitive deficits, often associated with the region of seizure onset and related neural pathways. Many cognitive domains can be impacted by seizures including language, attention, processing speed, executive function, and memory [2].

Cognitive impairment is a common comorbidity of epilepsy. The causes of cognitive impairment are thought to be multifactorial and include the impact of the underlying etiology; the effects of recurrent seizures; the side effects of antiepileptic drugs (AEDs), and psychosocial issues [3]. Studies of whole brain volumes have revealed associations between cognitive impairment and brain volume loss in patients with epilepsy [4].

Quantitative measures of whole brain atrophy are of interest in other neurologic disorders such as multiple sclerosis and Alzheimer's disease, viewed as potentially useful markers of disease severity and course, of demonstrated association with cognitive and disability status, and used with the hope that they may serve as useful outcome indices of treatment efficacy [5].

In the study of Hermann and colleagues [6], controls show a strong association between cognitive development and increasing cerebral tissue volume (especially white matter volume), an association that is absent in children with epilepsy. Modal cognitive profiles have been derived for several syndromes of epilepsy, and efforts have been undertaken to identify the shared versus unique cognitive abnormalities evident across epilepsy syndromes [6].

Quantitative MR volumetric have been used to characterize the nature and pattern of brain abnormality in adults with epilepsy, especially temporal lobe epilepsy [7].

Many studies using quantitative analyses of structural magnetic resonance imaging (MRI), such as volumetry, cortical thickness, and/or diffusion tensor imaging (DTI), have suggested structural brain abnormalities as the etiology of cognitive impairment in childhood epilepsy. Volumetric studies on pediatric epilepsy for example revealed abnormalities in the cerebrum, cerebellum, and hippocampus as well as temporal and extratemporal Gray Matter [8].

Quantitative MR volumetry has been used to characterize the nature and pattern of brain abnormalities in adults with epilepsy, especially temporal lobe epilepsy, and volumetric abnormalities are one of the clinical consequences, as demonstrated by their relationship with impaired cognition [7].

Using neuropsychological tests and surface-based morphometry, we investigated the neuropsychological status and brain volume alterations in a sample of adolescents and adults with epilepsy. In addition, we qualified the relationship between each cognitive domain and the whole brain volume in each patient group. Our aim was to evaluate the volumetric changes in brain of epileptic patients as a biomarker for cognitive dysfunction.

Type of the study
This is a comparative case control study.

Inclusion and exclusion criteria
Patients of both genders and 15-40 years' age group, diagnosed with idiopathic generalized epilepsy according to the ILAE criteria were included in the study. Patients with history of other neurological disorders, traumatic brain injury, intoxication, and encephalitis. Patients with psychiatric disorders and mental sub normality were excluded from the study as they can affect cognitive functions.

Study procedure
Data were collected from the patients and the accompanying relatives attending the outpatient epilepsy clinic together with data from the healthy controls. The data was recorded in a data sheet after taking informed consent from the adult patients, guardians of the patients under 18 years and healthy controls participating in the study, after informing them about the study rationale and their right to withdraw from the study at any time without any consequences. The data included demographic details, general and neurological history and examination, history of epilepsy and details of the treatment given.

Long term electroencephalogram EEG including sleep and awake recordings were done to all the patients.

Cognitive functions were done by the examiner to the patients and controls using Wechsler adult intelligence scale (WAIS), Wechsler Memory Scale (WMS), Wisconsin Card Sorting Test (WCST) and Trail Making Test (TMT). WAIS was done with subcategories of verbal IQ (VIQ) and performance IQ (PIQ). VIQ includes comprehension that reflects social judgment, similarities that reflects abstract thinking, arithmetic that reflects concentration and digit span with its two forms: forward that reflects auditory attention and backward that reflects the immediate memory. While PIQ includes picture completion that reflects perception,

block design that reflects constructional ability and viseomotor coordination and includes digit symbol that reflects psychomotor speed and sustained attention. Wechsler Memory Scale (WMS) was done with its subcategories information, orientation; mental control that reflects attention and concentration, logical memory that reflects short term memory and associate learning that reflects recent memory. Trail-Making Test (TMT) done with its two parts A and B that reflects attention. Wisconsin card sorting test was done that reflects the executive functions.

