An Investigation of Divided Attention Impairments in Huntington's Disease and Ageing

By

Eleftheria Vaportzis, BA (Hons) Psychology

This thesis is submitted in total fulfilment of the requirements for the degree of

Doctor of Philosophy (Psychology)



School of Psychology and Psychiatry

Faculty of Medicine, Nursing and Health Sciences

Monash University

Clayton, Melbourne, Australia

2013

Notice 1

Under the Copyright Act 1968, this thesis must be used only under the normal conditions of scholarly fair dealing. In particular no results or conclusions should be extracted from it, nor should it be copied or closely paraphrased in whole or in part without the written consent of the author. Proper written acknowledgement should be made for any assistance obtained from this thesis.

Table of Contents

Abstract	v
General Declaration	vii
Acknowledgements	viii
Publications and Conference Proceedings	ix
Abbreviations and Symbols	xii
List of Tables	xv
List of Figures	xvi

Chapte	r 1. (General Introduction	1				
1.	1.	Overview	2				
1.	2.	Genetics and Aetiology of HD	4				
1.	3.	Symptoms and Diagnosis of HD	5				
1.4	4.	Neuropathology of HD	6				
		1.4.1. Subcortical Changes	6				
		1.4.2. Cortical Changes	7				
		1.4.3. Functional MRI Changes					
		1.4.4. Basal Ganglia Circuitry	10				
1.	5.	Motor Deficits and Performance in HD					
1.	6.	Cognitive Changes and Assessment in HD	15				
		1.6.1. Executive Functions	16				
		1.6.2. Memory	16				
		1.6.2.1. Working and Short-Term Memory	17				
		1.6.3. Psychomotor Speed	19				
		1.6.4. Visuospatial Processing					
		1.6.5. Language Processing	22				
1.	7.	The Posner Model of Attention					
1.	8.	Theories of Divided Attention	25				
1.	9.	Divided Attention Tasks Versus Dual Tasks					
1.	10.	The Dual Task Paradigm					
1.	11.	Past Research on Dual Tasking in HD	Past Research on Dual Tasking in HD				
1.	12.	Dual Tasking in Neurologically Healty Individuals	33				
1.	13.	Does the Type of Concurrent Task Matter?	39				
1.	14.	Aims and Research Outline	40				

Chapter 2. Age Differences in Dual Task Performance	. 44
Preamble to Paper	. 45
Declaration for Thesis Chapter 2	. 46

Abstract	
Introduction	49
Method	53
Participants	53
Dual Task Description and Study Procedure	55
Design and Statistical Analyses	56
Results	58
Discussion	63
References	69

Preamble to Paper	5
Declaration for Thesis Chapter 3	6
Abstract	7
Introduction	7
Methods	8
Participants78	8
Dual Task Description	9
Statistical Analyses	0
Results	1
Simple Choice RT Task Performance	1
Simple Choice RT Dual Task Costs	1
Complex Choice RT Task Performance	1
Complex Choice RT Dual Task Costs	2
Digit Tasks Performance 82	2
Discussion	2
References	4

Chapter 4. Dual Task Performance in Huntington's Disease	36
Preamble to Paper	37
Declaration for Thesis Chapter 4	38
Abstract	9 0
Introduction	9 1
Method9	9 4
Participants9	94
Dual Task Description and Study Procedure	96
Design and Statistical Analyses	9 9
Results)1
Discussion10)5
References10)9

Chapter 5. A Comparison of Dual Tasks in Huntington's Disease	113
Preamble to Paper	
Declaration for Thesis Chapter 5	115
Abstract	117
Introduction	118
Method	
Participants	
Task Description	
Design	
Statistical Analyses	
Results	
Simple Choice RT Task Performance	
Complex Choice RT Task Performance	133
Digit Tasks Performance	
Discussion	
References	

Chapter 6.	General Discussion	
6.1.	Summary of Results	
6.2.	Implications of Findings	
6.3.	Theoretical Implications	
6.4.	Limitations and Future Research Directions	
6.5.	Concluding Remarks	
References		

Abstract

Divided attention, the ability to attend and respond simultaneously to two or more stimuli or tasks, has been typically investigated using dual task paradigms. Dual task paradigms have been extensively used to examine attentional demands in healthy people, including various age and patient groups. The effect of ageing on dual task performance is well-documented; however, dual task research on Huntington's disease (HD) is very limited, despite evidence suggesting poor dual task performance in this disease.

The overarching aim of this thesis was to investigate dual task performance in HD, and in younger (18-30 years) and older (> 60 years) healthy adults. To achieve this aim, we used a battery of dual tasks that varied in their input (e.g., visual, auditory) and output (e.g., motor, verbal) modalities. Each task was examined under two difficulty levels: easy and hard. Tasks were chosen based on past dual task research in HD and ageing, and divided attention theories (e.g., resource allocation theories).

Overall, our results showed that HD participants were slower and less accurate across all task conditions compared with controls. Similarly, older adults were slower and less accurate compared with younger adults. With a few exceptions, differences reached statistical significance either in terms of speed or accuracy within each set of tasks.

Our findings suggest differential effects of dual task performance in people with HD compared to healthy individuals, and between younger and older adults. Findings also highlight the importance of taking into account different measures of performance (e.g., speed, accuracy, dual task costs, etc.) since relationships between groups may differ

across measures. In regards to the effect of difficulty, overall, dual tasks were performed slower and less accurately than single tasks, and harder levels were performed slower and less accurately than easier levels.

A key outcome of our research is that HD participants and older adults may adopt differential behavioural strategies depending on the type of concurrent task, compared with controls and younger adults, respectively. Further investigation of dual tasking in HD and ageing, in conjunction with other tasks, will contribute to better understanding of attentional impairments that manifest with disease progression and older age. Consequently, this knowledge will assist with the development of adaptive strategies or treatments to improve functioning in people with HD and in the elderly.

General Declaration

In accordance with Monash University Doctorate Regulation 17 Doctor of Philosophy and Research Master's regulations the following declarations are made:

I hereby declare that this thesis contains no material which has been accepted for the award of any other degree or diploma at any university or equivalent institution and that, to the best of my knowledge and belief, this thesis contains no material previously published or written by another person, except where due reference is made in the text of the thesis.

This thesis includes four original papers published or submitted for publication in peer reviewed journals. The core theme of the thesis is *divided attention in Huntington's disease and ageing*. The ideas, development and writing up of all the papers in the thesis were the principal responsibility of myself, the candidate, working within the School of Psychology and Psychiatry under the supervision of *Professor Julie Stout* and *Professor Nellie Georgiou-Karistianis*.

Publication Nature and extent of Publication title Thesis status* candidate's contribution chapter 2 Age and task difficulty differences on dual Submitted Data collection and tasking using circle tracing and serial analysis, manuscript subtraction tasks synthesis and preparation 3 Published Data collection and Dual task performance in normal aging: A comparison of choice reaction time tasks analysis, manuscript synthesis and preparation 4 The impact of Huntington's disease and task Submitted Data collection and difficulty during dual task circle tracing analysis, manuscript synthesis and preparation 5 Dual task performance in Huntington's Data collection and Submitted disease: A comparison of choice reaction analysis, manuscript time tasks synthesis and preparation

In the case of chapters 2 to 5 my contribution to the work involved the following:

I have renumbered sections of submitted or published papers in order to generate a consistent presentation within the thesis.

Signed:

Date:

Acknowledgments

I would like to take the opportunity to express my gratitude to everyone who stood by me throughout this whole process. Without your support this thesis could not have come together in the manner in which it stands.

First and foremost, I would like to thank my supervisors *Professor Julie Stout* and *Professor Nellie Georgiou-Karistianis* for the guidance, encouragement, advice and insight they had provided throughout my time as their student. I could not have asked for more inspirational role models. They make me very proud of my academic roots.

I would also like to thank my participants and their families for taking the time out of their busy lives to support my research. In particular, I am indebted to those living with the burden of Huntington's disease, as they have been the inspiration for my research.

I am grateful to *Dr Andrew Churchyard* for his help in recruiting participants, which was my major concern when I started my PhD.

Finally, I am grateful to all the people in the *School of Psychology and Psychiatry* at Monash University, and especially to the members of the *Stout Lab* and *Experimental Neuropsychology Research Unit*, who have made the past few years a memorable and invaluable experience.

Publications and Conference Proceedings

Published and Submitted Manuscripts

- Vaportzis, E., Georgiou-Karistianis, N., & Stout, J. C. (2013). Dual task performance in normal aging: A comparison of choice reaction time tasks. *PLoS ONE*, 8, e60265.
- Vaportzis, E., Georgiou-Karistianis, N., & Stout, J. C. Age and task difficulty differences on dual tasking using circle tracing and serial subtraction tasks. Paper under review.
- Vaportzis, E., Georgiou-Karistianis, N., Churchyard, A., & Stout, J. C. Dual task performance in Huntington's disease: Comparing choice reaction time tasks. Paper under review.
- Vaportzis, E., Georgiou-Karistianis, N., Churchyard, A., & Stout, J. C. The impact of Huntington's disease and task difficulty during dual task circle tracing. Paper under review.

Abstracts

- Vaportzis, E., Georgiou-Karistianis, N., Churchyard, A., & Stout, J. (2012). Dual task performance in Huntington's disease using cancellation and auditory tasks. Abstract retrieved from http://www.frontiersin.org/Community/AbstractDetails.aspx?ABS_DOI=10.3389/ conf.fnhum.2012.208.00107&eid=1778&sname=ACNS-2012_Australasian_Cognitive_Neuroscience_Conference
- Vaportzis, E., Georgiou-Karistianis, N., Churchyard, A., & Stout, J. C. (2012). Dual task performance in Huntington's disease: Comparing choice reaction time tasks. *Journal of Neurology, Neurosurgery, & Psychiatry, 83*, A40.

Vaportzis, E., Georgiou-Karistianis, N., Churchyard, A., & Stout, J. (2011). The effects of Huntington's disease and task difficulty on dual-task performance. *Clinical Genetics*, 80(Supp 1), 59.

Posters

- Vaportzis, E., Georgiou-Karistianis, N., Churchyard, A., & Stout, J. (2012, December). Dual task performance in Huntington's disease using cancellation and auditory tasks. Poster presented at the 3rd Australasian Cognitive Neuroscience Conference, Brisbane, Australia.
- Vaportzis, E., Georgiou-Karistianis, N., Churchyard, A., & Stout, J. C. (2012, September). Dual task performance in Huntington's disease: Comparing choice reaction time tasks. Poster presented at the 7th European Huntington's Disease Network, Stockholm, Sweden.
- Vaportzis, E., Georgiou-Karistianis, N., Churchyard, A., & Stout, J. C. (2012, April). Dual task performance in Huntington's disease using circle tracing and counting backward tasks. Poster presented at the School of Psychology and Psychiatry Research Day, Monash University, Melbourne, Australia.
- Vaportzis, E., Georgiou-Karistianis, N., Churchyard, A., & Stout, J. (2011, September).
 The effects of Huntington's disease and task difficulty on dual-task performance.
 Poster presented at the World Congress on Huntington's Disease, Melbourne, Australia.

Oral Presentations

- Vaportzis, E., Georgiou-Karistianis, N., Churchyard, A., & Stout, J. C. (2013). The type of concurrent task does matter in dual task performance in Huntington's disease. Huntington's Disease and other Tandem Repeat Disorders Satellite Symposium, Melbourne, Australia.
- Vaportzis, E., Georgiou-Karistianis, N., Churchyard, A., & Stout, J. C. (2010). Divided attention in Huntington's disease. Huntington's Research Group Victoria Meeting, Melbourne, Australia.

Abbreviations and Symbols

ANOVA	Analysis of variance
CAG	Cytosine-adenine-guanine
cdm-GPi	Caudal dorsomedial internal globus pallidus
cl-SNr	Caudolateral substantia nigra pars reticulate
CRUNCH	Compensation-Related Utilization of Neural Circuits Hypothesis
df	Degrees of freedom
dl	Dorsolateral
DLPFC	Dorsolateral prefrontal cortex
DTC	Dual task costs
Ε	Easy
F	F-test
FEF	Frontal eye fields
GPe	External globus pallidus
GPi	Internal globus pallidus
Н	Hard
HD	Huntington's disease
IDS-SR	Inventory of Depressive Symptomatology-Self-Report
ISCED	International Standard Classification of Education
ldm-GPi	Lateral dorsomedial internal globus pallidus
LOF	Lateral orbitofrontal cortex
l-VAmc	Lateral ventralis anterior pars magnocellularis
M	Mean
MDmc	Medialis dorsalis pars magnocell ularis
mdm-GPi	Medial dorsomedial internal globus pallidus

MDpc	Medialis dorsalis pars parvocellularis
MDpl	Medialis dorsalis pars paralamellaris
MoCA	Montreal Cognitive Assessment
ms	milliseconds
m-VAmc	Medial lateral ventralis anterior pars magnocellularis
n	Number
р	<i>p</i> -value
pm-MD	Posteromedial medialis dorsalis
r	Pearson product-moment correlation
rd-SNr	Rostrodorsal substantia nigra pars reticulate
rl-GPi	Rostrolateral internal globus pallidus
rl-SNr	Rostrolateral substantia nigra pars reticulate
rm-SNr	Rostromedial, substantia nigra pars reticulate
RT	Reaction time
S	seconds
SD	Standard deviation
SMA	Supplementary motor area
SNpr	Substantia nigra pars reticulata
STN	Subthalamic nucleus
t	t-test
TFC	Total Functional Capacity
UHDRS	Unified Huntington's Disease Rating Scale
VApc	Ventralis anterior pars parvocellularis
vl-GPi	Ventrolateral internal globus pallidus
VLm	Ventralis lateralis pars medialis

VLo	Ventralis lateralis pars oralis
vl-SNr	Ventrolateral substantia nigra pars reticulate
vm	Ventromedial
VP	Ventral pallidum
VS	Ventral striatum
WTAR	Wechsler Test of Adult Reading
α	Alpha
η^2	Eta

List of Tables

Chapter 2

Table 1 (2.1)	Means	(standard	deviations)	across	all	task	conditions	for
younger and older participants						. 58		

Chapter 3

Table 1 (3.1)	Means (and	standard	deviations)	of	younger	and	older	adults
	across all tas	sks		••••			•••••	79

Chapter 4

Table 1 (4.1)	Demographic data for HD and control groups	. 96
Table 2 (4.2)	Means (standard deviations) across all task conditions for	HD
	and control groups	100

Chapter 5

Table 1 (5.1)	Demographic data for HD participants and controls	123
Table 2 (5.2)	Study design	127
Table 3 (5.3)	Means (and standard deviations) of HD participants and cont	trols
	across all tasks	129

Chapter 1

Figure 1 (1.1) Basal ganglia circuitry. Parallel organisation of the five basal ganglia-thalamocortical circuits. ACA = anterior cingulate area, cdm-GPi = caudal dorsomedial internal globus pallidus, cl-SNr = caudolateral substantia nigra pars reticulate, ldm-GPi = lateral dorsomedial internal globus pallidus, dl = dorsolateral, DLPFC = dorsolateral prefrontal cortex, FEF = frontal eye fields, LOF = lateral orbitofrontal cortex, l-VAmc = lateral ventralis anterior pars magnocellularis, mdm-GPi = medial dorsomedial internal globus pallidus, MDmc = medialis dorsalis pars magnocell ularis, MDpc = medialis dorsalis pars parvocellularis, MDpl = medialis dorsalis pars paralamellaris, m-VAmc = medial lateral ventralis anterior pars magnocellularis, rd-SNr = rostrodorsal substantia nigra pars reticulate, rl-GPi = rostrolateral internal globus pallidus, rl-SNr = rostrolateral substantia nigra pars reticulate, rm-SNr = rostromedial, substantia nigra pars reticulate, pm-MD = posteromedial medialis dorsalis, SMA = supplementary motor area, VApc = ventralis anterior pars parvocellularis, vl-GPi = ventrolateral internal globus pallidus, VLm = ventralis lateralis pars medialis, VLo = ventralis lateralis pars oralis, vl-SNr = ventrolateral substantia nigra pars reticulate, VP = ventral pallidum, VS = ventral striatum, vm = ventromedial (adapted with permission of the publisher from

Figure 2 (1.2)	Basal ganglia model showing the direct (left) and indirect (right)			
	striatal output pathways (used with permission of the published			
	from Andrews & Brooks, 1998)1			
Figure 3 (1.3)	Wickens's (2002) four-dimensional Multiple Resources Theorem			
	(used with permission of the publisher)			

Chapter 2

Figure 1 (2.1)	Number of rotations on the circle tracing task (easy, hard) as
	function of age (young, old). $E = Easy; H = Hard$. Standard error
	bars are included

Chapter 3

Figure 1 (3.1)	A non-target (R) and a target	t (X) trial of the simple choice RT
	task	

- **Figure 2 (3.2)** Target stimuli of the complex choice RT task conditions. On the left matrix, four Xs appear in a row (easy or hard conditions); on the right matrix, four Os appear in a row (hard condition).......78

Chapter 4

- Figure 2 (4.2) Circle tracing difficulty (easy, hard) as a function of serial subtraction difficulty (none, easy, hard) using dual task costs for speed. E = Easy; H = Hard. Standard error bars included 103
- Figure 3 (4.3)Speed-accuracy trade-offs for HD participants and controls
across all circle tracing task conditions. Asterisks next to the r
values represent significant correlations. ** p < .001;
* p < .05... 104

Chapter 5

Chapter 1

General Introduction

1.1. Overview

Huntington's disease (HD) is an inherited neurodegenerative condition causing impairment of movement, cognition and psychiatric function. Prevalence is approximately 1 in 10,000 individuals, although there is considerable regional variation (Harris et al., 2009). Onset is on average about the age of 40, but subtle symptoms are often present earlier (Walker, 2007). The progression of HD is generally slow with the striatum a main site of early pathology (Georgiou-Karistianis et al., 2013; Tabrizi et al., 2012). Cortical regions are also known to be affected early in the disease (Couette, Bachoud-Levi, Brugieres, Sieroff, & Bartolomeo, 2008), and they contribute to physical, emotional and cognitive symptoms (Deckel, Weiner, Szigeti, Clark, & Vento, 2000; Fenney, Jog, & Duval, 2008; Rosas et al., 2003).

Research on HD has advanced rapidly since the identification of the HD gene in 1993 (The Huntington's Disease Collaborative Research Group, 1993). Studies have investigated the clinical and neuropathological changes during the presymptomatic, early and advanced stages (Kirkwood et al., 2000; Klöppel et al., 2009; Reading et al., 2004; Rosas et al., 2006; Selemon, Rajkowska, & Goldman-Rakic, 2004; Tabrizi et al., 2011). Disease stage has been defined to reflect functional decline, as rated by the Total Functional Capacity (TFC) scale from the Unified Huntington's Disease Rating Scale (UHDRS; Huntington Study Group, 1996), an extensively employed measure of disease severity. Cognitive changes, such as attention impairments, have been widely investigated, although related functions, such as divided attention (the ability to respond simultaneously to two or more stimuli *or* tasks), have received little investigation. Divided attention is indispensable for simple tasks, such as listening to a friend while walking, as well as for more difficult and/or complex tasks, such as talking while

driving. The limited divided attention research in HD, as well as anecdotal reports from patients and their families, suggest that the ability to attend to multiple simultaneous stimuli is impaired in HD. However, it remains unknown whether dual task performance depends on the type of concurrent task. It is also unknown whether, compared to healthy individuals, HD is associated with relatively greater dual task interference when task difficulty increases. Studies of divided attention in HD may point to the involvement of specific cortical regions affected early in the disease process. If tests that are sensitive to divided attention impairments can be identified, they could be incorporated in batteries of tests aimed at determining the efficacy of treatments for HD.

Although divided attention is a relatively new and exciting area of research in HD, it has long been a topic of research in cognitive psychology. Furthermore, a number of theoretical frameworks have been put forward to explain difficulties in divided attention, such as resource allocation and processing speed theories. A substantial number of studies have investigated divided attention in ageing for both theoretical and practical reasons. To understand pathological cognitive changes in HD, it is important to investigate normal ageing, because it will allow us to compare the progression of HD directly with the progression of normal ageing. This first, introductory chapter provides a comprehensive review of the current literature on attention function in HD and ageing. Particular focus will be given on divided attention. The section below begins with an overview of the aetiology, neuropathology and cognitive changes in HD. Following, prominent theories of divided attention will be discussed, and their potency to account for findings in divided attention research in HD and ageing will be evaluated.

1.2. Genetics and Aetiology of HD

Gusella et al. (1983) localised the HD gene, IT15, on chromosome 4 using linkage analysis. Ten years later, the gene was identified as an expanded and unstable cytosine-adenine-guanine (CAG) trinucleotide repeat within the IT15 gene (The Huntington's Disease Collaborative Research Group, 1993). Normal individuals have fewer than 35 CAG repeats, whereas 39 or more are generally associated with the development of HD (Groen et al., 2010; Teo, Wang, Law, Lee, & Chong, 2008). Expansions between 36 and 39 are within the indeterminate range, and people may appear asymptomatic throughout their lives (Bates, Harper, & Jones, 2002; Hayward, 2004; Panegyres & Goh, 2011), whereas expansions greater than 60 are associated with juvenile onset (Andresen et al., 2006). Notably, there is an inverse association between CAG repeat length and age of onset (Andresen et al., 2006; Krobitsch & Kazantsev, 2011). Predictive testing for HD, which is now available in many countries, enables at-risk individuals to obtain confirmation of their genetic status (Tibben, 2007).

The IT15 gene codes the protein *huntingtin*. Loss of function of normal huntingtin, as well as gain of toxic function (i.e., a new function of a protein that is not part of its normal function) of mutant huntingtin that arises from the expanded CAG, has been suggested to contribute to HD pathogenesis (Gil & Rego, 2008; Krobitsch & Kazantsev, 2011). In addition, other neuropathological mechanisms, such as apoptosis (Ferreira et al., 2010), autophagy (Martinez-Vicente et al., 2010), excitotoxicity (Seong et al., 2005; Turner & Schapira, 2010), oxidative stress (Medina & Tunez, 2010), and mitochondrial dysfunction (Chen et al., 2007) have also been implicated in HD pathology (for a review see Gil & Rego, 2008). Several lines of evidence suggest that these mechanisms are not mutually exclusive. Some of these pathological processes may commence early in the

disease course, whereas others may develop later in more advanced stages. It is generally agreed that many of these factors contribute to a cascade of neuronal damage in HD.

Identification of the HD gene provided one of the first and most important steps in understanding the genome of HD, which is essential for studying disease progression. Understanding the effects of the expanded CAG repeat may ultimately provide insights into the nature of the neuropathological mechanisms at play in HD, and may also enable the development of interventions to delay onset and/or slow its progression.

1.3. Symptoms and Diagnosis of HD

A triad of symptoms including motor, cognitive and psychiatric disturbances are characteristic of HD. Motor symptoms include voluntary (Beste et al., 2009; Tabrizi et al., 2009) and involuntary (hyperkinetic and/or hypokinetic) abnormalities (Fenney et al., 2008; Thaut, Miltner, Lange, Hurt, & Hoemberg, 1999). Commonly reported cognitive symptoms include impairments in attention (Georgiou-Karistianis et al., 2012; Stout & Johnson, 2005; Wolf, Vasic, Schonfeldt-Lecuona, Ecker, & Landwehrmeyer, 2008), memory (Lawrence et al., 1996; van der Hiele et al., 2007), planning (Peinemann et al., 2005; Watkins et al., 2000), decision making (Eddy & Rickards, 2012; Stout, Rodawalt, & Siemers, 2001), visuospatial ability (Lawrence, Watkins, Sahakian, Hodges, & Robbins, 2000; Majerová et al., 2012), verbal fluency (Ho et al., 2002; Larsson, Almkvist, Luszcz, & Wahlin, 2008), procedural learning (Knopman & Nissen, 1991; Schmidtke, Manner, Kaufmann, & Schmolck, 2002), awareness (Hoth et al., 2007; Sitek et al., 2013) and perception (Aviezer et al., 2009; Finke et al., 2007; Sitek et al., 2008). Psychiatric symptoms include depression (Julien et al., 2007;

Paulsen et al., 2005), irritability (Chatterjee, Anderson, Moskowitz, Hauser, & Marder, 2005; Paulsen, Ready, Hamilton, Mega, & Cummings, 2001), anxiety (Decruyenaere et al., 2003; Soliveri et al., 2002), obsessive-compulsiveness (Duff et al., 2007), apathy (Burns, Folstein, Brandt, & Folstein, 1990; Naarding, Janzing, Eling, van der Werf, & Kremer, 2009) and personality disorders (Jensen, Fenger, Bolwig, & Sørensen, 1998; Vassos, Panas, Kladi, & Vassilopoulos, 2007). Cognitive and psychiatric symptoms have been identified during the presymptomatic stages (Duff et al., 2007; Solomon et al., 2007); however, by clinical convention, diagnosis of HD still requires the presence of chorea, which are jerky involuntary movements (Andresen et al., 2006; Paulsen et al., 2007).

1.4. Neuropathology of HD

The symptoms of HD that lead to eventual decline in every day functional capacity, are generally attributed to changes in brain structure, which are detectable during the presymptomatic (Ciarmiello et al., 2006; Georgiou-Karistianis et al., 2013; Nopoulos et al., 2007; Reading et al., 2004; Rosas et al., 2005; Tabrizi et al., 2009, 2011), early (Ciarmiello et al., 2006; Tabrizi et al., 2009, 2011), and advanced stages of disease (Ciarmiello et al., 2006; Montoya, Price, Menear, & Lepage, 2006; Rosas, Salat, Lee, Zaleta, Pappu, et al., 2008). The section below reviews the subcortical, cortical and functional brain changes that have been reported in HD, and also brain circuitry models, which are key to understanding the wide-ranging clinical symptoms in this disease.

1.4.1. Subcortical Changes

The earliest, most striking and most consistent neuropathological abnormalities are selective, with prominent cell loss and atrophy in the caudate and putamen (i.e.,

neostriatum) (Gutekunst, Norflus, & Hersch, 2002). The striatum shows significant degeneration early in the disease (Douaud et al., 2006; Kassubek et al., 2004; Peinemann et al., 2005; Rosas & Goldstein, 2004), and up to 12 years prior to onset (Aylward et al., 2004; Georgiou-Karistianis et al., 2013; Paulsen et al., 2004; Rosas et al., 2005; Tabrizi et al., 2012; Thieben et al., 2002). Douaud et al. (2006) reported approximately 50% reduced volume of the striatum in HD participants in comparison to controls. Striatal degeneration has been implicated in impaired attentional resources (Teichmann, Darcy, Bachoud-Levi, & Dupoux, 2009), inhibitory deficits (Aron, Schlaghecken, et al., 2003), impaired planning (Watkins et al., 2000) and executive dysfunction (Peinemann et al., 2005), among a range of other cognitive, motor and neuropsychiatric symptoms. Other affected subcortical regions include the hippocampus (Rosas, Salat, Lee, Zaleta, Hevelone, et al., 2008; Spargo, Everall, & Lantos, 1993), thalamus (Douaud et al., 2009; Fennema-Notestine et al., 2004; Heinsen et al., 1999; Rosas, Salat, Lee, Zaleta, Hevelone, et al., 2008; Ruocco, Bonilha, Li, Lopes-Cendes, & Cendes, 2008), hypothalamus (Douaud et al., 2006; Kremer et al., 1991), globus pallidus (Douaud et al., 2006, 2009; Fennema-Notestine et al., 2004), and amygdala (Douaud et al., 2006; Rosas et al., 2008).

1.4.2. Cortical Changes

Cortical degeneration has also been reported in HD. For instance, postmortem studies have established that both subcortical and cortical areas are affected in advanced stages (Gutekunst et al., 1999; Halliday et al., 1998; Mann, Oliver, & Snowden, 1993). In recent years, neuroimaging studies have shown cortical changes in presymptomatic stages of HD (Ciarmiello et al., 2006; Mühlau, Gaser, et al., 2007; Rosas et al., 2005; Thieben et al., 2002), and as early as within a year of diagnosis (Ciarmiello et al., 2006;

Halliday et al., 1998; Mühlau, Gaser, et al., 2007; Rosas, Salat, Lee, Zaleta, Pappu, et al., 2008), providing evidence of cortical degeneration over more than 12 years of estimated years to onset (for a description on how to calculate estimated years to onset see Langbehn, Brinkman, Falush, Paulsen, & Hayden, 2004). Cortical atrophy is regionally heterogeneous and advances with disease progression (Selemon et al., 2004). Several cortical regions, including the motor (Macdonald & Halliday, 2002; Orth et al., 2010; Thu et al., 2010), cingulate (Hobbs et al., 2011; Thu et al., 2010), sensorimotor (Dumas et al., 2012; Rosas et al., 2002; Rosas, Salat, Lee, Zaleta, Pappu, et al., 2008), visual (Rosas et al., 2002; Rosas, Salat, Lee, Zaleta, Pappu, et al., 2008), occipital (Mühlau, Weindl, et al., 2007), and dorsolateral prefrontal cortex (Rupp et al., 2011; Wolf, Vasic, Schönfeldt-Lecuona, Landwehrmeyer, & Ecker, 2007) have been implicated; however, it remains elusive whether cortical degeneration is secondary to striatal changes or independent of striatal pathology (Fennema-Notestine et al., 2004). The reciprocal neuroanatomical connections between cortical and subcortical regions add to the complexity of their pathological relationship, rendering it difficult to understand what the contribution of specific regions to specific neuroanatomical changes is.

1.4.3. Functional MRI Changes

Imaging studies have provided significant insight regarding functional changes in HD using a range of both cognitive and motor tasks, including Simon task (Georgiou-Karistianis et al., 2007; Thiruvady et al., 2007), set-shifting (Gray et al., 2013), Porteus maze (Clark, Lai, & Deckel, 2002; Deckel et al., 2000), tower (Bäckman, Robins-Wahlin, Lundin, Ginovart, & Farde, 1997; Lawrence et al., 1998; Pavese et al., 2003), line bisection (Ho et al., 2004), discrimination (Paulsen et al., 2004), serial reaction time

(Kim et al., 2004), working memory (Lawrence et al., 1998; Wolf, Sambataro, Vasic, Shonfeldt-Lecuona, et al., 2008; Wolf, Vasic, Schönfeldt-Lecuona, Ecker, & Landwehrmeyer, 2009), and interference tasks (Reading et al., 2004; Wolf et al., 2007). Overall, impaired behavioural task performance and decreased activation in various subcortical and cortical regions have been reported both in HD (Clark et al., 2002; Pavese et al., 2003; Wolf et al., 2009) and presymptomatic individuals (Reading et al., 2004; Wolf, Sambataro, Vasic, Shonfeldt-Lecuona, et al., 2008; Wolf et al., 2007), compared with controls. Some studies reported increased cortical activation during the symptomatic (Georgiou-Karistianis et al., 2007; Kim et al., 2004) and presymptomatic stages (Reading et al., 2004; Wolf et al., 2007) even when there was no evidence of striatal degeneration or cognitive impairment. Such findings have commonly been interpreted to be suggestive of a secondary compensatory mechanism for tasks that typically rely on subcortical areas (Clark et al., 2002; Georgiou-Karistianis et al., 2007). Overall, these findings suggest that functional imaging is sensitive for detecting reorganisation of functional neural processing that underlies cognitive and behavioural activities even presymptomatically.

A number of studies have reported that functional activation patterns increase or decrease depending on estimated years to onset at the time of imaging (Paulsen et al., 2004; Saft et al., 2008; Wolf et al., 2007; Zimbelman et al., 2007). During the disease continuum, variability in functional activation patterns maybe associated with other neuropathological changes (i.e., neuronal dysfunction), and be influenced by other factors, such as CAG repeat length and disease stage (for a review see Bohanna, Georgiou-Karistianis, Hannan, & Egan, 2008; Georgiou-Karistianis, 2009; Paulsen, 2009).

Collectively, functional imaging findings suggest that both subcortical and cortical regions contribute to cognitive deficits in HD, and that dysfunction in these regions precedes overt brain degeneration. However, it still remains elusive as to whether cortical degeneration arises due to striatal changes or whether it occurs independent of the striatum. The significance of cortical degeneration and its relationship to the progressive decline of cognitive functions is also sparse. The following section will discuss basal ganglia circuitry.

