Journal of Medicinal and Chemical Sciences

Journal homepage: http://www.jmchemsci.com/

Original Article

Oxidative Stress and Cognitive Performance in Children with Temporal Lobe Epilepsy

Marwa Elhady[1,*], Heba Tawfik Okda[1], Mohamed Farouk Ahmed[2], Rasha M. Gouda[1], Rasha Sobhy Elattar[3], Seham Eelsaid Abdelsadek[3], Talal Abd Allah Mohammed Dawa[4], Mohammad Fathi Abdulsalam[4], Fathy Mahmoud Mansour[4], Adel M. Othman[5], Doaa Ibrahim Hassan Ibrahim[6], Shaimaa A. Maklad[3], Shahinaz El Attar[7], Walaa Shipl[7], Rayyh A.M. Saleh[8], Esraa Ali[9]

[1]*Pediatric Department, Faculty of Medicine for Girls, Al-Azhar University, Cairo, Egypt*
[2]*Pediatric Department, Faculty of Medicine for Boys, Al-Azhar University, Cairo, Egypt*
[3]*Neurology Department, Faculty of Medicine for Girls, Al-Azhar University, Cairo, Egypt*
[4]*Neurology Department, Faculty of Medicine for Boys, Al-Azhar University, Cairo, Egypt*
[5]*Department of Neurology, Faculty of Medicine, Damitta, Al-Azhar University*
[6]*Psychiatric Department, Faculty of Medicine (for girls), Al-Azhar University, Cairo, Egypt*
[7]*Department of Medical Biochemistry, Faculty of Medicine for Girls, Al-Azhar University, Cairo, Egypt*
[8]*Department of Clinical Pathology, Faculty of Medicine for Girls, Al-Azhar University, Cairo, Egypt*
[9]*Department of Medical Biochemistry and Molecular Biology, Faculty of Medicine, Ain Shams University, Cairo, Egypt*

ARTICLE INFO

Article history

Receive: 2023-05-16
Received in revised: 2023-07-24
Accepted: 2023-07-24
Manuscript ID: JMCS-2307-2171
Checked for Plagiarism: **Yes**
Language Editor:
Dr. Fatima Ramezani
Editor who approved publication:
Dr. Ehab AlShamaileh

DOI:10.26655/JMCHEMSCI.2024.1.3

KEYWORDS

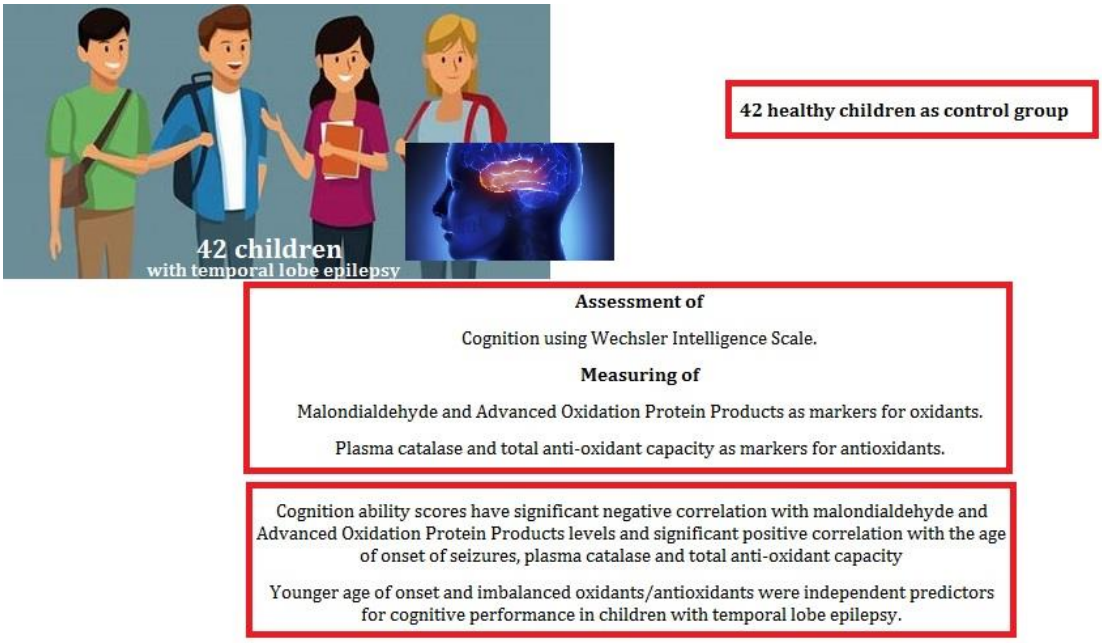
Pediatrics
Oxidants
Antioxidants
Cognitive function

