Recent Updates Concerning Co-morbid Cognitive Function Affection in Epilepsy Therapy

Submitted For Partial Fulfillment of
Master Degree of Neuropsychiatry

By

Karim Ashraf Mohamed

Supervised By

Prof. Dr. Samia Ashour M. Helal

Professor of Neurology
Faculty of Medicine - Ain-Shams University
Chair Person of the Neurology Department

Prof. Dr. Naglaa Mohamed El-Khayat

Professor of Neurology
Faculty of Medicine - Ain-Shams University

Dr. Amr Abdel Moniem Mohamed

Lecturer of Neurology
Faculty of Medicine - Ain-Shams University

Faculty of medicine
Ain Shams University
2011

التحديثات الأخيرة فيما يتعلق بتأثر الوظائف المعرفية في علاج الصرع

توطئة للحصول على درجة الماجستير
فى الأمراض العصبية والنفسية

بكالوريوس الطب والجراحة
كلية الطب - جامعة عين شمس

ا.د. سامية عاشور محمد هلال

أستاذ المخ والأعصاب والطب النفسي
جامعة عين شمس

ا.د. نجلاء محمد الخياط

أستاذ المخ والأعصاب والطب النفسي
جامعة عين شمس

د. عمرو عبد المنعم محمد

مدرس المخ والأعصاب والطب النفسي
جامعة عين شمس

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SUMMARY

Epilepsy is a complex set of brain disorders, with epileptic seizures being the quintessential defining element. The association between epilepsy plus or minus its therapy and mental functions has been a matter of mystification and controversy for centuries. More research has revealed the complexity of this relation with involvement of neurological, neuropsychological and psychosocial factors. The newly proposed ILAE definition for epilepsy is: A disorder of the brain characterized by an enduring predisposition to generate epileptic seizures and by the neurobiological, cognitive, psychological and social consequences of this condition.

The treatment of epilepsy is not restricted to the remission of seizures. In the last decade it has been recognized the importance of identifying and managing comorbid medical and psychiatric disorders with epilepsy therapy. Publications in the last two years reflect the increased interest in these problems.

The most widely used classification; proposed by the ILAE regards epileptic seizures as generalized or partial and for epilepsy syndromes as idiopathic, symptomatic and cryptogenic. Where Epilepsy syndromes that don't impair cognitive functions or development are often described as benign epilepsy syndromes.

بسم الله الرحمن الرحيم

(بل هو آيات بينات

في صدور الذين أوتوا العلم)

صدق الله العظيم

سورة العنكبوت الآية:٤٩

To My WIFE.....

ACKNOWLEDGEMENTS

This dissertation would not have been possible without the support of many people.

Foremost, I would like to express my sincere gratitude to my advisor ***Prof. Samia Ashour*** *for the continuous support of my Master's study, for her patience, motivation, enthusiasm, and immense knowledge. Her guidance helped me in all the time of reviewing and writing of this work.*

Besides my advisor, I would like to thank the rest of my thesis committee: ***Prof. Naglaa El-Khyat****,* ***Dr. Amr Abd El Moniem****, for their encouragement, insightful comments, and hard questions. This thesis would never have taken shape without the inspired problem solving of them.*

My sincere thanks go to ***Prof. Nahid Salah*** *and* ***Prof. Omar El Sirafy****, that in the midst of all their activities, they accepted to be members of the discussing committee. I was extremely delighted to interact with their excellence.*

I owe my deepest gratitude to *all the stuff of Neurology and Psychiatry department, faculty of medicine, Ain-Shams University for teaching me much.*

In particular, I'm sincerely grateful to ***Prof. Ossama Abdel Ghani*** *and* ***Prof. Mohamed Ghanem*** *for enlightening me the first glance of my clinical experience.*

I would like to thank my family: ***My mother*** *for her sleepless nights and for raising me up.* ***My father*** *for his precious advices, encouragement and financial assistance. Both of* ***My Parents*** *gave me everything at the first place and supported me spiritually throughout my life. Also* ***Eng. Walid Tawfik*** *and his wife; I could not have imagined having a better brother.*

I wish to express my warm and sincere thanks to many of my colleagues for supporting me.

Last but not the least; A special mention should be made to ***My Wife*** *without her encouragement, understanding & endless love; through the duration of my study, I would not have finished this degree if you were not beside me.*

To them all; I dedicate this work

And to GOD, who made all things possible

List of Abbreviations

ACTH	:	Adreno Cortico Tropic Hormone.
AD	:	Alzheimer Disease.
ADHD	:	Attention Deficient Hyperactive Disorder.
AEDs	:	Anti-Epileptic Drugs.
AMPA	:	Amino-3-hydroxy-5-Methyl-4-Isoxazole Propionic Acid.
ASDs	:	Autistic Spectrum Disorders.
BECT	:	Benign Childhood Epilepsy with Centro-Temporal (Rolandic).
BZD	:	Benzodiazepine.
CAM	:	Complementary and Alternative Medicine.
CBZ	:	Carbamazepine.
CDKL5	:	Cyclin-Dependent Kinase-Like 5.
CED	:	Convection-Enhanced Delivery.
CNS	:	Central Nervous System.
COX-2	:	CycloOXygenase 2.
CPT	:	Continuous Performance Task.
CRMP-2	:	Collapsin Response Medicate protein-2.
CSE	:	Convulsive Status Epilepticus.
CSF	:	CerebroSpinal Fluid.
DBS	:	Deep Brain Stimulation.
DZP	:	Diazepam.

