ORIGINAL PAPER

Gender and Hemispheric Differences in Epilepsy Diagnosed by Voxel-based Morphometry (VBM) Method: a Pilot Cortical Thickness Study

Shahid Bashir, Baradi, Raidah,
Fouad Al-Ghamdi

Neuroscience Center, King Fahd Specialist
Hospital Dammam, Dammam, Saudi Arabia

Corresponding author: Shahid Bashir.
Neuroscience Center, King Fahd Specialist
Hospital Dammam, Dammam, Saudi Arabia.
E-mail: sbashir10@gmail.com. ORCID ID: <http://www.orcid.org/0000-0000-0000-0000>.

doi: 10.5455/aim.2019.27.171-176

ACTA INFORM MED. 2019 SEP 27(3): 171-176

Received: Jul 15, 2019 • Accepted: Aug 10, 2019

ABSTRACT

Introduction: Voxel-based morphometry (VBM) is a neuroimaging analysis technique that allows investigation of focal differences in brain anatomy, using the statistical approach of statistical parametric mapping. Gender changes are probably expressed in the human brain in the form of functional and anatomical organization. **Aim:** Our aim was to study gender differences and anatomical abnormalities in epilepsy patients (EP) by voxel-based morphometry (VBM) methods. **Methods:** Cortical thickness analysis of whole brain was performed in 28 patients with EP and 30 controls for gender and hemispheric differences. **Results:** Cortical thickness abnormalities were more widespread in left side of the brain in EP; while in female changes were mostly seen in temporal areas, frontal regions were more affected in male. **Conclusion:** Our study confirmed that gender and laterality are important factors determining the brain damage in EP.

Keywords: Gender, Epilepsy, Voxel-based morphometry (VBM).

1. INTRODUCTION

Gender differences are predictable in the functional and anatomical organization of the human brain early in life (1-6). In 1960s, Taylor proposed the biological basis for a higher vulnerability of the male brain and of the left hemisphere (2). According to Taylor hypothesis in 1960, in female cerebral maturation would be more rapid, so that boys would be at a greater risk for a longer time in such a way that a potential seizure-producing insult would affect the less functionally active side, the left hemisphere. The temporal lobe epilepsy with mesial temporal sclerosis (TLE-MTS) has already been described in relation Sexual dimorphism (3, 4, 5).

Voxel-based morphometry (VBM) is a neuroimaging analysis technique that allows investigation of focal differences in brain anatomy, using the statistical approach of statistical parametric mapping (6). In traditional morphometry, volume of the whole brain or its subparts is measured by drawing regions of interest (ROIs) on images from brain scanning and calculating the volume enclosed (6).

Magnetic Resonance Imaging (MRI) study showed volume deficits in male brain areas other than ipsilateral hippocampus more than women (6). The glucose hypometabolism measured by PET showed gender-based differences (7). Finally, gender may differentially effect the degree of gliosis in EP patients (8).

Voxel-based morphometry (VBM), a fully automated computerized quantitative MRI analysis technique, is a widely used method to identify gray and white matter abnormalities in epilepsy field, which provides comprehensive analysis of global brain structure (9, 10)

2. AIM

Our aim was to study gender differences and anatomical abnormalities in epilepsy patients (EP) by voxel-based morphometry (VBM) methods.

3. METHODS

Subjects

Twenty-eight patients diagnosed with Epilepsy were included in this study. This evaluation consisted of a detailed clinical history, neurolog-

© 2019 Shahid Bashir, Baradi Raidah, Fouad Al-Ghamdi

This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (<http://creativecommons.org/licenses/by-nc/4.0/>) which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

ical examination, 3T brain MRI and neuropsychological assessment.

30 age and gender-matched healthy control subjects (15 males), members of the hospital personnel with no history of head injury or significant medical or psychiatric illnesses were submitted to 3T brain MRI under conditions identical to patients. All controls had normal MRI on visual inspection.