1.4.4. Basal Ganglia Circuitry

The basal ganglia are comprised of a group of structures including the globus pallidus, substantia nigra, subthalamic nucleus and the striatum (Lawrence et al., 2000). They are involved in a series of parallel cortico-subcortical circuits, which project from distinct cortical regions through the basal ganglia and thalamus and then back to their respective cortical areas of origin (Alexander, DeLong, & Strick, 1986; DeLong & Wichmann, 2007; Joel, 2001). These circuits are presented in Figure 1 (adapted from Alexander et al., 1986) and include the sensorimotor (motor and oculomotor), associative (dorsolateral prefrontal and lateral orbitofrontal circuits) and limbic (anterior cingulate) circuits (Alexander et al., 1986; Joel, 2001). The current organisational model of the basal ganglia holds that the sensorimotor, associative and limbic circuits are implicated in motor, cognitive and psychiatric symptoms, respectively (Grabli et al., 2004; Middleton & Strick, 2000; Paulsen et al., 2001). Individuals with HD endure gradual decline of cognitive function that often precedes motor function decline and overt movement disorders (Lawrence et al., 1998; Stout et al., 2011). In turn, this may suggest that the associative circuit is affected earlier in the course of the disease than the limbic

	Motor C		Oorsolateral Prefrontal	Lateral Orbitofrontal	Anterior Cingulate
	•		↓	•	•
Cortex	SMA	FEF	DLPFC	LOF	ACA
	↓	↓	↓ ↓	\downarrow	↓ ↓
Striatum	Putamen	Caudate	Caudate (dl)	Caudate (vm)	VS
	↓ ↓	↓ ↓	↓ ↓	↓	↓ ↓
Pallidum/	vl-GPi/	cdm-GPi/	ldm-GPi/	mdm-GPi/	rl-GPi, VP/
Sustantia nigra	cl-SNr	vl-SNr	rl-SNr	rm-SNr	rd-SNr
Thalamus	↓ VLo, VLm	↓ l-VAmc, MDpl	VApc, MDpc	↓ m-VAmc, MDmc	↓ pm-MD

circuit (Lawrence et al., 1996; Middleton & Strick, 2000), and therefore, divided attention impairments may be evident earlier.

Figure 1. Basal ganglia circuitry. Parallel organisation of the five basal gangliathalamocortical circuits. ACA = anterior cingulate area, cdm-GPi = caudal dorsomedial internal globus pallidus, cl-SNr = caudolateral substantia nigra pars reticulate, ldm-GPi= lateral dorsomedial internal globus pallidus, dl = dorsolateral, DLPFC = dorsolateral prefrontal cortex, FEF = frontal eye fields, LOF = lateral orbitofrontal cortex, l-VAmc = lateral ventralis anterior pars magnocellularis, mdm-GPi = medial dorsomedial internal globus pallidus, MDmc = medialis dorsalis pars magnocell ularis, MDpc = medialis dorsalis pars parvocellularis, MDpl = medialis dorsalis pars paralamellaris, m-VAmc = medial lateral ventralis anterior pars magnocellularis, rd-SNr = rostrodorsal substantia nigra pars reticulate, rl-GPi = rostrolateral internal globus pallidus, rl-SNr = rostrolateral substantia nigra pars reticulate, rm-SNr = rostromedial, substantia nigra pars reticulate, pm-MD = posteromedial medialis dorsalis, SMA = supplementary motor area, VApc = ventralis anterior pars parvocellularis, vl-GPi = ventrolateral internal globus pallidus, VLm = ventralis lateralis pars medialis, VLo = ventralis lateralis pars oralis, vl-SNr = ventrolateral substantia nigra pars reticulate, VP = ventral pallidum, VS = ventral striatum, vm = ventromedial (adapted with permission of the publisher from Alexander et al., 1986).

Models of basal ganglia function postulate that all circuits may be divided anatomically and functionally into two pathways: a direct pathway (responsible for action initiation), and an indirect pathway (responsible for action inhibition or switching between actions) (André et al., 2011; Berardelli et al., 1999). As seen in Figure 2, in the direct pathway, the main output of the striatum projects to the substantia nigra pars reticulata (SNpr) and the internal globus pallidus (GPi); in the indirect pathway, the main output of the striatum projects to the GPi via the external globus pallidus (GPe) and the subthalamic nucleus (STN) (Joel, 2001; Wichmann & DeLong, 1996). There is also some evidence suggesting that there is a third pathway, termed the hyperdirect pathway, that connects directly the motor cortex with the STN (Brunenberg et al., 2012; Jahfari et al., 2011). Chorea may be explained by degeneration of the indirect pathway. Rigidity (limb stiffness) and bradykinesia (slowing of movement), observed during more advanced stages, are likely due to degeneration of the direct pathway (André et al., 2011; Berardelli et al., 1999).

Within the ample literature that supports an early role of the basal ganglia regions in the manifestation of clinical symptoms in HD (Bonelli & Cummings, 2007; D'Esposito, Postle, & Rypma, 2000; Wolf, Sambataro, Vasic, Shonfeldt-Lecuona, et al., 2008), there is evidence of atrophy in other structures (i.e., thalamus and cortical regions) that could contribute to cognitive decline (Kassubek et al., 2004). The section below will discuss in more detail motor symptoms and motor task performance.

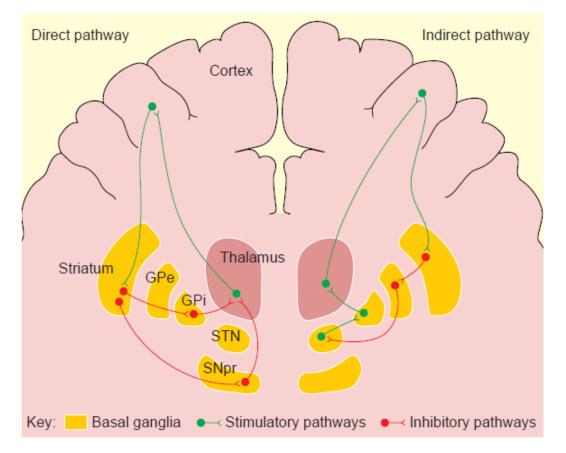


Figure 2. Basal ganglia model showing the direct (left) and indirect (right) striatal output pathways (used with permission of the publisher from Andrews & Brooks, 1998).

1.5. Motor Deficits and Performance in HD

Typically, the dominant movement disorders observed during the early stages are chorea and dystonia (overactivity of muscle groups), followed by bradykinesia (slowing of movement) and rigidity (limb stiffness) in the more advanced stages, although hypoactivity and hyperactivity movements may coexist (Bilney, Morris, & Denisenko, 2003; Michell et al., 2008). Movements in HD are usually slower, more variable and less efficient than healthy controls (Georgiou, Bradshaw, Phillips, Chiu, & Bradshaw, 1995; Georgiou, Bradshaw, Phillips, Bradshaw, & Chiu, 1995; Georgiou, Bradshaw, Phillips, Bradshaw, & Chiu, 1995; Georgiou, Phillips, Thaut et al., 1999) and can adversely affect motor function in terms of reaction time (RT) (Jahanshahi, Brown, & Marsden, 1993; Kim et al., 2004; Wechsler, 2009) and accuracy (Bilney, Morris, & Perry, 2003; Corbetta, Miezin, Dobmeyer, Shulman, & Petersen, 1991).

Some studies have examined voluntary movement by assessing continuous movements towards various visual targets (Georgiou, Phillips, et al., 1997; Smith et al., 2000), and circle tracing (Lemay, Fimbel, Beuter, & Chouinard, 2005; Say et al., 2011). In these studies, HD participants have been found to be slower and more error-prone than controls. Performance during circle tracing depends on the visual information provided by the circle, as well as on the visual and proprioceptive information of the moving arm, which together need to be transformed into a common spatial reference (Lemay et al., 2005). Since the basal ganglia have been implicated in sensorimotor transformation (Abbruzzese & Berardelli, 2003), it is not surprising that slower and more error-prone movements in HD have been reported. As fine motor skills deteriorate earlier than gross

motor skills in HD, tracing tasks may provide a very sensitive means by which to examine visuomotor integration in HD. The following section will review the nature and progression of the cognitive changes in HD.

1.6. Cognitive Changes and Assessment in HD

Cognitive changes underpin many aspects of functional capacity, such as occupational performance and daily living management. Changes in cognition may be detectable even far from clinical diagnosis and worsen with disease progression (Lemiere, Decruyenaere, Evers-Kiebooms, Vandenbussche, & Dom, 2002, 2004; Stout et al., 2007). Deficits are evident in executive function (Peinemann et al., 2005; Reedeker, Van Der Mast, Giltay, Van Duijn, & Roos, 2010; Rodrigues et al., 2009; Snowden, Craufurd, Thompson, & Neary, 2002), memory processes (Aretouli & Brandt, 2010; Brandt, Shpritz, Munro, Marsh, & Rosenblatt, 2005; Solomon et al., 2007; Wolf et al., 2009), psychomotor speed (Kassubek, Juengling, Ecker, & Landwehrmeyer, 2005; Snowden et al., 2002; Witjes-Ane et al., 2007), visuospatial abilities (Lawrence et al., 2000; Mohr et al., 1991), language processing (De Diego-Balaguer et al., 2008; Lepron, Péran, Cardebat, & Démonet, 2009; Murray, 2000; Saldert, Fors, Ströberg, & Hartelius, 2010; Teichmann et al., 2009; Teichmann et al., 2008), and attention (Aron, Watkins, et al., 2003; Couette et al., 2008; Delval et al., 2008; Georgiou-Karistianis et al., 2012; Georgiou, Bradshaw, Phillips, & Chiu, 1996, 1997; Hester, Kinsella, & Ong, 2004; Thompson et al., 2010). The section below is divided into various cognitive domains, and within each subsection major studies are presented.

1.6.1. Executive Functions

Executive function is a multidimensional construct that includes various cognitive functions reported to be affected in HD, such as working memory, planning, abstract thinking, attentional set-shifting and divided attention, some of which will be described in following subsections. Executive dysfunction in HD is similar to that observed in Parkinson's disease and frontal lobe patients (Como, 2006). Similarities in these patient groups may be explained by the connections between the basal ganglia and the frontal lobes (Saint-Cyr, 2003). Individuals with executive dysfunction may perform well on tasks that require a single response to the presence of a specific stimulus (i.e., single-choice tasks), but they may be impaired when they must select from multiple responses depending on the stimulus present (i.e., two-choice tasks) (Como, 2006).

More relevant to this thesis, interference between processing of more than one task at a time is considered to be the principal cause for the involvement of executive functions in divided attention (Baddeley, 1990). Therefore, executive functions are involved only in processing of multiple tasks, and not in single task processing. Indicators of interference include longer RT and/or greater error rates when dividing attention between tasks compared to single task performance, as well as increased neural activity (Szameitat, Schubert, Müller, & von Cramon, 2002). The following subsection deals with memory, one of the most integral mental processes.

1.6.2. Memory

Memory refers to the mental processes that are required to store, retain and retrieve information. Although memory functioning is impaired even in presymptomatic individuals, it deteriorates more precipitously closer to onset (Lawrence et al., 1996; Snowden et al., 2002), and even further with disease progression as indicated by longitudinal studies (Ho et al., 2003; Ward et al., 2006). Memory deficits in HD are typically characterised by poor encoding (Davis, Filoteo, & Kesner, 2007) and retrieval strategies (Ho et al., 2003) that are generally attributable to dysfunctional frontal cortex, secondary to striato-frontal degeneration (Snowden et al., 2002; Solomon et al., 2007). Some previous studies indicate that HD participants manifest worse performance on delayed recall than recognition tasks (Brandt, Leroi, O'Hearn, Rosenblatt, & Margolis, 2004; Delis, Massman, Butters, & Salmon, 1991; Fine et al., 2008; Lundervold, Reinvang, & Lundervold, 1994; Pillon, Deweer, Agid, & Dubois, 1993). This pattern has been interpreted as evidence for retrieval-based memory impairments. Despite that, a meta-analysis of studies investigating episodic memory in HD reported that both free recall and recognition capacities are impaired (Montoya, Pelletier, et al., 2006), suggesting that both domains are defective to some extent. Two important types of memory, working and short-term memory, that are essential for everyday functioning are discussed next.

1.6.2.1. Working and Short-Term Memory

Working memory is a limited capacity system that is responsible for processing and temporarily retaining information (Grégoire & Van Der Linden, 1997), whereas short-term memory is the simple ability to temporarily retain information (Dranias, Ju, Rajaram, & VanDongen, 2013). Working memory performance becomes increasingly impaired over the course of HD (Lemiere et al., 2002, 2004). Participants in the early stages perform poorly on working memory tasks compared with presymptomatic participants (Lemiere et al., 2004; Snowden et al., 2002) and controls (Lawrence et al.,

1998; Lemiere et al., 2004). In a similar fashion to working memory, short-term memory has also been found to be impaired in HD (Davis et al., 2007).

Digit span tasks have been routinely used to evaluate working memory and short-term memory performance. For instance, digit span forward is a simple measure of short-term memory as it requires storage and rehearsal of information; digit span backward is a measure of working memory, as it produces greater attentional and processing demands, since participants have not only to hold the digits in memory, but also perform an operation on them (Conway et al., 2005; Craik & Lockhart, 1979). Participants in the early stages of HD are consistently impaired on both measures (Lemiere et al., 2004; Snowden et al., 2002). Impairment in performance in the digit span backward may be explained by the involvement of working memory resources. However, it could be argued that the digit span forward task is not a passive task; hence, working memory resources may also be involved, albeit to a lesser extent than in digit span backward.

Counting backward is another attention-demanding task that has been used to reflect the operations of short-term memory or as a distractor task to "clean-out" short-term memory storage (Nairne & Healy, 1983). To perform this task, subjects are instructed to count backward aloud from a specific number by one, two or more digits. In order to maintain their position, subjects are required to check the current digit in their short-term memory and decide which digit is next in the sequence. Counting backward has been found to affect postural balance in the elderly (Swanenburg, de Bruin, Uebelhart, & Mulder, 2009) and motor performance in HD (Delval et al., 2008). These findings suggest that counting backward can stress an individual's attentional system, and therefore, could be used for the assessment of at-risk or patient populations.

Petrides (1994) proposed a model of memory retrieval according to which the ventrolateral frontal cortex mediates the organisation, selection and inhibition of short-term memory information, whereas the dorsolateral prefrontal cortex mediates monitoring and manipulating short-term memory information. Neuroimaging studies have also found the ventrolateral frontal cortex (Mayes, 1998; Owen, Evans, & Petrides, 1996; Owen et al., 1999) and the dorsolateral prefrontal cortex (D'Esposito et al., 1998; 2000; Wolf et al., 2007; Wolf & Walter, 2005) to make distinct functional contributions as the model holds. Therefore, short-term and working memory deficits apparent in HD may result from degeneration in the ventrolateral frontal and dorsolateral prefrontal cortices, respectively. The following subsection deals with psychomotor speed, which is of great interest in HD due to the movement disorder that characterises the disease, and also due to its sensitivity in HD.

1.6.3. Psychomotor Speed

Psychomotor speed is the time an individual requires to process, prepare and execute a response to a stimulus. Alteration in psychomotor function may be amongst the earliest changes, supporting the idea that cognitive impairments of various kinds may develop at different points in the progression of the disease (Aylward et al., 1996; Nehl, Ready, Hamilton, & Paulsen, 2001; Snowden et al., 2002). Psychomotor speed has been classified as involving both cognitive and motor ability (Hinton et al., 2007; Peavy et al., 2010; Snowden et al., 2002); therefore, the distinction is somewhat artificial.

RT is a basic measure that has been used to assess psychomotor speed. Simple and choice RT tasks have been extensively employed in cognitive and experimental

psychology. Normally, simple RT tasks require participants to detect and respond to a stimulus by pressing a button, whereas choice RT tasks are more complex as they require the processing of more than one stimulus prior to response. Although both simple and choice RT tasks have been found to show significant differences between various patient groups and controls, choice RT are more demanding tasks, and therefore even healthy people are usually slower on choice RT tasks (Ponsford & Kinsella, 1992; van Zomeren & Brouwer, 1994). Although some studies in HD reported no differences between simple and choice RT tasks, nevertheless, HD participants have been found to be slower than other patient groups in both measures (Georgiou, Bradshaw, Phillips, Bradshaw, et al., 1995; Jahanshahi et al., 1993; Sprengelmeyer, Canavan, Lange, & Hömberg, 1995).

RT tasks may be useful for discriminating between different levels of HD severity, providing insights about motor and cognitive progression, and specifically about progression declines in psychomotor speed. Although RT tasks are simple and easy to measure, subjects may vary in their approach to these tasks. For example, one notably troublesome issue with RT tasks is the speed-accuracy trade-off. Typically, in RT tasks, participants are instructed to perform as quickly and as accurately as possible. Despite that, some people are compelled to emphasise speed over accuracy and others take the opposite approach and emphasise accuracy over speed. Thus, the results from these tasks may not always mean the same thing. With respect to their inherent nature, RT measures may reflect a more complex picture than perhaps is sometimes assumed, given how simple these tasks appear. The following section will address visuospatial processing, which is a fundamental functional domain in neuropsychology.

1.6.4. Visuospatial Processing

Visuospatial processing is defined as the spatial perception, recognition and analysis of visual information (Sack, 2010). Visuospatial deficits are well-documented in HD. These deficits may arise due to difficulty in appreciating positioning of objects in space and integrating them into a logically connected spatial framework, or due to impairments in the ability to perform mental operations on spatial constructs (Georgiou-Karistianis, 2009). Several visual perception tests, such as line orientation (Girotti, Marano, Soliveri, Geminiani, & Scigliano, 1988; Soliveri et al., 2002), road map (Snowden, Craufurd, Griffiths, Thompson, & Neary, 2001; Snowden et al., 2002), motion discrimination (O'Donnell et al., 2003, 2008), mental rotation (Lineweaver, Salmon, Bondi, & Corey-Bloom, 2005), cancellation (Arango-Lasprilla et al., 2006; Gómez-Tortosa, del Barrio, Barroso, & Garcia Ruiz, 1996), and circle tracing (Lemay et al., 2005; Say et al., 2011) have indicated that HD participants perform worse than controls. Circle tracing tasks, also discussed in the motor section earlier in this chapter, have been employed under direct and indirect conditions (Lemay et al., 2005; Say et al., 2011). Participants traced a circle on a tablet screen with (direct) and without (indirect) view of their hand. In the indirect condition, visual feedback on performance was given through a monitor. Both Lemay et al. (2005) and Say et al. (2011) found greater error rates in the indirect condition suggesting that the visuospatial demands of circle tracing may be greater than the motor demands.

Presymptomatic individuals also manifest visuospatial deficits (Brandt, Shpritz, Codori, Margolis, & Rosenblatt, 2002; Lawrence et al., 2000; Lemiere et al., 2004; Snowden et al., 2002). Although visuospatial functions are subserved by posterior cortical regions (Gómez-Tortosa et al., 1996), visuospatial deficits in HD have been typically attributed to striatal degeneration (Brandt et al., 2002; Snowden et al., 2002). Evidence of atrophy in the occipital and parietal cortices before symptom onset may suggest the involvement of these regions in visuospatial deficits in the early stages of disease. Language processing is discussed below as the last cognitive subsection.

1.6.5. Language Processing

Language processing refers to the way the brain processes speech and writing to understand it as language. Language disorders are not traditionally associated with HD, but increasing evidence suggests that language deterioration comprise impairments in production (Lepron et al., 2009; Murray, 2000; Péran, Démonet, Pernet, & Cardebat, 2003), comprehension (Murray & Stout, 1999; Saldert et al., 2010), rule application (De Diego-Balaguer et al., 2008; Teichmann, Dupoux, Kouider, & Bachoud-Levi, 2006; Teichmann et al., 2005), syntax (Murray & Lenz, 2001), and phonology (Teichmann et al., 2009). Despite that, a meta-analysis of studies that reported impairments in several cognitive domains in HD found that language skills were the least impaired (Zakzanis, 1998). Recent evidence suggests that the basal ganglia have a language-specific role that pertains to rule application and word retrieval (Longworth, Keenan, Barker, Marslen-Wilson, & Tyler, 2005; Teichmann et al., 2005).

In summary, cognitive changes are not uniform in HD, and their nature and time course, as well as how they present across individuals, varies considerably. Different cognitive functions are affected at different disease stages, and subtle decline of symptoms precede clinical diagnosis. Attention, which is one of the most prominent cognitive deficits in HD, and the subject of this thesis, is discussed in the following section. As part of this, prominent divided attention theories and the effects of HD and normal ageing on divided attention will also be described.

1.7. The Posner Model of Attention

Most people appreciate instinctively what attention is. Despite that, attention is a complex construct that has offered researchers many challenges. For the purposes of this thesis, attention is defined as the cognitive process that selectively concentrates on a preferred stimulus while overlooking other irrelevant stimuli (Sheridan, Solomont, Kowall, & Hausdorff, 2003). Attentional dysfunction is one of the cognitive features that has been consistently reported in HD. Several types of attentional deficits have been demonstrated including problems with visual attention (Couette et al., 2008), task-set switching (Aron, Watkins, et al., 2003), attention shifting (Georgiou et al., 1996), selective attention (Hester et al., 2004) and divided attention (Delval et al., 2008). Divided attention deficits have been reported prediagnosis (Mazzoni & Wexler, 2009) suggesting that attentional problems are a fundamental feature of the disease.

Evidence from neuroimaging and lesion studies suggests that different attentional functions are accomplished by separate anatomical networks. For example, Posner and Petersen (1990) proposed a distributed network model of attention with three attentional systems in the brain: (1) a posterior automatic attention system, which involves the posterior parietal cortex, superior colliculi and pulvinar nuclei of the thalamus, and which is thought to be activated when a person is required to allocate attention to visual space; (2) an anterior voluntary attention system, which involves the prefrontal cortex and the anterior cingulate, and is thought to be activated when a person is required to allocate attention to visual stend to or select one out of multiple streams of cognitive processing; and (3) a

vigilance system, which involves the locus coeruleus, the cholinergic system, the right prefrontal cortex and the intralaminar thalamic nuclei, and which is thought to be activated when a person has to maintain a vigilant or alert state.

Some evidence suggests that the anterior attention system, which involves the prefrontal cortex, may be more sensitive to the effects of increasing age (West & Bell, 1997), and possibly to the effects of HD and divided attention, since the prefrontal cortex has been implicated in both. Filoteo et al. (1995) used a visuoperceptual Posner-like divided attention paradigm, which involved the presentation of global-local stimuli, to investigate attention shifts in HD and to compare performance with participants with Parkinson's and Alzheimer's diseases. RT of HD and Alzheimer's participants were significantly slower than controls, therefore, all participants showed some kind of impairment on this task. However, unlike participants with Parkinson's and Alzheimer's, who demonstrated impairments in disengaging and maintenance of attention, respectively, HD participants did not manifest impairments in attention shifting between these hierarchical levels. This was interpreted as suggesting that the visuoperceptual deficits in these diseases may be related to different attentional mechanisms (Filoteo et al., 1995). One interpretation that the authors put forward is that HD participants may have a visuoperceptual impairment that is independent of shifting attention impairments. Alternatively, they suggested the possibility that HD participants are impaired in *engaging* visual attention, rather that *disengaging* and *moving* components of attention.

1.8. Theories of Divided Attention

Several competing theories have attempted to explain dual task interference (i.e., impaired attention due to attending two sources of information concurrently) in HD, and in ageing healthy populations. Based on the observation that performance, and more specifically speed, declines with age, Salthouse (1985, 1996) proposed the Processing Speed Theory. According to this theory, age-related decrements in dual task performance, and cognitive performance in general, are due to a general slowing in processing speed. There is ample evidence that older adults have slower RT compared with younger adults (Crossley & Hiscock, 1992; Kemper, Herman, & Lian, 2003; Kemper, Schmalzried, Herman, Leedahl, & Mohankumar, 2009). Furthermore, processing speed may be one of the earliest indicators of HD onset and is sensitive to striatal dysfunction (Aylward et al., 2004; Maroof, Gross, & Brandt, 2011; Snowden et al., 2002).

Other theories, known as resource or capacity theories, propose that individuals have a limited availability of mental resources. One of the most influential of these theories is Kahneman's Unitary Resource Theory (1973). This theory states that attention is a limited resource that can be allocated to a single task or can be divided between a number of tasks. Thus, two or more tasks can be processed simultaneously or through time-sharing, which is an efficient and timely allocation of processing resources to tasks (Johnson & Proctor, 2004). The available amount of attention varies depending on the task (e.g., harder tasks demand more attention), and the individual's motivation and arousal levels. In cases where the demand exceeds the amount of attentional capacity, allocation strategies are used to establish on which tasks the attention resource should be allocated. Nevertheless, the Unitary Resource Theory cannot explain why two tasks

that can be performed together with perfect time-sharing, may interfere when combined with a third task (Johnson & Proctor, 2004). Similarly, the Unitary Resource Theory cannot explain why two seemingly equally hard tasks can have totally different effects on a third task, with one of them interfering with the third task and the other not interfering (Johnson & Proctor, 2004).

These observations gave rise to a multiple resource view of attention. Perhaps the most widely accepted theory of this kind is Wickens's (2002, 2008) four-dimensional Multiple Resources Theory (see Figure 3). This theory proposes that multiple resources account for information processing depending on four dichotomous dimensions (the original theory proposed by Wickens had three dichotomous dimensions): (1) processing stages, including perception-cognition and response, (2) perceptual modalities, including visual and auditory, (3) visual channels, including ambient and focal, and (4) processing codes, including spatial and verbal. When two tasks share common resources on the four dichotomous dimensions, divided attention deteriorates and dual task performance is less efficient. Therefore, cross-dimensional tasks that have the same perceptual modality (e.g., visual-visual). Although this model has been widely accepted, it cannot explain dual task interference when cross-dimensional tasks are performed.

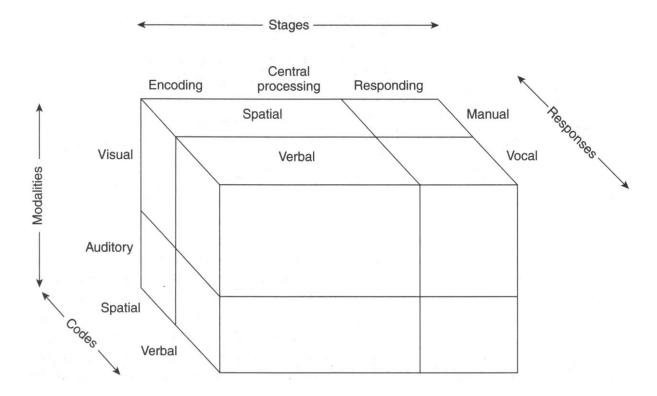


Figure 3. Wickens's (2002) four-dimensional Multiple Resources Theory (used with permission of the publisher).

Attentional deficits in HD have commonly been explained in terms of difficulty in allocating attentional resources (Delval et al., 2008; Georgiou-Karistianis, Churchyard, Chiu, & Bradshaw, 2002; Georgiou et al., 1996; Georgiou, Bradshaw, et al., 1997). This difficulty in resource allocation may be due to subcortical impairment and dysfunctional circuitry that links the basal ganglia with the frontal lobes (Georgiou et al., 1996). Some HD studies suggested that motor and cognitive circuits may not be dissociated (Delval et al., 2008) pointing towards a unitary resource framework. Other studies endorsed the notion that attention is a multidimensional system of related, but semi-independent processes (Müller et al., 2002; Sprengelmeyer, Lange, & Hömberg, 1995). There is no

study in either HD or ageing that has explicitly compared the unitary and multiple resources accounts.

In addition to processing speed and resource allocation theories, working memory architecture has also been used as a potentially useful framework for discussing divided attention impairments. According to Baddeley (2001), working memory consists of four components: the phonological rehearsal loop and the visuospatial sketchpad, which permit people to temporarily hold and manipulate verbal and visual information respectively; the episodic buffer, which integrates information and serves as an interface between working and long-term memory; and the central executive, which controls the deployment of attention and divided attention. Some overlap between working memory and multiple resources theories should be noted. Specifically, the concepts of phonological loop and visuospatial sketchpad proposed by working memory, and the verbal and spatial processing codes proposed by multiple resources theories, appear to be comparable. The central executive is usually seen as being similar to a central supervisory attention processor that schedules competing tasks (Norman & Shallice, 1980), and one of its main functions is to distribute attention in dual tasks (Sebastian, Menor, & Elosua, 2006). Working memory impairments that have been associated with HD (Brandt et al., 2002; Lemiere et al., 2004; Stout et al., 2011; Stout et al., 2007; Wolf et al., 2009) and ageing (Anguera, Reuter-Lorenz, Willingham, & Seidler, 2011; Kemper et al., 2003; Kemper et al., 2009) may reflect a limited capacity central executive. Studies with lesion patients and controls suggest that the central executive is implemented in the dorsolateral prefrontal cortex (Baddeley, 2003), and associated regions that have been found to have aberrant functional connectivity even in

presymptomatic HD (Wolf, Sambataro, Vasic, Schonfeldt-Lecuona, et al., 2008; Wolf, Sambataro, Vasic, Shonfeldt-Lecuona, et al., 2008).

1.9. Divided Attention Tasks versus Dual Tasks

Some confusion in the literature stems from the fact that the terms *divided attention task* and *dual task* are not clearly defined. In addition, a number of studies have used the two terms interchangeably (Azouvi et al., 2004; McDowd & Craik, 1988; Paré, Rabin, Fogel, & Pépin, 2009). Divided attention refers to the ability to respond simultaneously to two or more stimuli or tasks (Dannhauser et al., 2005). Divided attention tasks are separated into dual tasks and integration tasks. A dual task has two separate elements that require separate responses, such as driving a car and talking on a mobile phone at the same time. In contrast, an integration task also has two separate elements, but only a single response is required, for example comparing the kilometres left to approach a destination on a road sign with the kilometres displayed on a tour guide (Wickens & McCarley, 2008). What follows in the next section of this review focuses on *dual tasks* only, with the aim of considering evidence for whether responses to a single task are affected when a second response to a concurrent task is also required.

1.10. The Dual Task Paradigm

The dual task paradigm requires participants to perform two tasks concurrently (Armieri, Holmes, Spaulding, Jenkins, & Johnson, 2009). Typically, it involves the manipulation of the parameters of one task to vary difficulty level, and then examines whether changes in performance of a second, concurrent task, are observed (Rumbaugh & Washburn, 1996). Dual task paradigms have been used to evaluate trade-offs between

attentional demands in healthy individuals (Bherer et al., 2008; Hartley, Maquestiaux, & Silverman Butts, 2011) and in HD (Delval et al., 2008; Müller et al., 2002).

Previous research on divided attention suggested that dual task performance can be affected by three main factors: practice, task similarity and task difficulty. Practice can affect dual task performance, as it can lead to automatic, less controlled processing and reduced attentional load (Sarter & Turchi, 2002). When tasks become automatic their relationship with cognitive abilities declines (Ben-Shakhar & Sheffer, 2001). Furthermore, studies have found that similar tasks, which draw on the same resource pools, are more difficult to perform than dissimilar tasks that draw on different resource pools (Allport, 1980; McLeod, 1977; Navon & Gopher, 1979). Although task similarity is relatively easy to manipulate and test in the laboratory, when it comes to real life situations, it is much harder to determine how similar two tasks are (e.g., driving and playing tennis). In regards to task difficulty, Alberts et al. (2008) demonstrated that as dual task difficulty increased, cognitive and motor performance of individuals with Parkinson's disease deteriorated. Similar findings have been reported in ageing research (for a review see Woollacott & Shumway-Cook, 2002).

Divided attention performance has been found to improve with practice (Göthe, Oberauer, & Kliegl, 2007; McDowd, 1986), and decline with task difficulty (McDowd & Craik, 1988) in ageing research. Although practice effects have also been found in HD (Bachoud-Levi et al., 2001; Stout et al., 2012), the effect of practice, task difficulty and task similarity on divided attention in HD remains to be determined. The section below presents studies that have investigated divided attention in HD using the dual task paradigm.

1.11. Past Research on Dual Tasking in HD

To date, very limited systematic empirical research has investigated divided attention deficits in HD using the dual task paradigm. Among the few studies, Sprengelmeyer, Lange and Hömberg (1995) examined different aspects of attention, such as response flexibility, and intermodal integration, as well as divided attention in HD. Divided attention was tested with a visual-auditory dual task. For this task, participants were required to respond by pressing a button to a series of matrices when four Xs formed a square, and to a series of high and low pitched tones when a tone was followed by another tone of the same frequency. Results indicated that for both the HD and control groups, RT for the visual task was longer than for the auditory task. This finding may suggest that the visual task was more demanding as it required, amongst other things, preparation and execution of eye movements and visuo-perceptual processing, whereas the auditory task required only the detection of auditory targets. These authors additionally reported that HD was associated with slower RT on the visual task compared with controls, suggesting defective exploration of complex visual arrays or disordered visual perception. Although error rates were higher for HD participants in both the visual and the auditory tasks, the two types of tasks were not differentially affected. The authors suggested that this finding was due to visuo-perceptual or motor system deficits. Using the same divided attention task, Müller et al. (2002) also reported a similar pattern of significant differences in RT and error rates between HD and control groups. Both Sprengelmeyer et al. (1995) and Müller et al. (2002) advocated that attention is a multidimensional system of related, semi-independent processes.