ABSTRACT

Background: Cognitive impairment represents a major but under-determined comorbidity in children with temporal lobe epilepsy. Exposure to oxidation stress may induce cellular damage and functional disruption in the developing brain.
Method: This comparative study included 42 children with newly diagnosed temporal lobe epilepsy and 42 healthy children as a control group. Cognition was assessed using Wechsler Intelligence Scale. Malondialdehyde and Advanced Oxidation Protein Products were measured as markers for oxidants while plasma catalase and total antioxidant capacity was measured as markers for antioxidants. Biomarkers of oxidation stress were correlated to clinical data and cognition scores of included children.
Results: Children with temporal lobe epilepsy have significant higher circulating malondialdehyde, Advanced Oxidation Protein Products and lower catalase, total anti-oxidant capacity, and cognition ability scores than healthy controls. Cognition ability scores have significant negative correlation with malondialdehyde and Advanced Oxidation Protein Products levels and significant positive correlation with the age of onset of seizures, plasma catalase and total anti-oxidant capacity levels.
Conclusion: Oxidation stress may be associated with decreased cognitive abilities in children with newly diagnosed temporal lobe epilepsy. Treatment strategy for children with newly diagnosed temporal lobe epilepsy should be adjusted to decrease oxidation stress to avoid worsening of cognitive function.

* Corresponding author: Marwa Elhady
✉ E-mail: Marwaelhady@azhar.edu.eg

GRAPHICAL ABSTRACT



Introduction

Active seizures represent a major risk factor for oxidation stress in children with epilepsy. The developing brain is highly vulnerable to oxidation stress induced injury due to its great lipid content and high oxygen consumption. Neuronal exposure to oxidation stress enhances lipid peroxidation that may alter membrane excitability, disturb neurotransmitters and impairs both morphological and functional aspects of developing brain [1-6].

Production of free radicals and reactive oxygen/nitrogen species is tightly regulated by physiological anti-oxidant defense. Oxidation stress occurred due to imbalance in oxidants/antioxidant defense balance leading to activation of inflammatory signals, disruption of cellular morphology, and function. Endogenous antioxidants include both enzymatic molecules (e.g., glutathione peroxidase, glutathione reductase, catalase, superoxide dismutase, and glucose-6-phosphate dehydrogenase) and non-enzymatic molecules (e.g., vitamin C, E, omega-3, bilirubin, melatonin, coenzyme Q, reduced Glutathione, and uric acid) [7].

Cognitive impairment represents serious comorbidity of childhood epilepsy that adversely affects the quality of life and learning. The interaction between epilepsy and cognition is complex and multifactorial. Seizure activities in addition to use of antiepileptic medications are involved in the pathogenesis of cognitive dysfunction [8]. Epilepsy related factors include the underlying etiology, age of onset, frequency of seizures, duration, and type of epilepsy. Cognitive affection may precede the initiation of antiepileptic medications and can be persist even in those with controlled seizures. Cognitive dysfunction can be transient following seizure activity. However, several studies reported a long term cognitive impairment with ageing and dementia [9].

Malondialdehyde (MDA) is a lipid peroxidation end product that is produced by oxidation of polyunsaturated fatty acids. Advanced oxidation protein products (AOPP) is another biomarker that reflects protein damage induced by oxidative stress.

Both biomarkers are widely used as an indicator of increased oxidation stress in various tissues and organs. Evidence showed that oxidative stress toxicity involving cellular lipid and protein molecules are associated with increased the psychological comorbidities in subjects with temporal lobe epilepsy [10, 11].

Oxidation stress and free radicals formation together with impaired anti-oxidative defense capacity are involved in the initiation and progression of epilepsy and the development of its comorbidities [12, 13]. However, the impact of unbalanced oxidation stress on cognitive function in children with temporal lobe epilepsy apart from the effect of antiepileptic medications and refractory seizures is not fully explored. Evaluation of cognitive abilities and detection of risk factors that may add more burdens in such children can help individualization of treatment strategies.

The current study was conducted to explore the relation between oxidation stress/anti-oxidative imbalance, and cognitive function in children with newly diagnosed temporal lobe epilepsy.

Materials and Methods

Study design

A cross-sectional comparative study involved 42 children with newly diagnosed temporal lobe epilepsy who were recruited from children referred to Pediatric and Neurology Department at Al-Azhar University hospitals, Cairo, Egypt. A control group consisted of 42 healthy children of matched age and sex to epilepsy group was selected consecutively from attendance of pediatric outpatient clinics of Al-Azhar and Sayed Galal Hospital.

