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Volume changes of medial temporal lobe structures in patients with genetic generalized and temporal lobe epilepsy in relation to neuropsychological functions

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Abstract

Purpose: In patients with epilepsy (PWE), cognitive and behavioural dysfunctions are associated with abnormalities in various brain areas. The aim of the study was to compare the volume of the hippocampus (VHIP), amygdala (VAMG) and parahippocampal gyrus (VPHG) with the results of neuropsychological assessment in patients with temporal lobe epilepsy (TLE) and genetic generalized epilepsy (GGE).

Methods: 33 PWE were enrolled in the study (mean age 37.3), 10 with TLE and 23 GGE (12 with GGE with tonic-clonic seizure [GGE-GTCS], and 11 with juvenile myoclonic epilepsy). 19 healthy persons (mean age 32.2) were enrolled as the control group (CG). Measurements of VHIP, VAMG and VPHG were made with 3D completely balanced steady state (CBASS) and 3D T1-weighted sequence. All participants underwent a neuropsychological assessment using a multi-domain cognitive battery and emotional state questionnaires.

Results: The left hippocampus was significantly smaller in patients with left TLE (LTLE) and with GGE-GTCS, compared to the CG ($p = 0.0069$). In LTLE a significant enlargement of the right amygdala in comparison to the CG and other types of epilepsy were found ($p = 0.0015$). Among patients with LTLE and GGE-GTCS, impairment of attention and executive functions was statistically more common than in the CG. VHIP right ($r = 0.25$ $p < 0.01$) and VHIP left ($r = 0.26$ $p < 0.04$) were positively correlated with phonetic verbal fluency.

Conclusions: PWE showed changes in the volume of selected medial temporal lobe (MTL) structures. Selective impairment of attention and executive functions was found. Some neuropsychological findings correlate with volume changes in MTL structures. Antiseizure medications therapy could have an impact on the severity of neuropsychological dysfunctions.

Key words: temporal lobe epilepsy, MTL structures volumetry, amygdala enlargement, idiopathic generalized epilepsy, neuropsychological functions.

INTRODUCTION

Cognitive decline and emotional disturbances are common comorbidities among patients with epilepsy (PWE), mostly those with temporal lobe epilepsy (TLE) and idiopathic generalized epilepsy (IGE). Patients with IGE, including patients with idiopathic generalized tonic-clonic seizures (IGE-GTCS) and juvenile myoclonic seizures (JME), exhibit the selective impairment of visual and auditory speed of information processing, visuomotor coordination, visual working memory, semantic associative processing, auditory-verbal memory span and verbal learning [1-3]. Depression in epilepsy is common and recent epidemiological studies have shown that 9-37% of PWE suffered from depression and 11-25% from anxiety [4, 5]. The higher prevalence rates of depression among PWE compared to the general population have also been demonstrated in a large epidemiological study (the hazard ratio (HR) – 2.04 (95% CI: 1.97-2.09, $p < 0.001$)[6]. Mood disorders in PWE are characterized by a pleomorphic pattern of symptoms such as depression intermixed with euphoria, irritability, tearfulness, anergia and pain [4].

The medial temporal lobe (MTL) structures, such as the hippocampus (HIP) or amygdala (AMG), are sensitive to the pathophysiology of IGE-GTCSs and temporal TLE [6, 7]. Among the various types of IGE the IGE-GTCS are more likely to impair cognitive functions (such as attention, short-term memory, and information processing) than may happen in JME [8]. It has also been shown that repeated GTCS-s induce neuronal loss in the hippocampus, though the relationship between HIP volume and cognitive alterations in patients with IGE-GTCS remains unclear [1, 2].

Despite the importance of MTL structures for memory and emotional processing relatively few studies have been dedicated to analyzing the relationship between memory impairment or depression and volumes of the AMG and HIP structures measured by magnetic resonance imaging (MRI).

Antiseizure medications (ASMs) may impair neuropsychological functioning [8, 9]. Some ASMs, like topiramate (TPM) or levetiracetam (LEV), may cause cognitive decline or exacerbate existing mood and anxiety disorders or aggressiveness and other behavioral problems [9-11].