Brown, Jahanshahi and Marsden (1993) tested bimanual movements in six HD participants, as well as participants with Parkinson's disease, cerebellar disease, and

healthy controls. The dual task involved a peg placement and a button pressing task. Although HD participants carried out the peg placement task equally well in the single and dual task conditions, their performance on the button pressing task was reduced in the dual task condition. That is, the repetitive, less-demanding button pressing task was compromised more than the attentional, more demanding peg placement task. Although the button pressing task was performed relatively automatically by controls, it is possible that it was attentionally demanding for HD participants, and therefore, more affected by a second, concurrent task. This study found some dual task interference when two uni-dimensional tasks (i.e., motor-motor) were performed concurrently, providing some support to the Multiple Resources Theory.

A dual task study that sought to investigate the efficiency of voluntary movement, and to assess if a simultaneous task would affect movement efficiency in HD, found that overall performance of HD participants did not differentially worsen when they were required to do two things at the same time (Georgiou, Phillips, et al., 1997). For this study, participants performed a motor task and a digit-recall task. For the motor task participants had to generate, with both hands separately, a series of vertical zig-zag strokes of small or large targets over short or long extents on a graphics tablet. For the digit-recall task the experimenter called out a random sequence of five numbers between 0 and 9. Participants were instructed to rehearse the digits while performing the strokes on the graphics tablet, and then to recall them in the order of presentation when they completed the motor task. Although HD participants were less able than controls to adjust movement execution to target size and stroke length, and they manifested deficits in voluntary movements, their overall performance did not deteriorate in the presence of a second, simultaneous task. The authors suggested that HD participants may have

covertly paced each of their movements along with each digit rehearsal. Another possibility may be that the digit-recall task did not stress the attentional system of HD participants to an extent that compromised performance of the motor task. In any case, results are in line with the predictions of the multiple resources framework, as there was no interference between cross-dimensional concurrent tasks (i.e., motor-verbal).

The majority of previous studies suggests that dual task performance is differentially affected in HD compared to controls. Significant differences have been found even with small sample sizes (i.e., Brown et al., 1993). However, the findings are somewhat difficult to interpret in relation to the stage of HD or HD progression, given varied subject characteristics in many studies. For example, variability in disease duration is quite large in some studies, such as Müller et al. (3-13 years) and Sprengelmeyer et al. (1-9 years). These studies have grouped together participants in different disease stages, making it impossible to characterise early or late neuropathological profiles.

The number of studies that have investigated dual task performance in HD is limited, and the factors that contribute to dual task deficits in this disease are not well understood. Observing dual task performance in healthy individuals may assist in better understanding deficits in HD by allowing comparisons between the two groups. The following section presents dual task studies conducted with healthy subjects.

1.12. Dual Tasking in Neurologically Healthy Individuals

It is well-documented that dual tasks can result in task interference and consequently in impaired task performance even in healthy individuals. In a recent study, Armieri, Holmes, Spaulding, Jenkins and Johnson (2009) investigated the impact of a working memory task on gait by manipulating difficulty and articulation requirements of the working memory task. Healthy adults were presented with a sequence of three, five or seven digits and instructed to memorise this sequence. They were then asked to walk on a gait carpet, and then to report the digits at the end of the walking task. Articulation was also manipulated by requesting participants to continually rehearse digits either silently or loudly. Gait parameters suggested that the higher the levels of difficulty were, the greater the effect of articulation (i.e., velocity decreased). These findings suggest that manipulating difficulty of tasks may induce dual task interference as suggested by the Unitary Resource Theory.

Driven by Posner's (1966) suggestion, that attentional requirements of cognitive tasks can be manipulated by varying task difficulty, Pellecchia (2003) examined postural sway in healthy participants, who stood on a balance platform under four concurrent task conditions: digit reversal, digit classification, counting backward by threes and standing quietly. Results suggested that the concurrent cognitive tasks affected postural sway, with counting backward by threes having the greatest impact than all other cognitive task conditions as indicated by participants' high error rates. Therefore, different cognitive tasks may affect postural sway differently. Collectively, these studies suggest that performance on two concurrent tasks depends on the difficulty as well as on the type of the tasks.

Other studies have investigated brain activation while healthy participants performed dual tasks in order to unravel the neural circuitry underlying information processing during dual tasking. An fMRI study assessed the ability to divide attention between an auditory and a visual task in healthy males (Loose, Kaufmann, Auer, & Lange, 2003). This study used the visual-auditory dual task that has been used by Sprengelmeyer et al. (1995) and that was described previously in this review. Participants performed the tasks separately and concurrently. The findings indicated that RT for the visual task was longer than for the auditory task. The authors suggested that longer visual RT was due to particular characteristics of the stimuli. Specifically, in the visual task participants were required to discern a specific pattern within the stimulus, whereas in the auditory task they simply had to ascertain whether or not the tone was a stimulus, therefore, the auditory task was easier than the visual task. With more relevance to the question of dual task performance, RT during the dual task was significantly longer than in the single tasks. In the single task conditions (visual or auditory), the brain activity in the corresponding primary and secondary sensory areas (visual or auditory cortex) was activated. In contrast, in the dual task condition, the activation in the primary and secondary visual and auditory cortices decreased, and the left prefrontal area was activated, suggesting that the left prefrontal cortex may be important in the execution of controlled processing when two tasks had to be performed simultaneously. These results provide support that the prefrontal cortex is implicated in the central executive and regulates attention.

In another fMRI study, the posterior dorsolateral prefrontal cortex and the lateral parietal cortex were activated during dual task performance (Koechlin, Basso, Pietrini, Panzer, & Grafman, 1999). The aim of this study was to pinpoint the brain regions that are involved in dual task and delayed response performance. In the control condition, participants were presented with uppercase letters from the word *tablet*, and they had to decide whether or not two successively presented letters were also successive in the word *tablet*. In the dual task condition, participants had to respond both to uppercase

and lowercase letters. Similarly with Loose et al. (2003), the key brain structure showing consistent activation during dual tasking was the prefrontal cortex. On balance, the findings of Loose et al. (2003) and Koechlin et al. (1999) suggest that the prefrontal cortex may be an important region in the execution of controlled processing during divided attention performance, and also support the view that the prefrontal cortex is involved in the control of attention and information processing.

A large body of dual task research has focused on age differences. There is conflicting evidence as to whether older adults perform worse than younger adults when they have to divide their attention between two tasks. For example, McPhee, Scialfa, Dennis, Ho, and Caird (2004) investigated age differences in individual's ability to perform a visual search for traffic signs during a simulated conversation. Sixteen younger (M = 22.62) and 16 older adults (M = 64.19) performed the visual search task under single and dual task conditions in low- and high-cluttered scenes. An age-related increase in speed and error rates was shown in dual task conditions, especially with high-cluttered scenes, suggesting that not only the type of tasks, but also the level of difficulty may affect divided attention with increasing age.

A meta-analysis of 33 studies using speed as the performance measure, and 30 studies using accuracy, investigated the relationship between divided attention and ageing (Verhaeghen, Steitz, Sliwinski, & Cerella, 2003). As expected, the results indicated that both younger and older adults performed worse on dual task conditions than on single task conditions. Importantly, looking across the studies, Verhaeghen et al. (2003) found that the effect of dual tasking on speed and accuracy was larger in older than in younger adults, over and above the effect expected from age-related slowing. Despite that, Verhaeghen et al. (2003) also found that age effects on dual tasking were independent of task difficulty, suggesting that task difficulty may not be an important factor in explaining age differences in dual task performance.

Despite this, there is evidence that age differences may increase with greater task difficulty as well as task complexity. For instance, McDowd and Craik (1988) manipulated task difficulty to investigate age differences in participants who were asked to perform auditory and visual choice RT tasks as single and dual tasks. Both choice RT tasks had easy and hard conditions; therefore, participants completed four dual task combinations (easy auditory choice RT with easy visual choice RT, easy auditory choice RT with hard visual choice RT, hard auditory choice RT with easy visual choice RT, and hard auditory choice RT with hard visual choice RT). In a second study, using visual choice RT, complexity was also increased by manipulating the number of choices (two-, four- and eight-choice RT). Findings of both studies suggested that older adults had slower choice RT compared with younger adults, and their performance decreased in the harder dual task conditions. The authors suggested that mental operations may slow with increased age, and this slowing is exaggerated in dual tasks that require a greater number of operations.

Despite the many findings of age effects on dual tasking, some studies have found no age differences in divided attention. Della Sala, Foley, Beschin, Allerhand and Logie (2010) examined the effects of divided attention in a large sample (n = 436) of healthy adults whose age ranged between 16 and 88 years. Participants performed visual tracking and digit span tasks concurrently. For the tracking task participants had to draw a line through successive circles printed on a sheet of paper, whereas for the digit span

task they were presented with a series of numbers at an individual's digit span, and had to recall them immediately. The results showed negligible reductions in dual task performance, indicating that healthy individuals do not manifest difficulty in performing concurrent tasks in this set of conditions.

To determine whether there are age differences in divided attention, a study employed 9 tasks either alone or simultaneously (de Ribaupierre & Ludwig, 2003). There were 9 dual tasks, including target detection and perceptual clarification tasks, tracking and digit span tasks similar to those used by Della Sala et al. (2010), monitoring task (colour and size), and semantic judgment and word recall tasks. Eighty-one younger (M = 23.17) and 86 older adults (M = 72.24) participated. Age-related attentional costs were manifested for the monitoring (colour and size), target detection, perceptual, and tracking tasks, and were decreased after controlling for single task performance. In contrast with previous studies that found age effects on dual tasking, most of the age effects on dual tasks were accounted for by the age effects observed in the single task conditions, suggesting that divided attention performance does not worsen with increasing age.

In summary, past studies that investigated age differences in divided attention have yielded mixed results. However, although older adults are typically slower than younger adults when performing dual tasks (Crossley & Hiscock, 1992; de Ribaupierre & Ludwig, 2003), the effect of ageing on *accuracy* of dual task performance is less clear, with previous studies indicating no differences between younger and older adults (Hawkins, Kramer, & Capaldi, 1992), older adults making more errors (Cho, Gilchrist, & White, 2008; Hein & Schubert, 2004; Mutter & Goedert, 1997; Springer et al., 2006),

and older adults making fewer errors (Bherer et al., 2008; Kemper et al., 2009). An important drawback is that most previous studies have *either* provided measures of speed *or* accuracy. People may experience speed-accuracy trade-offs when performing tasks, and therefore, faster RT may be associated with increased error rates or vice versa (Smith & Brewer, 1995). Therefore, an investigation of both speed and accuracy may be more informative than either speed or accuracy alone. In addition, some studies (e.g., Armieri et al., 2009) used some tasks only under dual task conditions, therefore no baseline measure was provided.

1.13. Does the Type of Concurrent Task Matter?

Previous research both with healthy elderly (Beauchet, Dubost, Aminian, Gonthier, & Kressig, 2005) and Parkinson's disease patients (Galletly & Brauer, 2005) has indicated that dual task performance depends on the type of concurrent tasks. Beauchet et al. (2005) investigated the influence of verbal and arithmetic tasks on gait in older healthy adults. They found that stride time variability depended on the type of verbal task, with variation increasing significantly when participants performed the arithmetic task, but not when performing the verbal task. Galletly and Brauer (2005) asked Parkinson's disease participants to perform six motor and cognitive tasks while being seated, and also when walking 10 m with and without visual cues. For the motor task, participants had to use one of their thumbs to press a button on an electronic counter as many times as possible. For the cognitive tasks, they had to count backward by threes, and generate as many different words starting with F and S. Results suggested that stride length decreased with each of the cognitive tasks, but not with the motor task. Participants had significantly higher error rates in the cognitive tasks compared with the motor task suggesting that the motor task was the least difficult task. A review article on attention

and postural control and gait in healthy and balance-impaired individuals further supported that attentional demands of balance control depend on the type of concurrent task as well as its difficulty (Woollacott & Shumway-Cook, 2002).

Although research with healthy subjects and some patient groups suggests that dual tasking depends on the type of tasks involved and their difficulty, it remains unclear whether dual task performance is respective to the type of concurrent tasks in HD. Delval et al. (2008) found that HD participants had greater difficulty performing a cognitive task (counting backward) or walk while performing a motor task (carrying a tray with four glasses) than controls. Contrary to predictions based on Wickens's (2002) Multiple Resources Theory, HD participants had greater difficulty performing the cognitive task while walking (cognitive-motor dual task) than the motor task while walking (motor-motor dual task). A phenomenon, in which a person stops walking while talking, has been commonly observed in HD. This finding has been observed also in older adults (Faulkner et al., 2006), and suggests that highly automatic tasks, such as walking, may put demands on attentional load both in HD and older healthy adults.

1.14. Aims and Research Outline

To date, only a few studies have investigated divided attention in HD using the dual task paradigm (Delval et al., 2008; Müller et al., 2002; Sprengelmeyer, Lange & Homberg, 1995), and in each of these, only one dual task combination has been investigated. This may be an important limitation considering that there is some evidence that the type of concurrent task does matter in dual tasking. Understanding the difficulties that individuals with HD and older adults have when they attempt to perform two tasks at the same time has important theoretical and clinical implications, and will provide insights into the nature and control of dual task mental processes. With regard to HD, if dual task measures are found that are sensitive and clinically relevant, such tests may also become useful in clinical trials to test for cognitive effects of candidate drugs to treat HD. Overall, it will be practically important to provide a strong picture of the difficulties individuals with HD may have in performing concurrent tasks, as interventions using either cognitive training or strategies may be developed to reduce the impact of dual task requirements on function.

Therefore, the overall aim of the research presented in this thesis was to systematically investigate dual task performance in individuals with HD, and in neurologically healthy individuals across younger and older adulthood, by using a battery of tasks that pair different system modalities. Four sets of tasks were selected taking into consideration theories of divided attention and findings from past research studies. In particular, the dual tasks used in this thesis pair tasks that specifically vary in their input (e.g., visual) and output (e.g., motor) modalities. Because previous research suggested that dual task interference may emerge under more challenging conditions, each task was examined using two levels of difficulty: easy and hard. According to the Multiple Resources Theory (Wickens, 2002, 2008), tasks using separate input and output modalities should be performed concurrently quite efficiently as they draw on different cognitive resources. These findings will be the first documentation of dual task performance using several different pairs of tasks in either HD or at younger and older points within the lifespan. The value of examining both multiple pairs of tasks and two difficulty levels for each task lies in the fact that performance may deteriorate with task difficulty, and may be affected differently depending on the combination of tasks. Thus, it will help to form a more comprehensive picture of the impact of dual task requirements using different modalities in association with HD and with ageing.

To achieve the aims of this research, two separate studies were conducted. The first study (Chapters 2 and 3) was designed to investigate dual task performance in younger and older healthy adults. It was conducted to characterise the particular dual task combinations and difficulty levels in a general (non-pathological) population, thereby helping to establish the precise methodology for examining dual task performance in HD. Based on previous findings, it was predicted that older adults would be slower across all conditions compared with younger adults, and that speed would also decrease with higher task difficulty levels for both groups with older adults being more compromised than younger adults. It was also expected that error rates would increase with increased task difficulty for both groups. Supporting these hypotheses would suggest that older adults are worse in dual tasking relative to younger adults, and their performance further deteriorates with increased task difficulty. These results would provide support for a unitary resource framework.

The second study (Chapters 4 and 5) was designed to investigate dual task performance in individuals in the early stages of HD. It was predicted that HD participants would be slower and more error-prone across all conditions compared with healthy age-, sex- and education-matched controls. Consistent with the literature and our predictions in the ageing study, it was also expected that speed would decrease and error rates would increase with greater task difficulty for HD and control groups. Similar to the first study, supporting these hypotheses would suggest that HD participants are worse in dual tasking relative to healthy controls, and their performance further deteriorates with increased task difficulty. These results would also provide support for a unitary resource framework.

Note that this thesis is presented in line with Monash University guidelines and requirements as a "thesis by publication". Some chapters are comprised of published papers or papers under review. Therefore, due to the required format of the thesis, there is some unavoidable degree of overlap and repetition in content, such as methodology, for some chapters. The final chapter (Chapter 6) provides an overall discussion of the findings, limitations and implications of the studies, future directions and conclusion.

Chapter 2

Age Differences in Dual Task Performance

Preamble to Paper

Chapter 2 presents the first empirical study of this thesis. It examines upper limb proprioception ability in younger and older adults during dual task performance. The effect of ageing on dual task performance is well-documented; however, there has been a clear bias in the literature towards research of *lower* limb function. Therefore, this study examined how upper limb proprioceptive ability is affected by age and by the demands of a concurrent cognitive task. We examined dual task performance in younger and older adults using circle tracing and serial subtraction tasks. The results are discussed in the context of resource allocation theories, specifically the Unitary Resource and the Multiple Resources theories.

Declaration for Thesis Chapter 2

Declaration by candidate

In the case of Chapter 2, the nature and extent of my contribution to the work was the following:

Nature of contribution	Extent of
	contribution (%)
Conception and design of the study, attainment of ethics approval and	80%
ongoing reporting requirements, review of relevant literature and writing of	
manuscript	

The following co-authors contributed to the work. Co-authors who are students at Monash University must also indicate the extent of their contribution in percentage terms:

Name	Nature of contribution	Extent of contribution (%) for student co-authors only
Prof Julie C. Stout	Contributed to development of ideas	
	and critical revision of the paper	
Prof Nellie Georgiou-Karistianis	Contributed to development of ideas	
	and critical revision of the paper	

Candidate's Signature

Declaration by co-authors

The undersigned hereby certify that:

- (1) the above declaration correctly reflects the nature and extent of the candidate's contribution to this work, and the nature of the contribution of each of the co-authors.
- (2) they meet the criteria for authorship in that they have participated in the conception, execution, or interpretation, of at least that part of the publication in their field of expertise;
- (3) they take public responsibility for their part of the publication, except for the responsible author who accepts overall responsibility for the publication;
- (4) there are no other authors of the publication according to these criteria;
- (5) potential conflicts of interest have been disclosed to (a) granting bodies, (b) the editor or publisher of journals or other publications, and (c) the head of the responsible academic unit; and
- (6) the original data are stored at the following location(s) and will be held for at least five years from the date indicated below:

Location(s) School of	School of Psychology and Psychiatry, Monash University, Australia		
	Signature	Date	
Prof Julie C. Stout			
Prof Nellie Georgiou-Karistianis			

Date

Age and Task Difficulty Differences on Dual Tasking Using Circle Tracing and Serial Subtraction Tasks

Eleftheria Vaportzis, Nellie Georgiou-Karistianis and Julie C. Stout

School of Psychology and Psychiatry, Monash University

Acknowledgments

Financial support for this study was obtained from the School of Psychology and Psychiatry, Monash University. On behalf of all authors, the corresponding author states that there is no conflict of interest.

Address correspondence to Julie C. Stout, School of Psychology and Psychiatry, Monash University, Wellington Road, Clayton, Victoria 3800, Australia.

E-mail:

Abstract

The aim of this study was to investigate upper limb proprioceptive ability in younger and older adults under dual task conditions. Twenty-eight younger (18-30 years) and 28 older (> 60 years) healthy adults performed circle tracing and serial subtraction tasks separately and concurrently. Tasks had two levels of difficulty: easy and hard. The circle tracing task included direct (easy) and indirect (hard) visual feedback conditions, and it was paired with serial subtraction by twos (easy) or by threes (hard). We found that older adults were significantly slower than younger adults across all conditions, and had significantly greater dual task costs when they performed circle tracing with easy serial subtraction. Higher levels of task difficulty were associated with slower speed in both groups. We found no age differences in accuracy. Participants either traded speed for accuracy or accuracy for speed regardless of age group. Overall, the findings suggest that speed and accuracy may be affected differently during dual tasking. In addition, older adults may rely more extensively on proprioceptive feedback to guide upper limb movement compared with younger adults.

Keywords: Divided attention; Proprioception; Attention allocation; Speed-accuracy trade-off; Visuomotor integration.

Introduction

Dual tasking refers to the performance of two tasks simultaneously, such as cooking while talking. Although the effect of aging on dual tasking is well-documented, in the aging literature there has been a clear bias towards research of the *lower* limbs, and few studies have investigated *upper* limb performance (e.g., Crossley & Hiscock, 1992; Van Impe, Coxon, Goble, Wenderoth, & Swinnen, 2011). Furthermore, despite evidence indicating deterioration of proprioception (awareness of one's body position) with age, few studies have investigated proprioception in the upper limbs (for a review see Goble, Coxon, Wenderoth, Van Impe, & Swinnen, 2009).

To date, research on aging and dual tasking using upper limb tasks has yielded inconsistent results. For example, Crossley and Hiscock (1992) required 30 younger (20-40 years), 30 middle-aged (41-65 years) and 32 older (66-90 years) adults to perform a speeded finger tapping task with and without a concurrent cognitive task that was examined at two levels of difficulty. The decrement in tapping rate increased linearly with age from single to dual tasks, and tapping was slowed more by hard than by easy cognitive tasks. In addition, older adults' dual task performance was disproportionately affected by hard tasks, suggesting that age differences may emerge under more challenging conditions. This later finding was further supported by Kemper, Herman and Lian (2003), who examined speaking while performing several concurrent tasks (separately), including simple and complex finger tapping. Results showed that older (70-80 years) adults manifested *greater dual task costs* in the complex finger tapping task compared with younger (18-28 years) adults.

Kemper, Schmalzried, Herman, Leedahl and Mohankumar (2009) further assessed language production in 40 younger (18-34 years) and 40 older (65-85 years) adults who simultaneously performed a tracking task. Contrary to past research that has typically found *older* adults to incur greater dual task costs (Verhaeghen, Steitz, Sliwinski, & Cerella, 2003), in this study it was the *younger* adults who showed increased dual task costs in measures of tracking and language production. Kemper et al. (2009) suggested that slower, less complex speech protected older adults from dual task costs, whereas younger adults, who had faster, more complex speech, were more susceptible to dual task demands. These results were explained in terms of possible differential executive control strategies between different age groups.

A recent imaging study with 20 younger (20.7-32.6 years) and 20 older (62.3-76.5 years) adults found no dual task interference during circle drawing and serial addition in threes (Van Impe et al., 2011). Age-related increased brain activation was evident in the fronto-parietal network only during circle drawing, suggesting that compared to younger adults, older adults may rely more extensively on proprioceptive information to guide upper limb movement. The authors suggested that either over-learned tasks are protected against healthy aging effects or that serial addition may not have been challenging enough to elicit significant age differences. Another imaging study found that neural substrates responsible for dual task performance were similar between younger (19-25 years) and older (65-77 years) adults during colour and letter identification dual tasks, involving the medial prefrontal and lateral fronto-parietal networks (Hartley, Jonides, & Sylvester, 2011). However, this study also found that older adults had higher brain activation levels in occipital and polar prefrontal cortex during dual task performance. Thus, brains of older adults may work differently in order

to perform at accuracy levels similar to younger adults', possibly demonstrating that neural compensation is needed with aging to successfully maintain low levels of dual task interference.

Previous dual task studies report measures of speed and/or accuracy of performance. Older adults are typically slower than younger adults when performing dual tasks, even after age-related slowing is accounted for (Crossley & Hiscock, 1992; de Ribaupierre & Ludwig, 2003). Compared to speed, the effect of aging on *accuracy* of dual task performance is less clear, with previous studies indicating no differences between younger and older adults (Hawkins, Kramer, & Capaldi, 1992), older adults making more errors (Cho, Gilchrist, & White, 2008; Hein & Schubert, 2004; Mutter & Goedert, 1997; Springer et al., 2006), and older adults making fewer errors (Bherer et al., 2008; Kemper et al., 2009). In our view, an important drawback is that most previous studies have *either* provided measures of speed *or* accuracy. We know that people may experience speed-accuracy trade-offs when performing tasks, and therefore, faster reaction times may be associated with increased error rates or vice versa (Smith & Brewer, 1995). Therefore, an investigation of both speed and accuracy may be more informative than either speed or accuracy alone.

With regard to theoretical frameworks of dual tasking, competing theories have been proposed. For example, the Unitary Resource Theory proposes that attention is a *single, limited capacity resource* that depends on several factors, including task difficulty, and it can be allocated to a single task or divided between different tasks (Kahneman, 1973). Thus, in dual tasking, if one task is hard and requires a large proportion of this limited attentional resource, there will be little of this resource available to support the

performance of the other task, and performance will deteriorate. This theory also postulates that compared to younger adults, older adults have reduced attentional resources, and therefore, some operations are more demanding for older adults (Burke & Shafto, 2008).

In contrast to this view, there is evidence that two tasks can be performed concurrently even when difficulty is manipulated (Wickens & McCarley, 2008). This observation led to the Multiple Resources Theory, which proposes that there are *separate* resource pools (e.g., a visual resource pool, an auditory resource pool), each of which can be divided among concurrent tasks. According to this theory, interference occurs when tasks make concurrent demands on the same resources (Wickens, 2002; Wickens & McCarley, 2008). For example, the Multiple Resources Theory predicts minimal interference between a task that is presented visually (and requires manual response), and a concurrent task that is presented auditorily (and requires vocal response). Empirical evidence exists for and against both theories (e.g., Parkes & Coleman, 1990; Young & Stanton, 2007) suggesting that the theoretical basis for dual tasking requires additional development.

An important question is how upper limb proprioception is affected by age and by the demands of a concurrent task. To address this question, we examined dual task performance in younger and older adults by using circle tracing and serial subtraction tasks. We selected circle tracing to specifically tax upper limb proprioceptive ability. Evidence suggests changes in upper limb proprioception with age, as reflected by greater errors and prolonged, irregular movements (Adamo, Alexander, & Brown, 2007). Therefore, we expected that circle tracing

performance of older adults would be more compromised compared with younger adults. We selected serial subtraction because it has been previously used as an attention demanding task (Ingram et al., 2000), and is an effective distractor task of attention (Nicolson & Fawcett, 1990). In support of the Multiple Resources Theory, interference between circle tracing and serial subtraction should be minimal, because these tasks are likely to be processed by separate modalities-responses (visual-manual for circle tracing and auditory-vocal for serial subtraction). Unlike most previous studies that manipulated difficulty of only one of the tasks, we manipulated difficulty of both circle tracing and serial subtraction tasks. In support of the Unitary Resource Theory, manipulating task difficulty would induce resource allocation limitations, and therefore, age-related differences would emerge under the more challenging conditions. In view of previous findings, we expected older adults to be slower across all task conditions compared with younger adults, and speed of both groups to decrease with greater task difficulty. We also expected error rates of both groups to increase with greater task difficulty, and older adults to incur greater dual task costs than younger adults.

Method

Participants

Sixty younger (18-30 years) and older (61-90 years) healthy adults participated. Four older adults were excluded due to either low scores on the Montreal Cognitive Assessment (MoCA; Nasreddine et al., 2005) or inability to perform some of the tasks. The final sample consisted of 28 younger (15 females, M = 22.21, SD = 3.14) and 28 older (15 females, M = 71.96, SD = 7.84) participants. The MoCA is a 30-point cognitive screening test designed to detect cognitive impairment, and the suggested cut-off point (also adopted in this study) was 26. Other screening tests included the

Wechsler Test of Adult Reading (WTAR; Wechsler, 2001), and the Inventory of Depressive Symptomatology-Self-report (IDS-SR; Rush, Carmody & Reimitz, 2006). The WTAR is used to estimate verbal IQ, and is composed of 50 words that have irregular letter to sound translations. The IDS-SR is a 30-item questionnaire that assesses the severity of depression within the past 7 days for all symptom domains of major depression according to the Diagnostic and Statistical Manual-IV (American Psychiatric Association, 1994). Scores can range between 0 (= no depressive symptoms) and 84 (= very severe depressive symptoms).

The younger and older groups did not differ significantly on the MoCA ($M_Y = 28.07$, $SD_Y = 1.58$; $M_0 = 27.04$, $SD_0 = 1.87$), t(54) = 1.79, p = .08; WTAR ($M_Y = 107.50$, $SD_Y = 8.55$; $M_0 = 110.32$, $SD_0 = 5.89$), t(54) = -.143, p = .16; and IDS-SR ($M_Y = 11.96$, $SD_Y = 7.09$; $M_0 = 13.97$, $SD_0 = 8.34$), t(54) = -.435, p = .67. Education level was also assessed based on the International Standard Classification of Education (ISCED) system, according to which 0 indicates pre-primary education and 6 second stage tertiary education (UNESCO, 1997). Older adults had significantly fewer years of formal education than younger adults ($M_Y = 5.14$, $SD_Y = .35$; $M_0 = 4.21$, $SD_0 = .95$), t(54) = 4.81, p < .001. Education was used as a covariate in all experimental analyses, but was not found to be significant in any analysis.

All participants gave written informed consent, and self-reported that they were free of neurological disease, psychological disorders, and upper limb impairments. They had normal or corrected-to-normal vision and hearing, and they were fluent in English. Ethics approval was granted by the Monash University Human Research Ethics Committee.

Dual Task Description and Study Procedure

Participants were tested individually in a quiet room, and were advised to perform all tasks as quickly and as accurately as possible. For the dual task procedure, we combined circle tracing and serial subtraction tasks that both included an easy and a hard condition. The circle tracing task has been previously described by Say et al. (2011), who adapted a task described in Lemay, Fimbel, Beuter and Chouinard (2005). It was administered on a Lenovo ThinkPad® X61 (Morrisville, NC, USA) tablet, with the tablet positioned in front of the participants at comfortable reach. The tablet displayed a 90 mm diameter circle with a 5 mm thick white annulus on a gray background. For the hard circle tracing conditions, a desktop monitor, which was placed approximately 70 cm in front of the participants and displayed the same white annulus on a gray background, was also used. Participants traced the circle using a stylus that left a blue line indicating the circle tracing path trajectory. They started at the vertical apex of the circle, and traced it with their preferred hand in a clockwise direction. In the easy (direct) condition, participants could observe their arm and the circle tracing path on the tablet screen. In the hard (indirect) condition, participants' tracing arm and tablet were obscured by a box covering the tablet and a cloak covering the box and their arm. Thus, in contrast with the easy condition during which participants could *directly* observe their performance on the tablet, in the hard condition they could only monitor their progress *indirectly* on the desktop monitor.

For the serial subtraction task, participants were given 20 s and were instructed to count backward by twos (easy condition) or by threes (hard condition). Starting numbers ranged between 100 and 86 and half the trials commenced on an odd number.

Design and Statistical Analyses

Participants performed a practice circle tracing trial in the easy condition, and then, four single tasks separately and in the following order: (1) easy circle tracing, (2) hard circle tracing, (3) easy serial subtraction and (4) hard serial subtraction. Each circle tracing condition was repeated three times for 20 s each, and each serial subtraction condition was performed twice for 20 s each. Next, participants performed three trials of every possible combination of the circle tracing together with the serial subtraction tasks: (1) easy circle tracing with easy serial subtraction, (2) easy circle tracing with hard serial subtraction, and (4) hard circle tracing with easy serial subtraction, and (4) hard circle tracing with easy serial subtraction, and (4) hard circle tracing with hard serial subtraction. Each dual task trial lasted 20 s.

The circle tracing and serial subtraction dual task set was one of four sets of tasks that participants performed as part of a larger study, and the order of the four sets was counterbalanced across participants. In contrast, we did not counterbalance the eight conditions that make up the circle tracing and serial subtraction dual task set; all participants performed the eight task conditions *in the same order*. There were several reasons for this. First, with regard to the circle tracing and serial subtraction set, we wanted to ensure that hard tasks preceded by easy tasks as there is a learning component for each of these tasks. Secondly, because of the large number of conditions within each of the four sets of tasks, a task design containing all possible permutations of task order within and across sets would have required a much larger sample size. We also felt that within a task set, by presenting the easier tasks and task combinations first, we could maintain a level of control over the participants' previous experiences with the tasks, which could benefit them similarly as they reached the harder levels. The dependent variables for circle tracing were speed (total number of rotations in 20 s), and accuracy (number of errors per rotation). Errors were defined as the stylus moving beyond either the inner or outer edge of the white annulus for > 100 ms. For serial subtraction, the dependent variable was accuracy (percentage of incorrect responses). We also calculated the rate of responses by dividing the time to complete the task (20 s) by the number of responses per participant.