Inclusion criteria: Include children with confirmed temporal lobe epilepsy who were newly diagnosed and did not receive any previous antiepileptic drugs; their age ranged between 6 and 8 years old. Based on neurological examination and neuroimaging assay only those with idiopathic etiology were included. Control group were apparently healthy children who did not have family history of neuropsychiatric disorders or febrile seizures.

Exclusion criteria: Include children with any acute infection or inflammation, children with chronic medical disorders (e.g., metabolic, renal, hematological, cardiac, respiratory, and hepatic diseases), children with history of developmental delay, perinatal hypoxia or neuromuscular disability, children with structural brain abnormalities, children with mental retardation (IQ<70 by Wechsler intelligence quotient, the 3th edition), children with any psychological disorders and children who received any medications affect cognitive function within the previous 1 week as antihistaminic.

Diagnosis of epilepsy

A detailed medical history was obtained including socio demographic data (age, sex, level of education, and parent education), perinatal, developmental history, age of onset, seizures semiology, aura characteristics, seizures frequency, neurological manifestation, and previous investigations, or medications. Complete general and neurological clinical examinations were done.

Diagnosis of temporal lobe epilepsy was based on history of focal onset seizures either with retained or impaired awareness from reliable eye witness together with electroencephalography confirm the presence of temporal region epileptic discharge. Epilepsy was classified according to the principles of international league against epilepsy [14]. Interictal EEG was done using a Nihon Kohden 1200 digital EEG instrument at pediatric neurology unit of Al-Zahraa Hospital. Intermittent photic stimulation, sleep deprivation, and hyperventilation activation procedures were done for children with epilepsy to confirm temporal lobe epileptic discharge. Neuroimaging was done for children with epilepsy to exclude any underlying organic brain lesions (trauma, hypoxia, infections, mesial temporal sclerosis, or structural malformation).

Newly diagnosed epilepsy includes subjects with more than two unprovoked seizures who are initially diagnosed with epilepsy who have not received any antiepileptic medications before enrolling in the study.

Children with newly diagnosed temporal lobe epilepsy and healthy controls were age and gender matched. Likewise, with matched parent education, socio-economic status, and children level of education to eliminate the impact of other factors that may affect children cognitive abilities. Regarding nutrition all including children received ordinary traditional food with no history of specific medications affecting the cognitive functions (e.g., Omega-3, multivitamin, antihistamines, and antipsychotics).

Cognitive function assessment

All included children were interviewed and subjected to psychological assessment to exclude psychological disorders. Cognitive function was evaluated by the Arabic Version of Wechsler Intelligence Scale for Children-The Third Edition (WISC-III) [15]. This scale consists of performance and verbal subtests used to assess general intelligence and obtain total intelligence quotient (IQ) score, verbal IQ score, and performance IQ score. Verbal IQ score is obtained by doing 5 subscales (information that evaluate general knowledge and long term memory, similarities that evaluate logic thinking and verbal reasoning, arithmetic, digit span that evaluate working memory, and comprehension scales that evaluate social knowledge). While performance IQ score is score is obtained by doing another 5 subscales (picture completion that evaluate identification of related items, coding that evaluate organization, block design that evaluate analysis, designing, picture arrangement that evaluate visual-motor coordination, and object assembly scales that evaluate the identification of item parts). Total IQ score is based on the scores of both verbal and performance IQ scales. Assessment was done before initiating any antiepileptic medications. IQ score ≥130 is very superior, score 120-129 is superior, score 110-119 is high average, score 90-109 is average, score 80-89 is low average, score 70- 79 is borderline, and score ≤ 69 is extremely low. Time needed to complete the test ranges from 60 to 90 minutes.

Oxidants/antioxidants assay

Under complete aseptic condition, 4 ml venous blood were collected in ethylenediamine tetraacetic acid tubes (EDTA tubes), centrifuged for 15 minutes at 1000 x g within 30 minutes of collection and stored at -80°C according to manufacture till the time for analysis.

Plasma Human Advanced Oxidation Protein Products (AOPP) was measured by competitive enzyme-linked immunosorbent assay (ELISA) technique using Abbexa (Catalog No: abx258311) kits. The detection range was 61.7 ng/ml - 5000 ng/ml and the sensitivity was less than 23.7 ng/ml.