The Ethics Committee approved the study, and written informed consent was obtained from all participants before their inclusion in this protocol.

2.3. MRI data acquisition

A Siemens Magnetom Verio 3T MRI clinical scanner (Siemens AG, Healthcare Sector, Erlangen, Germany) and 12-channel phased-array head coil were used to acquire: (1) T1-weighted 3D magnetization-prepared rapid gradient-echo imaging (MPRAGE): TR=1600 ms, TE=2.19 ms, inversion time=900 ms, flip angle=9°, acquisition plane=sagittal, voxel size=1×1×1 mm³, FOV=256 mm, acquired matrix=256×256, acceleration factor (iPAT)=2; (2) Fluid attenuated inversion recovery (FLAIR): TR=9000 ms, TE=128 ms, inversion time=2500 ms, flip angle=150°, acquisition plane=axial, slice thickness=5 mm, FOV=220 mm, acquired matrix=256×196, acceleration factor (iPAT)=2.

2.5. Statistics

2.5.1. Clinical analysis

Descriptive analyses of quantitative variables were reported by mean and standard deviation (SD).

Prior to conducting analyses, measures were tested for normal distribution using Kolmogorov–Smirnov test. All categorical and quantitative variables were assessed according to side and gender using Chi-square and Mann–Whitney test, respectively. The level of statistical significance was set at $p < 0.05$.

Cortical thickness analysis

In order to investigate possible gender and hemispheric differences between males and females, right and left-EP patients, and control group, we employed the ANOVA with age and brain volume as covariates of no interest for all cortical thickness analyses.

4. RESULTS

4.1. Demographics

A total number of 58 patients have been enrolled in the study. Mean age for the study population (6.24 ± 0.39). Among these cases the mean age was (6.28 ± 0.60) while in the control group the mean age was (6.20 ± 0.51). There was no statistical difference in the age between groups with p -value 0.91. Most of the patients in the population were male 60.3%, while female patients were 39.7%. Among cases the male were 71.4% and female 28.6%. While in the control group male were 50%.

4.2. Gender differences

Areas of the brain with statistically significant in male compared to female patients for all 58 patients are summarized in Table 1.

When comparing between genders across all areas of the brain for all the population we found that there is statistically significant in: Cortex Volume ($p=0.001$, Table

1), Left and Right Hemisphere Cortex Volume ($p=0.001$ and $p=0.001$ respectively, Table 1), Cortical White Matter Volume ($p=0.007$, Table 1), Left and Right Hemisphere Cortical White Matter Volume ($p=0.009$ and $p=0.005$ respectively), Sub-Cortical Gray Matter Volume ($p=0.018$), Total Gray Matter Volume ($p=0.000$, Table 1), Left Lateral Ventricle ($p=0.034$), Left and Right Choroid Plexus ($p=0.018$ and $p=0.016$ respectively), Left Caudate ($p=0.022$), Right Accumbens Area ($p=0.015$), Left Putamen ($p=0.039$), Left Thalamus Proper ($p=0.046$), Left and Right Amygdala ($p=0.003$ and $p=0.026$ respectively), Left and Right Hippocampus ($p=0.021$ and $p=0.027$ respectively), Supra-Tentorial Volume with Ventricles ($p=0.001$), Supra-Tentorial Volume without Ventricles ($p=0.001$), Supra-Tentorial Volume Voxel Count ($p=0.001$), 4th Ventricle ($p=0.040$), Left and Right Cerebellum Cortex ($p=0.012$ and $p=0.011$ respectively, Table 1), Left Cerebellum White Matter ($p=0.033$), Mask Volume ($p=0.001$), Brain Segmentation Volume ($p=0.001$), Brain Segmentation Volume without Ventricles ($p=0.001$), Brain Segment Volume without Ventricles from Surface ($p=0.001$), Non White Matter Hypointensities ($p=0.006$), Right Hemisphere Surface Holes ($p=0.017$), Surface Holes ($p=0.034$) and Estimated Total Intracranial Volume ($p=0.001$).

