

SEXUAL DYSFUNCTION IN EPILEPTIC MALE PATIENTS

THESIS

*Submitted in the fulfillment of
The M.D. Degree in
Neurology*

By

Husam Salah Ahmed Mourad

(M.B., B.Ch., M.Sc. in Neuropsychiatry, Cairo University)

Supervised by

Professor Dr. Ahmed Talaat El Ghoneimy

*Professor of Neurology, Cairo University
Head of Neurology Department, Cairo University*

Professor Dr. Mohamed Mohamed Farid

Professor of Andrology, Cairo University

Professor Dr. Maged Abd El Naseer

Professor of Neurology, Cairo University

Professor Dr. Hatem Samir Mohamed

Assistant professor of Neurology, Cairo University

*FACULTY OF MEDICINE
CAIRO UNIVERSITY*

2009

بسم الله الرحمن الرحيم

"وقل رب زدني علماً"

صدق الله العظيم
(الآية 114 سورة طه)

ACKNOWLEDGEMENT

*First, I would like to express my sincerest gratitude and gratefulness to **Allah** who continues to bless and fill me with hope, faith and patience that enable me to carry out all my daily work.*

*My sincere appreciation and gratitude to Prof. Dr. **Ahmed Talaat El Ghoneimy**, Professor and Head of Neurology department, Faculty of Medicine, Cairo University, for his kind assistance, supervision and precious support, advises and guidance throughout this work.*

*I would like to extend my thanks to Prof. Dr. **Mohammed Farid**, Professor of Andrology, Faculty of Medicine, Cairo University for his kind advice and constant encouragement, giving me much of his time to make this work accomplished.*

*I am greatly thankful to Prof. Dr. **Maged Abd El Naseer**, Professor of Neurology, Faculty of Medicine, Cairo University for his endless effort, supervision and guidance throughout this work.*

*I would like to thank Prof. Dr. **Hatem Samir**, Assistant Professor of Neurology, Faculty of Medicine, Cairo University, for his encouragement, valuable advice and effort.*

*Many thanks go to Prof. Dr. **Ahmed Abo Mousa** Assistant Professor of Neurology and Dr. **Montaser Hegazy** Lecturer of Neurology for their help in this work.*

*It is with great pride and pleasure that I thank my family, especially **my father** for his help as regards the statistical methods of this work and **my lovely wife, Dr. Neveen ElFayoumy** for her help in the Neurophysiological procedures and her great support and encouragement throughout this work.*

I would also like to thank all my Professor and Colleagues in the Neurology department for their help and encouragement.

I would also like to thank all my colleagues in the Andrology department especially Dr Omar Abd Elgawad and Dr Ahmed Adel for their help.

Finally, I would like to thank every person who spent time or effort in helping me including the patients who endured and co-operated with me throughout this work.

Husam Salah
February, 2009

*TO MY big
and small
families*



CONTENTS

	Page
❑ Introduction and aim of the work	1
❑ Review of Literature:	3
▪ Anatomy of the Penis.	3
▪ Sexual function and dysfunction.	13
▪ Classification of epilepsy	70
▪ Epilepsy and sexual dysfunction.	86
❑ Subjects and Methods	121
❑ Results	137
❑ Discussion	192
❑ Summary and Conclusion	204
❑ Recommendations	209
❑ References	210
❑ Appendix	257
❑ Arabic Summary	

List of tables

No.	Title	Page
1	Male sexual function: relationships among the phase of sexual response cycle, neural pathways, end-organ and hemodynamic changes, and genital functional responses	15
2	Potency of various sex steroids, taking testosterone at a relative value of 100.	52
3	Causes of sexual dysfunction in the male classified by clinical manifestation	56
4	Means $\pm$ SD of ages included in the present study	137
5	Duration of epilepsy in different groups	138
6	Types of epilepsy in different groups	139
7	Frequency of seizures in different groups	141
8	Family history in epileptic patients	142
9	Antiepileptic drugs in monotherapy treated epileptic patients	142
10	Antiepileptic drugs in polytherapy treated epileptic patients	143
11	Doses of antiepileptic drugs in monotherapy and polytherapy groups	144
12	Epileptic discharges in EEG of epileptic patients	145
13	Laterality of epileptic discharges in EEG of CPS patients	146
14	Duration of sexual dysfunction in patients on monotherapy and polytherapy	147
15	Pattern of sexual dysfunction in epileptic patients on monotherapy and polytherapy	148
16	Descriptive results for sex hormones	150
17	Laboratory results for SHBG	151
18	Penile duplex and rigiscan	152