EEG	**:**	ElectroEncephaloGraphy.
EMEA	**:**	European Medicines Agency.
EPC	**:**	Epilepsia Partials Continua.
ESES	**:**	Electrical Status Epilepticus during Sleep.
ESM	**:**	Ethosuximide.
FBM	**:**	Felbamate.
FDA	**:**	Food Drug Administration.
FMRI	**:**	Functional Magnetic Resonance Imaging.
FMRP	**:**	Fragile X Mental Retardation Protein.
FXS	**:**	Fragile X Syndrome.
GABA	**:**	Gamma Amino Butyric Acid.
GBP	**:**	Gabapentin.
GCI	**:**	General Cognitive Index.
GEFS+	**:**	Generalized Epilepsy with Febrile Seizures plus.
GTCs	**:**	Generalized Tonic Clonic seizures.
I.Q.	**:**	Intelligence Quotient.
IDDs	**:**	Intellectual and Developmental Disabilities.
ILAE	**:**	International League Against Epilepsy.
JME	**:**	Juvenile Myoclonic Epilepsy.
LCM	**:**	Lacosmaide.
LEV	**:**	Levetiracetam.
LGS	**:**	Lennox-gastaut syndrome.

LMT	**:**	Lamotrigine.
LTP	**:**	Long term potentiation.
MeCP2	**:**	Methyl-CpG binding Protein 2.
mTOR	**:**	Mammalian Target Of Rapamycin.
NCSE	**:**	NonConvulsive Status Epilepticus.
NMDA	**:**	N-Methyl-D-Aspartate.
NO	**:**	Nitric Oxide.
OXC	**:**	Oxcarbazepine.
PAF	**:**	Palatelt Activating Factor.
PB	**:**	Phenoparbital.
PET	**:**	Positron Emission Topography.
PGB	**:**	Pregabalin.
PHT	**:**	Phyenytoin.
PIAT	**:**	Peabody Individual Achievement.
PRM	**:**	Primidone.
PRSE	**:**	Prolonged Refractory Status Epilepticcus.
PWEs	**:**	Patients With Epilepsies.
RSE	**:**	Refractory Status Epilepticus.
rTMS:	**:**	Repetitive Trans-Magnetic Stimulation.
RTT	**:**	Rett syndrome.
RUF	**:**	Rufinamide.
SE	**:**	Status Epilepsticus.

SMA	**:**	Supplementary Motor Area.
SPA	**:**	Seizure Prediction Algorithm.
TCI	**:**	Transient Cognitive Impairment.
TCS	**:**	Tuberous Sclerosis Complex.
TGB	**:**	Tiagabine.
TLE	**:**	Temporal Lobe Epilepsy.
TPM	**:**	Topiramte.
VaD	**:**	Vascular Dementia.
VGB	**:**	Vigabatrin.
VNS	**:**	Vagus Nerve Stimulation.
VPA	**:**	Valproate.
WAIS	**:**	Wechsler Adult Intelligence Scale.
WPPSI	**:**	Wechsler Preschool and Primary Scale of Intelligence.
WRAML	**:**	Wide Range Assessment of Memory and Learning.
WRAT-R	**:**	Wide Range Achievement Test.
ZBS	**:**	Zonisamide.

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INTRODUCTION

It is well known that neuropsychological impairment can be associated with chronic epilepsy. This work review a broad lifespan perspective of cognition in epilepsy should include consideration of:

a. Neurobiological factors that antedate the first seizure and influence cognition.

b. Epilepsy-related factors that influence brain growth and cognitive development after epilepsy is diagnosed and treated.

c. Clinical epilepsy and other risk factors associated with poor cognitive prognosis in the context of chronic epilepsy.

d. The modifiable and non-modifiable risk factors that influence cognitive aging in the general population ***(Hermann and Seidenberg 2007).***

Neuronal excitability is determined by the flux of ions through ion channels. Many types of ion channels are expressed in the central nervous system, each responsible for its own aspect of neuronal excitability, these mechanisms are tightly regulated to create a balance between excitation and inhibition. Disruption of this balance is thought to be the key in many neurological disorders, including epilepsy syndromes ***(Mizielinska, 2007)***.

Epilepsies are characterized by recurrent seizures, which can cause motor, sensory, cognitive, psychic or autonomic disturbances. The seizures themselves are the clinical manifestation of an underlying transient abnormality of cortical neuronal activity, and the phenotypic expression of each seizure

is determined by the point of origin of the hyperexcitability and its degree of spread in the brain. By convention, the diagnosis of epilepsy requires that the patient has had at least two unprovoked seizures ***(Steinlein, 2004)***.

Epileptogenesis, the transformation of the brain to a long-lasting state characterized by recurrent seizures, can occur due to genetic or acquired mechanisms ***(Acharya, 2002)***.

Proportion of incidence cases according to seizure type showed that the most common epileptic variants are complex partial type followed by generalized tonic clonic and Absence types ***(Sridharan, 2002)***.

This work will review also the anatomy and circuitry of skills that, like reading, calculating, recognizing, or remembering, are common abilities of humans. While the anatomical areas active are unique to each skill. There is considerable plasticity to the performance of skills. Practice may change the size or number of brain areas involved and alter the pathways used by the skill ***(Posner et al., 1997)***.

Regions specialized for learning/memory (i.e., plasticity) are most prone to seizures. In thinking about brain regions that are particularly seizure prone, we tend to focus on neocortical regions and particularly hippocampus, precisely those parts of the