We also found areas of near statistical significant: Right Lateral Ventricle ($p=0.165$), Right Caudate ($p=0.167$), Right Putamen ($p=0.080$), Right Thalamus Proper ($p=0.057$), Left and Right Ventral Diencephalon ($p=0.131$ and $p=0.103$ respectively), 3rd Ventricle ($p=0.072$), Brain Stem ($p=0.070$), Right Cerebellum White Matter ($p=0.060$), Left Hemisphere Surface Holes ($p=0.088$) and Right Vessel ($p=0.147$).

4.3. Hemispheric differences

Areas of the brain with statistically significant in the right hemisphere compared to the left hemisphere for all 58 patients are summarized in Table 2.

When comparing hemispheric differences across all areas of the brain for all the population we found that there is statistically significant in: Cortex Volume ($p=0.001$), Left and Right Hemisphere Cortex Volume ($p=0.001$ and $p=0.001$ respectively), Cortical White Matter Volume ($p=0.007$), Left and Right Hemisphere Cortical White Matter Volume ($p=0.009$ and $p=0.005$ respectively), Sub-Cortical Gray Matter Volume ($p=0.018$), Total Gray Matter Volume ($p=0.000$), Supra-Tentorial Volume with Ventricles ($p=0.001$), Supra-Tentorial Volume without Ventricles ($p=0.001$), Supra-Tentorial Volume Voxel Count ($p=0.001$), Mask Volume ($p=0.000$), Brain Segmentation Volume ($p=0.001$), Brain Segment Volume without Ventricles ($p=0.001$), Brain Segment Volume without Ventricles from Surface ($p=0.001$), Right Hemisphere Surface Holes ($p=0.017$), Surface Holes ($p=0.034$), Estimated Total Intracranial Volume ($p=0.001$). There is also an area of near statistically significant Left Hemisphere Surface Holes ($p=0.088$).

4.4. Gender differences

Areas of the brain with statistically significant in male compared to female patients for only 28 cases patients are summarized in Table 1.

When comparing between genders across all areas of the brain for only the cases we found that there is statis-