The aim of the present study was to assess volumetric differences in the HIP, AMG and parahippocampal gyrus (PHG) in patients with TLE, IGE-GTCS and JME, in whom disturbances in cognitive functioning and emotional disorders have been diagnosed by neuropsychological tests, and to compare the results with healthy controls (control group, CG) so as to search for the possible relations between these parameters.

METHODS

Participants

Thirty three epileptic patients from the 1st Department of the Neurology Institute of Psychiatry and Neurology in Warsaw, Poland (PWE) and 19 healthy persons (control group – CG) were enrolled between January 2014 and September 2016. All subjects gave their written informed consent to participate in the study; all the procedures were approved by a local bioethics committee.

The patients were recruited according to the following inclusion criteria: 1) age: 18-55; 2) duration of epilepsy of at least 3 years; 3) negative history of other neurological (except epilepsy) or psychiatric disorders, head trauma, substance abuse or encephalitis; 4) no pregnancy in women; 5) normal intelligence (IQ on the Wechsler Adult Intelligence Scale > 85); 6) lack of evidence of neocortical lesions in MRI (visually normal MR imaging); and 7) right handedness.

Classification of seizure type and epilepsy syndromes was made after a review of a patient's medical history, clinical findings, interictal and ictal (if available) video electroencephalography (VEEG) and neuroimaging findings according to the International League Against Epilepsy (ILAE) classification criteria. Other epilepsy variables, such as age at onset of seizures (years), duration of the epilepsy (years), seizure frequency (number of seizures per year) and treatment (monotherapy or polytherapy, the type and number of ASMs) were registered. All study participants had no abnormalities in their neurological examination and no history of cardiovascular, neurological, or psychiatric disease, diabetes, hypertension, or dyslipidemia.

The CG included healthy volunteers matched for gender, age, handedness, and education. All persons from the CG had normal MRI upon visual inspection. There were no significant differences between the CG and the PWE group as far as age, gender, educational level and occupation were concerned (Table 1).

Structural MRI scans

Structural MRI scans were performed using the Proview Philips Healthcare 1.5 T MRI system (The Nether-

Table 1. Demographic data of patients with epilepsy and healthy control subjects (mean ± SD)

Factor	EPI (*n* = 33)	LTLE (*n* = 10)	JME (*n* = 11)	IGE-GTCS (*n* = 12)	Controls (*n* = 19)	*p*
Age (years)	37.3 (± 10.9)	33.6 (± 8.5)	35.2 (± 10.1)	41.6 (± 14.1)	32.2 (± 8.7)	NS
Gender (F/M)	23/10 F = 62.8%	6/4 F = 63.2%	7/4 F = 70.0%	10/2 F = 83.3%	10/9 F = 55.0%	NS
Education, *n* (%)						
≥ 10 years	31 (81.4)	8 (73.7)	7 (100.0)	11 (83.3)	18 (90)	NS
< 10 years	7 (18.6)	3 (26.3)	–	2 (16.6)	2 (10.0)	NS
Age at onset of epilepsy (years)	16.9 (± 8.3)	14.8 (± 6.8)	14.7 (± 2.9)	21.5 (± 13.6)	–	NS
Duration of epilepsy (years)	20.3 (± 12.1)	18.8 (± 10.7)	20.4 (± 9.8)	20.2 (± 17.2)	–	NS
Seizure frequency (per year)	48.8 (± 65.4)	58.7 (± 78.2)	40.2 (± 66.2)	24.3 (± 47.2)	–	NS
Treatment, *n* (%)						
Monotherapy	15 (45.5%)	4 (40%)	6 (54.5%)	5 (41.8%)	–	NS
Polytherapy	18 (54.5%)	6 (60%)	5 (45.5%)	7 (58.2%)	–	NS

EPI – epilepsy, LTLE – left temporal lobe epilepsy, JME – juvenile myoclonic seizures, IGE-GTCS – idiopathic generalized tonic-clonic seizures, NS – not significant

lands). An MRI of the head was acquired for each patient to exclude pathological focal changes and to measure volume of HIP, PHG and AMG. These measurements were performed with fluid-attenuated inversion recovery sequence (FLAIR), T2-weighted FSE, three-dimensional (3D) completely balanced steady state (CBASS) sequence, and 3D T1-weighted sequence.