19	Difference in sex functions between generalized epilepsy & TLE groups on monotherapy with sexual dysfunction	156
20	Comparison between generalized epilepsy, TLE & FLE groups on polytherapy with sexual dysfunction as regards different sex functions	157
21	Comparison between epileptics on monotherapy and polytherapy as regards sex functions	158
22	Difference between sex functions in different seizure frequency groups in epileptics on monotherapy with sexual dysfunction	159
23	Comparison between different seizure frequency groups in epileptic on polytherapy with sexual dysfunction as regards different sex functions	160
24	Comparison between sex hormones and SHBG in different groups	162
25	Comparison between epileptics on monotherapy as regards sex hormones.	164
26	Comparison between epileptics on polytherapy as regards sex hormones	165
27	Comparison between epileptics with sexual dysfunction as regards sex hormones	166
28	Comparison between epileptics without sexual dysfunction as regards sex hormones	167
29	Comparison between sex hormones of epileptics with sexual dysfunction on PHT, CBZ and VPA as monotherapy	169
30	Comparison between sex hormones of epileptics on PHT monotherapy with & without sexual dysfunction	170
31	Comparison between sex hormones of epileptics on CBZ monotherapy with and without sexual dysfunction	171
32	Comparison between epileptics on PHT+CBZ with and without sexual dysfunction as regards sex hormones	173
33	Comparison between epileptics with sexual dysfunction on PHT+CBZ, VPA+CBZ & VPA+LTG as regards sex hormones	175
34	Comparison between generalized epilepsy and TLE patients on monotherapy with sexual dysfunction as regards sex hormones	176

35	Comparison between generalized epilepsy, TLE and FLE patients on polytherapy with sexual dysfunction as regards sex hormones.	178
36	Comparison between seizure frequencies in epileptics with sexual dysfunction on monotherapy as regards sex hormones and SHBG	179
37	Comparison between seizure frequencies in epileptics with sexual dysfunction on polytherapy as regards sex hormones and SHBG	181
38	Correlation between the age of different groups and sex hormones	182
39	Correlation between the duration of epilepsy in monotherapy and polytherapy groups with and without sexual dysfunction and sex hormones	183
40	Correlation between duration of sexual dysfunction in epileptic patients and sex hormones	184
41	Correlation between doses of PHT in monotherapy treated epileptic patients and sex hormones	185
42	Correlation between doses of CBZ in monotherapy treated epileptic patients and sex hormones	186
43	Correlation between doses of VPA in monotherapy treated epileptic patients with sexual dysfunction and sex hormones	187

List of figures

No.	Title	Page
1	cross section in the penis	4
2	arterial supply of the penis	11
3	Peripheral mechanisms involved in flaccidity and erection	20
4	Neuroanatomical connections and putative neurotransmitters in the central nervous system involved in penile erection	29
5	The illustration depicts the effects of normal (A) and abnormal (B) balance between smooth muscle contraction and relaxation on the entire erectile process.	36
6	The psychogenic and penodynamic events of the normal sexual cycle.	39
7	Diagram of the hypothalamic-pituitary-gonadal axis	49
8	Rigiscan	133
9	Age means between different groups.	138
10	Frequency of different types of epilepsy in different groups.	140
11	Penile duplex of a patient with arteriogenic erectile dysfunction	153
12	Penile duplex of a patient with corporo-venous leakage	154
13	Rigiscan showing organic erectile dysfunction	155
14	Difference between sex hormones and SHBG in different groups	163
15	Difference between Generalized and TLE patients on monotherapy with sexual dysfunction as regards sex hormones and SHBG	177
16	Impact of seizure frequency on sex hormones and SHBG in epileptic patients with sexual dysfunction on monotherapy	180