Group comparison	Brain region	Males brain volume, mm3	Females brain volume, mm3	P-Value
Comparing between genders for all cases and controls	Cortex Volume	578919.8 ± 10334.6	519105.9 ± 12121.4	0.000
	Left Hemisphere Cortex Volume	287522.9 ± 5241.8	258466.0 ± 6035.2	0.001
	Right Hemisphere Cortex Volume	291396.8 ± 5116.7	260639.8 ± 6095.6	0.000
	Cortical White Matter Volume	377808.3 ± 10512.0	330638.6 ± 13176.0	0.007
	Left Hemisphere Cortical White Matter Volume	187620.6 ± 5322.9	164718.0 ± 6570.9	0.009
	Right Hemisphere Cortical White Matter Volume	190187.6 ± 5201.7	165920.6 ± 6611.5	0.005
	Sub-Cortical Gray Matter Volume	56692.6 ± 1063.4	52459.0 ± 1396.6	0.018
	Total Gray Matter Volume	746028.4 ± 12795.6	671432.4 ± 14511.8	0.000
	Left Lateral Ventricle	5621.0 ± 562.9	3878.0 ± 497.9	0.034
	Left Choroid Plexus	979.4 ± 38.1	810.813 ± 62.520	0.018
	Right Choroid Plexus	1134.3 ± 48.5	937.2 ± 64.5	0.016
	Left Caudate	3611.3 ± 116.9	3225.3 ± 94.8	0.022
	Right Accumbens Area	661.9 ± 15.4	605.4 ± 14.9	0.015
	Left Putamen	5614.8 ± 117.5	5204.5 ± 158.5	0.039
	Left Thalamus Proper	7496.9 ± 198.0	6875.6 ± 224.3	0.046
	Left Amygdala	1482.8 ± 32.7	1287.7 ± 60.1	0.003
	Right Amygdala	1487.9 ± 36.3	1339.7 ± 58.2	0.026
	Left Hippocampus	4066.5 ± 95.3	3652.3 ± 159.7	0.021
	Right Hippocampus	4221.6 ± 124.2	3786.7 ± 142.7	0.027
	Supra-Tentorial Volume with Ventricles	1029002.5 ± 20266.7	914267.5 ± 23682.3	0.001
	Supra-Tentorial Volume without Ventricles	1016288.7 ± 20331.2	904657.6 ± 23785.3	0.001
	Supra-Tentorial Volume Voxel Count	1013834.2 ± 20248.5	902699.9 ± 23672.0	0.001
	4th Ventricle	1571.5 ± 82.9	1320.8 ± 75.7	0.040
	Left Cerebellum Cortex	55334.5 ± 1403.8	50126.8 ± 1215.2	0.012
	Right Cerebellum Cortex	55878.9 ± 1390.3	50548.9 ± 1349.7	0.011
	Left Cerebellum White Matter	13722.4 ± 533.1	11968.8 ± 569.3	0.033
	Mask Volume	1514215.2 ± 28738.7	1350562.6 ± 30442.2	0.000
	Brain Segmentation Volume	1166828.6 ± 23019.9	1038452.5 ± 26016.5	0.001
	Brain Segmentation Volume without Ventricles	1151029.7 ± 23093.8	1026085.7 ± 26097.1	0.001
	Brain Segmentation Volume without Ventricles from Surface	1150495.5 ± 23082.3	1025502.2 ± 26138.2	0.001
	Non White Matter Hypointensities	12.5 ± 1.2	7.5 ± 1.0	0.006
	Right Hemisphere Surface Holes	68.6 ± 4.2	53.0 ± 4.3	0.017
	Surface Holes	135.0 ± 8.3	107.3 ± 9.1	0.034
	Estimated Total Intracranial Volume	1403577.0 ± 25831.8	1265618.4 ± 27025.1	0.001
	Right Lateral Ventricle	4619.6 ± 492.7	3619.3 ± 452.2	0.165
	Right Caudate	3496.6 ± 102.6	3284.8 ± 101.6	0.167
	Right Putamen	5564.7 ± 111.3	5232.0 ± 155.5	0.080
	Right Thalamus Proper	6964.8 ± 142.3	6536.9 ± 163.4	0.057
	Left Ventral Diencephalon	3306.4 ± 80.9	3096.2 ± 116.3	0.131
	Right Ventral Diencephalon	3379.8 ± 75.8	3164.0 ± 112.0	0.103
	3rd Ventricle	873.5 ± 54.3	726.908 ± 53.6	0.072
	Brain Stem	17254.5 ± 522.2	15738.6 ± 628.5	0.070
	Right Cerebellum White Matter	13632.9 ± 543.3	12110.9 ± 517.6	0.060
	Left Hemisphere Surface Holes	66.4 ± 4.5	54.2 ± 5.135	0.088
	Right Vessel	40.0 ± 5.1	57.8 ± 12.697	0.147
	Cortex Volume	578919.8 ± 10334.6	519105.9 ± 12121.4	0.000
	Left Hemisphere Cortex Volume	287522.9 ± 5241.8	258466.0 ± 6035.2	0.001
	Right Hemisphere Cortex Volume	291396.8 ± 5116.7	260639.8 ± 6095.6	0.000
	Cortical White Matter Volume	377808.3 ± 10512.0	330638.6 ± 13176.0	0.007
	Left Hemisphere Cortical White Matter Volume	187620.6 ± 5322.9	164718.0 ± 6570.9	0.009
	Right Hemisphere Cortical White Matter Volume	190187.6 ± 5201.7	165920.6 ± 6611.5	0.005
	Sub-Cortical Gray Matter Volume	56692.6 ± 1063.4	52459.0 ± 1396.6	0.018
	Total Gray Matter Volume	746028.4 ± 12795.6	671432.4 ± 14511.8	0.000
	Left Lateral Ventricle	5621.0 ± 562.9	3878.0 ± 497.9	0.034
	Left Choroid Plexus	979.4 ± 38.1	810.813 ± 62.520	0.018
	Right Choroid Plexus	1134.3 ± 48.5	937.234 ± 64.553	0.016
	Left Caudate	3611.3 ± 116.9	3225.330 ± 94.8	0.022
	Right Accumbens Area	661.9 ± 15.4	605.4 ± 14.9	0.015