Plasma Total Antioxidant Capacity (TAC) was measured by competitive enzyme-linked immunosorbent assay (ELISA) technique using Cell Biolabs' OxiSelect™ TAC Assay Kit (Catalog Number STA-360).

Plasma Malondialdehyde (MDA) was measured by competitive enzyme-linked immunosorbent assay (ELISA) technique using Elabscience kits (Catalog No: E-EL-0060). The detection range was 31.25-2000 ng/mL and the sensitivity was 18.75 ng/mL.

Plasma catalase was measured by competitive enzyme-linked immunosorbent assay (ELISA) technique using Elabscience kits (Catalog No: E-BC-K031-M). The detection range was 1.12-150 U/ml and the sensitivity was 1.12 U/mL.

Ethical approval

The study follows the principles of the Declaration of Helsinki. Consent was obtained from caregivers of all children before they get enrolled in the study according to guideline of Local Ethics Committee of Al-Zharaa University.

Statistical analysis

Data analysis was done using the Statistical Package for Social Sciences (SPSS version 26, USA). Quantitative data were expressed as mean ± SD. Difference between groups was analyzed using independent student t-test and chi-square test. Correlations were performed using Pearson correlation coefficients. Logistic regression analysis was performed to detect predictors of cognitive dysfunction in children with epilepsy. P-value <0.05 was considered significant.

Results and Discussion

The current study included 42 children with newly diagnosed temporal lobe epilepsy (23 males and 19 females) and 42 healthy controls (21 males and 21 females). The age of onset of seizures ranged between 6 to 8 years. No significant difference was detected in age, sex, education, body weight, height, and body mass index between the two studied groups (Table 1).

There was a higher significant level of circulating malondialdehyde, advanced oxidation protein products, and lower catalase, total antioxidant capacity and cognition ability scores in children with temporal lobe epilepsy compared to the healthy controls (Table 2).

Cognition ability scores have a negative significant correlation with malondialdehyde and advanced oxidation protein products levels and significant positive correlation with the age of onset of seizures, circulating catalase, and total antioxidant capacity levels (Table 3).

Stepwise linear regression analysis revealed that younger age of onset and increased advanced oxidation protein products level represent independent predictors for cognitive performance in children with temporal lobe epilepsy as shown in (Table 4).

Epilepsy is a chronic neurologic disorder that adversely affects cognitive performance. Cognition impairment may persist even after seizures control and extend into adult life [16]. The relation between epilepsy and cognition is complex. Some hypotheses suggest the cognitive dysfunction is a consequence of epilepsy while others suggests that both disorders are related to the same underlying etiology [17].

Evidences showed that cognitive impairment is occurred at the early stage of epilepsy even before initiation of antiepileptic medications [18]. Our studies revealed lower cognitive abilities performance in children with newly diagnosed temporal lobe epilepsy than their healthy peers which is in a good agreement with previous studies indicating that cognitive impairment is already present at the time of diagnosis of epilepsy and may antedates the initial recognized seizure [19].

Table 1: Comparison of socio-demographic data between children with epilepsy and healthy controls

	Children with epilepsy N=42			Healthy children N=42			independent t test/ chi squire test	
	Mean	±	SD	mean	±	SD	T	P-value
Age (year)	6.669	±	0.563	6.943	±	0.664	-1.223	0.225
Male (N, %) Female (N, %)	23 (54.8%) 19 (45.2%)			21 (50%) 21 (50%)			0.191	0.662
Socio-economic status (N, %) Middle Low	34 (81%) 8 (19%)			32 (76.2%) 10 (23.8%)			0.283	0.595
Children education (N, %) Grade 1 Grade 2 Grade 3	32 (76.2%) 6 (14.3%) 4 (9.5%)			30 (71.4%) 5 (11.9%) 7 (16.7%)			0.974	0.615
Parental education (N, %) High school University degree	26 (61.9%) 16 (38.1%)			28 (66.7%) 14 (33.3%)			0.207	0.649
Body weight (kg)	21.234	±	2.528	21.173	±	2.642	0.108	0.914
Body height (cm)	118.762	±	2.752	118.176	±	2.443	1.032	0.305
BMI	16.783	±	1.452	16.683	±	1.473	-0.313	0.755

**Significant; BMI: Body Mass Index.*

Table 2: Comparison of cognition ability scores and circulating oxidants/antioxidants level between children with epilepsy and healthy controls