List of abbreviations

ACh	Acetyl choline
AEDs	Anti-epileptic drugs
ALT	Alanine Aminotransferase
AST	Aspartate Aminotransferase
BAE	Bio-active estradiol
BAT	Bio-active testosterone
cAMP	Cyclic adenosine monophosphate
cAOP	Cavernosal artery occlusion pressure
CBZ	Carbamazepine
cGMP	Cyclic guanosine monophosphate
CGRP	Calcitonin Gene-Related peptide
CNS	Central Nervous System.
CPS	Complex partial seizures
CSBs	Compulsive Sexual behaviors
CSFQ	Changes in Sexual Functioning Questionnaire
DA	Dopamine agonists
DHEA	Dehydroepiandrosterone
DHEAS	Dehydroepiandrosterone sulphate
DHT	Dihydrotestosterone
DICC	Dynamic infusion cavernosometry and cavernosography
DM	Diabetes mellitus
DSM-IV	Diagnostic and statistical manual- IV
E ₂	Estradiol
ECT	Electroconvulsive therapy
ED	Erectile dysfunction
EEG	Electroencephalography
EIAED	Enzyme-inducing antiepileptic drugs
eNOS	Endothelial nitric oxide synthase
EP ₂	Prostaglandin E receptor 2
EP ₄	Prostaglandin E receptor 4

ET _A	Endothelin receptor A
ET _B	Endothelin receptor B
FAI	Free androgen index
FBS	Fasting blood sugar
FLE	Frontal lobe epilepsy
FSH	Follicle stimulating hormone
FT	Free testosterone
GAs	Genital automatisms
GH	Growth hormone
GnRH	Gonadotropin releasing hormone
GTC	Generalized tonic-clonic
GTCs	Generalized tonic-clonic seizures
HbA1c	Glycosylated haemoglobin
HSD	Hypoactive sexual desire
5HT	5 hydroxy tryptamine
IIEF	International index of erectile function
ILAE	International League Against Epilepsy
L2	Lumbar 2
LH	Lutenizing hormone
LHRH	Lutenizing hormone releasing hormone
L-NAME	N- nitro-L-arginine methyl ester
LTG	Lamotrigine
M ₂	Muscarinic receptor 2
M ₃	Muscarinic receptor 3
M ₄	Muscarinic receptor 4
MAO	Mono amine oxidase
mCPP	m-chlorophenylpiperazine
MED	male erectile dysfunction
MHz	mega hertz
MPOA	medial preoptic area
MRI	Magnetic resonance imaging
NANC	Non-adrenergic non-cholinergic neuroeffector system

NHSLS	National Health and social life survey
NIH	National Institutes of Health
NO	Nitric oxide
NOS	Nitric oxide synthase
nPGi	Nucleus paragigantocellularis
NPT	Nocturnal penile tumescence
OXC	Oxcarbazepine
PB	Phenobarbitone
PDE-5	Phosphodiesterase-5
PEPS	Post-ejaculatory pain syndrome
PGE	Primary generalized epilepsy
PGE ₁	Prostaglandin E ₁
PGF _{2α}	Prostaglandin F _{2α}
PHT	Phenytoin
PO ₂	Partial oxygen pressure
Poly	Polytherapy
PPBS	Post-prandial blood sugar
PRL	Prolactin
PSV	Peak systolic velocity
PVN	Paraventricular nucleus
PWE	Patients with epilepsy
REM sleep	Rapid eye movement sleep
SES	Sexuality experience scales
SHBG	Sex hormone binding globulin
T12	Thoracic 12
TLE	Temporal lobe epilepsy
TPM	Topiramate
TRH	Thyrotropine- releasing hormone
TT	Total testosterone
VIP	Vasoactive intestinal peptide
VPA	Valproate

ABSTRACT

Sexual dysfunction in epilepsy appears to be multi factorial. We analyzed sexual functions and hormone blood levels in 90 male subjects (50 epileptics with sexual dysfunction, 20 epileptics without sexual dysfunction and 20 controls). We used the International Inventory of Erectile Function (IIEF) questionnaire to assess the patients' sexual functions. Assessment of blood levels of prolactin, total testosterone, sex hormone binding globulin, estradiol, dehydroepiandrosterone sulfate, follicle stimulating hormone and luteinizing hormone were performed.

(Key Words: sexual dysfunction-epilepsy-male-epileptic patients-hormone levels-IIEF- sex hormone binding globulin- testosterone)

INTRODUCTION AND AIM OF THE WORK