For circle tracing, trials with values more than 3.5 standard deviations from the individual's mean were removed prior to computing overall means and standard deviations for *speed* and for *error rates* (see Table 1). We computed a 2 X 2 X 3 mixed-model ANOVA with the between factor, age (young, old), and two within factors, circle tracing difficulty (easy, hard), and serial subtraction difficulty (none, easy, hard) for both speed and error rates. We report Greenhouse-Geisser corrected degrees of freedom due to violations of the sphericity assumption. Significant interactions of interest were followed with planned comparisons. Bonferroni post hoc tests were conducted for all post hoc pairwise comparisons. Alpha was set at 0.05.

Dual task costs were also computed to quantify participants' ability to perform two tasks simultaneously. We used a 2 X 2 X 2 mixed-model ANOVA with the between factor, age (young, old), and two within factors, circle tracing difficulty (easy, hard), and serial subtraction difficulty (easy, hard). As per previous studies (de Ribaupierre & Ludwig, 2003; Kemper et al., 2003) *dual task costs* were computed by calculating the relative ratio of the single task to dual task performance using the following formula: dual task cost = (single task-dual task)/single task. Positive dual task costs denote a decrease from single to dual task conditions. Finally, to examine speed-accuracy trade-

offs, we performed Pearson's correlations between speed and error rates for each of the

six circle tracing task separately for younger and older participants.

Table 1

Means (Standard Deviations) Across All Task Conditions for Younger and Older Participants

	Trac Spe	eing eed	Tra Err	<u> </u>	Tracing (Spe	1000	Subtra Err	action ors	Subtraction Rate	
	Young	Old	Young	Old	Young	Old	Young	Old	Young	Old
E Single Task	7.33 (3.42)	5.10 (2.59)	7.45 (6.83)	5.59 (5.92)			0.84 (1.73)	1.65 (2.51)	1.10 (.33)	1.17 (.27)
H Single Task	3.42 (1.63)	2.21 (1.28)	7.46 (3.87)	4.97 (3.75)			3.23 (4.50)	5.25 (7.11)	1.91 (.90)	2.08 (.81)
E Tracing-	5.27	3.11	4.86 2.96		.25 .37		$\begin{array}{ccc} 1.10 & 1.66 \\ (2.10) & (2.81) \end{array}$		1.38 1.66	
E Subtraction	(2.48)	(1.71)	(4.50) (3.32)		(.22) (.21)				(.53) (.45)	
E Tracing-	4.85	3.21	4.05	2.70	.30	.35	0.52	1.19	1.29	1.65
H Subtraction	(2.37)	(1.79)	(3.43)	(3.22)	(.26)	(.25)	(1.29)	(2.95)	(.47)	(.58)
H Tracing-	2.74	1.63	4.65	3.32	.16	.21	3.39	5.23	2.18	2.38
E Subtraction	(1.16)	(.83)	(3.04)	(3.04)	(.20)	(.22)	(5.13)	(6.61)	(1.04)	(.82)
H Tracing-	2.53	1.65	3.90	3.14	.21	.21	2.59	4.28	2.18	2.46
H Subtraction	(.97)	(.83)	(2.70)	(2.70)	(.21)	(.20)	(2.59)	(5.58)	(1.27)	(1.01)

Note. E = Easy; H = Hard. DTC = Dual task cost.

Results

In the following section, we first describe the circle tracing task performance (single and dual tasks), followed by dual task costs and speed-accuracy trade-offs. Finally, we briefly present serial subtraction performance.

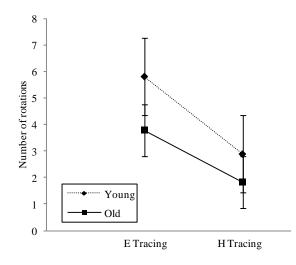


Figure 1. Number of rotations on the circle tracing task (easy, hard) as a function of age (young, old). E = Easy; H = Hard. Standard error bars are included.

As seen in Figure 1, older adults were slower than younger adults, and both groups were slower in the hard circle tracing conditions. Figure 2 shows that dual tasks (circle tracing with easy and hard serial subtraction) were performed slower than single tasks (no serial subtraction). Indeed, a three way ANOVA with speed as the dependent variable revealed significant main effects of age, F(1,54) = 12.98, p < .001, $\eta^2 = .19$, circle tracing, F(1.00,54.00) = 153.94, p < .001, $\eta^2 = .74$, and serial subtraction, F(1.23,66.70) = 58.60, p < .001, $\eta^2 = .52$. More importantly, we found a significant interaction between age and circle tracing, F(1.00,54.00) = 5.77, p = .02, $\eta^2 = .10$. Pairwise comparisons revealed that older adults were significantly slower when performing easy (p < .001) and hard (p < .001) circle tracing compared with younger adults. In addition, both groups were significantly (p < .001) faster in easy circle tracing compared with hard circle tracing. We also found a significant interaction between circle tracing. We also found a significant interaction between circle tracing. The also found a significant interaction between circle tracing and serial subtraction, F(1.28,69.13) = 34.43, p < .001, $\eta^2 = .39$. Pairwise comparisons revealed that performance on circle tracing (easy or hard) was significantly

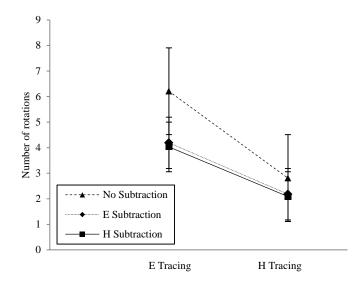


Figure 2. Number of rotations on the circle tracing task (easy, hard) as a function of serial subtraction difficulty (none, easy, hard). E = Easy; H = Hard. Standard error bars are included.

Both age groups maintained similar levels of accuracy across both levels of circle tracing task difficulty. The same ANOVA with error rates as the dependent variable showed a significant main effect of serial subtraction, F(1.36,54.00) = 40.09, p < .001, $\eta^2 = .42$, but no other significant main effects or interactions. Pairwise comparisons revealed that participants made significantly (p < .001) more errors in the absence of serial subtraction than when they performed easy or hard serial subtraction concurrently. In addition, error rates were significantly (p = .04) higher when circle tracing was performed concurrently with easy than hard serial subtraction.

Dual task costs for speed were greater in the easy circle tracing conditions compared with the hard circle tracing conditions, as suggested by a significant main effect of circle tracing, F(1.00,54.00) = 22.59, p < .001, $\eta^2 = .29$. We also found a significant two way interaction involving age and serial subtraction, F(1.00,54.00) = 4.79, p = .03, $\eta^2 = .08$ (see Figure 3). Pairwise comparisons revealed that older participants had marginally significantly (p = .05) greater dual task costs than younger participants when they performed circle tracing concurrently with easy serial subtraction compared with hard serial subtraction. We did not calculate dual task costs for error rates as both groups made fewer errors in the dual task conditions compared with the single task conditions.

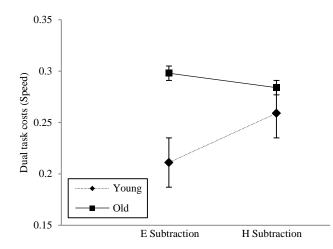


Figure 3. Dual task costs (speed) on the circle tracing task (easy, hard) as a function of age (young, old) and serial subtraction difficulty (none, easy, hard). E = Easy; H = Hard. Standard error bars are included.

Regardless of age group, individual participants performed the tasks either more slowly and made fewer mistakes (compromised speed for accuracy) or faster and with more errors (compromised accuracy for speed). Figure 4 clearly shows significant (p < .001) positive correlations for both groups across all circle tracing conditions.

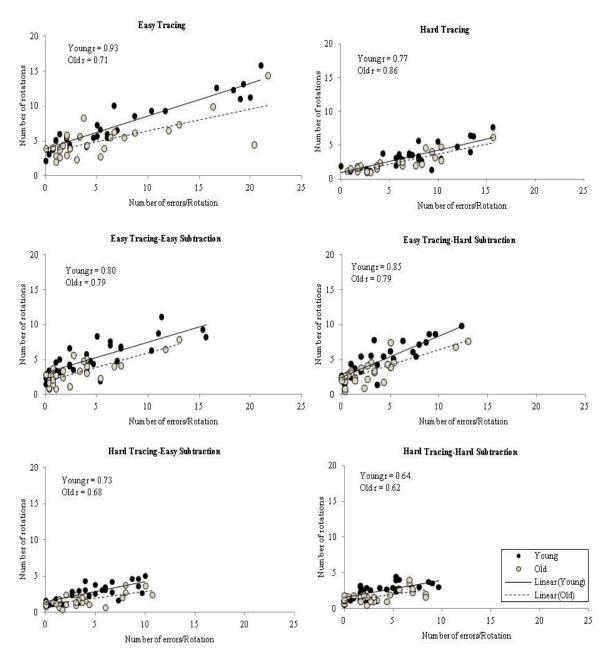


Figure 4. Correlational analyses between speed and error rates for all circle tracing conditions for younger and older participants. All correlations were significant (p < .001) suggesting speed-accuracy trade-offs for both groups.

Error rates for serial subtraction were below 6% for both groups. Due to this low error rate, no formal statistical analyses were performed. However, the data in Table 1 suggest that error rates for both younger and older participants increased from the single to the dual task conditions, and were greater when serial subtraction was performed concurrently with hard circle tracing rather than easy circle tracing. Response rate of older participants was slower than younger participants across all conditions, and when serial subtraction was paired with hard circle tracing rather than easy circle tracing task.

Discussion

The results of this study must be considered in light of three types of effects, including those associated with aging, those associated with task difficulty, and those associated with single versus dual tasks. In general, we found age-related differences in speed, but not in accuracy on circle tracing with serial subtraction tasks, highlighting the importance of investigating both speed and accuracy measures in dual task research. Circle tracing speed decreased with task difficulty and under the dual task conditions, whereas lower error rates were associated with higher levels of task difficulty and dual task performance.

Consistent with our hypothesis and previous studies that have used other combinations of tasks (Crossley & Hiscock, 1992), we found older age to be associated with slower performance in both easy and hard circle tracing, probably due to generalized psychomotor slowing, which is a characteristic of normal aging. Both groups were slower in circle tracing when they performed serial subtraction concurrently, corroborating that the addition of the serial subtraction task to the circle tracing task was associated with greater cognitive load than when the circle tracing task was performed on its own. Despite this, compared to the easy serial subtraction task, hard serial subtraction did not have differentially greater impact on circle tracing speed. This latter result may suggest that hard serial subtraction may not have been challenging enough to trigger greater decrease in speed than easy serial subtraction.

In line with past research (Crossley & Hiscock, 1992; Kemper et al., 2003) and with the Unitary Resource Theory, higher levels of task difficulty were associated with slower circle tracing performance in both groups. That is, both younger and older adults performed more slowly hard circle tracing, which used visual occlusion of the arm with only indirect feedback of the tracing path, compared to the easy circle tracing, in which the arm and its tracing path could be freely seen. This finding is consistent with Say et al. (2011) who also found slower performance in the indirect circle tracing may be explained by an additional sensorimotor transformation requirement that is necessary for integrating visual and proprioceptive information into a joint reference frame (Ingram et al., 2000; Messier & Kalaska, 1997; Say et al., 2011). Additionally, this differential finding for the direct and indirect circle tracing conditions may imply that the demands of the visuospatial element of the task (which varied for easy versus hard conditions).

Interestingly, the easy circle tracing task speed appeared to be more susceptible to dual task interference than the hard circle tracing task speed, and this finding was consistent across both groups. Our interpretation of this is that the hard circle tracing task may be more robust to the interference of the second task because performance is already

somewhat slow, thus allowing participants to incorporate the added demand of the second task without additional cost to their speed. With respect to the effect of aging, the dual task costs of performing circle tracing concurrently with easy serial subtraction was greater. However, with the hard serial subtraction task, performance of the two age groups was more similar. Overall, we interpret this pattern of effects as indicating that as tasks get more difficult, younger adults may adopt a more cautious approach, perhaps because they recognize the need of a slower performance speed to achieve reasonable accuracy. Alternatively, younger adults may be unable to perform the tasks more quickly due to their greater attentional requirements. In any case, the decrement in speed associated with task difficulty was greater for younger compared to older adults who were already performing the task more slowly.

In contrast to our hypotheses, the higher level of task difficulty was not associated with increased error rates on circle tracing. The greater proprioceptive demands of the hard circle tracing task seemed to only influence speed, but not errors for both groups. Therefore, the reduction in speed from easy to hard circle tracing seemed to engender sufficient control over performance, so that accuracy was maintained across both levels of difficulty for both younger and older adults.

Surprisingly, both groups performed the largest number of errors in circle tracing when it was performed as a single task (i.e., without serial subtraction), and the fewest errors when it was performed concurrently with hard serial subtraction. Consistent with this finding may be the explanation that because of the ease with which participants could perform the single tasks, perhaps they gave less effortful attention in single tasks compared to dual tasks, and therefore, performance was relatively more governed by automatic processes. In turn, under these more automatized performance conditions, errors may not have been as deliberately avoided, and thus occurred at higher rates. On the contrary, in dual task conditions, performance may have been necessarily more controlled due to the higher level of task difficulty, allowing participants to exercise better control over accuracy of performance, and in turn reducing error rates.

Overall, our results suggest that older adults may possibly rely more extensively on proprioceptive feedback to guide upper limb movement. Age-related deterioration in sensorimotor processing may affect upper limb position awareness, especially in harder task conditions (Adamo et al., 2009; Adamo et al., 2007; Goble & Brown, 2008). Despite that, older adults were significantly slower than younger adults in the easy circle tracing conditions as well, when visual feedback was given directly. Past research reported differential brain activation in older and younger adults during performance of motor (Goble et al., 2010; Heuninckx, Wenderoth, & Swinnen, 2008; Van Impe, Coxon, Goble, Wenderoth, & Swinnen, 2009) and cognitive tasks (Cabeza, 2001; Grady, 2008). These findings are typically explained in terms of increased functional demands exerted on the aging brain. With advancing age cognitive functions may become inflexible, and automaticity may decline (Maquestiaux, Lague-Beauvais, Ruthruff, Hartley, & Bherer, 2010). It is possible that the circle tracing task placed greater cognitive demands on older adults, even during the easy conditions, so that movement became less automated due to increased attentional resources required to maintain reasonable accuracy.

This study showed some resource sharing between two seemingly different tasks suggesting that the visual and auditory modalities *and* the manual and vocal responses are not utterly separate as the Multiple Resources Theory holds. Rather, our results

favor the explanatory framework of the unitary resource pool, although not conclusively, as we found deficits in dual task performance in speed, but not in error rates. In line with the Unitary Resource Theory (Kahneman, 1973), with increased task difficulty, the speed of both groups was reduced and dual task interference was induced. In further support of this theory, we found that compared with younger adults, performance of older adults was slower possibly because they reached a point where available attentional resources were not sufficient to perform the tasks quicker than younger adults (Burke & Shafto, 2008; Murphy, Craik, Li, & Schneider, 2000). However, we found no age-related differences or dual task interference in accuracy of performance. Therefore, our study demonstrates the importance of taking into account both measures in dual task research as each measure may yield different results.

We should point out certain limitations of our study. Firstly, most of the participants in the younger group were university students, whereas only about half of the older participants had completed a higher education degree. Despite this, analyses suggested that there were no significant education effects on dual task performance. Secondly, although we asked participants to perform the tasks as quickly and as accurately as possible, there may have been an aging effect on the balance between the competing goals of speed and accuracy. That is, participants may have intentionally emphasized either speed or accuracy, and this tendency may have been associated with the age grouping to which the participant belonged. Whether the speed-accuracy trade-off effects that we observed were more a result of conscious than automatic processes is unknown and remains an important question. Finally, another limitation was that conditions were not counterbalanced for single and dual tasks and therefore, results can only be interpreted in the context of single tasks occurring first and dual tasks occurring after all single tasks had been performed. Despite this, participants were faster in the single task conditions, and their performance deteriorated with increased task difficulty in the dual task conditions. Thus, if anything, counterbalancing may have increased the magnitude of the observed differences.

In summary, this study has demonstrated that older adults are differentially affected compared with younger adults when circle tracing is performed concurrently with serial subtraction, a finding broadly consistent with other studies using different combinations of tasks to examine dual task effect. Older adults were slower than, but as accurate as younger adults, partially supporting the Unitary Resource Theory. Both groups showed speed-accuracy trade-offs sustaining our view that both speed and accuracy measures are imperative when examining dual task performance. We also found age differences in dual task costs for some, but not all conditions, suggesting that dual task interference may emerge under certain conditions, and possibly during certain tasks. Further studies investigating dual tasking using upper limb motor with cognitive tasks are warranted and represent a potentially strong research framework.

References

- Adamo, D. E., Alexander, N. B., & Brown, S. H. (2009). The influence of age and physical activity on upper limb proprioceptive ability. *Journal of Aging and Physical Activity*, 17, 272-293.
- Adamo, D. E., Martin, B. J., & Brown, S. H. (2007). Age-related differences in upper limb proprioceptive acuity. *Perceptual and Motor Skills*, 104, 1297-1309.
- American Psychiatric Association (1994). *Diagnostic and statistical manual of mental disorders* (4th ed.). Washington, DC: American Psychiatry Association.
- Bherer, L., Kramer, A. F., Peterson, M. S., Colcombe, S., Erickson, K., & Becic, E. (2008). Transfer effects in task-set cost and dual-task cost after dual-task training in older and younger adults: Further evidence for cognitive plasticity in attentional control in late adulthood. *Experimental Aging Research*, 34, 188-219.
- Burke, D. M., & Shafto, M. A. (2008). Language and aging. In F. I. M. Craik & T. A. Salthouse (Eds.), *The handbook of aging and cognition* (pp. 373-443). New York: Psychology Press.
- Cabeza, R. (2001). Cognitive neuroscience of aging: Contributions of functional neuroimaging. *Scandinavian Journal of Psychology*, *42*, 277-286.
- Cho, C.-Y., Gilchrist, L., & White, S. (2008). A comparison between young and old adults in their ability to rapidly sidestep during gait when attention is divided. *Gerontology*, 54, 120-127.
- Crossley, M., & Hiscock, M. (1992). Age-related differences in concurrent-task performance of normal adults: Evidence for a decline in processing resources. *Psychology and Aging*, 7, 499-506.
- de Ribaupierre, A., & Ludwig, C. (2003). Age differences and divided attention: Is there a general deficit? *Experimental Aging Research, 29*, 79-105.

- Goble, D. J., & Brown, S. H. (2008). Upper limb asymmetries in the matching of proprioceptive versus visual targets. *Journal of Neurophysiology*, *99*, 3063-3074.
- Goble, D. J., Coxon, J. P., Van Impe, A., De Vos, J., Wenderoth, N., & Swinnen, S. P. (2010). The neural control of bimanual movements in the elderly: Brain regions exhibiting age-related increases in activity, frequency-induced neural modulation, and task-specific compensatory recruitment. *Human Brain Mapping, 31*, 1281-1295.
- Goble, D. J., Coxon, J. P., Wenderoth, N., Van Impe, A., & Swinnen, S. P. (2009). Proprioceptive sensibility in the elderly: Degeneration, functional consequences and plastic-adaptive processes. *Neuroscience and Biobehavioral Reviews*, 33, 271-278.
- Grady, C. L. (2008). Cognitive neuroscience of aging. Annals of the New York Academy of Sciences, 1124, 127-144.
- Hartley, A. A., Jonides, J., & Sylvester, C.-Y. C. (2011). Dual-task processing in younger and older adults: Similarities and differences revealed by fMRI. *Brain* and Cognition, 75, 281-291.
- Hawkins, H. L., Kramer, A. F., & Capaldi, D. (1992). Aging, exercise, and attention. *Psychology and Aging*, 7, 643-653.
- Hein, G., & Schubert, T. (2004). Aging and input processing in dual-task situations. *Psychology and Aging, 19*, 416-432.
- Heuninckx, S., Wenderoth, N., & Swinnen, S. P. (2008). Systems neuroplasticity in the aging brain: Recruiting additional neural resources for successful motor performance in elderly persons. *Journal of Neuroscience Methods*, 28, 91-99.

Ingram, H. A., van Donkelaar, P., Cole, J., Vercher, J.-L., Gauthier, G. M., & Miall, R.C. (2000). The role of proprioception and attention in a visuomotor adaptation task. *Experimental Brain Research*, 132, 114-126.

Kahneman, D. (1973). Attention and effort. New Jersey: Prentice-Hall.

- Kemper, S., Herman, R. E., & Lian, C. H. T. (2003). The costs of doing two things at once for young and older adults: Talking while walking, finger tapping, and ignoring speech or noise. *Psychology and Aging*, 18, 181-192.
- Kemper, S., Schmalzried, R., Herman, R., Leedahl, S., & Mohankumar, D. (2009). The effects of aging and dual task demands on language production. *Aging, Neuropsychology, and Cognition, 16*, 241-259.
- Lemay, M., Fimbel, E., Beuter, A., & Chouinard, S. (2005). Sensorimotor mapping affects movement correction deficits in early Huntington's disease. *Experimental Brain Research*, 165, 454-460.
- Maquestiaux, F., Laguë-Beauvais, M., Ruthruff, E., Hartley, A., & Bherer, L. (2010). Learning to bypass the central bottleneck: Declining automaticity with advancing age. *Psychology and Aging*, 25, 177-192.
- Messier, J., & Kalaska, J. F. (1997). Differential effect of task conditions on errors of direction and extent of reaching movements. *Experimental Brain Research*, 115, 469-478.
- Murphy, D. R., Craik, F. I. M., Li, K. Z. H., & Schneider, B. A. (2000). Comparing the effects of aging and background noise on short-term memory performance. *Psychology and Aging*, 5, 323-334.
- Mutter, S. A., & Goedert, K. M. (1997). Frequency discrimination vs frequency estimation: Adult age differences and the effect of divided attention. *The Journal of Gerontology*, *52B*, P319-P328.

- Nasreddine, Z. S., Phillips, N. A., Bediriam, V., Charbonneau, S., Whitehead, V.,
 Collin, I., . . . Chertkow, H. (2005). The Montreal Cognitive Assessment, MoCA:
 A brief screening tool for mild cognitive impairment. *Journal of the American Geriatrics Society*, 53, 695-699.
- Nicolson, R. I., & Fawcett, A. J. (1990). Automaticity: A new framework for dyslexia research? *Cognition*, 35, 159-182.
- Parkes, A. M., & Coleman, N. (1990). Route guidance systems: A comparison of methods of presenting directional information to the driver. In E. J. Lovesey (Ed.), *Contemporary ergonomics*. London: Taylor & Francis.
- Rush, A. J., Carmody, T., & Reimitz, P.-E. (2006). The Inventory of Depressive Symptomatology (IDS): Clinician (IDS-C) and Self-Report (IDS-SR) ratings of depressive symptoms. *International Journal of Methods in Psychiatric Research*, 9, 45-59.
- Say, M. J., Jones, R., Scahill, R. I., Dumas, E. M., Coleman, A., Dar Santos, R. C., . . . Investigators, t. T.-H. (2011). Visuomotor integration deficits precede clinical onset in Huntington's disease. *Neuropsychologia*, 49, 264-270.
- Smith, G. A., & Brewer, N. (1995). Slowness and age: Speed-accuracy mechanisms. *Psychology and Aging*, 10, 238-247.
- Springer, S., Giladi, N., Peretz, C., Yogev, G., Simon, E. S., & Hausdorff, J. M. (2006). Dual-tasking effects on gait variability: The role of aging falls, and executive function. *Movement Disorders*, 21, 950-957.
- UNESCO. (1997). International Standard Classification of Education from http://www.uis.unesco.org/ev.php?ID=7433_201&ID2=D0_TOPIC

- Van Impe, A., Coxon, J. P., Goble, D. J., Wenderoth, N., & Swinnen, S. P. (2009). Ipsilateral coordination at preferred rate: Effects of age, body side and task complexity. *Neuroimage*, 47, 1854–1862.
- Van Impe, A., Coxon, J. P., Goble, D. J., Wenderoth, N., & Swinnen, S. P. (2011). Age-related changes in brain activation underlying single- and dual-task performance:
 Visuomanual drawing and mental arithmetic. *Neuropsychologia*, 49, 2400-2409.
- Verhaeghen, P., Steitz, D. W., Sliwinski, M. J., & Cerella, J. (2003). Aging and dualtask performance: A meta-analysis. *Psychology and Aging*, 18, 443-460.
- Wechsler, D. (2001). *Wechsler Test of Adult Reading*. San Antonio: The Psychological Corporation.
- Wickens, C. D. (2002). Multiple resources and performance prediction. *Theoretical Issues in Ergonomics Science*, 3, 159-177.
- Wickens, C. D., & McCarley, J. S. (2008). Applied attention theory. Boca Raton: Taylor & Francis.
- Young, M. S., & Stanton, N. A. (2007). Miles away: Determining the extent of secondary task interference on simulated driving. *Theoretical Issues in Ergonomics Science*, 8, 233-253.

Chapter 3

A Comparison of Dual Tasks in Ageing

Preamble to Paper

Chapter 2 established that older adults are differentially affected compared with younger adults when circle tracing is performed concurrently with serial subtraction. This chapter sought to further extend the investigation of dual task performance in ageing by using two dual task sets that varied in difficulty and complexity. This paradigm provided a way to further explore whether age-related differences in dual task performance can be amplified due to increased task difficulty and complexity.

We employed two dual task sets: a simple dual task set that paired simple choice RT with digit forward, and a complex dual task set that paired complex choice RT with digit backward. Our findings provide information about the effects of both task difficulty and complexity on dual task performance in ageing, and have important implications for the Processing Speed Theory.

Declaration for Thesis Chapter 3

Declaration by candidate

In the case of Chapter 3, the nature and extent of my contribution to the work was the following:

Nature of contribution	Extent of contribution (%)
Conception and design of the study, attainment of ethics approval and ongoing reporting requirements, review of relevant literature and writing of manuscript	80%

The following co-authors contributed to the work. Co-authors who are students at Monash University must also indicate the extent of their contribution in percentage terms:

Name	Nature of contribution	Extent of contribution (%) for student co-authors only
Prof Julie C. Stout	Contributed to development of ideas	
	and critical revision of the paper	
Prof Nellie Georgiou-Karistianis	Contributed to development of ideas	
	and critical revision of the paper	

Candidate's Signature

Declaration by co-authors

The undersigned hereby certify that:

- (1) the above declaration correctly reflects the nature and extent of the candidate's contribution to this work, and the nature of the contribution of each of the co-authors.
- (2) they meet the criteria for authorship in that they have participated in the conception, execution, or interpretation, of at least that part of the publication in their field of expertise;
- (3) they take public responsibility for their part of the publication, except for the responsible author who accepts overall responsibility for the publication;
- (4) there are no other authors of the publication according to these criteria;
- (5) potential conflicts of interest have been disclosed to (a) granting bodies, (b) the editor or publisher of journals or other publications, and (c) the head of the responsible academic unit; and
- (6) the original data are stored at the following location(s) and will be held for at least five years from the date indicated below:

Location(s) School	of Psychology and Psychiatr	y, Monash University, Australia
	Signature	Date
Prof Julie C. Stout		
Prof Nellie Georgiou-Karistianis		

Date

Dual Task Performance in Normal Aging: A Comparison of Choice Reaction Time Tasks

Eleftheria Vaportzis, Nellie Georgiou-Karistianis, Julie C. Stout*

School of Psychology and Psychiatry, Faculty of Medicine, Nursing and Health Sciences, Monash University, Clayton, Victoria, Australia

Abstract

This study examined dual task performance in 28 younger (18–30 years) and 28 older (>60 years) adults using two sets of choice reaction time (RT) tasks paired with digit tasks. Set one paired simple choice RT with digit forward; set two paired complex choice RT with digit backward. Each task within each set had easy and hard conditions. For the simple choice RT, participants viewed single letters and pressed a specified keyboard key if the letter was X or Z or a different key for other letters (easy). For the hard condition, there were 4 target letters (X, Z, O, Y). Digit forward consisted of 4 (easy) or 5 (hard) digits. For the complex choice RT, participants viewed 4×4 matrices of Xs and Os, and indicated whether four Xs (easy) or four Xs or four Os (hard) appeared in a row. Digit backward consisted of 3 (easy) or 4 (hard) digits. Within each set, participants performed every possible combination of tasks. We found that in the simple choice RT tasks older adults were significantly slower than, but as accurate as younger adults. In the complex choice RT tasks, older adults were significantly less accurate, but as fast as younger adults. For both age groups and both dual task sets, RT decreased and error rates increased with greater task difficulty. Older adults had greater dual task costs for error rates in the simple choice RT, whereas in the complex choice RT, it was the younger group that had greater dual task costs. Findings suggest that younger and older adults may adopt differential behavioral strategies depending on complexity and difficulty of dual tasks.

Citation: Vaportzis E, Georgiou-Karistianis N, Stout JC (2013) Dual Task Performance in Normal Aging: A Comparison of Choice Reaction Time Tasks. PLoS ONE 8(3): e60265. doi:10.1371/journal.pone.0060265

Editor: Kevin Paterson, University of Leicester, United Kingdom

Received November 12, 2012; Accepted February 24, 2013; Published March 21, 2013

Copyright: © 2013 Vaportzis et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Funding: Financial support for this study was obtained from the School of Psychology and Psychiatry, Monash University. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Competing Interests: The authors have declared that no competing interests exist.

* E-mail:

Introduction

Choice reaction time (RT) tasks have been routinely used in aging research [1-8]. They are potent for discriminating between different age groups [1,7,9], are more sensitive measures of agerelated differences in psychomotor performance compared with simple RT tasks [4,10], and correlate significantly with higherorder cognitive processes in younger and older adults [8]. Previous studies have employed choice RT tasks to investigate the effect of dual tasking across various age groups [11-14]. The general agreement is that choice RT slows with aging and with increased task difficulty, which allegedly reflects competition for attentional resources. However, most previous aging studies have examined the effect of choice RT tasks on postural balance in healthy individuals and manipulated one of the dual tasks only [11,13]. Our understanding of the effect of aging on cognitive task performance under different levels of dual task difficulty remains limited. Extending this area of research allows us to tease apart the various mental operations that deteriorate with increased age, and how they may be amplified by task difficulty and complexity.

There is some evidence that age-related differences in performance are minimal at lower levels of task demand; as task demand increases, performance of older adults declines relative to that of younger adults [15]. This finding is also predicted by the Compensation-Related Utilization of Neural Circuits Hypothesis [CRUNCH; 16]. According to CRUNCH, the aging brain recruits more neural resources due to processing inefficiencies in order to achieve equivalent performance to that of younger adults'

PLOS ONE | www.plosone.org

brains [16,17]. CRUNCH predicts that this compensatory neural activation is efficient at low levels of task demand, however, with higher levels of task demand, age-related differences emerge [17].

Some studies investigated age-related dual task effects under different levels of task difficulty. For example, McDowd and Craik (1988) paired cognitive choice RT tasks and manipulated task difficulty to investigate age differences in participants who were required to perform auditory and visual choice RT tasks on their own and concurrently. Both choice RT tasks had easier and harder conditions producing four dual task combinations (easy auditory choice RT with easy visual choice RT; easy auditory choice RT with hard visual choice RT; hard auditory choice RT with easy visual choice RT; hard auditory choice RT with hard visual choice RT). In a second study, using visual choice RT, complexity was further increased by manipulating the number of choices (two-, four- and eight-choice RT). Results across both studies showed that older adults had slower choice RT compared with younger adults, and their performance further deteriorated under the harder dual task conditions. There was some support for an age-related decrease in dual task costs, which amplified with increased task complexity. The authors concluded that age differences are likely to be amplified by task difficulty and complexity, perhaps because mental operations slow with increased age. This slowing is exaggerated in dual task conditions that require a greater number of operations, providing a promising avenue in which to examine the effects of increased task complexity.