	Children with epilepsy N=42			Healthy children N=42			independent t test/ chi squire test	
	Mean	±	SD	mean	±	SD	T	P-value
Total IQ	105.429	±	6.918	116.143	±	7.662	-6.726	< 0.0001*
Performance IQ	99.952	±	5.401	103.667	±	3.303	-3.802	< 0.0001*
Verbal IQ	97.452	±	6.145	100.357	±	5.750	-2.237	0.028*
Intelligence categorization Average High average Superior Very superior	29 (69%) 12 (28.6%) 1 (2.4%) 0 (0%)			7 (16.7%) 23 (54.8%) 11 (26.2%) 1 (2.4%)			26.235	< 0.0001*
MAD (µmol/L)	13.281	±	3.010	8.227	±	1.483	9.761	< 0.0001*
AOPPs (ng/mL)	80.003	±	18.132	32.182	±	5.799	16.279	< 0.0001*
TAC (µmol/L)	2.125	±	0.482	3.291	±	0.593	-9.891	< 0.0001*
Catalase (K/mL)	5.846	±	1.334	9.223	±	1.986	-9.148	< 0.0001*

**Significant; AOPPs: Advanced Oxidation Protein Products, TAC: Total Antioxidant Capacity, MAD: Malondialdehyde, and IQ: Intelligence Quotient.*

Table 3: Correlation between age of onset of seizures, oxidants/antioxidants level, and cognitive ability scores

	Total IQ		Performance IQ		Verbal IQ	
	r	P-value	R	p-value	r	P-value
Age of onset (years)	0.407	<0.0001*	0.249	0.022*	0.169	0.125
MAD (µmol/L)	-0.630	<0.0001*	-0.440	<0.0001*	-0.348	0.001*
AOPPs (ng/mL)	-0.662	<0.0001*	-0.451	<0.0001*	-0.343	0.001*
TAC (µmol/L)	0.286	0.008*	0.151	0.169	0.066	0.549
Catalase (K/ml)	0.327	0.002*	0.180	0.101	0.128	0.247

**Significant; AOPPs: Advanced Oxidation Protein Products, TAC: Total Antioxidant Capacity, MAD: Malondialdehyde, and IQ: Intelligence Quotient.*

Table 4: Stepwise linear regression analysis for the association between circulating oxidants/antioxidants level, age of onset, and total intelligence quotient of the studied children

	Unstandardized Coefficients		Standardized Coefficients	T	P-value	95.0% Confidence Interval	
	B	Std. Error	Beta			Lower Bound	Upper Bound
(Constant)	2.627	0.152		17.318	<0.0001	2.325	2.928
AOPP (ng/mL)	-0.016	0.002	-0.584	-6.519	<0.0001	-0.021	-0.011
(Constant)	0.795	0.795		1.001	0.320	-0.786	2.377
AOPP (ng/mL)	-0.014	0.002	-0.532	-5.903	<0.0001	-0.019	-0.010
Age (year)	0.255	0.109	0.211	2.345	0.021	0.039	0.472
a. Dependent Variable: IQ							

**Significant; AOPPs: Advanced Oxidation Protein Products.*

Despite that IQ of children with idiopathic epilepsy is usually within the normal range, our findings showed that children with newly diagnosed temporal lobe epilepsy have about10 points lower mean IQ scores than healthy controls. Our study showed that children with newly diagnosed temporal epilepsy had lower scores for verbal and performance IQ than their healthy peers.

The presence of cognitive impairment at the time of epilepsy diagnosis in absence of structural brain lesion suggests the presence of a common pathophysiological mechanism inducing both disorders [20]. The current study investigated

oxidation stress as a link between epilepsy and cognition and revealed higher level of oxidants and lower level of antioxidants in children with newly diagnosed epilepsy. Furthermore, this oxidants/antioxidants imbalance was strongly correlated with lower cognitive ability scores in children with temporal lobe epilepsy.

Increased oxidation stress is one of the key factors involved in the process of epileptogenesis. The high lipid content of neuronal cells in addition to its high level of oxygen consumption making the brain at greater risk for oxidation stress induced cellular damage. When oxidation stress exceeds antioxidant capacity of the brain, those oxidants may disturb neuronal cells structural components, induce neuronal dysfunction leading to cell apoptosis or necrosis [21]. Moreover, exposure to oxidation stress may activate pro-inflammatory signaling pathways leading to release of pro-inflammatory cytokines that induce neuro-inflammation and neuro-degeneration leading to the development of numerous epilepsy comorbidities even when seizure activity is controlled [22].