tically significant in: Cortex Volume (p=0.038), Left and Right Hemisphere Cortex Volume (p=0.048 and p=0.030)

Comparing between genders in cases only	Left Putamen	5614.8 ± 117.5	5204.5 ± 158.5	0.039
	Left Thalamus Proper	7496.9 ± 198.0	6875.621 ± 224.3	0.046
	Left Amygdala	1482.8 ± 32.7	1287.7 ± 60.1	0.003
	Cortex Volume	582783.8 ± 14614.2	525810.2 ± 18788.7	0.038
	Left Hemisphere Cortex Volume	289390.8 ± 7468.2	261865.9 ± 9410.7	0.048
	Right Hemisphere Cortex Volume	293393.0 ± 7185.8	263944.280 ± 9407.9	0.030
	Total Gray Matter Volume	750779.6 ± 17353.9	677304.3 ± 20635.6	0.023
	Sub-Cortical Gray Matter Volume	56469.3 ± 1386.6	52128.5 ± 1847.8	0.093
	Supra-Tentorial Volume with Ventricles	1033316.7 ± 29599.5	941145.1 ± 31478.5	0.083
	Supra-Tentorial Volume without Ventricles	1020697.7 ± 29356.9	929655.4 ± 32023.0	0.085
	Supra-Tentorial Volume Voxel Count	1018098.4 ± 29233.0	927563.8 ± 32026.0	0.086
	Mask Volume	1521503.3 ± 40845.6	1404639.8 ± 41657.3	0.108
	Brain Segment Volume	1172276.5 ± 32823.8	1065091.0 ± 34031.1	0.069
	Brain Segmentation Volume without Ventricles	1156590.6 ± 32538.8	1050482.3 ± 34637.8	0.070
	Brain Segmentation Volume without Ventricles from Surface	1156001.1 ± 32503.8	1050006.980 ± 34658.6	0.070
	Left Hemisphere Surface Holes	70.7 ± 6.7	50.5 ± 4.7	0.083
	Right Hemisphere Surface Holes	70.650 ± 6.450	51.500 ± 3.736	0.082
	Surface Holes	141.350 ± 12.576	102.000 ± 7.063	0.067
	Estimated Total Intracranial Volume	1411955.614 ± 37167.799	1306996.512 ± 37802.272	0.112

Table 1. Areas of the brain with statistically significant in male compared to female patients for all 58 patients.