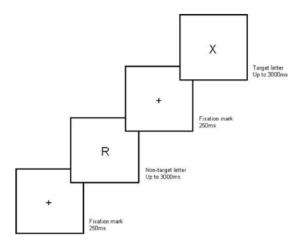


Figure 1. A non-target (R) and a target (X) trial of the simple choice RT task. doi:10.1371/journal.pone.0060265.g001

The generalized slowing, observed with increased age, is predicted by the Processing-Speed Theory. This theory postulates that age-related differences, observed during cognitive task performance, are likely to be underpinned by changes in processing speed [18]. According to this theory, age-related differences should be more pronounced in more cognitively demanding tasks, which are assumed to embody several simpler cognitive processing stages. Past research has suggested that RT becomes slower and more variable with increased age; a finding supported by longitudinal studies [5,7]. However, when measuring accuracy, the effect of age is remarkably mixed. Some studies have reported no differences in error rates between younger and older adults [19], younger adults making fewer errors [20-24] or more errors [25,26]. It should be noted, however, that a limitation of several previous studies is that they either reported RT or error rates, but not both. This presents a potential limitation since including both variables offers a more holistic view of dual task performance than viewing speed and accuracy individually, allowing speed-accuracy trade-offs to be taken into account.

In light of previous findings, we sought to investigate whether age-related differences in dual task performance emerge when choice RT tasks are performed concurrently with cognitive tasks, and whether they are more pronounced with increased task complexity and difficulty. We extended past research by employing and comparing two sets of dual tasks that differed in their degree of complexity. The first task combination paired simple choice RT with digit forward (termed the simple dual task set), and the second combination paired complex choice RT with digit backward (termed the complex dual task set). We selected digit forward and backward, because both have been previously used to assess attention and working memory [27], and are comparable to each other, but vary in complexity. Previous studies have suggested that older adults perform well on short-term memory tasks that require passive storage of information (e.g., digit forward), whereas age-related impairments emerge in working memory tasks that require participants to not only hold information in memory, but also perform an operation (e.g., digit backward) [28]. Therefore, age differences are expected to be minimal in digit forward, but greater in digit backward. We also manipulated the difficulty of each task within the dual task sets, by adopting easy and hard conditions for both the choice RT and

PLOS ONE | www.plosone.org

2

Dual Task Performance in Normal Aging

digit tasks. We predicted that older adults would be slower across all task conditions compared with younger adults, and that RT would be slower with higher levels of task difficulty across both age groups. Based on previous findings and the Processing-Speed Theory, age - related differences in RT were predicted to be more pronounced in the more complex dual task set. We also predicted that error rates would be higher with increased task difficulty across both groups.

Methods

Participants

Participants were 28 younger (18–30 years) and 32 older (61– 90 years) adults. Four older participants were excluded due to either low scores on the Montreal Cognitive Assessment [MoCA; 29] or inability to perform some of the tasks. The final sample comprised 28 younger (15 females, M=22.21, SD=3.14) and 28 older (15 females, M=71.96, SD=7.84) adults. The MoCA is a 30-point cognitive screening test that emphasizes executive functioning and attention. We adopted the suggested cut-off of 26 for mild impairment. The average MoCA scores were not significantly different between the two groups (MY = 28.07, SDY = 1.58; MO = 27.04, SDO = 1.87), t(54) = 1.79, p = .08.

Participants were also screened with the Wechsler Test of Adult Reading [WTAR; 30]. The WTAR consists of 50 words that have irregular letter to sound translations, and provides an estimate of verbal IQ by emphasizing previous word knowledge for correct pronunciations. There was no significant difference in the WTAR scores for the two groups (MY = 107.50, SDY = 8.55; MO= 110.32, SDO = 5.89), t(54) = -.143, p = .16. The Inventory of Depressive Symptomatology-Self-report [IDS-SR; 31] was also administered to assess depression severity within the past 7 days for all criterion domains of major depression according to the Diagnostic and Statistical Manual-IV [32]. Scores can range between 0 and 84, with lower scores indicating no depressive symptoms and higher scores very severe depressive symptoms. We found no differences in the IDS-SR scores for the two groups (MY = 11.96, SDY = 7.09; MO = 13.97, SDO = 8.34), t(54) = -.435, p = .67. Education level was assessed based on the International Standard Classification of Education [ISCED; 33] system (e.g., 0 = pre-primary education; 6 = second stage tertiary education). Younger participants had significantly more formal education than older participants, t(54) = 4.81, p<.001; years of education was used as a covariate in all analyses.

Ethics approval was granted by the Monash University Human Research Ethics Committee. All participants gave written informed consent and reported that they had normal or correctedto-normal vision and hearing, and that that they were free of neurological disease, psychological disorders, and upper limb

0	0	0	х	0	0	0	0
х	х	х	х	0	0	X	X
х	0	х	0	x	x	X	0
0	х	0	0	x	x	0	X

Figure 2. Target stimuli of the complex choice RT task conditions. On the left matrix, four Xs appear in a row (easy or hard conditions); on the right matrix, four Os appear in a row (hard condition).

doi:10.1371/journal.pone.0060265.g002

		CVIATION	of or younder			CACED III						
	Simple Choice RT (RT)	. (RT)	Simple Choice RT (Errors)	RT (Errors)	Digit Forward (Errors)	d (Errors)	Complex C	Complex Choice RT (RT)	Complex Choice RT (Errors)	ce RT (Errors)	Digit Backward (Errors)	d (Errors)
	Voung 0	old	Young	old	Young	OId	Young	pio	Young	old	Young	Old
E Single Task	496 61	618	3.17	4.05	<mark>00</mark> .	00.	1615	1697	7.50	21.72	7.85	6.42
	(78) (8	(83)	(2.52)	(3.82)	(00)	(.00)	(475)	(463)	(7.51)	(10.71)	(8.75)	(8.2.6)
H Single Task	518 651	1	3.21	2.46	5.00	5.00	2168	2235	13.33	24.16	17.14	20.71
	(73) (8)	(87)	(2.71)	(2.36)	(2.93)	(7.45)	(644)	(633)	(7.59)	(8.63)	(16.06)	(21.59)
E Choice RT-E Digit	613 801	1	3.65	4.36	1.61	3.86	2425	2745	16.66	36.30	11.18	14.36
	(123) (1	(173)	(3.48)	(4.50)	(4.06)	(6.05)	(502)	(581)	(9.51)	(12.74)	(14.93)	(11.64)
E Choice RT-H Digit	663 80	801	3.84	3.66	5.86	4.57	2431	2647	22.23	35.55	13.43	12.24
	(179) (179)	(174)	(3.76)	(2.59)	(11.50)	(7.75)	(580)	(909)	(12.36)	(10.29)	(14.84)	(15.49)
H Choice RT-E Digit	639 79	798	4.84	5.79	13.16	13.43	2521	2609	20.95	32.96	29.80	30.94
	(120) (1	(1.2.1)	(3.96)	(5.78)	(15.53)	(15.10)	(572)	(519)	(13.11)	(10.91)	(28.06)	(27.26)
H Choice RT-H Digit	695	866	6.79	7.82	14.70	14.97	2611	2755	24.10	38,88	30.77	26.67
	(194) (2	(211)	(3.80)	(4.56)	(16.55)	(15.83)	(432)	(398)	(14.12)	(10.86)	(29.29)	(22.71)
Note. RT = Reaction time; E = Easy; H doi:10.1371/journal.pone.0060265.t001	Note. RT = Reaction time; E = Easy; H = Hard. doi:10.1371/journal.pone.0060265.t001	łard.										

Table 1. Means (and standard deviations) of younger and older adults across all tasks

PLOS ONE | www.plosone.org

3

Dual Task Performance in Normal Aging

impairments. They were also fluent in English, and their MoCA, WTAR and IDS-SR scores were all within the normal range.

Dual Task Description

Participants performed two sets of dual tasks: the simple dual task set paired simple choice RT with digit forward, and the complex dual task set paired complex choice RT with digit backward. Paré, Rabin, Fogel and Pépin [34] used a similar simple choice RT task to examine dual task performance in individuals with mild traumatic brain injury. Müller et al. [35] employed a similar complex choice RT task to examine dual task performance in Huntington's disease. Each of the tasks within each set had easy and hard conditions. The choice RT tasks were administered on a Lenovo ThinkPad X61 laptop running Windows XP. The laptop was placed in front of the participants within comfortable reach. Participants used the laptop's keyboard to respond to stimuli that were presented in the centre of the screen: they pressed the left arrow with their left index finger to respond to target stimuli, and the right arrow with their right index finger to respond to non-target stimuli. The ratio of target to nontarget stimuli was approximately the same. We recorded RT and error rates. RT was the time taken from the moment each stimulus appeared on the screen until participants' response. Error rates were the percentage of incorrect responses across trials. Responding to a target or non-target stimulus with the appropriate keyboard arrow constituted a correct response.

For simple choice RT, stimuli were specific letters of the alphabet, which were designated as target and non-target letters. In the easy condition the target letters were X and Z, and in the hard condition they were X, Z, O and Y. Non-target letters were other letters of the alphabet. Each trial commenced with a "get-ready" sign (+) that remained on the screen for 250 ms. A letter followed in the same position, and until the participant responded or for a maximum of 3000 ms (see Figure 1). Because hard digit forward requires more time, we adjusted the number of simple choice RT trials so that there were enough trials to last throughout the hard digit task. Thus, there were 45 simple choice RT trials performed concurrently with easy digit forward.

For complex choice RT, stimuli were 4×4 matrices of regular arrays of eight Xs and eight Os. In the easy condition the target matrices had four Xs in a row, either horizontally, vertically, or diagonally. In the hard condition, they had either four Xs or four Os in a row (see Figure 2). Non-target matrices did not have four

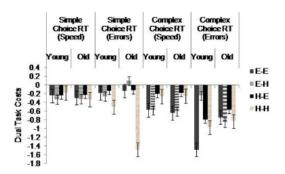


Figure 3. Dual task costs for the choice RT tasks. E-E = Easy choice RT with easy digit; E-H = Easy choice RT with hard digit; H-E = Hard choice RT with easy digit; H-H = Hard choice RT with hard digit. Standard error bars are included. doi:10.1371/journal.pone.0060265.g003

March 2013 | Volume 8 | Issue 3 | e60265

Xs or four Os in a row; they appeared in any location that did not constitute a row. Each stimulus was displayed on the screen until response was made or for a maximum of 3000 ms with an interstimulus interval of 500 ms. There were 30 complex choice RT trials when performed concurrently with easy digit backward and 40 trials performed concurrently with hard digit backward.

For *digit forward*, stimuli were 4-digit (easy) and 5-digit (hard) numbers; for *digit backward*, stimuli were 3-digit (easy) and 4-digit (hard) numbers. Digits ranged between 0 and 9, and each digit appeared only once in any given number. The experimenter read each series of numbers at a rate of approximately 1 s. Participants were then required to repeat each series aloud and in the correct order. As soon as participants recalled a series, the experimenter presented the next one. Incorrect digits or digits out of order were counted as errors. These errors were summed across trials and divided by the total number of trials in that condition to obtain the error percentage, which we then used for data analysis. There were 10 trials for the single tasks for each task set. In dual tasks, the number of trials varied from one participant to another as the digit tasks ended only when participants had completed the choice RT tasks.

For the dual task conditions, participants were required to press the Enter button on the keyboard in order to commence the choice RT tasks. As soon as they commenced each of the choice RT tasks, the experimenter started reading a series of numbers which's length depended on the condition (e.g., easy, hard). The experimenter moved on to the next series of numbers as soon as the participant recalled the previous series.

Participants were tested individually in a quiet room. They were instructed to perform all tasks as quickly and as accurately as possible. For each of the sets, participants first performed the four single tasks. Taking for example the simple dual task set, participants performed the single tasks in the following order: easy simple choice RT, hard simple choice RT, easy digit forward, and hard digit forward. Participants performed practice trials prior to each of the single tasks. Next, for the dual tasks, participants performed every possible combination of the simple choice RT with the digit forward tasks: (1) easy simple choice RT with easy digit forward, (2) easy simple choice RT with hard digit forward, (3) hard simple choice RT with easy digit forward, and (4) hard simple choice RT with hard digit forward. The same order was followed for the complex dual task set.

The simple and complex dual task sets were two of four sets of tasks that participants performed as part of a larger study, and the order of the four sets was counterbalanced across participants. Therefore, half of the participants in each of the groups performed

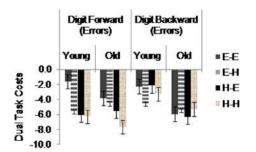


Figure 4. Dual task costs for the digit tasks. E–E = Easy digit with easy choice RT; E–H = Easy digit with hard choice RT; H–E = Hard digit with easy choice RT; H–H = Hard digit with hard choice RT. Standard error bars are included. doi:10.1371/journal.pone.0060265.g004

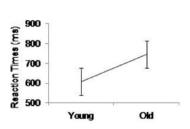


Figure 5. Main effect of Age (young, old) on reaction times of the simple choice RT task. Standard error bars are included. doi:10.1371/journal.pone.0060265.q005

the simple dual task set first, and the other half of participants performed the complex dual task set first. We did not counterbalance the order of the conditions, because a full permutation with all the different conditions for all the different sets of tasks was deemed impractical due to the large number of conditions within each set of tasks as well as the sample size. Also, since there is a learning component it was appropriate for the hard tasks to be preceded by easy tasks.

Statistical Analyses

For RT and error rates across all tasks, trials with values more than 3.5 standard deviations from the individual mean were excluded before computing overall means and standard deviations (see Table 1). Taking, for example the simple dual task set, separate 2×2×3 mixed model ANOVAs were computed for RT and for errors rates, with Age as a between subjects factor (young, old), and two within factors, Simple Choice RT Task Difficulty (easy, hard), and Digit Forward Task Difficulty (none, easy, hard). The same model was used for the complex dual task set. Due to violations of the sphericity assumption, we report Greenhouse-Geisser corrected degrees of freedom. Education level was included as a covariate in all specified models below, but it was not found to be significant in any model. Thus, all subsequent analyses were performed without education as a covariate. Significant interactions of interest were followed with appropriate post hoc analyses: simple main effects or planned comparisons. For all pairwise comparisons we conducted Bonferroni post hoc tests $(\alpha = .05).$

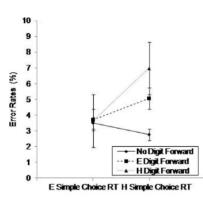


Figure 6. Percentage of error rates on the Simple Choice RT (easy, hard) as a function of Digit Forward Task Difficulty (none, easy, hard). E = Easy; H = Hard. Standard error bars are included.

doi:10.1371/journal.pone.0060265.g006

4

March 2013 | Volume 8 | Issue 3 | e60265

Dual Task Performance in Normal Aging

To assess participants' ability to perform concurrent tasks, we computed dual task costs separately for RT and error rates for the simple and complex choice RT tasks, as well as for error rates for the digit tasks (see Figures 3 and 4). Taking, for example the simple dual task set, we used a 2×2×2 mixed-model ANOVA with the between factor Age (young, old) and two within factors, Simple Choice RT Task Difficulty (easy, hard) and Digit Forward Task Difficulty (easy, hard). We used the same model for complex choice RT dual task costs. For the digit tasks, we added a value of 1 to each data point prior to computing dual task costs due to a large number of participants not committing any errors in the single tasks. In accord with previous studies [14,36,37] we used the formula: dual task cost = (single task-dual task)/single task to calculate the relative ratio of single task to dual task that controls for single task performance. Negative dual task costs suggest that RT and accuracy decreased in the dual task conditions compared with the single task conditions.

Results

Age and condition effects on RT and error rates were examined in order to investigate dual task performance in younger and older adults. We first present the simple choice RT task performance followed by the complex choice RT task. Finally, we present performance on the digit tasks.

Simple Choice RT Task Performance

Using RT as the dependent variable, a three way ANOVA revealed a significant main effect of Age, F(1,52) = 19.55, p < .001, $\eta^2 = .27$, with older adults being significantly slower than younger adults (see Figure 5). We also found significant main effects of Simple Choice RT, F(1.00,52.00) = 9.88, p = .01, $\eta^2 = .16$, with significantly faster performance in easy compared with hard simple choice RT, and Digit Forward, F(1.39,72.57) = 72.09, p < .001, $\eta^2 = .58$, with significantly faster performance in the single digit tasks compared with the dual digit tasks. Easy digit forward conditions were also performed significantly (p = .03) faster than hard digit forward conditions. There were no significant interactions.

Using error rates as the dependent variable, the same model revealed significant main effects of Simple Choice RT, F(1.00,50.00) = 15.63, p < .001, $\eta^2 = .23$ and Digit Forward, F(1.88,94.03) = 11.54, p < .001, $\eta^2 = .18$. There was also a significant interaction between Simple Choice RT and Digit Forward, F(1.90,95.31) = 12.89, p < .001, $\eta^2 = .20$ (see Figure 6). Post hoc

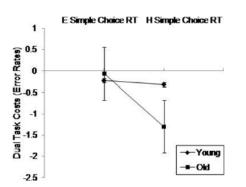


Figure 7. Dual task costs (error rates) on the Simple Choice RT Task Difficulty (easy, hard) as a function of Age (young, old). E = Easy; H = Hard. Standard error bars are included. doi:10.1371/journal.pone.0060265.g007

Dual Task Performance in Normal Aging

analysis of the simple main effects showed no differences on the easy simple choice RT. For hard simple choice RT we found significant (p<.05) differences between the single and dual tasks, and between the easy and hard digit forward conditions; error rates increased with increased difficulty. Overall, the results of the simple choice RT tasks suggest aging effects in RT, but not in error rates. There was no evidence of speed-accuracy trade-offs, as slower responses were associated with greater error rates.

Simple Choice RT Dual Task Costs

For dual task costs, a three way ANOVA for RT revealed a significant main effect of Digit Forward, F(1.00,54.00) = 7.58, p=.01, $\eta^2=.12$, with significantly greater dual task costs in easy digit forward compared with hard digit forward. The same model for error rates revealed a significant main effect of Simple Choice RT, F(1.00,54.00) = 9.86, p=.01, $\eta^2=.15$, and a significant interaction between Age and Simple Choice RT, F(1.00,54.00)= 7.31, p=.01, $\eta^2=.12$ (see Figure 7). As indicated by pairwise comparisons, older adults had significantly (p<.001) more costs in the hard simple choice RT, whilst the other conditions had similar costs. We found no age difference on easy simple choice RT.

Complex Choice RT Task Performance

Using RT as the dependent variable, a three way ANOVA revealed significant main effects of Complex Choice RT, F(1.00,52.00) = 39.59, p<.001, $\eta^2 = .43$, and Digit Backward, F(1.31,68.58) = 112.27, p<.001, $\eta^2 = .68$, and a significant interaction between Complex Choice RT and Digit Backward (see Figure 8). Post hoc analysis of the simple main effects showed that easy complex choice RT was performed significantly (p<.001) faster than hard complex choice RT only in the single tasks.

Using error rates as the dependent variable, the same model revealed a significant main effect of Age, F(1,50) = 47.85, p<.001, $\eta^2 = .48$, with older adults making significantly more errors than younger adults (see Figure 9). We also found significant main effects of Complex Choice RT, F(1.00,52.00) = 11.21, p = .002, $\eta^2 = .17$, with significantly more errors in the easy than hard complex choice RT conditions; and Digit Backward, F(1.47,76.61) = 11.54, p < .001, $\eta^2 = .48$. Participants made significantly fewer errors in the single tasks compared with the dual tasks, and also significantly fewer errors in easy compared with hard digit

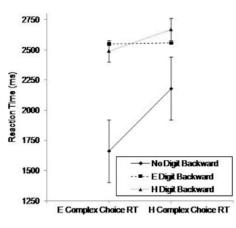


Figure 8. Reaction times on the Complex Choice RT (easy, hard) as a function of Digit Backward Task Difficulty (none, easy hard). E = Easy; H = Hard. Standard error bars are included. doi:10.1371/journal.pone.0060265.g008

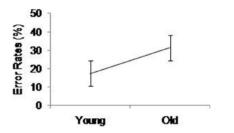


Figure 9. Main effect of Age (young, old) on error rates of the complex choice RT task. Standard error bars are included. doi:10.1371/journal.pone.0060265.g009

backward. Contrary with the simple choice RT tasks, the results of the complex choice RT tasks suggest aging effects in error rates, but not in RT. Similarly with the simple choice RT task, slower responses were associated with greater error rates suggesting no speed-accuracy trade-offs.

Complex Choice RT Dual Task Costs

For dual task costs, a three way ANOVA for RT revealed only a significant main effect of Complex Choice RT, F(1.00,54.00) = 33.81, p<.001, $\eta^2 = .382$. The same model for error rates revealed significant main effects of Complex Choice RT, F(1.00,54.00) = 6.44, p=.01, $\eta^2 = .11$, and Digit Backward, F(1.00,54.00) = 17.36, p<.001, $\eta^2 = .24$. There was also a significant interaction between Age and Complex Choice RT, F(1.00,54.00) = 4.31, p=.04, $\eta^2 = .07$ (see Figure 10). Pairwise comparisons suggested that there were significantly (p<.001) greater dual task costs for the younger adults in the easy complex choice RT tasks.

In order to see whether there were differences in dual task costs between the simple and complex choice RT tasks, we calculated dual task cost ratios for RT and error rates separately for each condition using the following formula: simple choice RT/complex choice RT. We found that the majority of both younger and older participants had greater costs in the complex choice RT, with only very few participants having similar costs between the two tasks or greater costs on the simple choice RT. Mann-Whitney tests showed no significant age-related differences between dual task cost ratios for any of the conditions.

Digit Tasks Performance

For digit forward, a three way ANOVA revealed a significant main effect of Digit Forward, F(1.00,49.00) = 37.49, p<.001, $\eta^2 = .43$, with significantly fewer errors in the easy than hard conditions. There was also a significant main effect of Simple Choice RT, F(1.82,75.71) = 17.47, p<.001, $\eta^2 = .26$, with significantly fewer errors in the single tasks compared with the dual tasks. There were no significant interactions.

For *digit backward*, the same model revealed a significant main effect of Digit Backward, F(1.00,52.00) = 53.62, p<.001, $\eta^2 = .51$, with significantly fewer errors in easy than hard conditions. We also found a significant main effect of Complex Choice RT, F(1.54,80.43) = 13.39, p<.001, $\eta^2 = .20$, with significantly fewer errors in the single tasks compared with the dual tasks. There were no significant interactions.

For dual task costs of digit forward, we found a significant main effect of Digit Forward, F(1.00,54.00) = 5.18, p = .02, $\eta^2 = .08$, with significantly greater dual task costs in hard digit forward compared with easy digit forward. We found no other significant main effects or interactions for digit forward or digit backward.

Discussion

This study examined whether concurrent performance of choice RT and cognitive tasks varies depending on differences in task complexity and difficulty in younger and older adults. We found age-related differences in speed, but not in accuracy in the simple choice RT tasks with older adults having greater dual task costs only in the hard simple choice RT conditions. For the complex choice RT tasks, we found age-related differences in accuracy, but not in speed with younger adults having greater dual task costs only in the easy complex choice RT conditions. Collectively, our results suggest that younger and older adults differ in their dual task performance, with differences depending on both the complexity and difficulty of dual tasks probably due to implementation of different strategies.

Most previous studies, using different combinations of dual tasks, found that older adults were slower than younger adults [7,13]. Our findings indicate that under more cognitively demanding conditions, age differences in speed may be eliminated, albeit at the expense of accuracy. Despite our instructions, which put equal emphasis on the importance of both speed and accuracy, older adults may have either opted for a more careful approach or could not perform the choice RT tasks any faster due to generalized slowing as suggested by Processing-Speed Theory [18]. However, age differences in speed were not more pronounced in the complex dual task set that was presumably more cognitively demanding, a finding not in support of the Processing-Speed Theory [18], although age differences in accuracy emerged. It may be possible that under the more cognitively demanding conditions younger adults slowed down due to the increased attentional demands of the tasks in order to attain a level of satisfactory accuracy. Overall, the results indicate age-differences in the strategy adopted by different groups. In support of this notion, Davidson, Amso, Cruess Anderson and Diamond [38] have also found that younger adults adjusted their speed to preserve reasonable accuracy on difficult trials.

In any case, we found no age differences in dual task costs for speed in either the simple or the complex dual task sets. Thus, both groups maintained their baseline levels of speed during the dual task conditions. In line with previous studies [14,39], the accuracy of older adults for dual task costs decreased from baseline to the harder simple choice RT dual tasks compared with younger adults. However, a different pattern emerged in the complex choice RT tasks during which accuracy of younger adults

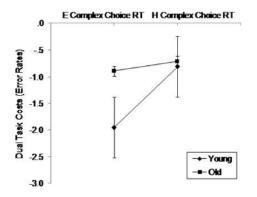


Figure 10. Dual task costs (error rates) on the Complex Choice RT Task Difficulty (easy, hard) as a function of Age (young, old), E = Easy; H = Hard. Standard error bars are included. doi:10.1371/journal.pone.0060265.g010

6

March 2013 | Volume 8 | Issue 3 | e60265

Dual Task Performance in Normal Aging

decreased from baseline to the harder dual tasks compared with older adults, although in the context of the results in speed. This finding is unexpected given that past research has typically found that older adults incur greater dual task costs [39]. Despite this, there are a few studies that have found greater dual task costs in younger adults [e.g., 40, 41]. For example, Kemper et al. (2003) investigated language production and suggested that younger adults may experience greater dual task costs than older adults due to their faster and more complex speech at baseline, which became similar to older adults' speech under the more demanding dual task conditions. Similarly, our findings suggest that performing the hard choice RT concurrently with a secondary task had more detrimental effects on the performance of younger than older adults. This is most likely due to their comparatively lower error rates at baseline that increased under dual task conditions. Taken as a whole, our findings indicate that dual task costs are affected by the complexity of the task being performed. Although our participants were able to maintain their baseline RT under dual task conditions, their accuracy changed. One might assume that increasing task complexity changed participants' response from emphasizing speed to emphasizing accuracy; however, this is unlikely, as we found no speed-accuracy trade-offs. Therefore, our participants' accuracy decreased under more demanding dual task conditions, and baseline speed was maintained.

Previous neuroimaging studies have investigated the neural basis of processing speed [42,43], as well as patterns of cortical activation [44,45]. Recently, Takeuchi et al. [46] used functional magnetic resonance imaging to examine differences between the speed of simple and complex working memory tasks in 23 healthy males using an N-Back task. Significantly increased activation of the right dorsolateral prefrontal cortex and fronto-parietal network was found during faster and more complex tasks, compared with the slower and easier tasks. The authors suggested that these regions may mediate differences between the speed of simple and complex cognitive processes in line with other studies that have found increased cognitive load to be associated with increased brain activation specifically in the prefrontal cortex [47-49]. Moreover, past research has shown a positive relationship between speed of complex cognitive processes and psychometric measures of intelligence [e.g., 50]. The fronto-parietal network has been typically ascribed to cognitive functions, and has been found to be over-activated in older compared with younger adults [51,52], and during dual-task performance [52,53]. Age-related increased activation may reflect a compensatory strategy employed by older adults as an attempt to maintain task performance at an accurate level, especially under more cognitively demanding conditions. Overall, these studies emphasize the importance of the frontoparietal network as playing a critical role in age-related differences in the speed of both simple and complex cognitive processes.

Consistent with our hypothesis, and past research [11,13], our findings showed that performance slowed and became less accurate with higher levels of task difficulty in both groups and across both sets of tasks. Both groups were slower and made more errors in the choice RT tasks when they performed the digit tasks concurrently, highlighting the increased cognitive load in the dual task conditions. Past research investigating age differences in dual tasking has produced inconsistent results in regards to error rates [19,21,24]. Our findings suggest that age-related differences in error rates emerge under more complex dual tasks. Older adults' already slowed RT may have provided a "protective" mechanism in the more complex dual task set (against the need to slow down even further); however, maintaining RT was at the expense of accuracy. Alternatively, older adults may not be able to regulate their RT as effectively as younger adults to adapt to different

Dual Task Performance in Normal Aging

conditions. Although results suggested no speed-accuracy tradeoffs within each set of tasks, there were age-related differences in RT, but not in error rates in the simple set of tasks, and age-related differences in error rates, but not in RT in the complex set of tasks. Differences in the pattern of age effects across sets of dual tasks suggest that different age groups may implement differential strategies depending on the type and complexity of tasks.

Our study has implications for the Processing-Speed Theory. For example, Salthouse [54] argues that age-related differences in cognitive performance, such as working memory, can be explained by age-related differences in processing speed. Our results indicate that age-related differences are not explained solely by processing speed. Rather, we find clear age-related differences that are best demonstrated by two measures, RT and accuracy, with the relationships between these measures and aging varying with levels of task difficulty. Under conditions of simple processing, older participants' RT was slower relative to younger participants, whereas accuracy was similar; however, under harder processing conditions older participants' RT was similar to younger participants, but they were less accurate. These findings are consistent with past research which asserts that participants are likely to share resources between a number of factors, including processing speed and processing accuracy [55].

The current findings showed that older adults performed worse overall in both simple and complex choice RT tasks, but employed different strategies with speed-accuracy trade-offs based on the complexity of dual tasks: older adults traded speed for accuracy in the simple dual task set, and accuracy for speed in the complex dual task set. Accumulator models of speed-accuracy trade-offs assume that sensory evidence accumulates over time from signal onset until a decision threshold [56]. Depending on the task and individual differences, such as capability and age, accumulation of evidence may proceed more or less slowly and more or less accurately. Relevant to our results, accumulator models predict either changes in speed or accuracy by changing the decision threshold: emphasizing the speed of responding lowers the decision threshold relative to emphasizing accuracy and vice versa [56]. Overall, our results highlight the need to characterise dual task performance using a more comprehensive readout of behaviour, including speed and accuracy, and to include conditions that span a variety of difficulty levels. It remains to be determined whether the different pattern of results across the simple and complex choice RT tasks is under conscious control.

Our findings should be considered in light of some study limitations. Despite instructing participants to perform the tasks as quickly and as accurately as possible, it is likely that the complexity of tasks affected the competing goals of speed and accuracy differently. In addition, our conclusions must be tempered by possible task order effects since, for practical reasons, we did not counterbalance single and dual task conditions. However, given that practice effects would be expected to accrue with increased experience, together with the fact that participants' performances actually deteriorated in the higher task difficulty conditions which were presented later (i.e., with the greatest amount of practice), suggests that, if anything, counterbalancing would have strengthened our findings.

An important contribution of this study was to compare different combinations of cognitive dual tasks, and to manipulate the task difficulty of both tasks within each set, so as to further tease apart mental operations in younger and older adults. Most previous studies have used one dual task only, and manipulated task difficulty of only one of the tasks. In addition, previous studies have typically employed choice RT tasks concurrently with postural balance tasks rather than cognitive tasks.