Several studies revealed that unbalanced oxidation stress is linked to psycho-behavioral comorbidities in children with newly diagnosed, refractory epilepsy or even in healthy subjects [23, 24]. Animal models showed that oxidation stress may implement in cognitive decline through inducing endothelial dysfunction and impairing cerebral blood flow [25]. In human studies oxidation stress is one of the hypothesized mechanisms included in age related decline in learning and memory [26]. Our study demonstrated that younger age of onset, higher levels of oxidants and lower level of antioxidants defenses were significantly associated with lower cognitive performance in children with temporal lobe epilepsy. Previous studies showed a strong association between oxidative stress and cognitive dysfunction in several disorders. However, no sufficient data was reported in epilepsy. Liu et al. [27] reported that elevated MDA level represent an independent predictor of post-stroke cognitive impairment [28]. Previous studies reveled decreased total antioxidant capacity in newly diagnosed and untreated epileptic subjects improved after initiation of antiepileptic medications and achieving seizure control [29, 30]. Animal model of epilepsy showed improved cognition and memory performance using medications that eliminate the oxidative stress [31]. Pearson et al. [32] demonstrated that exposure to oxidative stress in animal model of temporal lobe epilepsy induce cognitive dysfunction. Furthermore, pharmacological removal of reactive oxygen species may improve cognitive performance in such animal model.

Identification of baseline cognitive abilities at the time of diagnosis of epilepsy and regular monitoring of cognitive performance are required to adjust treatment plan, and avoid further cognition impairment and learning disabilities especially in children with younger age of onset of seizures.

Study Limitations

The first limitation is the small number of the studied children. The second limitation is the cross sectional designs of this study that interferes with assessment of cause-effect relationship.

Conclusion

Oxidation stress may be associated with impaired cognitive abilities in children with newly diagnosed temporal lobe epilepsy. Treatment strategy for children with newly diagnosed temporal lobe epilepsy should be adjusted to decrease oxidation stress to avoid worsening of cognitive performance.

Conflict of Interest

The authors declare that there is no conflict of interest in this article.

Funding

Authors did not receive any funding source to declare.

Author's Contributions

All authors contributed to data analysis, drafting, and revising of the article and agreed to be responsible for all the aspects of this work.

ORCID

Marwa Elhady
https://orcid.org/0000-0002-7785-3736
Heba Tawfik Okda
https://orcid.org/0009-0009-5085-493X
Mohamed Farouk Ahmed
https://orcid.org/0009-0008-9060-2422
Rasha M. Gouda
https://orcid.org/0000-0003-3112-0323
Rasha Sobhy Elattar
https://orcid.org/0000-0002-4629-0088
Seham Eelsaid Abdelsadek
https://orcid.org/0000-0001-7783-153X
Talal Abd Allah Mohammed Dawa
https://orcid.org/0009-0004-3964-9867
Mohammad Fathi Abdulsalam
https://orcid.org/0009-0001-1772-5548
Fathy Mahmoud Mansour
https://orcid.org/0009-0008-8627-1691
Adel M. Othman
https://orcid.org/0009-0005-6341-8249
Shaimaa A.Maklad
https://orcid.org/0000-0001-8322-2589
Shahinaz El Attar
https://orcid.org/0000-0001-9293-756X
Walaa Shipl
https://orcid.org/0000-0002-2589-4245
Rayyh A.M. Saleh
https://orcid.org/0000-0003-4627-6558
Esraa Ali
https://orcid.org/0000-0001-7067-9416

References

[1]. Geronzi U., Lotti F., Grosso S., Oxidative stress in epilepsy, *Expert Review of Neurotherapeutics*, 2018, **18**:427 [Crossref], [Google Scholar], [Publisher]

[2]. Saedi S., Saedi A., Ghaemi M.M., Milani Fard M., Assessed the Complication of Central Nervous System in COVID-19 Patients: A Systematic Review and Meta-Analysis, *Eurasian Journal of Science and Technology*, 2022, **2**:185 [Crossref], [Google Scholar], [Publisher]

[3]. Rostamzadeh Mansour S., Sohrabi-Gilani N., Nejati P., Synthesis and characterization of a nanomagnetic adsorbent modified with Thiol for magnetic and investigation of its adsorption behavior for effective elimination of heavy metal ions, *Advanced Journal of Chemistry-Section A*, 2022, **5**:31 [Crossref], [Google Scholar], [Publisher]

[4]. Abida A.M., Asif M., Study of Some Hyndantion Derivatives as Anticonvulsant Agents, *Progress in Chemical and Biochemical Research,* 2020, **3**:93 [Crossref], [Google Scholar], [Publisher]