Patients and controls were subjected to Structural MRI brain using 1.5 Tesla machine (Achieva, Philips, Best the Netherlands), applying epilepsy protocol according to the unit of diagnostic radiology Ain Shams university. Sagittal 3D T1 weighted images were acquired using a standard head coil. Images were then converted from DICOM to NIFTI format and analyzed using Free Surfer software v5.3.0, which is documented and freely available for download online (http://surfer.nmr.mgh.harvard.edu/) to determine whole brain volume, cortical thickness measures and subcortical structures volume including bilateral hippocampi, bilateral thalami and bilateral amygdala.

Data analysis

All data recording and statistical analysis were done using the 'Statistical Package for Social Science (SPSS) version 23'. The results were tabulated, grouped and statistically analyzed using the following procedures:

- Chi square test to compare mean of non-parametric values between different groups.
- ANOVA test with Tukey HSD as a post HOC test to compare mean of parametric values between different groups.
- Pearson chi-squared test ($\chi 2$): to detect whether there is a significant association between different categorical variables.
- Spearman rho test: to detect whether there is a significant association between different non categorical variables.
- P-value: is used to indicate the level of significance: $P > 0.05$: Insignificant, $P < 0.05$: Significant and $P < 0.01$: Highly significant.

Results

The study was conducted on 61 patients with epilepsy including 20 patients with idiopathic generalized epilepsy (IGE), 21 patients with temporal lobe epilepsy (TLE) and 20 patients with frontal lobe epilepsy (FLE) recruited from the epilepsy outpatient clinic of Ain Shams university hospitals in addition to 23 matching healthy controls.

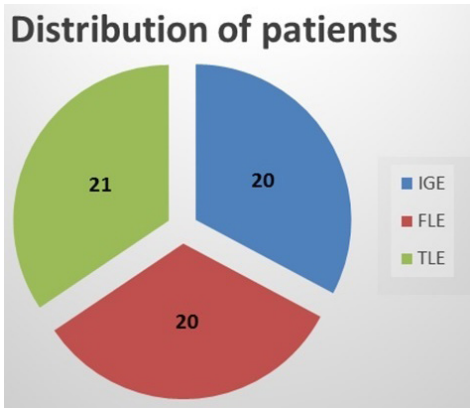

Figure 1: Pie chart showing patients distribution in the epileptic groups.

		Case group			Control group	ANOVA	
		IGE	TLE	FLE		F	Sig.
Comprehension	mean ± SD	10.95 ± 2.99	11.21 ± 3.43	11.77 ± 2.75	13.45 ± 2.68	2.82	0.045*
	Tukey HSD	IGE - TLE	IGE-FLE	TLE-FLE	IGE-Control	TLE-Control	FLE-Control
		0.993	0.841	0.944	0.047*	0.098	0.324
Similarities	mean ± SD	9.40 ± 2.37	7.89 ± 2.307	8.82 ± 2.767	10.30 ± 2.430	3.262	0.026*
	Tukey HSD	IGE - TLE	IGE-FLE	TLE-FLE	IGE-Control	TLE-Control	FLE-Control
		0.234	0.893	0.673	0.657	0.017*	0.274
Arithmetic	mean ± SD	7.80 ± 2.526	7.16 ± 3.404	8.00 ± 2.475	6.75 ± 1.860	0.918	0.437
Digit span	mean ± SD	7.65 ± 1.424	7.79 ± 3.276	7.06 ± 2.657	7.30 ± 3.097	0.275	0.843
Picture Completion	mean ± SD	9.55 ± 2.235	8.26 ± 2.330	9.88 ± 2.421	9.75 ± 1.832	2.143	0.102
Block design	mean ± SD	8.10 ± 2.269	8.11 ± 2.580	8.94 ± 2.585	8.80 ± 2.215	0.644	0.589
Digit symbol	mean ± SD	8.70 ± 3.130	10.00 ± 3.199	10.24 ± 3.456	12.50 ± 2.819	5.031	0.003*
	Tukey HSD	IGE - TLE	IGE-FLE	TLE-FLE	IGE-Control	TLE-Control	FLE-Control
		0.583	0.455	0.996	0.002*	0.078	0.138
VIQ	mean ± SD	93.30 ± 11.952	91.79 ± 16.199	92.06 ± 14.868	96.50 ± 14.032	0.443	0.723
PIQ	mean ± SD	93.75 ± 12.969	93.11 ± 16.960	96.94 ± 17.509	105.25 ± 13.436	2.661	0.054
TIQ	mean ± SD	92.80 ± 12.142	91.79 ± 16.427	94.47 ± 14.786	100.25 ± 12.548	1.438	0.239
Information	mean ± SD	4.84 ± 1.167	4.76 ± 1.091	5.24 ± 0.831	5.20 ± 1.473	0.754	0.524
Orientation	mean ± SD	5.11 ± 1.286	5.18 ± 1.131	5.71 ± 0.772	5.90 ± 0.308	3.223	0.028*
	Tukey HSD	IGE - TLE	IGE-FLE	TLE-FLE	IGE-Control	TLE-Control	FLE-Control
		0.996	0.236	0.367	0.051	0.103	0.924