In summary, our findings suggest that under dual task demands, older adults adopt different strategies than younger adults, and these depend on both complexity and difficulty level of the cognitive tasks. The differential pattern of performance across the lifespan affects both processing speed and processing accuracy. Compared with younger adults, older adults were significantly slower than, but as accurate in simple choice RT tasks, and significantly less accurate, but as fast in complex choice RT tasks. RT decreased and error rates increased with greater task difficulty for both age groups, and both dual task sets. Finally, older adults showed greater costs for error rates in the simple choice RT tasks, whereas in the complex choice RT tasks, it was the younger group that showed greater costs. Findings suggest that younger and older

References

- Der G, Deary IJ (2006) Age and sex differences in reaction time in adulthood: Results from the United Kingdom Health and Lifestyle Survey. Psychology and Aging 21: 62–73.
- Williams BR, Hultsch DF, Strauss EH, Hunter MA, Tannock R (2005) Inconsistency in reaction time across the life span. Neuropsychology 19: 88–96. 3. Kolev V, Falkenstein M, Yordanova J (2006) Motor-response generation as a source
- ging-related behavioural slowing in choice-reaction tasks. Neurobiology of Aging 27: 1719-1730.
- 4. Yordanova J, Kolev V, Hohnsbein J, Falkenstein M (2004) Sensorimotor slowing with agging is mediated by a functional dysregulation of motor-generation processes: Evidence from high-resolution event-related potentials. Brain 127: 351–362.
- 5. Deary IJ, Der G (2005) Reaction time, age, and cognitive ability: Longitudinal findings from age 16 to 63 years in representative population samples. Aging, Neuropsychology, and Cognition 12: 187–215.
- Deary IJ, Johnson W, Starr JM (2010) Are processing speed tasks biomarkers of cognitive aging? Psychology and Aging 25: 219–228.
- 7. Deary IJ, Der G (2005) Reaction time, age, and cognitive ability: Longitudinal findings from age 16 to 63 years in representative population samples. Aging, Neuropsychology, and lognition 12: 187-215
- 8. Deary IJ, Der G, Ford G (2001) Reaction times and intelligence differences: A population based cohort study. Intelligence 29: 389-399.
- 9. Moore H, Dudchenko P, Bruno JP, Sarter M (1992) Toward modeling age-related changes of attentional abilities in rats: Simple and choice reaction time tasks and vigilance. Neurobiology of Aging 13: 759-772.
- 10. Benton A (1986) Reaction time in brain disease: Some reflections, Cortex 22: 129-140. 11. Shurnway-Cook A, Woollacott M (2000) Attentional demands and postural control: The
- effect of sensory context. The Journals of Gerontology 55A: M10-M16. 12. Mendelson DN, Redfern MS, Nebes RD, Jennings JR (2010) Inhibitory processes
- relate differently to balance/reaction time dual tasks in young and older adults. Aging, Neuropsychology, and Cognition 17: 1-18.
- 13. Huxhold O, Li S-C, Schmiedek F, Lindenberger U (2006) Dual-tasking postural control: Aging and the effects of cognitive demand in conjunction with focus of attention. Brain Research Bulletin 69: 294-305.
- McDowd JM, Craik FIM (1988) Effects of aging and task difficulty on divided attention performance. Journal of Experimental Psychology: Human Perception and Performance 14: 267–280.
- 15. Mattay VS, Fera F, Tessitore A, Hariri AR, Das S, et al. (2002) Neurophysiological Initially Vos Cola 1, Cosmol Cr., Human motor function. Neurology 58: 630–635.
 Reuter-Lorenz PA, Lustig C (2005) Brain aging: Rorganizing discoveries about the aging
- ind. Current Opinion in Neurobiology 15: 245-251.
- Reuter-Lorenz PA, Cappell KA (2008) Neurocognitive aging and the compensation hypothesis. Current Directions in Psychological Science 17: 177–182.
- Salthouse TA (1996) The processing-speed theory of adult age differences in cognition Psychological Review 103: 403–428.
- Hawkins HL, Kramer AF, Capaldi D (1992) Aging, exercise, and attention. Psychology and Aging 7: 643–653.
 Springer S, Giladi N, Peretz C, Yogev G, Simon ES, et al. (2006) Dual-tasking
- effects on gait variability: The role of aging, falls, and executive function. Movement Disorders 21: 950–957.
- Hein G, Schubert T (2004) Aging and input processing in dual-task situations. Psychology and Aging 19: 416–432.
- 22. McPhee LC, Scialfa CT, Dennis WM, Ho G, Caird JK (2004) Age differences in visual search for traffic signs during a simulated conversation. Human Factors 46: 674-685
- Mutter SA, Goedert KM (1997) Frequency discrimination vs frequency estimation: Adult age differences and the effect of divided attention. The Journal of Gerontology 52B: P319–P328.
- 24. Cho C-Y, Gilchrist L, White S (2008) A comparison between young and old adults in their ability to rapidly sidestep during gait when attention is divided. Gerontology 54: 120-127.
- 25. Bherer L, Kramer AF, Peterson MS, Colcombe S, Erickson K, et al. (2008) Transfer effects in task-set cost and dual-task cost after dual-task training in older and y adults: Further evidence for cognitive plasticity in attentional control in late adulthood. Experimental Aging Research 34: 188-219.

Dual Task Performance in Normal Aging

adults may adopt differential behavioral strategies depending on complexity and difficulty of dual tasks.

Acknowledgments

The authors wish to thank all the participants for their time.

Author Contributions

Editing-Proofreading: NG-K ICS. Conceived and designed the experiments: EV NG-K JCS. Performed the experiments: EV. Analyzed the data: EV. Contributed reagents/materials/analysis tools: EV. Wrote the paper: EV.

- 26. Kemper S, Schmalzried R, Herman R, Leedahl S, Mohankumar D (2009) The effects of aging and dual task demands on language production. Aging, Neuropsychology, nd Cognition 16: 241-259.
- Grégoire J, Van Der Linden M (1997) Effect of age on forward and backward digits. 27.
- Aging, Neuropsychology, and Cognition 4: 140–149. Babcock RL, Salthouse TA (1990) Effects of increased processing demands on age differences in working momory. Psychology and Aging 5: 421–428. 28.
- 29 Nasreddine ZS, Phillips NA, Bédiriam V, Charbonneau S, Whitehead V, et al. (2005) The Montreal Cognitive Assessment, MoCA: A brief screening tool for mild cognitive nbainment, Journal of the American Geriatrics Society 53: 695-699.
- 30. Wechsler D (2001) Wechsler Test of Adult Reading. San Antonio: The Psychological Corporation
- Rush AJ, Carmody T, Reimitz P-E (2006) The Inventory of Depressive Symptomatology 31. (IDS): Clinician (IDS-C) and Self-Report (IDS-SR) ratings of depressive symptoms. International Journal of Methods in Psychiatric Research 9: 45-59.
- American Psychiatric Association (1994) Diagnostic and statistical manu ial of mental disorders Fourth edition Washington DC: American Psychiatry Association 33.
- UNESCO (1997) International Sundard Classification of Education. Available from: http://www.uis.unesco.org/ev.php?ID = 7433_201&ID2 = DO_TOPIC.
 Paré N, Rabin IA, Fogel J, Pépin M (2009) Mild traumatic brain injury and its
- 34. equelae: Characterisation of divided attention defiaits. Neuropsychological rehabilitation 19: 110-137.
- Müller SV, Jung A, Preinfalk J, Kolbe H, Ridao-Alonso M, et al. (2002) Disturbance of "extrinsic alertness" in Huntingtons disease. Journal of Clinical and Experimental Neuropsychology 24: 517–526.
- Swanenburg J, de Bruin ED, Hegemann S, Uebelhart D, Mulder T (2010) Dual 36 tasking under compromised visual and somatosensory input in elderly fallers and non-fallers. The Open Rehabilitation Journal 3: 169–176.
- 37. de Ribaupierre A, Ludwig C (2003) Age differences and divided attention: Is there a general deficit? Experimental Aging Research 29: 79-105.
- 38. Davidson MC, Amso D, Cruess Anderson L, Diamond A (2003) Development of cognitive control and executive functions from 4 to 13 years: Evidence from unipulations of manory, inhibition, and task switching. Neuropsychologia 44: 2037–2078.
 Loose R, Kaufinann C, Auer DP, Lange KW (2003) Human prefrontal and sonsory
- rtical activity during divided attention tasks. Human Brain Mapping 18: 249-259. Kemper S, Hoffman L, Schmalzried R, Herman R, Kieweg D (2011) Tracking 40.
- Recipcition, Homman L, German et al., Recipcition R, Recency D (2011) Financial talking: Dual task costs of planning and producing speech for young tersus older adults. Aging, Neuropsychology, and Cognition 18: 257–279.
- Matthews A, Garry MI, Martin F, Summers J (2006) Neural correlates of performa trade-offs and dual-task interference in bimanual coordination: An ERP investigation. Neuroscience Letters 400: 172–176.
- Menon V, Rivera SM, White CD, Glover GH, Reiss AL (2000) Dissociating 42. prefrontal and parietal cortex activation during arithmetic processing. Neuroimage 12: 357 365
- 43. Loose R, Kaufmann C, Tucha O, Auer DP, Lange KW (2006) Neural networks of response shifting: Influence of task speed and stimulus material. Brain Research 1090: 146-155.
- Wolf RC, Vasic N, Schönfeldt-Lecuona C, Landwehrmeyer B, Ecker D (2007) Dorsolateral prefrontal cortex dysfunction in presymptomatic Huntington's disease; Evidence from event-related fMRI. Brain 130: 2845–2857.
- Barch DM, Braver TS, Cohen JD, Nystrom LE, Forman SD, et al. (1997) Dissociating working memory from task difficulty in human prefrontal cortex. Neuropsycho-45. logia 35: 1373-1380
- 46. Cohen JD, Perlstein WM, Braver TS, Casey BJ, Servan-Schreiber D, et al. (1997) Temporal dynamics of brain activation during a working memory task. Nature 386: 604-608
- 47. Bors DA, Forrin B (1995) Age, speed of information processing, recall, and fluid intelligence. Intelligence 20: 229–248. Van Impe A, Coxon JP, Goble DJ, Wenderoth N, Swinnen SP (2011) Age-related
- changes in brain activation underlying single- and dual-task performance: Visuomanual drawing and mental arithmetic. Neuropsychologia 49: 2400-2409.
- 49. Goble DJ, Coxon JP, Van Impe A, De Vos J, Wenderoth N, et al. (2010) The neural control of bimanual movements in the elderly: Brain regions exhibiting age-related

8

March 2013 | Volume 8 | Issue 3 | e60265

Dual Task Performance in Normal Aging

- increases in activity, fraquency-induced neural modulation, and task-specific compensatory recruitment. Human Brain Mapping 31: 1281-1295.
 50. D' Esposito M, Detre JA, Alsop DC, Shin RK, Atlas S, et al. (1995) The neural basis of the central accentice system of working memory. Nature 378: 279-281.
 51. Verhaeghen P, Steitz DW, Sliwinski MJ, Cerella J (2003) Aging and dual-task performance: A meta-analysis. Psychology and Aging 18: 443-460.
 52. Kemper S, Herman RE, Lian CHT (2003) The costs of doing two things at once for young and older adults: Talking while walking, finger tapping, and ignoring speech or noise. Psychology and Aging 18: 181-192.
- Murray LI, Holland AL, Beeson PM (1998) Sokon language of individuals with mild fluent aphasia under focused and divided-attention conditions. Journal of Speech, Language & Hearing Research 41: 213-227.
 Salthouse TA (1994) The aging of working memory. Neuropsychology 8: 535-543.
 Brebion G (2003) Working monory, language comprehension, and aging: Four experiments to understand the deficit. Experimental Aging Research 29: 269-301.
 Ivanoff J, Branning P, Marois R (2008) fMRI widence for a dual process account of the speed-accuracy tradeoff in decision-making. PLoS ONE 3: e2635.

Chapter 4

Dual Task Performance in Huntington's Disease

Preamble to Paper

The previous two chapters focussed on dual task performance in younger and older healthy adults. Chapter 2 investigated age-related differences in dual tasking by employing circle tracing with serial subtraction tasks, and Chapter 3 compared two different dual task sets. This chapter provides the first empirical study to examine dual task performance in HD. In particular, this chapter applied the same dual task paradigm as Chapter 2 (circle tracing with serial subtraction) to investigate differences in dual tasking between HD participants and healthy controls.

Circle tracing has been previously used to examine visuomotor performance in HD. This study extended past research by investigating the effect of a concurrent cognitive task on circle tracing performance in HD under different difficulty levels. This paradigm provided an avenue to explore dual task performance in HD, an area of research that has been relatively overlooked in this disease. Our results are discussed within the context of the Unitary Resource and Multiple Resources theories.

Declaration for Thesis Chapter 4

Declaration by candidate

In the case of Chapter 4, the nature and extent of my contribution to the work was the following:

Nature of contribution	Extent of contribution (%)
Conception and design of the study, attainment of ethics approval and	80%
ongoing reporting requirements, review of relevant literature and writing of	
manuscript	

The following co-authors contributed to the work. Co-authors who are students at Monash University must also indicate the extent of their contribution in percentage terms:

Name	Nature of contribution	Extent of contribution (%) for student co-authors only
Prof Julie C. Stout	Contributed to development of ideas and critical revision of the paper	
Prof Nellie Georgiou-Karistianis	Contributed to development of ideas and critical revision of the paper	
Dr Andrew Churchyard	Assisted with recruitment of participants and input on manuscripts	

Candidate's Signature

Date

Declaration by co-authors

The undersigned hereby certify that:

- (1) the above declaration correctly reflects the nature and extent of the candidate's contribution to this work, and the nature of the contribution of each of the co-authors.
- (2) they meet the criteria for authorship in that they have participated in the conception, execution, or interpretation, of at least that part of the publication in their field of expertise;
- (3) they take public responsibility for their part of the publication, except for the responsible author who accepts overall responsibility for the publication;
- (4) there are no other authors of the publication according to these criteria;
- (5) potential conflicts of interest have been disclosed to (a) granting bodies, (b) the editor or publisher of journals or other publications, and (c) the head of the responsible academic unit; and
- (6) the original data are stored at the following location(s) and will be held for at least five years from the date indicated below:

```
Location(s)
```

School of Psychology and Psychiatry, Monash University, Australia

	Signature	Date
Prof Julie C. Stout		
Prof Nellie Georgiou-Karistianis		
Dr Andrew Churchyard		20/4/13
		100

Effects of Task Difficulty During Dual Task Circle Tracing in Huntington's Disease

Eleftheria Vaportzis and Nellie Georgiou-Karistianis

School of Psychology and Psychiatry, Monash University

Andrew Churchyard

School of Psychology and Psychiatry, Monash University Department of Neurology, Monash Medical Centre

Julie C. Stout

School of Psychology and Psychiatry, Monash University

Acknowledgments

This research was supported by the School of Psychology and Psychiatry, Monash University. We thank our participants and their families for their time and effort.

Address correspondence to Julie C. Stout, School of Psychology and Psychiatry, Monash University, Wellington Road, Clayton, Victoria 3800, Australia.

E-mail:

Abstract

We examined dual task performance in Huntington's disease (HD) in 15 HD participants and 15 controls. Participants performed direct circle tracing (able to view arm) and indirect circle tracing (arm obscured) paired with serial subtraction by twos and by threes. HD participants were significantly slower and less accurate than controls, and were more compromised in the indirect circle tracing conditions. Despite this, we found no group differences in dual task costs. Overall, our findings suggest that although HD participants differ from controls in dual task performance, neither group was susceptible to dual task interference.

Keywords: Divided attention; Proprioception; Attention allocation; Speed-accuracy trade-off; Visuomotor integration.

Introduction

Huntington's disease (HD) is associated with deficits in a range of attentional functions, including divided attention, which is the ability to attend to and respond simultaneously to two or more stimuli or tasks (Dannhauser et al., 2005). Divided attention has been typically investigated using a dual task paradigm that requires individuals to perform two tasks simultaneously (Armieri, Holmes, Spaulding, Jenkins, & Johnson, 2009). Past studies investigating dual tasking in HD are limited, and the cognitive basis of dual task impairments is still unclear. However, previous explanations have included impairments in resource allocation (Georgiou, Bradshaw, Phillips, & Chiu, 1996), attentional set-shifting (Lawrence et al., 1998), and lack of automaticity (Thompson et al., 2010).

A number of theories, including the Unitary Resource Theory and the Multiple Resources Theory, have attempted to explain dual task interference in healthy individuals. The Unitary Resource Theory views attention as a *single, limited capacity resource* that can be allocated to a single task or divided between tasks (Kahneman, 1973). This resource depends on various factors, including task difficulty. Dual task interference is expected when a task is difficult and requires a large proportion of the limited attention resource, leaving little of this resource to support performance of a second task. In contrast, the Multiple Resources Theory states that attention has *separate* resource pools (e.g., a visual resource pool, an auditory resource pool), each of which can be divided among concurrent tasks (Wickens & McCarley, 2008). Accordingly, dual task interference is expected when tasks make concurrent demands on the same resources (Wickens, 2002; Wickens & McCarley, 2008). Our study was designed to test these theories, and to investigate the influence of cognitive demands on motor outputs in HD. To achieve this aim we adopted motor and cognitive tasks that allowed quantifiable manipulations of task difficulty.

Most previous studies suggest that dual task performance is differentially affected in HD compared with controls. For example, both Sprengelmeyer, Lange and Homberg (1995) and Müller et al. (2002) used the same visual-auditory dual task and reported significant differences between HD and control groups in reaction times and error rates. More recently, Thompson et al. (2010) employed a simple, tone-paced finger-tapping task with one hand (single task) and with both hands concurrently (dual task). HD participants demonstrated greater variability in bimanual tapping than controls, and reported that the dual task was more difficult than the single task. The results suggest that impaired automaticity might be a possible reason for dual task deficits in HD. Similarly, Brown, Jahanshahi and Marsden (1993) found that compared with controls, HD participants were more impaired during dual task performance, and also were more challenged by a simple button pressing task than by a more challenging peg placement task.

Although there is evidence that adding a second task leads to improvements, such as better automaticity of motor tasks in some dual task combinations (Georgiou, Phillips, Bradshaw, Cunnington, & Chiu, 1997), past research also suggests ample evidence of impairments in some dual task combinations in HD. Adding to the complexity in interpreting these findings, stage and/or duration of disease in the HD samples also vary considerably (Müller et al. 3-13 years; Sprengelmeyer et al. 1-9 years), making it difficult to discriminate the impact of early and late neuropathological profiles on dual tasking. Therefore, the current study included participants in the early stages of HD only.

Our dual task paradigm employed visuomotor (circle tracing) and cognitive (serial subtraction) tasks. We manipulated the difficulty level of both tasks to examine the influence of cognitive demands on different difficulty levels of motor behavior. To our knowledge, no study has manipulated difficulty of the concurrent tasks in HD. We selected circle tracing since previous studies have shown HD participants to be impaired in both speed and accuracy on this task (Lemay, Fimbel, Beuter, & Chouinard, 2005). These findings were further substantiated by our group in both presymptomatic and symptomatic stages of HD (Say et al., 2011). Lemay et al. (2005) and Say et al. (2011) both investigated visuomotor integration under two conditions: direct and indirect circle tracing. In particular, the circle tracing task required participants to trace an annulus using a tablet and a stylus. In the direct condition, participants could view their arm and tracing path whilst tracing the circle. In the indirect circle tracing condition, however, their arm was covered, and the annulus and their tracing path were displayed on a separate monitor. HD and controls both performed worse in the indirect condition, and this effect was more detrimental to HD participants' performances than controls (Lemay et al., 2005; Say et al., 2011). Using a serial subtraction task as a second task condition, this study extends the work of Lemay et al. (2005) and Say et al. (2011) by examining direct and indirect circle tracing under dual task conditions. We selected serial subtraction because it has been found to be an effective distractor task (Nicolson & Fawcett, 1990), previously used as an attention demanding task (Ingram et al., 2000), and difficulty can be easily manipulated.

In consideration of past research and theories, we predicted that HD participants would be slower and less accurate across all task conditions compared with controls. Moreover, we expected speed to be slower and error rates to be higher with increased task difficulty across both groups. Consistent with the Unitary Resource Theory, differences in performance were expected to emerge under the harder conditions, as manipulating task difficulty can induce limitations in resource allocation. However, if impaired automaticity is the reason for dual task deficits in HD, then one would expect either worse performance in the simpler (i.e., direct circle tracing with serial subtraction) rather than the more difficult (i.e., indirect circle tracing with serial subtraction) dual task conditions or in the single rather than dual tasks. Consistent with the Multiple Resources Theory, interference between the circle tracing and serial subtraction should be minimal, as these tasks are likely to be processed by separate modalities-responses (i.e., visual-manual and auditory-vocal).

Method

Participants

Fifteen individuals with HD and 15 age-, sex- and education-matched healthy controls participated. HD participants were diagnosed by an experienced neurologist (AC) on the basis of genetic confirmation of the disease, and the presence of motor symptoms. Years since diagnosis ranged from 2 to 7. Motor symptom severity was rated using the motor scale of the Unified Huntington's Disease Rating Scale (UHDRS; Huntington Study Group, 1996). The range of scores was from 7 to 34, out of a possible 60 (higher scores = worse motor symptoms). Using the Total Functional Capacity Scale of the UHDRS, the range of scores was from 3 to 13, out of a possible 13 (higher scores = better functioning).

Sample characterization measures included the Montreal Cognitive Assessment (MoCA; Nasreddine et al., 2005), the Wechsler Test of Adult Reading (WTAR;

Wechsler, 2001), and the Inventory of Depressive Symptomatology-Self-report (IDS-SR; Rush, Carmody & Reimitz, 2006). The MoCA is a 30-point cognitive screening test designed to detect cognitive impairment, with scores of 26 and below considered to be indicative of cognitive impairment. Items from the MoCA emphasize executive functioning and attention. The WTAR is used to estimate verbal IQ, and is composed of 50 words that have irregular letter to sound translations. The IDS-SR is a 30-item questionnaire that assesses the severity of depression within the past 7 days for all symptom domains of major depression according to the Diagnostic and Statistical Manual-IV (American Psychiatric Association, 1994). A score of 0 indicates no depressive symptoms, whereas a score of 84 indicates very severe depressive symptoms. Education level was assessed based on the International Standard Classification of Education (ISCED) system, according to which 0 indicates preprimary education and 6 second stage tertiary education (UNESCO, 1997). ISCED, WTAR and IDS-SR scores did not significantly (p > .05) differ between HD participants and controls. However, MoCA scores were significantly lower for HD participants compared with controls, t(28) = 2.40, p = .023 (see Table 1).

All participants gave written informed consent, were fluent in English and self-reported that they were free of upper limb impairments (i.e., wrist injuries), neurological disease and psychological disorders, and that they had normal or corrected-to-normal vision and hearing. Ethics approval was granted by the Monash University Human Research Ethics Committee.

	HD n = 15	Controls n = 15
Sex (F:M)	4:11	4:11
Age (years)	58.40 (8.87)	55.53 (12.33)
MoCA	24.60 (3.06)	27.07 (2.43)
WTAR	109.13 (6.27)	109.85 (8.49)
IDS-SR	14.35 (9.28)	11.60 (6.87)
ISCED	4.06 (0.79)	4.46 (1.12)
Disease duration (years)	4.67 (1.91)	
UHDRS Total Functional Capacity	10.20 (3.05)	
UHDRS Motor score	21.21 (8.86)	
CAG repeat	42.36 (1.82)	

 Table 1

 Demographic Data for HD and Control Groups

Note. CAG = Cytosine-adenine-guanine trinucleotide repeat; IDS-SR = Inventory of Depressive Symptomatology-Self-Report; ISCED = International Standard Classification of Education; MoCA = Montreal Cognitive Assessment; UHDRS = Unified Huntington's Disease Rating Scale; WTAR = Wechsler Test for Adult Reading.

Dual Task Description and Study Procedure

To investigate dual task performance, participants were required to trace a circle on a computer tablet using a stylus while performing a serial subtraction task. The circle tracing *and* serial subtraction tasks both had easy *and* hard difficulty level conditions. Participants first performed these tasks individually: circle tracing without serial subtraction, and serial subtraction without circle tracing. Specifically, after a practice trial in the easy circle tracing condition, participants performed easy circle tracing, then hard circle tracing, followed by easy serial subtraction, and finally hard serial subtraction. There were three 20 s trials for each circle tracing condition, and two 20 s trials for each serial subtraction condition.

Following performance of these single tasks, participants performed three trials of all possible combinations of difficulty levels of the circle tracing and serial subtraction tasks: (1) easy circle tracing with easy serial subtraction, (2) easy circle tracing with hard serial subtraction, (3) hard circle tracing with easy serial subtraction, and (4) hard circle tracing with hard serial subtraction. Dual task trials lasted 20 s each.

The circle tracing with serial subtraction dual task set was one of four dual task sets that was performed as part of a larger study. The order of the four dual task sets was counterbalanced across participants; however, within the circle tracing with serial subtraction dual task set, the eight conditions were administered in a single standard order. Across all participants, we used the same order of the eight task conditions for several reasons. Firstly, we wanted hard tasks to be preceded by easy tasks to allow mastery of the easy task before adding to the difficulty level. Secondly, we provided experience with the single tasks before the dual tasks to facilitate mastery of the single tasks before the dual tasks. Finally, due to the large number of conditions within each task set, a study design with all possible permutations of task order within and across sets would not have been feasible within reasonable testing duration. It would have also required a larger sample size to ensure there were sufficient samples within each test order condition.

For the circle tracing task we used a Lenovo ThinkPad® X61 (Morrisville, NC, USA) tablet positioned in front of the participant at comfortable reach. For the hard condition of the circle tracing task, a separate desktop monitor was placed about 70 cm in front of the participant. A 90 mm diameter circle with 5 mm thick white annulus on a gray background was presented on the tablet for the easy condition, and on the desktop

monitor for the hard condition. Participants were required to trace the circle, with their preferred hand, using a stylus that left a blue line indicating the trajectory of circle tracing path. Participants were instructed to start at the vertical apex of the circle, and to trace the circle clockwise, as quickly and as accurately as they could. Participants were instructed that only the tip of the stylus, and no part of their hand, was allowed to touch the tablet. In the *easy condition*, participants could observe their arm in motion, and could monitor the circle tracing path on the tablet. In the *hard condition*, participants' views of the tablet and their tracing arm were obscured by a box covering the tablet and a cloak covering the box and their arm. Therefore, in the easy condition participants could *directly* observe their performance on the tablet, whereas in the hard condition they could only observe their progress *indirectly* on the separate desktop monitor. Dependent variables were speed (total number of rotations in 20 s), and error rates number of errors per rotation). Errors were defined as the stylus moving beyond either the inner or outer edge of the white annulus for > 100 ms.

For the serial subtraction task, participants counted backward by twos (easy) or by threes (hard) for 20 s. Starting numbers ranged between 100 and 86 with half of the trials commencing on an even number. The dependent variable was error rates (percentage of incorrect responses). We also calculated rate of responses for serial subtraction by dividing the time to complete the task (20 s) by the number of responses per participant. We advised participants to perform all tasks as quickly and as accurately as possible.

Design and Statistical Analyses

Trials with values more than 3.5 standard deviations from the individual's mean were removed prior to computing overall means and standard deviations for speed and for error rates (see Table 2). To determine the effect of HD and task conditions, we examined the effects of dual task performance for both speed and error rates. We computed 2 X 2 X 3 mixed-model ANOVAs with the between factor, Group (HD, controls), and two within factors, Circle Tracing difficulty (easy, hard), and Serial Subtraction difficulty (none, easy, hard). We examined main effects, two- and threeway interactions. We report Greenhouse-Geisser corrected degrees of freedom due to violations of the sphericity assumption. A Bonferroni adjustment was applied and alpha was set to .05. We also computed dual task costs in order to quantify participants' ability to perform two concurrent tasks. We used a 2 X 2 X 2 mixed-model ANOVA with the between factor, Group (HD, controls), and two within factors, Circle Tracing difficulty (easy, hard), and Serial Subtraction difficulty (easy, hard). As per previous studies (de Ribaupierre & Ludwig, 2003; Kemper, Herman, & Lian, 2003; McDowd & Craik, 1988; Swanenburg, de Bruin, Hegemann, Uebelhart, & Mulder, 2010), dual task *costs* for speed were computed using the following formula: dual task cost = (single taskspeed-dual task speed)/single task speed, to calculate the relative ratio of single task to dual task speed, controlling for single task speed. Positive dual task costs indicate that participants' speed was reduced in the dual task conditions compared with the single task conditions. Lastly, in order to examine speed-accuracy trade-offs, we calculated Pearson's correlations between speed and error rates for all conditions separately for each group.

Means (Standard Deviations) Across All	s) Across A	ll Task Conc	litions for	Task Conditions for HD and Control Groups	ttrol Gro	sdn				
	Circle	Circle Tracing Speed	Circle Er	Circle Tracing Errors	Circle	Circle Tracing DTC (Speed)	Serial S E	Serial Subtraction Errors	Serial	Serial Subtraction Rate
	Ð	Controls	日	Controls	Ð	Controls	HD	Controls	HD	Controls
E Single task	3.85 (1.30)	6.20 (1.66)	10.06 (5.89)	8.13 (5.65)			1.85 (5.20)	0.81 (2.30)	1.85 (0.65)	1.30 (.50)
H Single task	1.71 (1.00)	2.39 (0.75)	16.37 (9.35)	9.57 (6.38)			4.02 (7.88)	5.77 (9.10)	3.27 (1.36)	2.35 (1.19)
E Tracing-E Subtraction	2.72 (1.37)	3.51 (1.77)	8.86 (5.31)	4.24 (4.23)	.31 (23)	.43 (.19)	2.16 (5.89)	3.76 (6.89)	3.38 (2.35)	1.93 (.61)
E Tracing-H Subtraction	2.92 (1.97)	3.31 (1.67)	8.77 (6.66)	3.57 (4.29)	.85 (1.27)	1.25 (1.07)	1.61 (4.37)	.84 (1.81)	2.77 (1.24)	1.66 (.47)
H Tracing-E Subtraction	1.43 (0.74)	1.77 (0.63)	15.26 (12.51)	5.15 (3.69)	.11 (27)	24 (20)	4.31 (7.59)	2.89 (4.24)	5.99 (9.66)	2.62 (1.38)
H Tracing-H Subtraction	1.37 (0.83)	1.66 (0.61)	14.28 (12.58)	4.59 (4.30)	.14 (.31)	28 (23)	3.41 (5.62)	2.47 (4.54)	5.18 (4.19)	2.64 (1.42)
<i>Note</i> . DTC = Dual task cost; E = Easy; H	; E = Easy;	H = Hard.								

	Contr
	and
	HD O
	for
	sk Conditions
	Ta
	All
	Across
	d Deviations)
	Standar
Table 2	Means (

Results

Overall, HD participants were slower and less accurate on circle tracing (single and dual tasks), compared with controls. In addition, performance of both groups was worse in the hard, compared with the easy, circle tracing conditions. In this section, we first present the effects of dual tasking on circle tracing task performance, followed by dual task costs and speed-accuracy trade-offs. Lastly, we present serial subtraction performance.

A three-way ANOVA with speed as the dependent variable revealed significant main effects of Group, F(1,28) = 4.51, p = .043, $\eta^2 = .14$, Circle Tracing difficulty, $F(1.00,28.00) = 136.00, p < .001, \eta^2 = .82$, and Serial Subtraction difficulty, F(1.21,33.92) = 34.61, p < .001, $\eta^2 = .55$. There was a significant three-way interaction involving Group, Circle Tracing and Serial Subtraction difficulty, F(1.53,42.82) =13.03, p < .001, $\eta^2 = .31$ (see Figure 1), with significant two-way interactions between Group and Circle Tracing difficulty, F(1.00,28.00) = 4.52, p = .042, $\eta^2 = .13$, Group and Serial Subtraction difficulty, F(1.21,33.92) = 7.06, p = .002, $\eta^2 = .20$, and Circle Tracing and Serial Subtraction difficulty, F(1.53,42.82) = 51.87, p < .001, $\eta^2 = .64$. To understand the different effects within the HD and control groups, we used two-way ANOVAs with Circle Tracing and Serial Subtraction as factors. In the HD group, we found a significant main effect of Circle Tracing difficulty, F(1,84) = 38.35, p < .001, η^2 = .31, with slower performance on hard (indirect) circle tracing compared to easy (direct) circle tracing. We found no other main effects or interactions. For controls, we found significant main effects of Circle Tracing difficulty, F(1,84) = 77.33, p < .001, η^2 = .47, and Serial Subtraction difficulty, F(2,84) = 18.02, p < .001, $\eta^2 = .30$, and a significant two-way interaction between Circle Tracing and Serial Subtraction

difficulty, F(2,84) = 6.67, p = .002, $\eta^2 = .13$. A post-hoc analysis revealed that controls performed significantly (p < .001) faster in the easy circle tracing task on its own than when performed concurrently with either easy or hard serial subtraction.

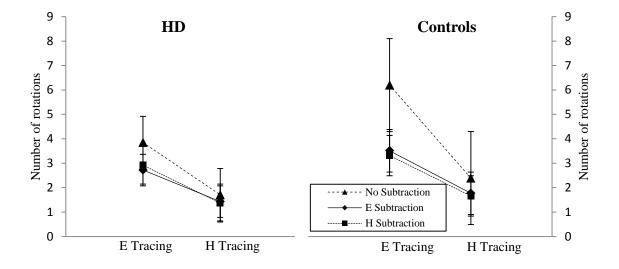


Figure 1. Circle tracing difficulty (easy, hard) as a function of serial subtraction difficulty (none, easy, hard) in (A) HD participants and (B) controls using speed as the dependent variable. E = Easy; H = Hard. Standard error bars included.

A three-way ANOVA with error rates as the dependent variable revealed significant main effects of Group, F(1,28) = 11.77, p < .002, $\eta^2 = .29$, with HD participants making more errors than controls, and Circle Tracing difficulty, F(1.00,28.00) = 6.49, p = .01, $\eta^2 = .18$, with more errors in hard than easy circle tracing. We also found a significant main effect of Serial Subtraction difficulty, F(1.37,38.45) = 7.35, p < .001, $\eta^2 = .20$ with single tasks being significantly (p < .05) more accurate than dual tasks. There were no significant interactions.

