بسم الله الرحمن الرحيم

MONA MAGHRABY

شبكة المعلومات الجامعية

التوثيق الالكتروني والميكروفيلم

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جامعة عين شمس

التوثيق الإلكتروني والميكروفيلم

قسم

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MONA MAGHRABY

Predictors of gait impairment in Parkinson's disease

Thesis

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Engy Nady Sadik

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List of Abbreviations

Abbr.	Full-term
AD	: Alzheimer's disease
BBS	: Berg Balance Scale
BDI	: Beck depression inventory
CI	: Cognitive impairment
CMA	: Chaperone-mediated autophagy
CNS	: Central nervous system
ChE-I	: Cholesterase inhibitors
CSVDs	: Cerebral small vessel diseases
DBS	: Dep brain stimulation
DTI	: Diffusion tensor imaging
FOG	: Freezing of gait
FMRI	: Functional magnetic resonance imaging
GPi	: Globus pallidus internus
H & Y	: Hoehn and Yahr
LM	: Logical memory
MCI	: Mild cognitive impairment
MDS	: Movement Disorder Society
MDS-UPDRS	: Movement Disorders Society-Unified Parkinson's Disease Rating Scale
M-EDL	: Motor Aspects of Experiences of Daily Living
MLR	: Mesencephalic locomotor region
MMSE	: Mini mental state examination
MPTP	: 1-methyl-4-phenyl-1,2,5,6-tetrahydropyridine
MRI	: Magnetic resonance imaging
N-FOG	: New freezing of gait questionnaire
NM-EDL	: Non-Motor Aspects of Experiences of Daily Living
NMS	: Non-motor symptoms
NMSS	: Non-motor symptoms scale

PD : Parkinson's disease
PDD : PD with dementia
PET : positron emission tomography
PIGD : Postural instability and gait disturbance
PPNd : dorsal Pedunculopontine nucleus
QOL : Quality of life
REM : Rapid eye movement
SNr : Substantianigra pars reticularis
STN : Sub-thalamic nucleus
TDCS : Transcranial direct current stimulation
TMS : Transcranial magnetic stimulation
UPDRS : Unified Parkinson's Disease Rating Scale
UPS : Ubiquitin-proteasome system
VPA : Verbal Paired Associates
WCST : Wisconsin card sorting test
WMH : White matter hyperintensities
WMS : Wechsler Memory Scale

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Introduction

Parkinson's disease (PD) is the most common movement disorder besides essential tremor and the second most common neurodegenerative disease **(Tanner et al., 2000).** Egypt has higher prevalence of PD about 35 in 100000 as was studied previously **(Khedr et al., 2015).**

The prevalence of PD in industrialized countries is generally estimated at 0.3% of the entire population and about 1% in people over 60 years of age **(DeLau and Breteler, 2006)**. The prevalence increases with advancing age both for men and women ages **(De Rijk et al., 1997).** In Europe, the prevalence at ages 85–89 has been reported as 3.5% **(Clarke and Moore, 2007).**

Braak et al. (2003) have mapped PD into six neuropathological stages. In the pre-symptomatic stages of the disease (stages 1–2), the inclusion bodies are confined to the medulla oblongata/pontine tegmentum and olfactory bulb/ anterior olfactory nucleus. With progression of the disease, substantia nigra and other nuclei of the midbrain and forebrain become affected (stages 3–4). It has been suggested that patients develop clinical symptoms of the disease at this stage. In the end stage (stage 5–6), the process enters the neocortex with a wide variety of clinical manifestations **(Braak et al., 2004).**

Gait is a learned, complex and almost automatic task with limited involvement of higher cognitive control in healthy individuals till old age **(Holtzer et al., 2006).** These automatic and rhythmic motor activity patterns are generated by spinal networks of motor neurons and interneurons, also called the "central pattern generators" **(Dietz, 2003).** The activity of these spinal networks is modulated and initiated by the basal ganglia and the brainstem nuclei **(Pahapill & Lozano, 2000)**. The basal ganglia and their two-way connections with cortical regions and cerebellum play a central role in movement initiation **(Yogev-Seligman et al., 2008).**

Gait difficulties are one of the first problems reported in people with PD, indicating the onset of disability **(Shulman et al., 2008).** Parkinsonian gait is often slow and characterized by short shuffling steps. Such problems are often accompanied by falling, which occurs in 40–70% of patients with PD **(Pickering et al., 2007).**

Understanding gait difficulties and developing criteria to identify people with PD who are at risk for falling are crucial to interrupt this devastating cycle of falls and injuries **(Bloem et al., 2004).**

Freezing of gait (FOG) is a disabling gait disorder defined as a ‘‘brief, episodic absence or marked reduction of forward progression of the feet despite the intention to walk’’ **(Nutt et al., 2011).**

Longer disease duration and greater disease severity often increase the likelihood of developing FOG **(Giladi et al., 2001)**. FOG is less efficiently improved with dopaminergic medication **(Espay et al., 2012),** so early risk identification of FOG may improve its treatment in the near future **(Rascol et al., 2011).**

Cognitive impairment (CI) is a common non-motor complication of PD and is associated with significant disability for patients and burden for caregivers. Similar to motor symptoms, the characteristics of CI in PD can be quite variable, both in terms of what cognitive domains are impaired and the timing of onset and rate of progression **(Aarsland et al., 2005).**

PD with dementia (PDD) has a cross-sectional prevalence of approximately 30% and a life-long risk of up to 80% **(Hely et al., 2008).**

Research suggests an association between global cognition and postural instability/gait disturbance (PIGD) in PD, but the relationship between specific cognitive domains and PIGD symptoms is not clear **(Kellya et al., 2015)**.

Moreover, fall risk factors among patients with PD include disease severity, motor function, and level of mobility **(Kerr et al., 2010)**; studies also identified cognitive impairment as an independent contributing factor **(Allcock et al., 2009).**