Volumetric measurements were performed using volume of interest (VOI)-based volumetry with Brain Suite (Ahmanson-Lovelace Brain Mapping Center, University of California, Los Angeles) and MIPAV (Medical Image Processing, Analysis and Visualization, National Institutes of Health, Bethesda, Maryland) computer programs running on a Mac computer with a 64-bit operating system. Volumetric 3D sequences of T1-weighted brain pictures in DICOM format were used as the source data. DICOM series were converted to a single image file with MRI Convert software (https://surfer.nmr.mgh.harvard.edu/fswiki/mri_convert#AdditionalInformation). The skin, skull and other non-brain structures were eliminated from MR brain images with the use of a BSE (Brain Surface Extractor) algorithm implemented either in the MIPAV program or Brain Suite software. Then, after a series of transformations, the 3D volume of the cerebrum, cerebral hemispheres and cerebellum were isolated and saved in separate files. Next, using Brain Suite software a 3D picture of the cerebrum underwent semi-automatic segmentation with superimposed predefined volume of interests (VOI-s) of different brain structures and the cerebellum (the units of VOI-s in volumetric analysis are mm^3).

All participants underwent the same MRI machine scan, and the images were used for the automated volumetric procedures. In addition, experienced neurologists visually confirmed good or fair parcellation in each volumetric analysis. Volumetric analysis was performed with the use of the data of 19 subjects in the control group, 10 subjects with left TLE, 12 subjects with IGE-GTCS and 11 subjects with JME.

Neuropsychological assessment

A multi-domain cognitive battery was used for the assessment of different aspects of neuropsychological functions: the Trail Making Test (TMT) part A and part B to assess mental speed, visual attention and executive functions; Rey's Complex Figure Test (RCFT) – copy and reproduction – to assess constructional praxis and immediate recall of visual-spatial stimuli; the Naming Test based on the Boston Naming Test (BNT) to assess semantic memory; Verbal Fluency Tasks (VFTs) in two categories, i.e., the phonetic category (words beginning with the letter "k") and the semantic category (names of animals), in order to examine semantic memory and executive functions; and Rey's Auditory Verbal Learning Test (AVLT) to assess verbal learning and memory (the first and the fifth trial of immediate recall, the sum of total learning, the short delayed recall and the long delayed recall) [12]. The raw scores of neuropsychological tests were taken into statistical analysis. The analysis of group differences was made with the Mann-Whitney test.

The following questionnaires were used to assess the participant's emotional state: the Beck Depression Inventory (BDI) for the assessment of depressive symptoms, and the Polish adaptation of the State-Trait Anxiety Inventory (STAI) for the evaluation of anxiety symptoms considered as a state and as a trait [13, 14].

Statistical analysis

Numerical data are depicted as means ± standard error (SE). Statistica ver. 12 (StatSoft USA) software was used for the statistical analyses. Parametric variables were compared with the use of ANOVA, and the Mann-Whitney test was used in the case of data not passing the normality test. To compare the volumes of brain structures the Kruskal-Wallis test, together with a post hoc Dunn's test were used. Correlations between volumetric data, neuropsychological data and clinical features were evaluated by Pearson correlation or Spearman correlation (according to distribution of variables).

RESULTS

Clinical characteristics of the patients

The study population consisted of 33 PWE: 10 with left TLE (LTLE), 12 with IGE-GTCS, 11 with JME, and 19 healthy subjects matched for age and educational level as the CG. The demographic and clinical characteristics of the subgroups are presented in Table 1.

Volumetric analysis

We compared the volumes of HIP, AMG and PHG and in the PWE group and in the CG. It was found that the left hippocampi (LHIP) were significantly smaller in patients with LTLE (median 2401 ± 65 mm^3) and with IGE-GCTS (median 2446 ± 56 mm^3), when compared to the CG (2835 ± 125 mm^3, $p = 0.0069$, $H = 12,15$). However, the PHG of subjects with all types of epilepsy differed significantly in volume from the control group (Table 2).

