Faculty of medicine

Gait and Cognitive Functions

Essay Submitted for Partial Fulfillment of the Requirement of the Master Degree in Neurology and Psychiatry

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كليـة الطـب

المشية والوظائف المعرفية

رسالة
توطئة للحصول على درجة الماجستير في أمراض المخ والأعصاب والطب النفسى

مقدمة من
الطبيب / **أيمن تفيد على محمد جاويش**
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بسم الله الرحمن الرحيم

وَأَنْزَلَ اللهُ

عَلَيْكَ الْكِتَابَ

والْحِكْمَةَ

وَعَلَّمَكَ مَا لَمْ

تَكُنْ تَعْلَمُ

وَكَانَ فَضْلُ

اللهِ عَلَيْكَ

عَظِيمًا

Dedication

This work is dedicated to …

My beloved Parents, to whom I owe everything I ever did in my life and will achieve

My beloved wife and my lovely daughter **(Roqaya)** for being the light of my life

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Abbreviations

AChE	acetylcholinesterase
ACTIVE	Advanced Cognitive Training for Independent and Vital Elderly study
AD	Alzheimer's disease
bvFTD	behavioral variant Frontotemporal Dementia
CGI	cognitive-gait intervention
CNS	central nervous system
CR	conditioned responses
CS	conditioned stimuli
CSF	cerebrospinal fluid
CT	computed tomography
DAT	Dementia of Alzheimer type
DBS	deep brain stimulation
DLB	dementia with Lewy bodies
DT	dual task
EF	Executive functions
FLD	frontal lobe dementia
FLD-ALS	frontal lobe degeneration– amyotrophic lateral sclerosis complex
fMRI	Functional Magnetic Resonance Imaging
FTD	Frontotemporal Dementia
FTDP-17	frontotemporal dementia with parkinsonism linked to chromosome 17
GABA	Gamma Amino Butyric Acid
GPi	globus pallidus interna
GV	gait velocity
HD	Huntington's disease
iNPH	idiopathic normal pressure hydrocephalus
MCI	Mild Cognitive Impairment
MMSE	Mini Mental State Examination
MPH	Methylphenidate
MRI	Magnetic Resonance Imaging
MSA	Multiple System Atrophy
NAc	nucleus accumbens
NPH	Normal Pressure Hydrocephalus
PD	Parkinson's disease
PDD	Parkinson's disease with dementia
PET	positron emission tomography
PFC	prefrontal cortex

PPN	Pedunculo-pontine Nucleus
PSP	Progressive Supranuclear Palsy
RCT	randomized controlled trial
SMA	supplementary motor area
SPECT	Single-photon emission computed tomography
SRT	sequential reaction time task
STN	subthalamic nucleus
SVE	subcortical vascular encephalopathy
TMS	transmagnetic stimulation
TT	treadmill training
UR	unconditioned responses
US	unconditioned stimuli
VAD	Vascular dementia
VR	virtual reality
WMH	white matter hyper intensities
WMSAs	White matter signal abnormalities

INTRODUCTION

The relationship between higher-level cognitive function and gait disturbances has received considerable attention in recent years **(Yogev et al., 2008)**.Until recently gait has been considered as an automated motor activity independent from cognitive function. However, recent arguments suggest a strong link between gait and cognition, in particular in neurodegenerative disorders such as Alzheimer's disease and related disorders. Executive functions seem to play a central role in these gait disorders due to deficits in cognition **(Allali et al., 2010).**

Gait is a learned, complex and almost automatic task with limited involvement of cognitive control in healthy individuals until the onset of old age. Previous studies have established the importance of cognitive control on gait in older adults; gait slowing is more prevalent in people with cognitive impairment and slow gait in healthy older adults is associated with a higher risk of cognitive impairment, including dementia **(Holtzer et al., 2006).** A slow gait velocity has been associated with an increased risk of falls, hospitalization and mortality **(Verghese et al., 2010).**

Changes in cognitive functions contribute to changes in the variability and stability of the gait pattern. Walking under dual task conditions and quantifying gait using dynamical parameters can improve detecting walking disorders and might help to identify those elderly who are able to adapt walking ability and those who are not and thus are at greater risk for falling **(Lamoth et al., 2011).** Managing gait disorders at early stages can help prevent further deconditioning and mobility impairment **(Lam, 2011).**

Previous findings underscore the fact that gait and complex cognitive functioning are closely related. Gait should no longer be considered a simple automatic motor activity that is independent of cognition; it should be treated as a higher level of cognitive functioning **(Hausdorff et al., 2005).**

The executive functions (EF) integrates cognitive and behavioral components necessary for effective, goal-directed actions and for the control of intentional resources thus enabling the human being to manage independent daily activities **(Stuss and Levine, 2002).** White matter hyper-intensities on magnetic resonance imaging were associated with a decline of EF, but not with the level of general intelligence **(Gunning-Dixon and Raz, 2003).**

Loss of dentritic branching in the prefrontal cortex is also associated with a decline in performance on EF tests. Age-associated decline in dopaminergic Activity in the frontal areas is also related to poorer performance on executive tasks **(Burke and Barnes, 2006)** Impairment of one or more of EF components reduces the ability to walk efficiently and safely **(Yogev-Seligman et al., 2008)** For example, poor self-awareness of limitations, an aspect of impaired volition, increases the risk of falling in elderly patients with dementia **(Van Iersel et al., 2006).** In older adults with mild cognitive impairment (MCI), low working memory performance was associated with slow gait velocity (GV). Dual-task conditions showed the strongest associations with gait slowing. The findings suggest that cortical control of gait is associated with decline in working memory in people with MCI **(Montero-Odasso et al., 2009a).**

The contribution of cognition to gait is particularly evident in patient with Parkinson’s disease (PD) with gait disorders who have a reduced ability to perform multiple tasks simultaneously, either because the central processing abilities have become too limited, or because patients fail to properly prioritize their balance control over other less important tasks **(Yogev-Seligman et al., 2008)**. While there have been several studies of comprehensive, multidisciplinary rehabilitation programs for individuals with PD, none have included any cognitive assessments nor interventions aimed at cognitive rehabilitation **(Wade et al., 2003).** Therefore, studies in Alzheimer’s disease must be examined to explore the potential of cognitive therapy and its possible application in Parkinson’s disease patients **(Loewenstein et al., 2004).**

Gait disorders are more prevalent in dementia than in normal aging and are related to the severity of cognitive decline. Dementia-related gait changes (DRGC) mainly include decrease in walking speed provoked by a decrease in stride length and an increase in support phase. More recently, dual-task related changes in gait were found in Alzheimer’s disease (AD) and non-Alzheimer dementia, even at an early stage **(Beauchet et al.,2008).**Predicting and anticipating disturbances in higher level gait is particularly relevant for patients with dementia as higher level gait appears to be closely related to higher level cognitive functioning **(Scherder et al ., 2011).** Decreased executive function plays an important role in increased gait variability in dementia patients; a fact that should be considered when designing fall risk interventions for this population. Furthermore, results indicate that measures of