Mental control	mean ± SD	6.42 ± 1.835	6.12 ± 1.833	7.12 ± 1.833	8.00 ± 1.556	4.255	0.008*
	Tukey HSD	IGE - TLE	IGE-FLE	TLE-FLE	IGE-Control	TLE-Control	FLE-Control
		0.955	0.639	0.355	0.033*	0.010*	0.432
Logical memory	mean ± SD	6.895 ± 2.8017	6.618 ± 2.3883	7.265 ± 2.4310	8.175 ± 2.9748	1.221	0.309
Forward digit span	mean ± SD	5.37 ± 1.116	5.53 ± 1.068	5.12 ± 0.697	5.60 ± 1.142	0.770	0.515
Backward digit span	mean ± SD	3.79 ± 1.398	4.18 ± 1.425	3.76 ± 1.393	3.25 ± 1.650	1.236	0.303
Associate learning	mean ± SD	13.447 ± 3.2313	11.676 ± 4.0386	12.265 ± 3.2554	13.825 ± 3.3650	1.518	0.218
TMA	mean ± SD	69.47 ± 22.169	77.18 ± 32.073	61.29 ± 17.769	59.00 ± 9.947	2.634	0.057
TMB	mean ± SD	164.05 ± 48.929	182.24 ± 73.980	157.65 ± 48.866	153.00 ± 43.298	0.985	0.405
Conceptual level responses	mean ± SD	0.475 ± 0.280	0.454 ± 0.212	0.564 ± 0.254	0.527 ± 0.251	0.662	0.579
Categories completed	mean ± SD	3.75 ± 2.380	3.53 ± 1.908	4.25 ± 2.236	4.68 ± 1.797	1.103	0.354

Table 1: Cognitive functions comparison among case and control groups with POST HOC test.
IGE: Idiopathic generalized epilepsy, TLE: Temporal lobe epilepsy, FLE: Frontal lobe epilepsy VIQ: Verbal intelligence quotient, PIQ: Performance intelligence quotient, TIQ: Total intelligence quotient, TMA: Trail making test part A, TMB: Trail making test part B.

In table 1 comparison among patients and controls are done where collective comparison is done between cases and controls in each category of the cognitive tests and then individual comparison is done between each type of epilepsy with the other and each type with the healthy controls.

Our results showed statistically significant difference in comprehension subcategory of the Wechsler adult intelligence scale (WAIS) between patients with IGE (mean ± SD = 10.95 ± 2.99) and healthy controls (mean ± SD = 13.45 ± 2.68) (p=0.047) denoting poorer social judgment in the IGE group. The IGE group also showed poorer performance (mean ± SD = 8.70 ± 3.13) than control group (mean ± SD = 12.50 ± 2.819) in digit symbol subcategory of the same test denoting worse psychomotor speed and sustained attention (Table 1).

Also, significant difference in similarities subcategory (p=0.017) was found between TLE group (mean ± SD = 7.89 ± 2.307) and control group (mean ± SD =10.30 ± 2.43) denoting poorer abstract thinking among the TLE group.

The IGE and TLE groups also showed lower attention and concentration as compared with the control group in the mental control subcategory of the Wechsler memory scale (WMS) (p=0.033 and 0.01 respectively) yet failed to show superiority over each other (p=0.955). As regards orientation subcategory of WMS there was a significant difference revealed by ANOVA (p=0.028) among the four groups yet the post hoc analysis using Tukey test showed no superiority among them.