Significant differences were also found in the volumes of right amygdala (RAMG) in patients with LTLE, when compared to both the control group and other types of epilepsy. The mean volume of RAMG in LTLE patients was 1223 ± 30 mm^3 ($n = 11$) vs. 1028 ± 33 mm^3 ($n = 19$) in the CG, 1057 ± 35 mm^3 in patients with IGE-GCTS and 1162 ± 21 mm^3 in patients with IME ($p = 0.0015$, $F = 5,96$, ANOVA). However, the mean volume of the left amygdale (LAMG) of LTLE subjects was not significantly different from the CG and other types of epilepsy.

Table 2. Results of mean volumes of hippocampi, parahippocampal gyri, and amygdala in control group subjects and patients with epilepsy (mm^3, mean ± SE)

	Median (mm^3)	SE (mm^3)	*p*	Median (mm^3)	SE (mm^3)	*p*
	Right hippocampus			**Left hippocampus**		
Control group	3059	66	Kruskal-Wallis	**2764**	80	Kruskal- Wallis
LTLE	2851	72	$p = 0.63$	**2297**	65	**$p = 0.0069$**
IGE-GTCS	3019	107	$H = 1.73$	**2467**	56	$H = 12.15$
JME	2788	80		2377	113	
	Right amygdala			**Left amygdala**		
Control group	**1028**	33	ANOVA	1128	31	ANOVA
LTLE	**1223**	31	**$p = 0.0015$**	1195	37	$p = 0.72$
IGE-GTCS	1058	35	$F = 5.966$	1089	31	$F = 0.44$
JME	1163	22		1099	28	
	Right parahippocampal gyrus			**Left parahippocampal gyrus**		
Control group	6570	280	ANOVA	6581	292	ANOVA
LTLE	6854	306	$p = 0.76$	6633	265	$p = 0.81$
IGE-GTCS	6900	383	$F = 0.27$	6351	230	$F = 0.2$
JME	6468	317		5915	258	

LTLE – left temporal lobe epilepsy, IGE-GTCS – idiopathic generalized tonic-clonic seizures, JME – juvenile myoclonic seizures

Neuropsychological assessment

In the neuropsychological assessment, selective differences were found in several tests. The whole of the PWE group gained lower scores than the control group in tests assessing mental speed and visual attention (TMT part A, $p = 0.02$), and verbal phonetic fluency (VFT – "k" letter, $p = 0.04$). Patients with TLE showed a lower level of performance than the control group in task assessing, mental speed, visual attention and executive functions (TMT part A, $p = 0.03$; TMT part B, $p = 0.03$). The IGE-GTCS group showed a lower level of phonetic fluency (VFT – "k" letter; $p = 0.01$) than the control group.

An analysis of the level of behavioral (depressive and anxiety) symptoms did not show any differences between epilepsy groups and the control group (Table 3).

Correlational analysis between volumes of selected MTL structures – LHIP, RHIP, LAMG, RAMG – and the results of the neuropsychological tests in the PWE group showed that the volumes of RHIP ($r = 0.25$, $p < 0.01$) and LHIP ($r = 0.26$, $p < 0.04$) were significantly positively correlated with phonetic VFT.

No other statistically significant correlations between volumes of HIP, AMG and the results of the neuropsychological test scores were found.

The results of the correlation of neuropsychological test scores with the type and number of ASMs are presented in Table 4.

Treatment with carbamazepine (CBZ) was correlated with anxiety in epilepsy patients, and use of valproic acid (VPA) was negatively correlated with verbal fluency. Lamotrigine (LTG) treatment correlated with reduction of mental speed and deficits of visual attention. Treatment with topiramate (TPX) correlated negatively with naming ability, word generation, episodic auditory-verbal memory, and visual-spatial memory. Lacosamide (LCM) use was correlated negatively with naming ability, word generation and deficits of verbal memory.