Group comparison	Brain region	Right & Left hemisphere brain volume, mm ³	P-Value
Comparing both hemispheres for all cases and controls	Cortex Volume	555200.5 ± 8715.0	0.000
	Left Hemisphere Cortex Volume	276000.3 ± 4360.0	0.001
	Right Hemisphere Cortex Volume	279200.1 ± 4368.3	0.000
	Cortical White Matter Volume	359103.1 ± 8699.9	0.007
	Left Hemisphere Cortical White Matter Volume	178538.5 ± 4359.9	0.009
	Right Hemisphere Cortical White Matter Volume	180564.5 ± 4347.6	0.005
	Sub-Cortical Gray Matter Volume	55013.7 ± 883.6	0.018
	Total Gray Matter Volume	716447.3 ± 10701.7	0.000
	Supra-Tentorial Volume with Ventricles	983504.1 ± 16998.6	0.001
	Supra-Tentorial Volume without Ventricles	972021.2 ± 16961.5	0.001
	Supra-Tentorial Volume Voxel Count	969763.7 ± 16887.8	0.001
	Mask Volume	1449318.5 ± 23485.5	0.000
	Brain Segmentation Volume	1115920.8 ± 19066.4	0.001
	Brain Segmentation Volume without Ventricles	1101482.9 ± 19019.7	0.001
	Brain Segmentation Volume without Ventricles from Surface	1100929.2 ± 19024.7	0.001
	Right Hemisphere Surface Holes	62.4 ± 3.2	0.017
	Surface Holes	124.0 ± 6.4	0.034
	Estimated Total Intracranial Volume	1348869.3 ± 20781.7	0.001
Comparing between hemispheres in cases only	Left Hemisphere Surface Holes	61.6 ± 3.4	0.088
	Left Choroid Plexus	920.1 ± 49.8	0.039
	Left Cerebellum Cortex	54265.2 ± 1298.5	0.025
	Right Cerebellum Cortex	54632.3 ± 1362.2	0.046
	Right Choroid Plexus	1090.4 ± 58.2	0.095
	Left Caudate	3507.4 ± 125.4	0.117
	Left Accumbens Area	598.4 ± 27.6	0.192
	Right Accumbens Area	633.2 ± 19.4	0.063
	Left Putamen	5280.8 ± 150.5	0.061
	Right Putamen	3435.7 ± 116.5	0.119
	Right Thalamus Proper	6865.6 ± 149.4	0.173
	Left Amygdala	1422.7 ± 38.2	0.056
	Right Amygdala	1425.7 ± 35.1	0.085
	Left Hippocampus	3977.8 ± 111.1	0.140
	Right Hippocampus	4113.2 ± 150.0	0.182
	Non White Matter Hypointensities	11.4 ± 1.2	0.098

Table 2.

respectively), Total Gray Matter Volume ($p=0.023$). We also found areas of near statistical significant: Sub-Cortical Gray Matter Volume ($p=0.093$), Supra-Tentorial Volume with Ventricles ($p=0.083$), Supra-Tentorial Volume without Ventricles ($p=0.085$), Supra-Tentorial Volume Voxel Count ($p=0.086$), Mask Volume ($p=0.108$), Brain Segmentation Volume ($p=0.069$), Brain Segmentation Volume without Ventricles ($p=0.070$), Brain Segment Volume without Ventricles from Surface ($p=0.070$), Left and Right Hemisphere Surface Holes ($p=0.083$ and $p=0.082$ respectively), Surface Holes ($p=0.067$) and Estimated Total Intracranial Volume ($p=0.112$).

4.5. Hemispheric differences

Areas of the brain with statistically significant in the right hemisphere compared to the left hemisphere for only 28 cases patients are summarized in Table 2.

When comparing hemispheric differences across all areas of the brain for only the cases we found that there is statistically significant in: Left Choroid Plexus ($p=0.039$) and Left and Right Cerebellum Cortex ($p=0.025$ and $p=0.046$ respectively). There are also areas of near statistical significant: Right Choroid Plexus ($p=0.095$), Left Caudate ($p=0.117$), Left and Right Accumbens area ($p=0.192$ and $p=0.063$ respectively). Left and Right Putamen ($p=0.061$ and $p=0.119$ respectively), Right Thalamus Proper ($p=0.173$), Left and Right Amygdala ($p=0.056$ and $p=0.085$ respectively), Left and Right Hippocampus ($p=0.140$ and $p=0.182$ respectively, Table 2) and Non White Matter Hypointensities ($p=0.098$).

5. DISCUSSION

CH The result of our data showed 34 statically significant areas comparing between genders for 28 patients with TLE and 30 controls. Males have showed higher ANOVA score than females in all the significant areas. Moreover, hemispheric differences were significant for 18 areas in all cases and controls. Keller has described 26 foci in the brain which were found to be associated with volume reduction in association with TLE which could be ipsilateral and contralateral to the epileptic focus (9). However, the association between volume reduction and VBM in relation to gander was not studied. This study showed significant value of gander differentiation as an augmenting tool to be used with Voxel Based Morphometry to investigate TLE patients.