[5]. Alimoradzadeh R., Moosavi N., Karimkoshteh A., sadeghi Z., Milanifard M., Ismaili A. Investigation of the Chemistry of Metformin by Targeting the Nrf2 Signaling Pathway (A response Surface Methodology Approach). *Chemical Methodologies*, 2022, **6**:166 [Crossref], [Publisher]

[6]. Atghaei M., Rezaie M.R., Baghizadeh A., Mirshekarpour H. Investigation of Gamma-Ray Effect on Physiological and Biochemical Traits of Triticale Plant under Salinity Stress. *Chemical Methodologies*, 2023, **7**:447 [Crossref], [Publisher]

[7]. Kotha R.R., Tareq F.S., Yildiz E., Luthria D.L., Oxidative Stress and Antioxidants-A Critical Review on In Vitro Antioxidant Assays, *Antioxidants (Basel)*, 2022, **11**:2388 [Crossref], [Google Scholar], [Publisher]

[8]. Mirabel H., Guinet V., Voltzenlogel V., Pradier S., Hennion S., Social cognition in epilepsy: State of the art and perspectives, *Revue neurologique*, 2020, **176**:468 [Crossref], [Google Scholar], [Publisher]

[9]. Dahab M.A., Khalid I., Bahary H., Bahgat K., Elhadi M., Clinical & electroencephalographic and cognitive function correlation in epileptic children, *Journal of the Neurological Sciences*, 2013, **33**:E53 [Crossref], [Google Scholar], [Publisher]

[10]. Tsikas D., Assessment of lipid peroxidation by measuring malondialdehyde (MDA) and relatives in biological samples: Analytical and biological challenges, *Analytical biochemistry*, 2017, **524**:13-30. [Crossref], [Google Scholar], [Publisher]

[11]. Maes M., Supasitthumrong T., Limotai C., et al. Increased Oxidative Stress Toxicity and Lowered Antioxidant Defenses in Temporal Lobe Epilepsy and Mesial Temporal Sclerosis: Associations with Psychiatric Comorbidities,

Molecular neurobiology, 2020, **57**:3334 [Crossref], [Google Scholar], [Publisher]
[12]. Pearson-Smith J.N., Patel M., Metabolic dysfunction and oxidative stress in epilepsy, *International Journal of Molecular Sciences*, 2017, **18**:2365 [Crossref], [Google Scholar], [Publisher]
[13]. Elhady M., Youness E.R., Mostafa R.S.I., Abdel Aziz A., Hussein R., Oxidative stress contribution to attention deficit hyperactivity disorder in children with epilepsy, *Applied Neuropsychology: Child,* 2019, **8**:347 [Crossref], [Google Scholar], [Publisher]
[14]. Fisher R.S., The new classification of seizures by the International League Against Epilepsy 2017, *Current neurology and neuroscience reports*, 2017, **17**:48 [Crossref], [Google Scholar], [Publisher]
[15]. Seashore H, Wesman A, Doppelt J. The standardization of the Wechsler intelligence scale for children. *J Consult Psychol*., 1950, **14**:99-110. [Crossref], [Google Scholar], [Publisher]
[16]. Holmes G.L., Cognitive impairment in epilepsy: the role of network abnormalities, *Epileptic Disorders*, 2015, **17**:101 [Crossref], [Google Scholar], [Publisher]
[17]. Wang L., Chen S., Liu C., Lin W., Huang H., Factors for cognitive impairment in adult epileptic patients, *Brain and behavior*, 2020, **10**:e01475 [Crossref], [Google Scholar], [Publisher]
[18]. Witt J.A., Helmstaedter C., Cognition in epilepsy: current clinical issues of interest, *Current opinion in neurology*, 2017, **30**:174 [Crossref], [Google Scholar], [Publisher]
[19]. Rathouz P.J., Zhao Q., Jones J.E., Jackson D.C., Hsu D.A., Stafstrom C.E., Seidenberg M., Hermann B.P., Cognitive development in children with new onset epilepsy, *Developmental Medicine & Child Neurology*, 2014, **56**:635 [Crossref], [Google Scholar], [Publisher]
[20]. Kim E.H., Ko T.S., Cognitive impairment in childhood onset epilepsy: up-to-date information about its causes, *Korean journal of pediatrics*, 2016, **59**:155 [Crossref], [Google Scholar], [Publisher]
[21]. Aguiar C.C.T., Almeida A.B., Araújo P.V.P., Abreu R.N.D.C.D., Chaves E.M.C., Vale O.C.D., Macêdo D.S., Woods D.J., Fonteles M.M.D.F., Vasconcelos S.M.M., Oxidative stress and epilepsy: literature review, *Oxidative medicine and cellular longevity*, 2012, **2012**:795259 [Crossref], [Google Scholar], [Publisher]
[22]. Solleiro-Villavicencio H., Rivas-Arancibia S., Effect of chronic oxidative stress on Neuroinflammatory response mediated by CD4(+)T cells in neurodegenerative diseases, *Frontiers in cellular neuroscience*, 2018, **12**:114 [Crossref], [Google Scholar], [Publisher]
[23]. Shatla R., Elsayed R.M., Sayyah H.E., Azzam H., Korraa S.S., Child psychopathology and oxidative stress in newly diagnosed children with epilepsy, *Journal of Pediatric Neurology*, 2013, **11**:221 [Crossref], [Google Scholar], [Publisher]
[24]. Hajjar I., Hayek S.S., Goldstein F.C., Martin G., Jones D.P., Quyyumi A., Oxidative stress predicts cognitive decline with aging in healthy adults: an observational study, *Journal of neuroinflammation*, 2018, **15**:17 [Crossref], [Google Scholar], [Publisher]
[25]. Logan S., Royce G.H., Owen D., Farley J., Ranjo-Bishop M., Sonntag W.E., Deepa S.S., Accelerated decline in cognition in a mouse model of increased oxidative stress, *Geroscience*, 2019, **41**:591 [Crossref], [Google Scholar], [Publisher]
[26]. Kumar A., Yegla B., Foster T.C., Redox Signaling in Neurotransmission and Cognition During Aging, *Antioxidants & Redox Signaling*, 2018, **28**:1724 [Crossref], [Google Scholar], [Publisher]
[27]. Liu Z., Liu Y., Tu X., Shen H., Qiu H., Chen H., He J., High Serum Levels of Malondialdehyde and 8-OHdG are both Associated with Early Cognitive Impairment in Patients with Acute Ischaemic Stroke, *Scientific Reports*, 2017, **7**:9493 [Crossref], [Google Scholar], [Publisher]
[28]. Wu C., Gao B., Gui Y., Malondialdehyde on postoperative day 1 predicts postoperative cognitive dysfunction in elderly patients after hip fracture surgery, *Bioscience Reports*, 2019, **39**:BSR20190166 [Crossref], [Google Scholar], [Publisher]
[29]. Keskin Guler S., Aytac B., Durak Z.E., Gokce Cokal B., Gunes N., Durak I., Yoldas T., Antioxidative-oxidative balance in epilepsy patients on antiepileptic therapy: a prospective case-control study, *Neurological Sciences*, 2016, **37**:763 [Crossref], [Google Scholar], [Publisher]