The number of ASMs taken was correlated negatively with mental speed and attention, visual-spatial and constructional functions, and naming and memory (auditory-verbal memory as well as visual-spatial memory).

DISCUSSION

The MTL is a part of the limbic system that plays an important role in memory encoding and retrieval. In humans, the MTL consists of the cortical region composed of the HIP, AMG and PHG. In a previous study it was proved that in patients with either left or right TLE the HIP ipsilateral to the seizures focus was smaller than in normal controls. The HIP may also be more vulnerable in patients with IGE-GTCS [6, 7].

Cognitive impairment is a major complication of epilepsy, associated with the etiology of epilepsy, seizure type, seizure frequency and age at epilepsy onset [4, 7]. A correlation between cognitive decline and HIP volume reduction has been documented in many studies. Patients with LHIP pathologies performed poorly in verbal memory tests. In the current study, the whole PWE group presented significantly lower mental speed and visual attention, and lower levels of verbal fluency in comparison to the CG.

Patients with TLE hippocampal sclerosis (HS) present the most common histopathological findings, which may

Table 3. Scores in neuropsychological tests (mean ± SD)

Test	EPI (*n* = 33)	LTLE (*n* = 10)	JME (*n* = 11)	GGE-GTCS (*n* = 12)	Control (*n* = 19)	*p*
TMT						
TMT – part A	37.9[1] ± 17.7	42.5[2] ± 20.6	36 ± 14.8	31.3 ± 9.3	27.2[1 2] ± 8.9	* [1 2]
TMT – part B	73.0 ± 47.7	69.4[1] ± 36.3	102 ± 84.9	53.9 ± 17.2	56.9[1] ± 21.3	* [1]
RCFT						
RCFT – recall	21.3 ± 3.4	19.5 ± 9.1	23.3 ± 3.3	21.9 ± 5.1	21.4 ± 5.2	NS
NT						
Correct	20.0 ± 3.4	18.4 ± 6.0	20.6 ± 0.8	20.9 ± 0.3	20.8 ± 0.5	NS
VFT						
Animal	21.3 ± 7.7	21.2 ± 10.7	20.3 ± 7.9	22.1 ± 6.1	22.3 ± 6.1	NS
Word "k"	13.1[1] ± 5.8	14.1 ± 9.1	14.0 ± 3.4	11.7[2] ± 4.7	16.2[1 2] ± 4.5	* [1 2]
AVLT						
AVLT_1	6.7 ± 2.4	6.9 ± 3.2	7.3 ± 1.9	7.0 ± 2.5	6.9 ± 1.2	NS
AVLT_5	12.2 ± 2.9	11.1 ± 4.1	13.1 ± 1.9	13.3 ± 2.1	13.2 ± 1.5	NS
AVLT 1-5	51.3 ± 12.8	47.3 ± 18.1	55.0 ± 7.9	55.2 ± 10.1	53.9 ± 6.2	NS
AVLT short delay recall	10.4 ± 3.4	10.5 ± 3.9	11.4 ± 2.7	11.7 ± 2.6	11.1 ± 2.2	NS
AVLT long delay recall	10.6 ± 4.0	9.8 ± 5.1	12.0 ± 2.6	12.2 ± 3.4	11.6 ± 2.1	NS
BDI						
BDI	12.5 ± 11.4	7.0 ± 12.9	10.0 ± 11.9	14.9 ± 8.5	9.9 ± 7.2	NS
STAI						
STAI – state	5.0 ± 2.2	4.7 ± 2.9	3.7 ± 1.7	5.9 ± 1.7	5.1 ± 1.9	NS
STAI – trait	5.5 ± 2.1	3.7 ± 2.0	5.2 ± 2.2	6.3 ± 1.9	5.0 ± 1.7	NS

**Statistically significant differences between groups: p < 0.05 (Mann-Whitney test), NS – not significant, TMT – Trail Making Test, RCFT – Rey's Complex Figure Test, NT – Naming Test, VFT – Verbal Fluency Test, AVLT – Rey's Auditory Verbal Learning Test (AVLT_1 – the first trial of learning, AVLT_5 – the fifth trial of learning, AVLT 1-5 – total learning), BDI – Beck Depression Inventory, STAI – State-Trait Anxiety Inventory*