For dual task costs, a three-way ANOVA for speed as the dependent variable revealed significant main effects of Circle Tracing difficulty, F(1.00,28.00) = 33.47, p < .001, $\eta^2 = .54$, and Serial Subtraction difficulty, F(1.00,28.00) = 14.24, p < .001, $\eta^2 = .34$. There was also a significant two-way interaction between Circle Tracing and Serial Subtraction difficulty, F(1.00,28.00) = 12.25, p = .002, $\eta^2 = .30$ (see Figure 2). Post-hoc analysis revealed significantly (p < .001) higher dual tasks costs when easy circle tracing was performed concurrently with hard serial subtraction. We did not calculate dual task costs for error rates as they increased from single to dual task conditions for both groups.

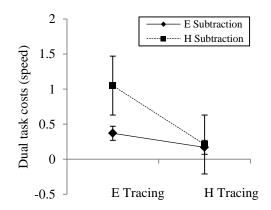


Figure 2. Circle tracing difficulty (easy, hard) as a function of serial subtraction difficulty (none, easy, hard) using dual task costs for speed. E = Easy; H = Hard. Standard error bars included.

To investigate whether HD participants were more inclined to trade speed for accuracy and vice versa, we performed a series of correlational analyses between speed and error rates for each of the six circle tracing task (single and dual tasks) conditions separately for HD participants and controls. We found significant (p < .05) positive correlations, indicating speed-accuracy trade-offs in controls across all conditions except hard circle tracing with easy serial subtraction. In contrast, the HD group showed this trade-off only in the easy circle tracing single task (see Figure 3).

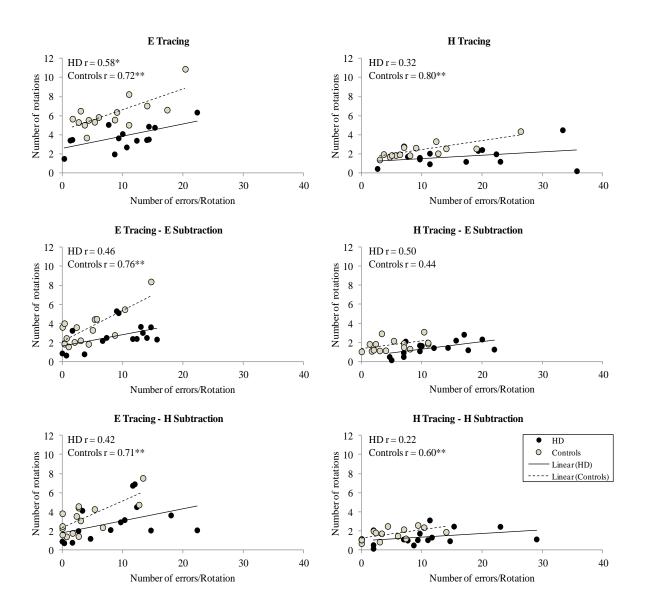


Figure 3. Speed-accuracy trade-offs for HD participants and controls across all circle tracing task conditions. Asterisks next to the r values represent significant correlations. ** p < .001; * p < .05.

For serial subtraction, error rates were below 6%. Rates of responding were comparable for the two groups, and increased with task difficulty. Due to the low error rates and poor distributional qualities, Mann-Whitney U tests were performed across all serial subtraction conditions to investigate group comparisons. None of the tests reached statistical significance (p > .05).

Discussion

Consistent with our predictions, HD participants were significantly slower and less accurate than controls. Both groups were slower and less accurate in the hard circle tracing conditions with HD participants being disproportionately compromised. Despite this, and in contrast to our predictions, there were no group differences in dual task costs. Instead, accuracy increased from single to dual tasks for both groups. Furthermore, HD participants were less susceptible to speed-accuracy trade-offs than controls. Our results provide partial support for the Unitary Resource Theory, and show that although HD participants differ in dual task performance compared with controls, neither group showed susceptibility to dual task interference.

Consistent with previous studies that used different dual task paradigms (Müller et al., 2002; Sprengelmeyer et al., 1995), HD was associated with slower performance in both circle tracing conditions, a finding that may reflect declines in psychomotor function. The HD group was less accurate across all conditions, and was also disproportionately compromised during the hard circle tracing conditions. Say et al. (2011) has also reported disproportionately reduced accuracy in hard circle tracing in HD. Our data extend these findings into a dual task paradigm. Previous studies have suggested that slowed performance in indirect circle tracing may be due to the increased sensorimotor

transformation demand which allows visual and proprioceptive information to be integrated into a common reference frame (Ingram et al., 2000; Messier & Kalaska, 1997; Say et al., 2011). Furthermore, the differences between the direct and indirect circle tracing tasks may suggest that the visuospatial demands of the task, which differed for direct and indirect circle tracing, were greater than the motor demands of the task, which were the same for direct and indirect circle tracing.

Although both groups maintained their single task *speed* during dual tasks, *accuracy was poorer for single tasks than dual tasks*. It is possible that because the single tasks were relatively easy, participants gave less effortful attention, or perhaps performed in more automatized fashion, reducing their monitoring of accuracy. Dual task performance, however, because it is more attentionally demanding and effortful, may have led participants to exert greater control, and therefore increased monitoring of accuracy. Our results are consistent with previous findings that showed simple tasks to place attentional demands on HD participants (Jahanshahi, Brown, & Marsden, 1993; Thompson et al., 2010). However, because controls showed a similar pattern, our results do not substantiate previous findings of impaired automaticity in HD.

The finding that HD was not associated with speed-accuracy trade-offs (with a single exception), but that speed-accuracy trade-offs were consistently present in controls, may be considered in the context of accumulator models. Specifically, accumulator models of speed-accuracy trade-offs assume that sensory evidence accumulates over time from signal onset until a decision threshold (Ivanoff, Branning, & Marois, 2008). Accumulation of evidence may proceed more or less slowly *and* more or less accuracy trade-offs

have been found to be implemented by a prefrontal network (Ivanoff et al., 2008; Romo & Salinas, 2003), which has also been implicated in HD (Thiruvady et al., 2007; Wolf et al., 2008; Wolf, Vasic, Schönfeldt-Lecuona, Landwehrmeyer, & Ecker, 2007). Therefore, although our instructions emphasized equally speed and accuracy, it is possible that controls used different strategies that emphasized either speed or accuracy, whereas HD participants were unable to implement such strategies due to this dysfunctional prefrontal network. Therefore, controls showed speed-accuracy trade-offs, whereas HD participants did not manifest trade-offs. This point may be clarified by instructions that systematically emphasize the speed or accuracy of performance.

As predicted by the Unitary Resource Theory, participants' speed decreased with task difficulty; however, in contrast to predictions from this theory, accuracy increased. Therefore, our results provide only partial support to the unitary resource framework. In addition, our findings highlight the importance of taking into account both speed and accuracy, as their relationship may vary with task difficulty or particular cognitive impairments. Contrary to predictions of the Multiple Resources Theory, our finding of interference between the circle tracing and serial subtraction is evidence of resource sharing between two apparently different tasks, suggesting that the visual and auditory modalities *and* the manual and vocal responses are not entirely separate.

In terms of limitations of our study, it is important to note that for practical reasons, counterbalancing the order of single and dual tasks was not possible, thus the results should be interpreted in the context of dual tasks being performed after single tasks. Participants' speed decreased with increased task difficulty, which may reflect practice effects on task performance. In addition, despite our instructions to perform the tasks as

quickly and as accurately as possible, our results suggest that the two groups were affected differently by the competing goals of speed and accuracy. Furthermore, the serial subtraction task conditions may not have been a sufficient manipulation of difficulty level, as there was no change in performance associated with difficulty level.

In summary, we demonstrated that HD was associated with overall slowing and less accuracy in dual tasking compared to controls. Dual task performance in HD was more compromised in the hard circle tracing tasks compared to controls, regardless of the difficulty of the second task, suggesting that higher levels of visuomotor task demands differentially affected HD participants. Despite this, we found no group differences in dual task costs, suggesting that group differences ceased to exist when single task performance was taken into account. Rather, accuracy increased from single to dual tasks. Interestingly, in both groups accuracy increased from single to dual tasks. Furthermore, in contrast to controls, HD participants were not susceptible to speed-accuracy trade-offs. Overall, we do not find support for the Multiple Resource Theory, but our findings provide partial support for the Unitary Resource Theory, and show that despite differences in dual task performance, neither group was more compromised in the dual task conditions after taking single task performance into account.

References

- American Psychiatric Association. (1994). *Diagnostic and statistical manual of mental disorders* (4th ed.). Washington, DC: American Psychiatry Association.
- Armieri, A., Holmes, J. D., Spaulding, S. J., Jenkins, M. E., & Johnson, A. M. (2009). Dual task performance in a healthy young adult population: Results from a symmetric manipulation of task complexity and articulation. *Gait & Posture, 29*, 346-348.
- Brown, R. G., Jahanshahi, M., & Marsden, C. D. (1993). The execution of bimanual movements in patients with Parkinson's, Huntington's and cerebellar disease. *Journal of Neurology, Neurosurgery, & Psychiatry, 56*, 295-297.
- Dannhauser, T. M., Walker, Z., Stevens, T., Lee, L., Seal, M., & Shergill, S. S. (2005). The functional anatomy of divided attention in amnestic mild cognitive impairment. *Brain*, 128, 1418-1427.
- de Ribaupierre, A., & Ludwig, C. (2003). Age differences and divided attention: Is there a general deficit? *Experimental Aging Research*, 29, 79-105.
- Georgiou, N., Bradshaw, J. L., Phillips, J. G., & Chiu, E. (1996). The effect of Huntington's disease and Gilles de la Tourette's syndrome on the ability to hold and shift attention. *Neuropsychologia*, 34, 843-851.
- Georgiou, N., Phillips, J. G., Bradshaw, J. L., Cunnington, R., & Chiu, E. (1997). Impairments of movement kinematics in patients with Huntington's disease: A comparison with and without a concurrent task. *Movement Disorders, 12*, 386-396.
- Huntington Study Group. (1996). The Unified Huntington's Disease Rating Scale: Reliability and consistency. *Movement Disorders*, 11, 136-142.

- Ingram, H. A., van Donkelaar, P., Cole, J., Vercher, J.-L., Gauthier, G. M., & Miall, R.C. (2000). The role of proprioception and attention in a visuomotor adaptation task. *Experimental Brain Research*, 132, 114-126.
- Ivanoff, J., Branning, P., & Marois, R. (2008). fMRI evidence for a dual process account of the speed-accuracy tradeoff in decision-making. *PLoS ONE*, *3*, e2635.
- Jahanshahi, M., Brown, R. G., & Marsden, C. D. (1993). A comparative study of simple and choice reaction time in Parkinson's, Huntington's and cerebellar disease. *Journal of Neurology, Neurosurgery, & Psychiatry, 56*, 1169-1177.

Kahneman, D. (1973). Attention and effort. New Jersey: Prentice-Hall.

- Kemper, S., Herman, R. E., & Lian, C. H. T. (2003). The costs of doing two things at once for young and older adults: Talking while walking, finger tapping, and ignoring speech or noise. *Psychology and Aging*, 18, 181-192.
- Lawrence, A. D., Hodges, J. R., Rosser, A. E., Kershaw, A., ffrench-Constant, C., Rubinsztein, D. C., . . . Sahakian, B. J. (1998). Evidence for specific cognitive deficits in preclinical Huntington's disease. *Brain*, 121, 1329-1341.
- Lemay, M., Fimbel, E., Beuter, A., & Chouinard, S. (2005). Sensorimotor mapping affects movement correction deficits in early Huntington's disease. *Experimental Brain Research*, 165, 454-460.
- McDowd, J. M., & Craik, F. I. M. (1988). Effects of aging and task difficulty on divided attention performance. *Journal of Experimental Psychology: Human Perception* and Performance, 14, 267-280.
- Messier, J., & Kalaska, J. F. (1997). Differential effect of task conditions on errors of direction and extent of reaching movements. *Experimental Brain Research*, 115, 469-478.

- Müller, S. V., Jung, A., Preinfalk, J., Kolbe, H., Ridao-Alonso, M., Dengler, R., &
 Münte, T. F. (2002). Disturbance of "extrinsic alertness" in Huntingtons disease.
 Journal of Clinical and Experimental Neuropsychology, 24, 517-526.
- Nasreddine, Z. S., Phillips, N. A., Bédiriam, V., Charbonneau, S., Whitehead, V.,
 Collin, I., . . . Chertkow, H. (2005). The Montreal Cognitive Assessment, MoCA:
 A brief screening tool for mild cognitive impairment. *Journal of the American Geriatrics Society*, 53, 695-699.
- Nicolson, R. I., & Fawcett, A. J. (1990). Automaticity: A new framework for dyslexia research? *Cognition*, *35*, 159-182.
- Romo, R., & Salinas, E. (2003). Flutter discrimination: Neural codes, perception, memory and decision making. *Nature Reviews Neuroscience*, *4*, 203-218.
- Rush, A. J., Carmody, T., & Reimitz, P.-E. (2006). The Inventory of Depressive Symptomatology (IDS): Clinician (IDS-C) and Self-Report (IDS-SR) ratings of depressive symptoms. *International Journal of Methods in Psychiatric Research*, 9, 45-59.
- Say, M. J., Jones, R., Scahill, R. I., Dumas, E. M., Coleman, A., Dar Santos, R. C., . . . Investigators, the TRACK-HD. (2011). Visuomotor integration deficits precede clinical onset in Huntington's disease. *Neuropsychologia*, 49, 264-270.
- Sprengelmeyer, R., Lange, H., & Hömberg, V. (1995). The pattern of attentional deficits in Huntington's disease. *Brain*, *118*, 145-152.
- Swanenburg, J., de Bruin, E. D., Hegemann, S., Uebelhart, D., & Mulder, T. (2010). Dual tasking under compromised visual and somatosensory input in elderly fallers and non-fallers. *The Open Rehabilitation Journal*, *3*, 169-176.

- Thiruvady, D. R., Georgiou-Karistianis, N., Egan, G. F., Ray, S., Sritharan, A., Farrow,
 M., . . . Cunnington, R. (2007). Functional connectivity of the prefrontal cortex in
 Huntington's disease. *Journal of Neurology, Neurosurgery, & Psychiatry*, 78, 127-133.
- Thompson, J. C., Poliakoff, E., Sollom, A. C., Howard, E., Craufurd, D., & Snowden, J. S. (2010). Automaticity and attention in Huntington's disease: When two hands are not better than one. *Neuropsychologia*, 48, 171-178.
- UNESCO. (1997). International Standard Classification of Education from http://www.uis.unesco.org/ev.php?ID=7433_201&ID2=D0_TOPIC
- Wechsler, D. (2001). *Wechsler Test of Adult Reading*. San Antonio: The Psychological Corporation.
- Wickens, C. D. (2002). Multiple resources and performance prediction. *Theoretical Issues in Ergonomics Science*, 3, 159-177.
- Wickens, C. D., & McCarley, J. S. (2008). Applied attention theory. Boca Raton: Taylor & Francis.
- Wolf, R. C., Sambataro, F., Vasic, N., Shonfeldt-Lecuona, C., Ecker, D., & Landwehrmeyer, B. (2008). Aberrant connectivity of lateral prefrontal networks in presymptomatic Huntington's disease. *Experimental Neurology*, 213, 137-144.
- Wolf, R. C., Vasic, N., Schönfeldt-Lecuona, C., Landwehrmeyer, B., & Ecker, D. (2007). Dorsolateral prefrontal cortex dysfunction in presymptomatic Huntington's disease: Evidence from event-related fMRI. *Brain*, 130, 2845-2857.

Chapter 5

A Comparison of Dual Tasks in Huntington's Disease

Preamble to Paper

Chapter 5 is the last empirical study presented in this thesis. Here we extend our previous study by investigating whether HD-related differences in dual tasking increase with increased task difficulty, as well as complexity. To achieve this aim, we employed the same two dual task sets that were presented earlier in Chapter 3. This paradigm provided insight into the importance of manipulating task difficulty and complexity in dual tasking in HD. It also provided evidence supporting that the type of concurrent task may affect dual task performance in HD.

Declaration for Thesis Chapter 5

Declaration by candidate

In the case of Chapter 5, the nature and extent of my contribution to the work was the following:

Nature of contribution	Extent of
	contribution (%)
Conception and design of the study, attainment of ethics approval and	80%
ongoing reporting requirements, review of relevant literature and writing of	
manuscript	

The following co-authors contributed to the work. Co-authors who are students at Monash University must also indicate the extent of their contribution in percentage terms:

Name	Nature of contribution	Extent of contribution (%) for student co-authors only
Prof Julie C. Stout	Contributed to development of ideas and critical revision of the paper	
Prof Nellie Georgiou-Karistianis	Contributed to development of ideas and critical revision of the paper	
Dr Andrew Churchyard	Assisted with recruitment of participants and input on manuscripts	

Candidate's Signature

Declaration by co-authors

The undersigned hereby certify that:

- (1) the above declaration correctly reflects the nature and extent of the candidate's contribution to this work, and the nature of the contribution of each of the co-authors.
- (2) they meet the criteria for authorship in that they have participated in the conception, execution, or interpretation, of at least that part of the publication in their field of expertise;
- (3) they take public responsibility for their part of the publication, except for the responsible author who accepts overall responsibility for the publication;
- (4) there are no other authors of the publication according to these criteria;
- (5) potential conflicts of interest have been disclosed to (a) granting bodies, (b) the editor or publisher of journals or other publications, and (c) the head of the responsible academic unit; and
- (6) the original data are stored at the following location(s) and will be held for at least five years from the date indicated below:

Location(s)

School of Psychology and Psychiatry, Monash University, Australia

	Signature	Date
Prof Julie C. Stout		
Prof Nellie Georgiou-Karistianis		
Dr Andrew Churchyard		20/4/12
		11-1

Date

Dual Task Performance in Huntington's Disease: A Comparison of Choice Reaction Time Tasks

Eleftheria Vaportzis and Nellie Georgiou-Karistianis

School of Psychology and Psychiatry, Monash University

Andrew Churchyard

School of Psychology and Psychiatry, Monash University Department of Neurology, Monash Medical Centre

Julie C. Stout

School of Psychology and Psychiatry, Monash University

Acknowledgments

We would like to thank our participants and their families for donating their time and effort to our study.

Address correspondence to Julie C. Stout, School of Psychology and Psychiatry, Monash University, Wellington Road, Clayton, Victoria 3800, Australia.

E-mail:

Abstract

Individuals with Huntington's disease (HD) have difficulty in performing concurrent tasks. This difficulty has been explained in terms of attentional *and* automaticity impairments. In addition, several theories have attempted to explain dual task interference, including the Unitary Resource and Multiple Resources theories. This study investigated whether simple tasks make disproportionately high demands in HD compared with controls, and also tested the unitary and multiple resources frameworks. Thirteen HD participants and 13 controls completed two dual task sets that varied in difficulty and complexity: set one paired simple choice reaction time (RT) with digit forward, and set two paired complex choice RT with digit backward. We found that HD participants were overall slower; however, although they maintained similar levels of accuracy in the simple choice RT tasks with controls, their accuracy decreased in the complex choice RT tasks. In addition, we found that HD participants were more susceptible to speed-accuracy trade-offs. Despite that, they did not show greater dual task costs than controls. Overall, our findings support the attentional impairment hypothesis in HD, and also the Unitary Resource Theory, although not conclusively.

Keywords: Choice reaction time; Divided attention; Dual task costs; Huntington's disease; Multitasking; Resource theories.

Introduction

Dual tasking refers to the performance of two tasks concurrently. From an ecological point of view, being able to perform multiple tasks at the same time is vital for independent functioning, as this makes it possible to execute everyday tasks, such as cooking while talking. The limited multitask research in Huntington's disease (HD), and anecdotal reports of HD patients and their families, suggest that multitasking is impaired in HD. Explanations for this impairment have been suggested, including deficits in resource allocation (Georgiou, Bradshaw, Phillips, & Chiu, 1996), attentional set-shifting (Lawrence et al., 1998), and lack of automaticity (Thompson et al., 2010). Although these explanations are plausible, the definitive basis of multitasking impairments in HD is still unclear.

The progression of HD is generally slow with the striatum the main site of early pathology (Georgiou-Karistianis et al., 2013; Tabrizi et al., 2012). Cortical regions are also affected early (Couette, Bachoud-Levi, Brugieres, Sieroff, & Bartolomeo, 2008), and are likely to contribute to physical, emotional and cognitive symptoms (Deckel, Weiner, Szigeti, Clark, & Vento, 2000; Fenney, Jog, & Duval, 2008; Rosas et al., 2003). Of particular interest is how HD participants multitask activities, which is often a source of complaint from both patients and family members.

Multitasking is usually studied using dual task paradigms. A number of theoretical frameworks have also been developed to explain dual task interference, including unitary resource and multiple resources theories. For instance, according to the Unitary Resource Theory, attention is a *single, limited capacity resource* that can be allocated to a single task or divided between different tasks, and which is affected by task difficulty

(Kahneman, 1973). According to this theory, dual task performance deteriorates if one task is difficult and requires a large proportion of this limited attentional resource, because there is little left to support the performance of the other task. However, in contrast to the predictions of the Unitary Resource Theory, findings indicate that two tasks can be performed concurrently even when difficulty is manipulated. To account for this observation, the Multiple Resources Theory (Wickens & McCarley, 2008) was proposed, which theorises that attention has *multiple separate resource pools* (e.g., a visual resource pool, an auditory resource pool), each of which can be divided among concurrent tasks. According to this theory, dual task performance would deteriorate when tasks make concurrent demands on the same resources (Wickens, 2002; Wickens & McCarley, 2008). Therefore, cross-dimensional tasks (e.g., visual-auditory) should lead to better processing than uni-dimensional tasks (e.g., visual-visual). At present there is empirical evidence for and against both theories (e.g., Parkes & Coleman, 1990; Young & Stanton, 2007) suggesting that the theoretical basis for dual tasking requires additional development. The current study aimed to examine the Unitary and Multiple Resources theories by manipulating task difficulty and complexity in HD.

Empirical evidence on dual tasking in HD is sparse. Although dual task impairments have been reported in HD, no study has addressed the issue of Unitary versus Multiple Resources theories. For example, Sprengelmeyer et al. (1995) and Müller et al. (2002) used the same visual-auditory dual task paradigm that required participants to press a button to specific stimuli and a different button to discriminative stimuli. Therefore, although the input of the tasks was cross-dimensional (i.e., visual-auditory), the output was uni-dimensional (i.e., motor-motor). For one task of the dual task pair, participants viewed matrices formed by Xs and Os, and were asked to respond by pressing a button

when they identified four Xs (from within a given matrix) that formed a square. The second task in the pair, which was performed simultaneously with the matrix task, required participants to listen to a series of high- and low-pitched tones, and respond when a tone was followed by another tone of the same frequency. Overall, HD participants were slower and less accurate than controls on choice reaction time (RT) tasks when administered within dual task contexts. Due to the different inputs, but same task outputs, it is difficult to draw conclusions on the multiple resources theory. It is possible, also endorsed by the authors, that the evidence points at a multi-dimensional system of semi-independent processes.

We extended past research by using and comparing two sets of dual tasks that differed in their degree of complexity. Our paradigm has been previously used to investigate dual task differences in healthy younger and older adults (Vaportzis, Georgiou-Karistianis, & Stout, 2013). The first task combination (termed the *simple dual task set*) paired simple choice RT with digit forward, and the second task combination (termed the *complex dual task set*) paired complex choice RT with digit backward. Choice RT tasks have been previously used to investigate dual task performance in HD, and have been found powerful for distinguishing between different patient groups (Jahanshahi, Brown, & Marsden, 1993). Previous studies have also found HD participants to be significantly impaired in digit forward and backward tasks (Beste, Saft, Güntürkün, & Falkenstein, 2008; Snowden, Craufurd, Thompson, & Neary, 2002; Wolf, Vasic, Schönfeldt-Lecuona, Ecker, & Landwehrmeyer, 2009). These tasks are comparable, but differ in complexity. Digit forward requires passive storage of information, whereas digit backward requires participants to hold information in memory and perform an operation on it (Babcock & Salthouse, 1990). For the current study, we used dual tasks to examine elements of both the Unitary and Multiple Resources theories. To examine the Multiple Resources Theory, we selected a combination of tasks (i.e., choice RT and digit tasks) likely to be processed by separate modalities-responses (i.e., visual-manual and auditory-vocal), thus leading to minimal interference. To examine the Unitary Resource Theory, we manipulated task difficulty within the dual task sets, by using easy and hard conditions for both the choice RT and digit tasks. According to the Unitary Resource Theory, differences are expected to emerge under the harder conditions, because manipulating task difficulty induces resource allocation limitations. With regard to HD, if a fundamental deficit is the ability to automatise responses, then one might expect greater impairments in the simpler, less demanding tasks. On the contrary, if attention is the primary deficit in HD, then greater impairments in the more complex and demanding tasks would be expected.

In light of dual task theories and past research, we predicted that HD participants would be slower and less accurate across all task conditions compared with controls. We expected speed to be slower and error rates to be higher with increased task difficulty and from single to dual tasks across both groups. In keeping with the resource allocation account, we expected disproportionate HD-related differences in speed and error rates in the complex dual task set; differences in the simple dual task set would support that simpler tasks make disproportionately high demands in HD.

Method

Participants

Thirteen participants in the early stages of HD and 13 age-, sex- and education-matched healthy controls participated. HD participants were diagnosed by an experienced neurologist (AC) on the basis of genetic confirmation of the disease, and the unequivocal presence of motor symptoms associated with HD. Years of diagnosis prior to participation in this study ranged from 2 to 7. Motor symptom severity was rated using the motor scale of the Unified Huntington's Disease Rating Scale (UHDRS; Huntington Study Group, 1996). The range of scores in our sample was between 7 and 34, out of a possible 60. The Total Functional Capacity Scale of the UHDRS was also assessed. The range of scores in our sample was between 3 and 13 out of a possible 13. Sample characterisation measures included the Montreal Cognitive Assessment (MoCA; Nasreddine et al., 2005), the Wechsler Test of Adult Reading (WTAR; Wechsler, 2001), and the Inventory of Depressive Symptomatology-Self-report (IDS-SR; Rush, Carmody & Reimitz, 2006). The MoCA is a 30-point cognitive screening test designed to detect cognitive impairment. The suggested cut-off point for mild impairment is 26 (Nasreddine et al., 2005). All control participants performed over 26 on the MoCA. The WTAR is used to estimate verbal IQ, and is composed of 50 words that have irregular letter to sound translations. The IDS-SR is a 30-item questionnaire that assesses the severity of depression within the past 7 days for all symptom domains within major depression according to the Diagnostic and Statistical Manual-IV (American Psychiatric Association, 1994). A score of 0 indicates no depressive symptoms, whereas a score of 84 indicates very severe depressive symptoms. Education level was assessed based on the International Standard Classification of Education (ISCED) system, according to which 0 indicates pre-primary education and 6 second stage tertiary education (UNESCO, 1997). ISCED, WTAR and IDS-SR scores did not significantly (p < .05) differ between HD participants and controls; MoCA scores were significantly lower for HD participants, t(23) = 2.90, p = .008.

Demographic and disease characteristics of participants are presented in Table 1. All participants gave written informed consent, were fluent in English, and self-reported that they were free of upper limb impairments (e.g., wrist injuries), neurological disease and psychological disorders, and that they had normal or corrected-to-normal vision and hearing. Ethics approval was granted by the Monash University Human Research Ethics Committee.

	HD n = 13	Controls n = 13
Sex (F:M)	3:10	3:10
Age (years)	58.15 (9.23)	55.31 (11.36)
MoCA	25.31 (2.62)	27.83 (1.52)
WTAR	109.46 (6.70)	111.25 (7.68)
IDS-SR	13.83 (7.49)	10.46 (5.22)
ISCED	4.15 (0.80)	4.54 (1.05)
Disease duration (years)	4.46 (1.94)	
UHDRS Total Functional Capacity	10.08 (3.17)	
UHDRS Motor score	21.42 (9.15)	
CAG repeat	42.42 (1.92)	

Table 1

Demographic Data for HD Participants and Controls

Note. CAG = Cytosine-adenine-guanine trinucleotide repeat; IDS-SR = Inventory of Depressive Symptomatology-Self-Report; ISCED = International Standard Classification of Education; MoCA = Montreal Cognitive Assessment; UHDRS = Unified Huntington's Disease Rating Scale; WTAR = Wechsler Test for Adult Reading.

Task Description

Participants were tested individually in a quiet room, and were instructed to perform all tasks as quickly and as accurately as they could. We used two sets of dual tasks: the simple dual task set paired simple choice RT with digit forward, and the complex dual task set paired complex choice RT with digit backward. Each task within each set had an easy and a hard condition.

We administered both choice RT tasks on a Lenovo ThinkPad® X61 (Morrisville, NC, USA) laptop. The laptop was placed in front of the participants within comfortable reach. Participants responded on the keyboard to stimuli that were presented in the centre of the screen. They pressed the left arrow with their left index finger to respond to target stimuli, and the right arrow with their right index finger to respond to non-target stimuli. The ratio of target/non-target stimuli was similar. RT and error rates were recorded. RT was the time required from the moment each stimulus appeared on the screen until participant's response. Error rates were the percentage of incorrect responses across all trials. A correct response was recorded when participants responded with the designated keyboard arrow to a target or non-target stimulus.

In the *simple choice RT* task, stimuli were letters of the alphabet, some of which were designated as target letters, and the rest as non-target letters. The target letters were X and Z in the easy condition, and X, Z, O and Y in the hard condition. Non-target letters were other letters of the alphabet. Trials started with a "get-ready" sign (+) that remained on the screen for 250 ms. Then, a letter appeared in the same position, and until the participant responded or for up to 3000 ms (see Figure 1A). Because hard digit forward requires more time, we adjusted the number of simple choice RT trials so that

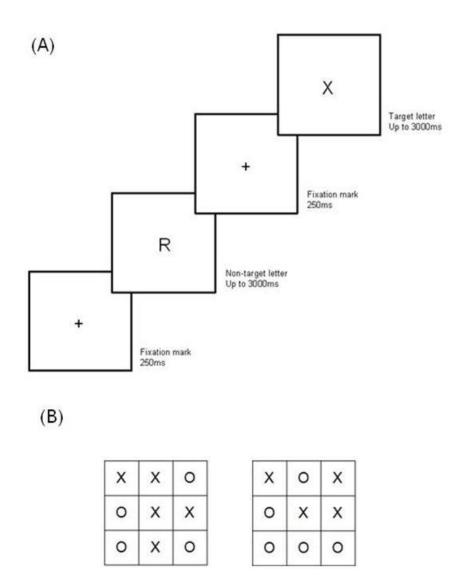


Figure 1. (A) A non-target (R) and a target (X) trial of the simple choice RT task. (B) Target stimuli of the complex choice RT task conditions. On the left matrix, three Xs appear in a row (easy or hard conditions); on the right matrix, three Os appear in a row (hard condition).

In the *complex choice RT* task, stimuli were 3 X 3 matrices of regular arrays of Xs and Os. In the easy condition, the target matrices had three Xs in a row, either horizontally or vertically. In the hard condition, they had either three Xs *or* three Os in a row (see Figure 1B). In non-target matrices, Xs and Os appeared in any location that did not constitute a row. Each stimulus was displayed on the screen until the participant responded or for up to 3000 ms. The interstimulus interval was 500 ms. The number of complex choice RT trials was 30 when it was performed concurrently with easy digit backward, and 40 when it was performed concurrently with hard digit backward.

For *digit forward*, stimuli were 4-digit (easy) and 5-digit (hard) numbers, and for *digit backward*, stimuli were 3-digit (easy) and 4-digit (hard) numbers. Digits ranged between 0 and 9, and each digit appeared only once in any given number. The series of numbers was read out at a rate of approximately 1 s, and then participants had to repeat them aloud in the correct order. As soon as participants recalled a series, the researcher presented the following one. Error rates were recorded as the percentage of incorrect responses across trials. For the single tasks, participants completed 10 trials. For the dual tasks, the number of trials varied from participant to participant since the digit tasks ended once participants had finished the choice RT tasks.

For the dual task conditions, participants started the choice RT tasks by pressing the Enter button on the keyboard. At the same time, the experimenter started reading a series of numbers, the length of which depended on the condition (e.g., easy, hard). As soon as the participant recalled a series, the experimenter read out the following one.