As regard MRI study:

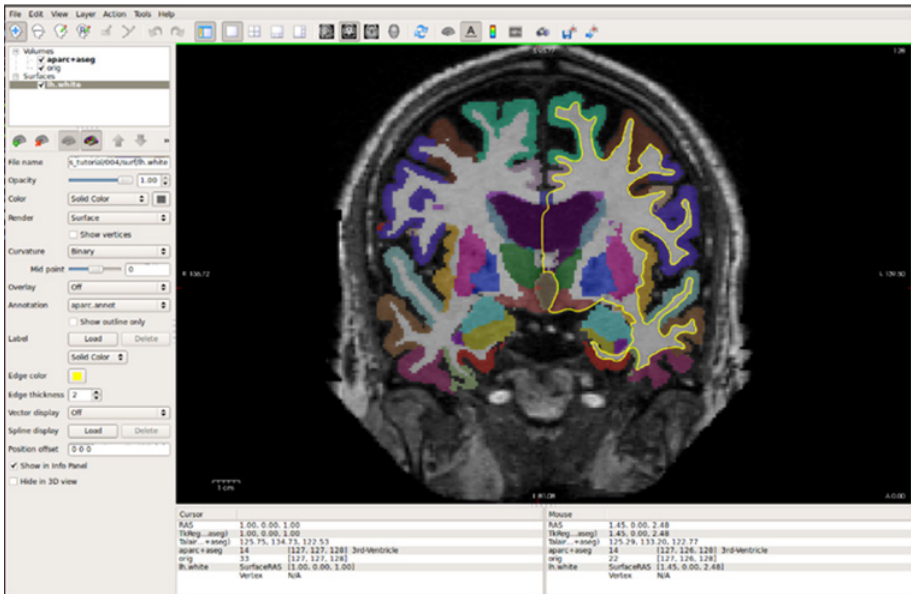

Figure 2: Example of the output of free surfer software showing brain regions in different colors.

		Case group			Control group	ANOVA	
		IGE	TLE	FLE		F	Sig.
Whole brain volume mm^3	mean ± SD	1080987.90 ± 117706.645	1014727.90 ± 72769.076	1043786.60 ± 46720.98	1046514.23 ± 88912.71	2.010	0.120

Table 2: MRI volumetric comparison among case and control groups with POST HOC test.

On comparing the whole brain volume between cases and control groups there was no statistically significant results (Table 2).

		Whole brain volume		
		IGE	TLE	FLE
comprehension	Pearson	-.178	.122	.342
	Sig.	.454	.631	.179
similarities	Pearson	-.282	.050	.242
	Sig.	.228	.844	.349
arithmetic	Pearson	.155	.180	.577*
	Sig.	.514	.476	.015
digit span	Pearson	.044	.227	.139
	Sig.	.855	.365	.594
picture completion	Pearson	-.183	-.108	.016
	Sig.	.439	.671	.950
block design	Pearson	.182	-.023	.081
	Sig.	.443	.928	.758
digit symbol	Pearson	.316	.239	-.155
	Sig.	.175	.355	.552
VIQ	Pearson	-.152	.103	.420
	Sig.	.522	.683	.094
PIQ	Pearson	.104	.078	.015
	Sig.	.662	.758	.954
TIQ	Pearson	-.009	.151	.220
	Sig.	.971	.551	.397
Information	Pearson	.180	.056	.166
	Sig.	.462	.836	.524
orientation	Pearson	-.075	-.112	-.102
	Sig.	.761	.679	.696
mental control	Pearson	.033	.183	-.240
	Sig.	.892	.497	.353
logical memory	Pearson	-.407	-.150	-.042
	Sig.	.084	.579	.873
forward digit span	Pearson	-.017	-.199	.272
	Sig.	.944	.461	.290
backward digit span	Pearson	-.037	.118	-.016
	Sig.	.880	.664	.950
associate learning	Pearson	.018	-.445	.159
	Sig.	.943	.084	.542
TMA	Pearson	-.096	-.155	-.072
	Sig.	.697	.566	.783
TMB	Pearson	.060	.017	.169
	Sig.	.808	.951	.516
conceptual level responses	Pearson	.016	.082	.235
	Sig.	.952	.763	.382
categories completed	Pearson	-.043	.203	.073
		.875	.450	.789

Table 3: Pearson Correlation between MRI volumetric and cognitive functions in patients with IGE, TLE and FLE.

On comparing the MRI volumetric parameters with the different subcategories of the used cognitive scales in the group of patients with FLE, a statistically significant direct relationship was found between the arithmetic subcategory of WAIS and the whole brain volume of the patients (p=0.015) denoting that the higher the whole brain volume the better the concentration and mathematical problem saving among the patients of the FLE group (Table 3).