TMT part A: EPI < Control, LTLE < Control

TMT part B: LTLE < Control

VFT word "k": EPI < Control, IGE < Control

Table 4. Statistically significant correlations between neuropsychological tests scores and the kind and number of antiseizure medications

Test	CBZ	VPA	LTG	TPX	LCM	Number of ASM
TMT – part A	–0.16	0.12	**0.33**	0.29	0.17	**0.38**
TMT – part B	0.04	0.20	0.16	0.20	0.20	**0.45**
RCFT– copy	–0.09	–0.20	–0.21	–0.08	0.03	**–0.40**
RCFT – recall	–0.06	0.00	–0.27	**–0.35**	–0.27	**–0.40**
NT – correct	0.02	–0.17	0.02	**–0.68**	**–0.54**	**–0.43**
VFT – animal	0.00	**–0.33**	0.10	**–0.35**	–0.24	–0.30
VFT – word "k"	0.02	–0.11	0.00	**–0.41**	**–0.32**	–0.29
AVLT_1	0.09	–0.15	–0.31	**–0.36**	–0.29	**–0.41**
AVLT_5	–0.07	0.06	–0.06	**–0.43**	**–0.33**	–0.26
AVLT 1-5	0.00	–0.14	–0.21	**–0.45**	**–0.37**	**–0.37**
AVLT – short delay recall	–0.04	–0.07	–0.02	**–0.37**	–0.24	–0.26
AVLT – long delay recall	–0.07	–0.14	–0.09	**–0.43**	**–0.32**	**–0.39**
BDI	–0.13	–0.29	0.05	0.14	–0.14	0.10
STAI – state	**–0.43**	–0.15	–0.32	–	-	–0.14
STAI – trait	0.12	–0.33	–0.12	–	-	–0.09

Statistically significant Spearman's correlations are in bold.

ASM – antiseizure medications, CBZ – carbamazepine, VPA – valproic acid, LTG – lamotrigine, TPX – topiramate, LCM – lacosamide

be established on FLAIR or T-2 weighted images. In our study we found, similarly to others [15], that the volume reduction of the HIP may be noted also in the patients with normal MR imaging.

The analysis regarding MTL structure volume reduction between different types of epilepsy in comparison to the CG showed significant changes of HIP and AMG in patients with LTLE, HIP volume reduction in IGE-GTCS.

In LTLE patients, besides a statistically significant LHIP volume reduction, an enlargement of right-side AMG was found. Enlarged AMG was considered to be an epileptogenic region [16, 17]. Patients with this abnormality are characterized by later age of epilepsy onset and frequent occurrence of complex partial seizures, which are more frequent than convulsive seizures. Ipsilateral AMG enlargement was reported by Peng *et al.* [17], and according to their suggestion could contribute to either verbal or non-verbal memory impairment. AMG enlargement may be localized ipsi- or contralateral to HS [18]. In our study, similarly to the data analyzed by Coan *et al.*, enlargement of AMG volume was observed contralaterally to the epileptic zone [19]. According to actual hypothesis AMG plays a lesser role in the mechanism enabling memory formation, but in memory consolidation linked to emotional experiences [20, 21]. The predominant mechanisms enabling the consolidation of the emotion are based on AMG stimulation by norepinephrine. Recent studies prove that the effect of this hormone on memory consolidation depends upon the binding of norepinephrine to β-adrenergic receptors in the basolateral complex of the AMG [18, 22]. In patients with TLE without HS, the enlargement of the AMG has been investigated as the possible localization of seizure onset at rates that range from 12% to 63% [16]. In these cases, the neuroimaging, clinical and histopathological characteristics of TLE are heterogeneous, which challenges the hypothesis of a distinct TLE subtype [16, 23, 24].