[30]. Ashrafi M.R., AziziMalamiri R., Shams S., Ranjbar N.R., Nasrabadi S.E., Ashtiani M.H., ... & Zarch V.V., Serum Total Antioxidant Capacity of Epileptic Children before and after Monotherapy with Sodium Valproate, Carbamazepine, and Phenobarbital, *Iranian Journal of Child Neurology*, 2018, **12**:24 [Google Scholar], [Publisher]

[31]. Mishra P., Mittal A.K., Rajput S.K., Sinha J.K., Cognition and memory impairment attenuation via reduction of oxidative stress in acute and chronic mice models of epilepsy using antiepileptogenic Nux vomica, *Journal of Ethnopharmacology*, 2021, **267**:113509 [Crossref], [Google Scholar], [Publisher]

[32]. Pearson J.N., Rowley S., Liang L.P., White A.M., Day B.J., Patel M., Reactive oxygen species mediate cognitive deficits in experimental temporal lobe epilepsy, *Neurobiology of disease*, 2015, **82**:289 [Crossref], [Google Scholar], [Publisher]

HOW TO CITE THIS ARTICLE

Marwa Elhady, Heba Tawfik Okda, Mohamed Farouk Ahmed, Rasha M. Gouda, Rasha Sobhy Elattar, Seham Eelsaid Abdelsadek, Talal Abd Allah Mohammed Dawa, Mohammad Fathi Abdulsalam, Fathy Mahmoud Mansour, Adel M. Othman, Doaa Ibrahim Hassan Ibrahim, Shaimaa A.Maklad, Shahinaz El Attar, Walaa Shipl, Rayyh A.M. Saleh, Esraa Ali. Oxidative stress and cognitive performance in children with temporal lobe epilepsy. *J. Med. Chem. Sci*., 2024, 7(1) 24-33.
DOI: https://doi.org/10.26655/JMCHEMSCI.2024.1.3
URL: https://www.jmchemsci.com/article_178706.html