Discussion

In our study, patients with IGE had poorer social judgment than healthy controls, while patients with TLE and FLE did not. This correlates with the results of the study done by Giorgi and colleagues [9] on 20 juvenile myoclonic epilepsy (JME) patients and twenty matched controls that showed altered social cognition in JME. However, this contradicted the results of Farrant and colleagues [10] in a study done on 14 patients with FLE showing impaired social cognition in patients with FLE and the results of Hennion and colleagues [11] in a study done on 50 patients with TLE that also showed impaired social cognition in TLE. The reason for this contradiction in the last two studies is probably due to their use of a different detailed tool of assessment which is the theory of mind.

Our results also showed that patients with IGE had worse psychomotor speed, sustained attention and concentration than healthy controls. Similar results were described by Iqbal and co-workers [12] in their study on twenty-two sibling pairs, one with JME, were compared with 44 matched controls.

Also, in our study patients with TLE showed lower attention and concentration together with poorer abstract thinking despite normal IQ. This was consistent with the study done by Guimarães and colleagues [13] on 25 patients with TLE and compared them with 25 normal children that showed impaired attention in children with TLE despite normal IQ together with poor abstract resolution.

Similar results were also found by Oyegbile and coworkers [14] in their study done on 96 patients with temporal lobe epilepsy and 82 healthy control subjects who were assessed with a comprehensive neuropsychological battery. The results of this study showed that patients with temporal lobe epilepsy exhibited not only worse memory function but worse performance across measures of intelligence, language, executive function, and motor speed which is similar to our results.

Another study with similar results to ours done by Rzezak and colleagues [15] on patients with TLE. Although patients had IQ score in the normal range, they showed lower IQ scores than controls. When IQ was not considered in the analyses, patients had worse performance in verbal and visual memory (short and long-term), semantic memory, sustained, divided and selective attention, mental flexibility and mental tracking for semantic information.

This was inconsistent with the study done by Hermann and co-workers [16] done on 107 patients with TLE (66 of which had hippocampal sclerosis (MTLE), and 41 did not have evidence of

significant hippocampal sclerosis. In this study the syndrome of MTLE was associated with considerable generalized cognitive impairment (in intelligence, academic achievement, language, and visuospatial functions), but not related to adequacy of performances in other selected cognitive domains (attention or concentration, executive functions). The difference in the results between our study and this study is probably due to our enrollment of all TLE patients whether lateral or medial, and lesional and non lesional TLE.

Also in contrast to our results, the study by Matricardi and colleagues [17] done on patients with FLE showed a significant difference in almost all assessed cognitive domains compared with controls, mainly in frontal functions and memory. The difference in the results from ours is probably due the different age groups and the different tools of assessment used.

Also in the study done by Longo and colleagues [18] including 19 youth with intractable FLE and 47 youth with intractable TLE, participants completed the Wisconsin Card Sorting Test (WCST), verbal fluency, Trail Making Test (Trails A and B), Digit Span Forward (DSF), and Digit Span Backward (DSB), both groups performed significantly below the normative sample levels on attention and working memory tasks which is similar to our results as regards poorer attention and concentration in TLE group yet different from the FLE group that showed no difference as regards attention and working memory when compared to control group in our study.

On comparing the MRI volumetric parameters among cases and control groups, our results showed no difference between both groups as regards the whole brain volume. This was inconsistent with the study done by Zelko and colleagues [19] including 108 individuals with uncomplicated non-syndromic epilepsy (NSE) and 36 healthy age- and gender-matched controls that revealed that total brain volume was significantly smaller in cases.

This was also the same in the study of Lawson and co-workers [20] on 231 children with non-intractable epilepsy and 44 normal childhood control subjects that revealed significant decrease in the whole brain volumes among the patients group. The difference in our results in contrast to the latter two studies is probably to the larger number of patients enrolled in both of them.

In the study of Zelko and colleagues [19] total brain volume TBV showed small associations with intellectual indices of verbal and perceptual ability, working memory and overall IQ which is quite similar to our results that only showed association between the larger TBV and the better performance in arithmetic subcategory in the patients with FLE that indicates better concentration and mathematical problem solving abilities.

The conclusion of the latter study was that the lack of consistent associations between case–control differences in brain volumes and cognitive functioning suggests that brain volumes have limited explanatory value for cognitive functioning in childhood epilepsy.

