بسم الله الرحمن الرحيم

MONA MAGHRABY

شبكة المعلومات الجامعية

التوثيق الالكتروني والميكروفيلم

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جامعة عين شمس

التوثيق الإلكتروني والميكروفيلم

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MONA MAGHRABY

Cognitive Assessment of A Sample of Egyptian Patients with Amyotrophic Lateral Sclerosis

Thesis

Submitted for Partial Fulfillment of Master Degree in Neuropsychiatry

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بسم الله الرحمن الرحيم

﴿وَعَلَّمَكَ مَا لَمْ تَكُنْ تَعْلَمُ وَكَانَ فَضْلُ اللهِ عَلَيْكَ عَظِيمًا﴾

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Nourhan Belal

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List of Abbreviations

Abb.	Full term
ACE	Addenbrooke's cognitive examination
AD	Alzheimer's disease
AES	Apathy evaluation scale
AES-C	Clinician administrated apathy evaluation scale
AES-I	Informant administrated apathy evaluation scale
AES-S	Self-administrated apathy evaluation scale
ALS	Amyotrophic lateral sclerosis
ALS2	Alsin mediated ALS
ALS-BCA	ALS-brief cognitive assessment
ALSbi	Amyotrophic lateral sclerosis with behavioural impairment
ALS-CFB	ALS-computerized frontal battery
ALSci	Amyotrophic lateral sclerosis with cognitive impairment
ALS-FRS R	ALS functional rating scale revised
ALS-FTD	ALS frontotemporal dementia
ALS-FTSD	ALS frontotemporal spectrum disorder
ANOVA	Analysis of variance
BBI	The Beaumont behavioural inventory
b-DAS	Brief dimensional apathy scale
bv-FTD	Frontotemporal dementia behavioural variant
C9orf72 gene	Chromosome 9 open reading frame 72
C-ALS	Classical ALS
CNS	Central nervous system
CT	Computerized tomography

List of Abbreviations Cont...

Abb.	Full term
DAS	Dimensional apathy scale
DM	Diabetes Mellitus
DNA	Deoxyribonucleic acid
DTI	Diffusion tensor imaging
ECAS	Edinburgh cognitive and behavioural ALS screen
EMG	Electromyography
FAB	Frontal assessment battery
FALS	Familial Amyotrophic lateral sclerosis
FBI	Frontal behavioural inventory
FDA	The food and drug administration
FH	Family history
FTD	Frontotemporal dementia
FTLD	Frontotemporal lobar degeneration
FTLD-TDP	Frontotemporal lobar degeneration with TDP-43 pathology
FUS	Fused in sarcoma gene
GHQ	General health questionnaire
HTN	Hypertension
IQ	Intelligence quotient
LL	Lower limb
LMN	Lower motor neuron
LMNL	Lower motor neuron lesion
Max	Maximum
MCI	Mild cognitive impairment
MiND-B	The motor neuron disease behavioural instrument

List of Abbreviations Cont...

Abb.	Full term
MiTos	The Milano–torino staging
MMSE	Mini mental state examination
MoCA	The montreal cognitive assessment
MRI	Magnetic resonance imaging
mRNA	Messenger ribonucleic acid
NCS	Nerve conduction study
NPI	The neuropsychiatric inventory
NPI-C	The neuropsychiatry inventory clinical based
NPI-NH	The neuropsychiatric inventory nursing home
NPI-Q	The neuropsychiatric inventory questionnaire
PET	Positron emission tomography
PH	Past history
PLS	Primary lateral sclerosis
PMA	Progressive muscular atrophy
PSSEFT	The penn state screening examination of frontal and temporal lobe dysfunction
ROS	Reactive oxygen species
SALS	Sporadic Amyotrophic lateral sclerosis
SD	Standard deviation
SETX	Senataxin protein
SOD1	Superoxide dismutase 1
SPECT	Single-photon emission computerized tomography
SPSS	Statistical package for social science
SSRI	Serotonin reuptake inhibitor
T6	6^{th} thoracic vertebrae

List of Abbreviations Cont...

Abb.	Full term
TBK1	TANK-binding kinase 1 or TNF –alpha-activated protein kinase
TCA	Tricyclic antidepressant
TDP-43	Transactive response DNA binding protein 43
UCSF-SB	The university of California and San Francisco screening battery
UK	United Kingdom
UL	Upper limb
UMN	Upper motor neuron
UMNL	Upper motor neuron lesion
VBM	Voxel based marphometry

INTRODUCTION

Amyotrophic lateral sclerosis (ALS) is a fatal neurodegenerative disorder affecting the human motor system, which was first described by Jean Martin Charcot in 1869 as a pure motor neuron disease but is now recognized as a multisystem neurodegenerative, characterized by heterogeneity in phenotype, pathological substrate and genetic predisposition with its core feature being degeneration of both upper motor neuron (neurons which project from the cortex to brainstem and spinal cord) and lower motor neurons (whose cell bodies present in the ventral horn of the spinal cord or the brain stem motor nuclei of the cranial nerves that have motor modalities) ***(Masrori et al., 2020).***

Lower motor neuron lesions are characterized by specific signs as atrophy, fasciculations and weakness while upper motor neuron lesions are characterized by spasticity, hyperreflexia and Babinski signs which are present across multiple spinal and bulbar segments ***(Brooks et al., 2000).***

It has multiple synonyms as amyotrophic lateral sclerosis, motor neuron disease, Charcot's disease, or Lou Gehrig's disease ***(Brown et al., 2017).***

It was found that 30-50% of ALS patients may suffer from cognitive and behavioral decline along the course of their illness ***(Xu et al., 2017)***, the most reported cognitive functions to be affected are executive functions with deficit in letter fluency,

otherwise, the most reported behavioral change is apathy, especially initiation apathy, also reported irritability, inflexibility, restlessness, and disinhibition ***(Huynh et al., 2020).***

On the other hand, some recent studies demonstrated that there may be a relation between cognitive changes and disease progression, which assessed by ALS functional rating scale (ALSFRS-R) and staging of disease according to involvement of upper limbs, lower limbs, respiratory and nutritional aspects ***(Crockford et al., 2018).***

Moreover, a new term known as ALS with cognitive impairment (ALSci) has been announced referring to the subpopulation that has distinct cognitive impairment which does not meet the criteria for frontotemporal dementia, in addition to another term known as ALS with behavioral impairment (ALSbi) referring to the subpopulation that predominantly exhibit behavioral changes which does not fulfill criteria for frontotemporal dementia. Therefore, determining the cognitive and behavioral status of ALS patients is important, especially that severe forms have a worse prognosis than the previously described terms ***(Watanabe et al., 2020).***

Many studies showed the significance of early identification of cognitive and behavioral impairment in ALS patient as they are associated with worse quality of life with an increase in the care giver burden and a decrease in the survival rates ***(Gosselt et al., 2020).***