Patients with idiopathic generalized epilepsies (IGE) presented deficits of visual and auditory attention, reduction of speed of information processing and selective memory impairment, but it should be stressed that IGE comprise a group of different syndromes characterized by a variable combination of absence, generalized tonic-clonic (GTC) and myoclonic seizures. In our study the IGE-GTCS group showed deficits of verbal fluency, but different subtypes of IGE may reflect a different mechanism and different morphological changes. For this reason we divided this group separately for IGE-GTCS and JME.

In our study the IGE-GTCS patients had a significant decrease of the LHIP volume in comparison to the CG. Such changes were the most consistent findings in previously published studies. Zhou *et al.* found significant asymmetry with the LHIP being smaller than the right, suggesting that the LHIP was more vulnerable to IGE-GTCS than the RHIP [7].

Among the various seizure types, IGE-GTCS is more likely to correlate with impairment of cognitive functions. Cognitive problems may reflect cortical tone deregulation inherent in IGE-GTCS pathophysiology [2]. However, in the most recent study by Abarrategui *et al.* the lowest scores on cognitive assessment and the highest anxiety index were found in patients with childhood absence epilepsy (CAE) and juvenile absence epilepsy (JAE) compared to IGE-GTCS, which showed the most favorable scores [1]. Similarly, Patrikelis *et al.* found that IGE patients, both JME and IGE-GTCS, presented impaired visual- and auditory-related functions, and that JME patients' results were significantly worse than the IGE-GTCS [3].

JME is a well-defined heterogeneous clinical syndrome predominantly characterized by symmetric or myoclonic jerks, mostly affecting the upper limbs, or generalized tonic-clonic seizures and, more rarely, absence seizures related to several independent genetic abnormalities. Routine brain imaging shows no abnormalities, but advanced imaging studies like the quantitative analysis of high-resolution MRI have identified changes in the medial prefrontal cortex [8, 25]. Patients in whom the first seizure was an absence one more often have a smaller HIP in comparison to a CG [27]. In patients without absence seizures a thinning of the cortical layer in the right hemisphere including the right post-central, lingual, orbitofrontal, inferior temporal and lateral occipital has been documented [8], contrarily to patients with absence in whom an enlargement of right AMG has been observed [27, 28]. In our study in patients with JME we have documented an insignificant enlargement of RAMG. Some authors have reported that enlargement of the AMG may be related to psychiatric disorders, but other observations have not substantiated this conception. Thalamo-frontocortical network disorders play an important role in cognitive functions such as working memory, executive functions and prospective memory. The prevalence of these disorders supports the concept of a genetically determined Thalamo-frontocortical network dysfunction [8, 26]. In our study, in the JME group of patients the data from neuropsychological tests did not differ statistically from the control group, perhaps because we have a clinically heterogenic group of patients.

One-third of PWE suffer from depression and anxiety [2, 4]. PWE feel stigmatized and their quality of life is likely to be worse. However, in our study the severity of depressive symptoms was not significantly different between epilepsy groups and the CG. Neither was the prevalence of anxiety symptoms different between the PWE and CG groups.

Many studies have investigated the influence of ASM therapy on mood and cognitive function. All ASMs have the potential to exert detrimental effects on cognitive function but the older ASMs have a great impact [11, 29, 30].

We found a negative correlation between LCM treatment and naming ability, word generation and deficits of verbal memory. The use of LTG correlated negatively with mental speed and visual attention. Treatment with TPX had a negative influence on verbal fluency and learning, recalling information and visual-spatial memory. The use of VPA was related with a reduction of verbal fluency.

LIMITATIONS OF THE STUDY

The limitations of the study are the small sample size and heterogeneity of groups in relation to the number of seizures and the duration of illness and type of treatment, despite classifying the patients on the basis of type of epilepsy. The observed differences may reflect a varying severity of disease and may be responsible for structural changes, as the brain is a dynamic structure with its own plasticity and individual ability to respond to changes occurring in the environment. It is problematic to assume in a small group of patients the extent to which the differences between groups may have been associated with individual diversity.

CONCLUSIONS

PWE showed selective cognitive impairment of attention and executive functions as compared with the CG. HIP volumes in PWE were significantly positively correlated with phonetic VFT. AMG enlargement is a common pathology in patients with JME.

Conflict of interest

Absent.

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Absent.

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