Limitations

The differences in cognitive functions and volumetric studies in various types of epilepsy could not be detected as the number of patients in each group, were insufficient for separate analyses. Future long-term prospective investigations with larger patient populations and individualized studies in each epileptic subgroup are required.

Also, the volumetric studies rely mostly on the resolution of the acquired images which is usually done by a higher resolution MRI which can give better and more accurate results as regard the studied structures.

References

1. Hart YM. Epidemiology, natural history and classification of epilepsy. Medicine. 2012; 40: 471-476.
2. Busch RM, Najma I, Hermann BP, et al. Genetics of cognition in epilepsy. Epilepsy & Behavior. 2014; 41: 297-306.
3. Baker GA, Taylor J, Aldenkamp AP. Newly diagnosed epilepsy: Cognitive outcome after 12 months. Epilepsia. 2011; 52: 1084-1091.
4. Braakman HMH, van der Kruijs SJM, Vaessen MJ, et al. Microstructural and functional MRI studies of cognitive impairment in epilepsy. Epilepsia. 2012; 53: 1690-1699.
5. Oyegbile TO, Bhattacharya A, Seidenberg M, et al. Quantitative MRI Biomarkers of Cognitive Morbidity in Temporal Lobe Epilepsy. Epilepsia. 2006; 47: 143-152.
6. Hermann B, Jones J, Sheth R, et al. Children with new-onset epilepsy: neuropsychological status and brain structure. Brain. 2006; 129: 2609-2619.
7. Bernasconi N, Duchesne S, Janke A, et al. Whole-brain voxel-based statistical analysis of gray matter and white matter in temporal lobe epilepsy. NeuroImage. 2004; 23: 717-723.
8. Lee JH, Kim SE, Park C, et al. Gray and White Matter Volumes and Cognitive Dysfunction in Drug-Naïve Newly Diagnosed Pediatric Epilepsy. BioMed Research International. 2015; 923861.
9. Giorgi FS, Guida M, Caciagli L, et al. Social cognition in Juvenile Myoclonic Epilepsy. Epilepsy Research. 2016; 128: 61-67.
10. Farrant A, Morris RG, Russell T, et al. Social cognition in frontal lobe epilepsy. Epilepsy & Behav. 2005; 7: 506-516.
11. Hennion S, Delbeuck X, Duhamel A, et al. Characterization and prediction of theory of mind disorders in temporal lobe epilepsy. Neuropsychology. 2015; 29: 485-492.
12. Iqbal N, Caswell H, Muir R, et al. Neuropsychological profiles of patients with juvenile myoclonic epilepsy and their siblings: An extended study. Epilepsia. 2015; 56: 1301-1308.
13. Guimarães CA, Li LM, Rzezak P, et al. Temporal Lobe Epilepsy in Childhood: Comprehensive Neuropsychological Assessment. Journal of Child Neurology. 2007; 22: 836-840.
14. Oyegbile TO, Dow C, Jones J, et al. The nature and course of neuropsychological morbidity in chronic temporal lobe epilepsy. Neurology. 2004; 62: 1736-1742.
15. Rzezak P, Guimarães CA, Guerreiro MM, et al. The impact of intelligence on memory and executive functions of children

with temporal lobe epilepsy: Methodological concerns with clinical relevance. European Journal of Paediatric Neurology. 2017; 21: 500-506.
16. Hermann BP, Seidenberg M, Schoenfeld J, et al. Neuropsychological Characteristics of the Syndrome of Mesial Temporal Lobe Epilepsy. Arch Neurol. 1997; 54: 369-376.
17. Matricardi S, Deleo F, Ragona F, et al. Neuropsychological profiles and outcomes in children with new onset frontal lobe epilepsy. Epilepsy & Behavior. 2016; 55: 79-83.
18. Longo CA, Kerr EN, Smith ML. Executive functioning in children with intractable frontal lobe or temporal lobe epilepsy. Epilepsy & Behavior. 2013; 26: 102-108.
19. Zelko FA, Pardo HR, Blackstone SR, et al. Regional brain volumes and cognition in childhood epilepsy: Does size really matter? Epilepsy Research. 2014; 108: 692-700.
20. Lawson JA, Vogrin S, Bleasel AF, et al. Predictors of Hippocampal, Cerebral, and Cerebellar Volume Reduction in Childhood Epilepsy. Epilepsia. 2000; 41: 1540-1545.