The concept of using VBM as a tool to investigate epilepsy was used before in multiple previous studies. Mueller has used Voxel-based T2 Relaxation Rate Measurements in Temporal Lobe Epilepsy (TLE) with and without Mesial Temporal Sclerosis. He found ipsilateral significant that exceeds the limits of temporal lobe and extend to extra temporal areas (11). However, using VBM N. Bernasconi found the extension of gray matter disease will involve cingulum, thalamus and frontal lobe, but white matter involvement was exclusive for ipsilateral to the elliptic focus site with involvement of temporal tracks only (REFS) (12). The result of our study showed bilateral hemispheric involvement for both hemispheres including gray and white matter changes. The gray matter changes were compatible with Mullar result, but the white matter change was

involving both hemispheres as Mullar showed ipsilateral involvement. Cortex Volume, Left and Right Hemisphere Cortex and Total Gray Matter Volume are the areas which were most significant for TLE patients (11). These findings augment the previous evidence provided by Maria which showed to gender and hemispheric differences as factors representing the nature and severity of TLE with bilateral hemispheric involvement (13). Also, this study proposes TLE to have generalized pathological extension to entire brain regions. The effectivity of VBM technique to monitor brain changes were shown in many conditions including, schizophrenia, temporal lobe epilepsy (TLE), mild cognitive impairment (MCI) and Alzheimer's disease (AD) (14).

Limitation of the study

Limitations included a small sample size. We believe that this trade-off to be sound as replication using identical methods is uncommonly carried out. Nevertheless, in a future paper we plan to carry out an analysis using whole brain measurement.

6. CONCLUSION

Further research using VBM to study patients with TLE is recommended to understand the nature of disease and to modify the treatment plan.

- **Declaration of patient consent:** The authors certify that they have obtained all appropriate patient consent forms.
- **Author's contribution:** Each author gave substantial contribution to the conception or design of the work and in the acquisition, analysis and interpretation of data for the work. Each author had role in drafting the work and revising it critically for important intellectual content. Each author gave final approval of the version to be published and they agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.
- **Conflict of interest:** There are no conflicts of interest.
- **Financial support and sponsorship:** Nil.

REFERENCES

1. Voxel based morphometry. URL: <http://voxel-based-morphometry> (retrieved on May 2nd, 2019).
2. Geschwind N, Galaburda AM. Cerebral lateralization, biological mechanisms, associations, and pathology: I. A hypothesis and a program for research. *Arch Neurol*. 1985; 42(5): 428-459.
3. Taylor DC. Differential rates of cerebral maturation between sexes and between hemispheres. *Lancet*. 1969; 294(7612): 140-142.
4. Rémillard GM, Andermann F, Testa GF, et al. Sexual ictal manifestations predominate in women with temporal lobe epilepsy: a finding suggesting sexual dimorphism in the human brain. *Neurology*. 1983; 33(3): 323-330.
5. Janszky J, Schulz R, Janszky I, et al. Medial temporal lobe epilepsy: gender differences. *J Neurol Neurosurg Psychiatry*. 2004 May; 75(5): 773-775.
6. Chiesa V, Gardella E, Tassi L, et al. Age-related gender differences in reporting ictal fear: analysis of case histories and review of the literature. *Epilepsia*. 2007; 48(12): 2361-2364.
7. Briellmann RS, Berkovic SF, Jackson GD. Men may be more vulnerable to seizure-associated brain damage. *Neurology*.

- 2000; 55: 1479-1485.
8. Scharfman HE, MacLusky NJ. Sex differences in the neurobiology of epilepsy: a preclinical perspective. *Neurobiol Dis.* 2014; 72 Pt B: 180-192.
9. Doherty MJ, Rostad SW, Kraemer DL, et al. Neocortical gliosis in temporal lobe epilepsy: gender-based differences. *Epilepsia.* 2007 Aug; 48(8): 1455-1459.
10. Keller SS, Roberts N. Voxel-based morphometry of temporal lobe epilepsy: an introduction and review of the literature. *Epilepsia.* 2008 May; 49(5): 741-757.
11. Ashburner J, Friston KJ. Voxel-based morphometry – the methods. *Neuroimage.* 2000 Jun; 11(6 Pt 1): 805-821.
12. Mueller SG, Laxer KD, Schuff N, et al. Voxel-based T2 relaxation rate measurements in temporal lobe epilepsy (TLE) with and without mesial temporal sclerosis. *Epilepsia.* 2007; 48(2): 220-228.
13. 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 Oct; 23(2): 717-723.
14. Santana GCTM, Jackowski AP, dos Santos Britto F, et al. Gender and hemispheric differences in temporal lobe epilepsy: A VBM study. *Seizure.* 2014; 23: 274-279.

International Medical Informatics Association

[About Us](#)
[IMIA Members](#)
[Publications](#)
[MedInfos](#)
[IMIA WGs & SIGs](#)
[IMIA NI SIG](#)
[IAHSI](#)

Welcome to IMIA, the International Medical Informatics Association

IMIA General Assembly Meeting (2019) will be held on Monday, August 26th, 2019 in Lyon, France

The meeting will be held in conjunction with MedInfo 2019, please visit the MedInfo 2019 website for more details ... [MedInfo 2019](#)

IMIA Code of Ethics – 2016 Revision and accompanying Handbook Now Available

Thank you again to Dr. Eike-Henner W. Kluge for his dedication and time to IMIA on this important work.

Greetings to everyone and welcome to IMIA!

Greetings from the President of IMIA, Dr. Chris Lehmann

About IMIA

The International Medical Informatics Association (IMIA) is the world body for health and biomedical informatics. As an 'association of associations', IMIA acts as a bridging organisation, bringing together the constituent organisations and their members. IMIA provides leadership and expertise to the multidisciplinary, health focused community and to policy makers, to enable the transformation of healthcare in accord with the world-wide vision of improving the health of the world population.

Inherent in IMIA's role is to bring together, from a global perspective, scientists, researchers, users, vendors, developers, consultants and suppliers in an environment of cooperation and sharing.

IMIA's vision is that there will be a world-wide systems approach for healthcare. Clinicians, researchers, patients and people in general will be supported by informatics tools, processes and behaviors that make it easy to do the right thing, in the right way, at the right time to improve health care for all. This systems approach will incorporate and integrate research, clinical care and public health. To achieve this vision will require everyone being supported by informatics-based information and communication systems and technologies. As an organization committed to promoting best practice in the use of information and communication technologies within biomedical informatics and in health and healthcare, and seeing technology as transformational, IMIA will promote research and develop the concepts needed to support the organizations of the world.

IMIA Vision Statement

Login

Username

Password

☐ Remember Me

Login →

IMIA – Latest News

IMIA ANNOUNCES DR. SUZANNE BAKKEN AS THE RECIPIENT OF THE 2019 IMIA FRANÇOIS GRÉMY AWARD OF EXCELLENCE
 June 18, 2019

CALL FOR BIDS FOR MEDINFO 2023 NOW OPEN
 February 23, 2019

2019 NOMINATIONS FOR IMIA BOARD POSITIONS – DEADLINE APRIL 1, 2019
 February 23, 2019

2019 CALL FOR NOMINATIONS IMIA FRANÇOIS GRÉMY AWARD OF EXCELLENCE: DEADLINE MARCH 18, 2019
 December 17, 2018

IMIA NEW CAREER OPPORTUNITY – W2 PROFESSORSHIP IMIS KIEL UNIVERSITY MEDICAL FACULTY