Design

For each dual task set, participants first performed the four single tasks followed by every possible combination of the choice RT with digit tasks as described in Table 2. Participants performed practice trials prior to each of the single tasks only. The simple and complex dual task sets were two of four sets of tasks that participants performed as part of a larger study. The order of the four sets was counterbalanced across participants, and thus, half of the participants performed the simple dual task set first, whereas half of the participants performed the complex dual task set first. We did not counterbalance the order of the conditions, because a full permutation with all the different conditions for all the different sets of tasks as well as the sample size. Furthermore, we wanted easy tasks to precede hard tasks in order to allow mastery of the easy task before increasing task difficulty. Similarly, we wanted single tasks to precede dual tasks in order to allow mastery of the single tasks before adding the challenge of a concurrent task.

Т	abl	le	2	

Order	Simple Dual Task Set	Hard Dual Task Set
1	Simple Choice RT E	Complex Choice RT E
2	Simple Choice RT H	Complex Choice RT H
3	Digit Forward E	Digit Backward E
4	Digit Forward H	Digit Backward H
5	Simple Choice RT E + Digit Forward E	Complex Choice RT E + Digit Backward E
6	Simple Choice RT E + Digit Forward H	Complex Choice RT E + Digit Backward H
7	Simple Choice RT H + Digit Forward E	Complex Choice RT H + Digit Backward E
8	Simple Choice RT H + Digit Forward H	Complex Choice RT H + Digit Backward H

Note. RT = Reaction time; E = Easy; H = Hard.

Statistical Analyses

Trials with values more than 3.5 standard deviations from the individual mean were excluded prior to computing overall means and standard deviations for *RT* and *error rates* across all tasks (see Table 3). For each dependent variable, mixed model ANOVAs were used to examine effects of groups and task conditions. Taking for example the simple dual task set, 2 X 2 X 3 mixed model ANOVAs were computed separately for RT and errors rates, with Group as a between subjects factor (HD, controls), and two within factors: Simple Choice RT Task difficulty (easy, hard), and Digit Forward Task difficulty (none, easy, hard). The same model was used for the complex dual task set. We report Greenhouse-Geisser corrected degrees of freedom due to violations of the sphericity assumption. Significant interactions of interest were followed with Bonferroni post hoc tests ($\alpha = .05$).

We also computed *dual task costs* separately for RT and error rates for the simple and complex choice RT tasks, as well as for error rates for the digit tasks, to assess performance costs associated with completing tasks concurrently. In line with past studies (de Ribaupierre & Ludwig, 2003; McDowd & Craik, 1988; Swanenburg, de Bruin, Hegemann, Uebelhart, & Mulder, 2010), we used the formula dual task cost = (single task-dual task)/single task to calculate the relative ratio of single task to dual task that controls for single task performance. Taking for example the simple dual task set, we used a 2 X 2 X 2 mixed-model ANOVA with the between factor Group (HD, controls) and two within factors: Simple Choice RT Task difficulty (easy, hard) and Digit Forward Task difficulty (easy, hard). We used the same model for complex choice RT and digit tasks. Negative dual task costs indicate that RT decreased and error rates increased in the dual tasks in comparison to the single tasks.

andard Dev	viations) c	andard Deviations) of HD Participants a	pants and	Controls Across All Tasks	ossAll Ia	SKS						
	Simple	Simple Choice	Simple (Choice	Digit F	Digit Forward	Complex	Complex Choice	Complex Choice	x Choice	Digit Backward	ckward
	RT (RT)	RT)	RT(E	(Errors)	(En	(Errors)	RT (RT (RT)	RT (Errors)	(rrors)	(Errors)	ors)
	HD	Controls	HD	Controls	HD	Controls	HD	Controls	HD	Controls	HD	Controls
	778	586	5.46	4.10	1.53	0.76	1479	1274	20.51	10.25	10.53	6.15
	(182)	(108)	(5.63)	(4.04)	(3.75)	(2.77)	(408)	(405)	(13.93)	(11.01)	(11.43)	(11.92)
	851	622	5.98	2.22	12.30	5.38	1957	1700	23.58	12.30	33.84	20.76
	(244)	(103)	(5.90)	(2.72)	(15.89)	(10.50)	(477)	(526)	(10.22)	(10.57)	(22.18)	(18.46)
Digit	1110	813	11.45	4.78	9.80	7.69	30.37	2295	39.99	19.48	32.43	18.68
	(406)	(250)	(14.36)	(5.35)	(16.97)	(13.12)	(491)	(571)	(16.33)	(12.89)	(27.77)	(22.22)
IDigit	1001	753	17.26	5.58	11.14	11.65	1799	1601	30.25	26.41	20.40	20.89
	(319)	(199)	(16.46)	(4.36)	(11.96)	(20.48)	(491)	(485)	(15.83)	(18.46)	(21.63)	(17.46)
Digit	1177	799	12.47	5.64	20.62	17.78	2921	2266	36.41	18.46	55.25	29.13
	(411)	(194)	(17.62)	(4.68)	(18.03)	(18.01)	(561)	(458)	(13.84)	(6.29)	(19.73)	(21.27)
I Digit	1017	746	19.82	10.08	20.09	21.95	1908	1604	41.79	27.17	54.45	28.25
	(321)	(195)	(16.93)	(4.85)	(23.15)	(21.88)	(416)	(590)	(14.88)	(11.57)	(26.45)	(26.77)
action time.	; E = Easy	action time; $E = Easy; H = Hard$.										

undard Deviations) of HD Participants and Controls Across All Tasks

Results

Overall, HD participants were slower and less accurate on the choice RT tasks. In addition, performance of both groups was worse in the dual tasks compared with the single tasks. In this section, we first present the simple choice RT task performance (single and dual tasks) followed by the complex choice RT task performance (single and dual tasks). Finally, we present performance on the digit tasks.

Simple Choice RT Task Performance

For the simple choice RT (single and dual tasks), slowing was associated with being in the HD group, performing dual tasks, and easy digit forward. Using RT as the dependent variable, a three-way ANOVA revealed significant main effects of Group, F(1,24) = 8.19, p = .009, $\eta^2 = .25$, with HD participants being significantly slower than controls, and Digit Forward, F(1.54,37.04) = 51.25, p < .001, $\eta^2 = .68$, with significantly slower performance in the dual tasks (easy and hard digit forward) compared with single tasks (no digit forward). Surprisingly, the easy digit forward conditions were performed significantly (p < .001) slower than the hard digit forward conditions. As there were no significant interactions, we did not find evidence that having HD unduly compromised performance of dual tasks compared to controls.

For error rates, a three-way ANOVA revealed that error rates were more affected by the difficulty level of the digit forward task in HD. Specifically, we found a significant main effect of Digit Forward, F(1.60,38.39) = 16.33, p < .001, $\eta^2 = .40$, and an interaction between Group and Digit Forward, F(1.60,38.39) = 3.54, p = .04, $\eta^2 = .13$ (see Figure 2). Post hoc analysis showed that HD participants made significantly (p < .001)

.05) more errors in the dual tasks (easy and hard digit forward) compared with the single tasks (no digit forward).

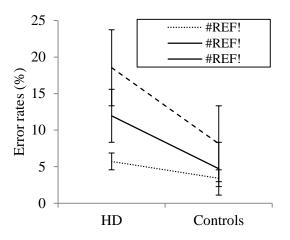


Figure 2. Error rates on the Simple Choice RT as a function of Group (HD, controls) and Digit Forward Task difficulty (none, easy, hard). E = Easy; H = Hard. Standard error bars are included.

For dual task costs, we did not find any interactions or HD-related differences for either RT or error rates suggesting that neither group was more susceptible to dual task demands. For dual task costs of *RT*, we found significant main effects of Simple Choice RT, F(1.00,24.00) = 4.41, p = .04, $\eta^2 = .15$, with significantly greater costs in the easy simple choice RT, and Digit Forward, F(1.00,24.00) = 20.09, p < .001, $\eta^2 = .45$, with significantly greater costs in the easy digit forward. For dual task costs of *error rates*, we found a significant main effect of Digit Forward, F(1.00,24.00) = 8.93, p = .006, $\eta^2 = .27$, with significantly greater costs in the hard digit forward conditions.

To investigate whether HD participants were more inclined to sacrifice accuracy for speed, we performed a series of correlational analyses between speed and error rates for each of the six simple choice RT conditions separately for the two groups. We found significant (p < .05) positive correlations across a number of conditions suggesting speed-accuracy trade-offs for the HD group only. Specifically, we found speed-accuracy trade-offs in all conditions for HD participants with exception the single condition of the easy simple choice RT task (see Figure 3).

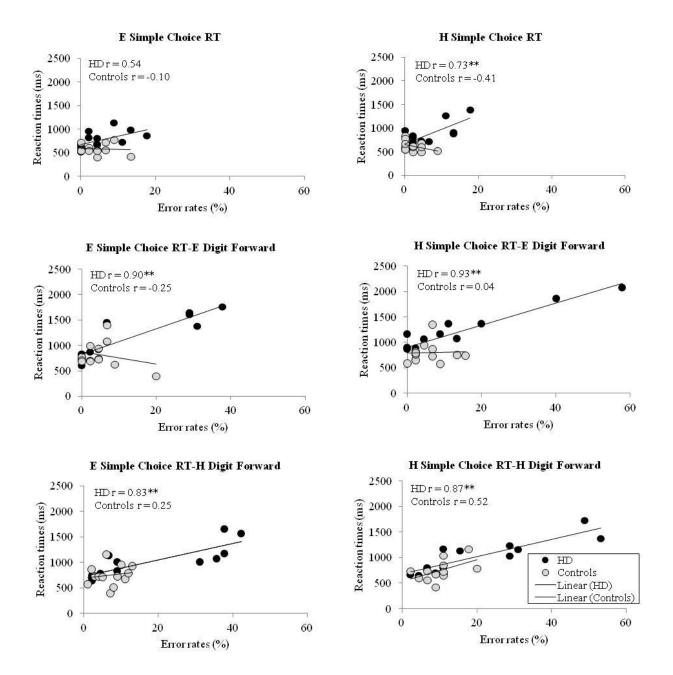


Figure 3. Speed-accuracy trade-offs for HD participants and controls across all conditions of the simple dual task set. E = Easy; H = Hard. ** p < .001.

Complex Choice RT Task Performance

For the complex choice RT (single and dual tasks), slowing was associated with being in the HD group, performing dual tasks, hard complex choice RT, and easy digit forward. Using RT as the dependent variable, a three-way ANOVA revealed significant main effects of Group, F(1,24) = 6.03, p = .022, $\eta^2 = .20$, Complex Choice RT, F(1.00,24.00) = 13.88, p = .001, $\eta^2 = .36$, and Digit Backward, F(1.86,44.67) = 120.01, p < .001, $\eta^2 = .83$. We also found a significant interaction between Group and Digit Backward, F(1.86,44.67) = 6.66, p = .01, $\eta^2 = .21$ (see Figure 4). Post hoc analysis showed that both groups were significantly (p < .001) slower in the easy digit backward conditions, compared with the hard digit backward and single task conditions.

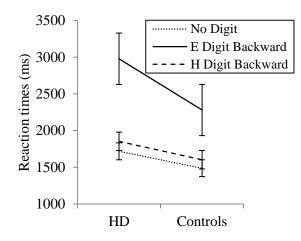


Figure 4. Reaction times on the Complex Choice RT as a function of Group (HD, controls) and Digit Backward difficulty (none, easy, hard). E = Easy; H = Hard. Standard error bars are included.

In addition, we found a significant interaction between Complex Choice RT and Digit Backward, F(1.79,43.04) = 121.08, p < .001, $\eta^2 = .46$. Post hoc analysis revealed that hard complex choice RT task was performed significantly (p < .001) slower than easy complex choice RT task in the single tasks (no digit backward). We also found that the easy digit backward conditions were performed significantly (p < .001) slower than the single tasks and the hard digit backward conditions regardless of complex choice RT difficulty.

For error rates, a three-way ANOVA showed that HD participants were less accurate. Specifically, we found a significant main effect of Group, F(1,24) = 11.28, p = .003, $\eta^2 = .32$, with HD participants making significantly more errors than controls. We also found a significant main effect of Digit Backward, F(1.61,38.74) = 28.90, p < .001, $\eta^2 = .54$, and an interaction between Complex Choice RT and Digit Backward, F(1.93,46.45) = 4.61, p = .01, $\eta^2 = .16$. Post hoc analysis showed that all participants made significantly (p < .01) more errors in the dual tasks (easy and hard digit backward) compared with the single tasks (no digit backward).

For dual task costs, we did not find any interactions or HD-related differences for RT; however, for error rates, we found that HD participants were less susceptible to dual task demands in the hard digit backward conditions. More specifically, for dual task costs for *RT*, we found significant main effects of Complex Choice RT, F(1.00,24.00) =44.71, p < .001, $\eta^2 = .65$, with significantly greater costs in easy complex choice RT, and Digit Backward, F(1.00,24.00) = 76.32, p < .001, $\eta^2 = .76$, with significantly greater costs in easy digit backward. For dual task costs for *error rates*, we found a significant interaction between Group and Digit Backward, F(1.00,24.00) = 6.15, p =.02, $\eta^2 = .20$ (see Figure 5). Post hoc analysis showed that HD participants had significantly (p = .01) lower costs in the hard digit backward, compared with the easy digit backward; controls showed no significant difference.

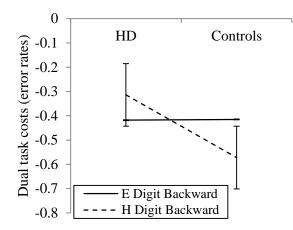


Figure 5. Dual task costs (error rates) on the Complex Choice RT (easy, hard) as a function of Group (HD, controls). E = Easy; H = Hard. Standard error bars are included.

Similarly with the simple choice RT tasks, we performed a series of correlational analyses between speed and error rates for each of the six complex choice RT conditions separately for the two groups. We found significant (p < .05) positive correlations across a number of conditions. Specifically, we found that HD participants sacrificed speed for accuracy in all dual task conditions, but not in the single task conditions. Controls showed speed-accuracy trade-offs only in the easy complex choice RT dual tasks (see Figure 6).

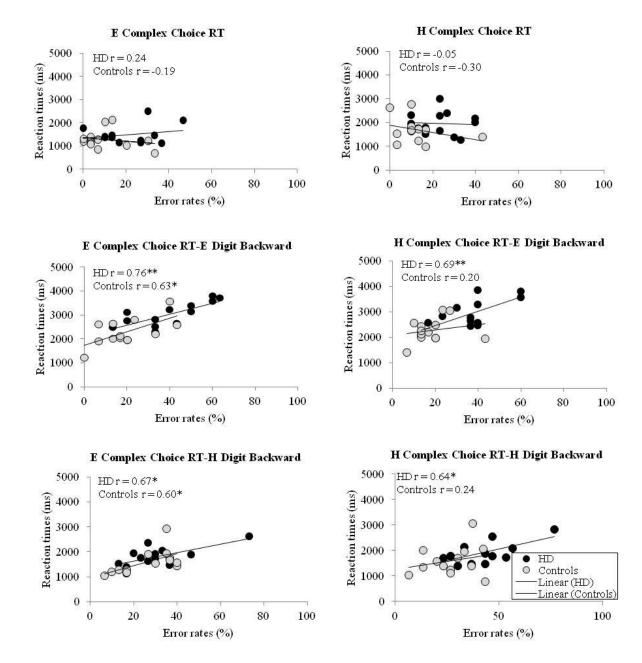


Figure 6. Speed-accuracy trade-offs for HD participants and controls across all conditions of the complex dual task set. E = Easy; H = Hard. ** p < .001; * p < .05.

Digit Tasks Performance

Performance of the two groups did not differ on the digit forward tasks. For the digit backward tasks, however, HD participants made significantly more errors. Specifically, for *digit forward*, a three-way ANOVA revealed a significant main effect of Digit Forward, F(1.00,24.00) = 21.48, p < .001, $\eta^2 = .47$, with significantly more errors in the hard conditions. There was also a significant main effect of Simple Choice RT, F(1.78,42.73) = 10.44, p < .001, $\eta^2 = .30$, with significantly more errors in the dual tasks compared with the single tasks. There were no significant interactions.

For *digit backward*, a three-way ANOVA showed significant main effects of Group, $F(1,24) = 4.82, p = .0.3, \eta^2 = .17$, with HD participants making significantly more errors than controls; Digit Backward, $F(1.00,24.00) = 50.47, p < .001, \eta^2 = .68$, with significantly more errors in the hard conditions compared with the easy conditions; and Complex Choice RT, $F(1.93,46.33) = 14.77, p < .001, \eta^2 = .38$, with significantly more errors in the dual tasks compared with the single tasks. There were no significant interactions. For dual task costs, we did not find any interactions or HD-related differences for either digit forward or digit backward.

Discussion

This study examined whether simple tasks make disproportionately high demands in HD compared with controls, and tested the Unitary Resource and Multiple Resources theories. We employed two dual task sets that varied in difficulty and complexity, and expected HD participants to be slower and less accurate across all conditions.

In line with our prediction, and consistent with Müller et al. (2002) and Sprengelmeyer et al. (1995), we found that HD participants were overall slower. However, although they maintained similar levels of accuracy with controls in the simple choice RT tasks, their accuracy decreased in the complex choice RT tasks. Therefore, performance in HD was more compromised in the more demanding dual task set. Thompson et al. (2011) demonstrated impaired automaticity in HD using tapping tasks, and suggested that the automaticity principle extends to cognitive tasks as they found tapping variability to be correlated with neuropsychological measures, such as the Stroop test. We argued that difficulty in automatising responses in HD would be manifest by greater impairments in the simpler, less demanding tasks, whereas greater impairments in the more complex and demanding tasks, would suggest attentional impairments in HD. We found that HD participants were more compromised in the more challenging dual task set, thus our findings are in keeping with the attentional impairment hypothesis.

In support of the Multiple Resources Theory, we expected minimal interference between the choice RT and digit tasks; in support of the Unitary Resource Theory, we expected differences to emerge with increased task difficulty. Overall, our findings showed some resource sharing between two seemingly different tasks, suggesting that the visual and auditory modalities *and* the manual and vocal responses are not as utterly separate as the Multiple Resources Theory posits. Although not conclusively, these results favour the Unitary Resource Theory (Kahneman, 1973), as with increased task difficulty performance of both groups deteriorated. In further support of this theory, performance of HD participants was slower, possibly because they came to a point where attentional resources were not enough to perform the tasks quicker than controls. However, we found HD-related differences in error rates only in the complex choice RT tasks. Thus, our study highlights the importance of manipulating task difficulty and complexity, as well as taking into account speed and accuracy measures, as the relationships between HD and these measures may vary with task difficulty and complexity.

Both groups were slower and made more errors in the choice RT tasks when they performed the digit tasks concurrently, strengthening the notion that the dual task conditions increased cognitive load. Surprisingly, we found that HD participants had *lower dual task costs* in *error rates* when *complex choice RT* was performed with *hard digit backward*, and this was the only significant group difference that we found in dual task costs. We suggest that perhaps HD participants were more robust to the demands of the second concurrent task because their performance was already sufficiently compromised in the single task conditions, therefore, making it possible for them to incorporate the second task without further reduction in their accuracy.

Furthermore, we found that HD participants were more inclined to speed-accuracy trade-offs probably due to inability to maintain speed at reasonable accuracy and vice versa, and despite our instructions that emphasised both. This finding may be explained by accumulator models of speed-accuracy trade-offs. Accumulator models posit that sensory evidence accumulates over time from stimulus onset until a decision threshold (Ivanoff, Branning, & Marois, 2008). Speed-accuracy trade-offs may surface depending on the task and individual differences, and therefore, accumulation of evidence may progress more or less slowly and accurately (Ivanoff et al., 2008). Studies have suggested that speed-accuracy trade-offs are implemented by a prefrontal network (Ivanoff et al., 2008; Romo & Salinas, 2003), which has also been implicated in HD

(Gray et al., 2013; Thiruvady et al., 2007; Wolf et al., 2008; Wolf, Vasic, Schönfeldt-Lecuona, Landwehrmeyer, & Ecker, 2007). It remains to be determined whether the different pattern of results between the two groups can be modulated by instructions that emphasise either speed or accuracy of performance.

In terms of the caveats of our study, although we instructed participants to perform the tasks as quickly and as accurately as they could, our results suggest that it is likely that HD participants were affected differently than controls with respect to the competing goals of speed and accuracy. An important question that remains is whether the speed-accuracy trade-offs that we observed were a result of conscious rather than automatic processes. Furthermore, our conclusions must be considered in light of possible order effects since, for practical reasons, we did not counterbalance single and dual tasks. However, because we found that participants' performance deteriorated in the harder tasks, which were presented later (i.e., with the greatest amount of practice), if anything, counterbalancing would most likely have further strengthened our findings. Finally, our control group did not execute the simple choice RT dual tasks as efficiently as the single tasks, suggesting that even this simple combination of tasks placed some demand on conscious attention, and could not be entirely automatised.

A major aim of the current study was to compare different sets of dual tasks that differed in complexity. We also manipulated task difficulty of both tasks within each set. Research in dual tasking in HD is limited, and most previous studies have used only one dual task, and did not examine dual task performance at different difficulty levels. We found that HD participants were slower across all tasks, however, accuracy differences emerged with increased task complexity, suggesting some attentional impairment in HD. These findings, along with our results indicating speed-accuracy trade-offs mainly for HD participants, highlight the importance of taking into account measures of both speed and accuracy. Despite that, HD participants did not show greater dual task costs than controls; in fact, they showed lower costs in error rates of the complex choice RT task when performed with hard digit backward. Overall, we found a differential effect of dual task performance between HD participants and controls that depends on both the difficulty and complexity level of dual tasks. Although not conclusive, performance of both groups deteriorated with task difficulty giving some support to the Unitary Resource Theory, and also with task complexity, giving support to the attentional impairment hypothesis in HD. Further investigation in multi-tasking is warranted as it is vital for independent living.

References

- American Psychiatric Association. (1994). *Diagnostic and statistical manual of mental disorders* (4th ed.). Washington, DC: American Psychiatry Association.
- Babcock, R. L., & Salthouse, T. A. (1990). Effects of increased processing demands on age differences in working memory. *Psychology and Aging*, *5*, 421-428.
- Beste, C., Saft, C., Güntürkün, O., & Falkenstein, M. (2008). Increased cognitive functioning in symptomatic Huntington's disease as revealed by behavioral and event-related potential indices of auditory sensory memory and attention. *The Journal of Neuroscience*, 28, 11695-11702.
- Couette, M., Bachoud-Levi, A.-C., Brugieres, P., Sieroff, E., & Bartolomeo, P. (2008). Orienting of spatial attention in Huntington's disease. *Neuropsychologia*, 46, 1391-1400.
- de Ribaupierre, A., & Ludwig, C. (2003). Age differences and divided attention: Is there a general deficit? *Experimental Aging Research, 29*, 79-105.
- Deckel, A. W., Weiner, R., Szigeti, D., Clark, V., & Vento, J. (2000). Altered patterns of regional cerebral blood flow in patients with Huntington's disease: A SPECT study during rest and cognitive or motor activation. *The Journal of Nuclear Medicine*, 41, 773-780.
- Fenney, A., Jog, M. S., & Duval, C. (2008). Bradykinesia is not a "systematic" feature of adult-onset Huntington's disease; Implications for basal ganglia pathophysiology. *Brain Research*, 1193, 67-75.
- Georgiou, N., Bradshaw, J. L., Phillips, J. G., & Chiu, E. (1996). The effect of Huntington's disease and Gilles de la Tourette's syndrome on the ability to hold and shift attention. *Neuropsychologia*, *34*, 843-851.

- Georgiou-Karistianis, N., Stout, C. J., Dominquez, J. F., Carron, S. P., Ando, A., Churchyard, A., . . . Egan, G. F. (2013). Functional magnetic resonance imaging of working memory in Huntington's disease: Cross-sectional data from the IMAGE-HD study, *Human Brain Maping*, in press 12 March 2013.
- Gray, M. A., Egan, G. F., Ando, A., Churchyard, A., Chua, P., Stout, J. C., & Georgiou-Karistianis, N. (2013). Prefrontal activity in Huntington's disease reflects cognitive and neuropsychiatric disturbances: The IMAGE-HD study. *Experimental Neurology*, 239, 218-228.
- Huntington Study Group. (1996). TheUnified Huntington's Disease Rating Scale: Reliability and consistency. *Movement Disorders*, 11, 136-142.
- Ivanoff, J., Branning, P., & Marois, R. (2008). fMRI evidence for a dual process account of the speed-accuracy tradeoff in decision-making. *PLoS ONE*, *3*, e2635.
- Jahanshahi, M., Brown, R. G., & Marsden, C. D. (1993). A comparative study of simple and choice reaction time in Parkinson's, Huntington's and cerebellar disease. *Journal of Neurology, Neurosurgery, & Psychiatry, 56*, 1169-1177.

Kahneman, D. (1973). Attention and effort. New Jersey: Prentice-Hall.

- Lawrence, A. D., Hodges, J. R., Rosser, A. E., Kershaw, A., ffrench-Constant, C., Rubinsztein, D. C., . . . Sahakian, B. J. (1998). Evidence for specific cognitive deficits in preclinical Huntington's disease. *Brain*, 121, 1329-1341.
- McDowd, J. M., & Craik, F. I. M. (1988). Effects of aging and task difficulty on divided attention performance. *Journal of Experimental Psychology: Human Perception* and Performance, 14, 267-280.
- Müller, S. V., Jung, A., Preinfalk, J., Kolbe, H., Ridao-Alonso, M., Dengler, R., & Münte, T. F. (2002). Disturbance of "extrinsic alertness" in Huntingtons disease. *Journal of Clinical and Experimental Neuropsychology*, 24, 517-526.

- Nasreddine, Z. S., Phillips, N. A., Bédiriam, V., Charbonneau, S., Whitehead, V., Collin, I., . . . Chertkow, H. (2005). The Montreal Cognitive Assessment, MoCA:
 A brief screening tool for mild cognitive impairment. *Journal of the American Geriatrics Society*, 53, 695-699.
- Parkes, A. M., & Coleman, N. (1990). Route guidance systems: A comparison of methods of presenting directional information to the driver. In E. J. Lovesey (Ed.), *Contemporary ergonomics*. Mahwah, NJ: Erlbaum.
- Romo, R., & Salinas, E. (2003). Flutter discrimination: Neural codes, perception, memory and decision making. *Nature Reviews Neuroscience*, 4, 203-218.
- Rosas, H. D., Koroshetz, W. J., Chen, Y. I., Skeuse, C., Vangel, M., Cudkowicz, M. E.,
 . . . Goldstein, J. M. (2003). Evidence for more widespread cerebral pathology in early HD: An MRI-based morphometric analysis. *Neurology*, 60, 1615-1620.
- Rush, A. J., Carmody, T., & Reimitz, P.-E. (2006). The Inventory of Depressive Symptomatology (IDS): Clinician (IDS-C) and Self-Report (IDS-SR) ratings of depressive symptoms. *International Journal of Methods in Psychiatric Research*, 9, 45-59.
- Snowden, J. S., Craufurd, D., Thompson, J., & Neary, D. (2002). Psychomotor, executive, and memory function in preclinical Huntington's disease. *Journal of Clinical and Experimental Neuropsychology*, 24, 133-145.
- Sprengelmeyer, R., Lange, H., & Hömberg, V. (1995). The pattern of attentional deficits in Huntington's disease. *Brain*, *118*, 145-152.
- Swanenburg, J., de Bruin, E. D., Hegemann, S., Uebelhart, D., & Mulder, T. (2010). Dual tasking under compromised visual and somatosensory input in elderly fallers and non-fallers. *The Open Rehabilitation Journal*, *3*, 169-176.

- Tabrizi, S. J., Reilmann, R., Roos, R. A. C., Durr, A., Leavitt, B., Owen, G., . . . investigators, the TRACK-HD. (2012). Potential endpoints for clinical trials in premanifest and early Huntington's disease in the TRACK-HD study: Analysis of 24 month observational data. *The Lancet*, 11, 42-53.
- Thiruvady, D. R., Georgiou-Karistianis, N., Egan, G. F., Ray, S., Sritharan, A., Farrow,
 M., . . . Cunnington, R. (2007). Functional connectivity of the prefrontal cortex in
 Huntington's disease. *Journal of Neurology, Neurosurgery, & Psychiatry*, 78, 127-133.
- Thompson, J. C., Poliakoff, E., Sollom, A. C., Howard, E., Craufurd, D., & Snowden, J.S. (2010). Automaticity and attention in Huntington's disease: When two hands are not better than one. *Neuropsychologia*, 48, 171-178.
- UNESCO. (1997). International Standard Classification of Education from http://www.uis.unesco.org/ev.php?ID=7433_201&ID2=D0_TOPIC
- Vaportzis, E., Georgiou-Karistianis, N., & Stout, C. J. (2013). Dual task performance in normal aging: A comparison of choice reaction time tasks. *PLoS ONE*, 8, e60265.
- Wechsler, D. (2001). *Wechsler Test of Adult Reading*. San Antonio: The Psychological Corporation.
- Wickens, C. D. (2002). Multiple resources and performance prediction. *Theoretical Issues in Ergonomics Science*, 3, 159-177.
- Wickens, C. D., & McCarley, J. S. (2008). Applied attention theory. Boca Raton: Taylor & Francis.
- Wolf, R. C., Sambataro, F., Vasic, N., Shönfeldt-Lecuona, C., Ecker, D., & Landwehrmeyer, B. (2008). Aberrant connectivity of lateral prefrontal networks in presymptomatic Huntington's disease. *Experimental Neurology*, 213, 137-144.

- Wolf, R. C., Vasic, N., Schönfeldt-Lecuona, C., Ecker, D., & Landwehrmeyer, G. B. (2009). Cortical dysfunction in patients with Huntington's disease during working memory performance. *Human Brain Mapping*, *30*, 327-339.
- Wolf, R. C., Vasic, N., Schönfeldt-Lecuona, C., Landwehrmeyer, B., & Ecker, D.
 (2007). Dorsolateral prefrontal cortex dysfunction in presymptomatic Huntington's disease: Evidence from event-related fMRI. *Brain 130*, 2845-2857.
- Young, M. S., & Stanton, N. A. (2007). Miles away: Determining the extent of secondary task interference on simulated driving. *Theoretical Issues in Ergonomics Science*, 8, 233-253.

Chapter 6

General Discussion

6.1. Summary of Results

Behavioural and neuroimaging research, as outlined in Chapter 1, has shown that HD and ageing are associated with difficulties in dual tasking. Although the basis of these difficulties remains unresolved, a number of explanations that have been put forward include impairments in resource allocation in HD and limited availability in mental resources in ageing. Processing Speed (Salthouse, 2000), Multiple Resources (Wickens & McCarley, 2008) and Unitary Resource (Kahneman, 1973) theories have also attempted to provide a theoretical explanation for dual task difficulties in these populations.

The overall aim of this thesis was to systematically examine dual task performance in HD and healthy younger and older adults. Previous studies and theories have suggested that dual task performance can be affected by task similarity and task difficulty. For this reason, we selected four sets of tasks that have been previously used in HD or other clinical populations. Each task varied in its input (e.g., visual) and output (e.g., motor) modalities, *and* also in its level of difficulty (easy and hard). We examined several dual task sets because previous research in healthy subjects and other patient groups has shown that dual task performance depends on the type of concurrent task. Therefore, by investigating more than one type of concurrent task, and different combinations of tasks, we reasoned that we could make more generalisable conclusions about dual tasking in HD.

The first study, presented in Chapters 2 and 3 (submitted and published manuscripts, respectively), was conducted with healthy younger and older adults to characterise the parameters of the tasks in a healthy population, and to investigate the potential

suitability of the tasks for measuring dual task performance in the subsequent studies with HD. Chapter 2 describes a study that used circle tracing with serial subtraction tasks. For the easy level of the circle tracing task, participants traced a circle on a tablet that was placed in front of them. Similarly, for the hard level, participants traced a circle on a tablet; however, in this condition their arm was covered, and they had to monitor their progress on a second monitor screen that was placed in front of them. For serial subtraction, participants counted backward by twos (easy) and by threes (hard). Results indicated that older adults were significantly slower than younger adults across all conditions, and had significantly greater dual task costs when they performed circle tracing with the easy level of serial subtraction. Higher levels of task difficulty were associated with slower speed in both groups. We found no age-related differences in accuracy. We also found speed-accuracy trade-offs regardless of age group. These findings suggest that different measures of performance may be affected differently during dual tasking. Furthermore, with increased age, people may rely to a greater extent on proprioceptive feedback to guide upper limb movement.

Chapter 3 presents a study comparing two dual task sets with similar types of demands, but varied in complexity. The first set paired simple choice RT with digit forward, and the second set paired complex choice RT with digit backward. For simple choice RT, participants viewed single letters and pressed a specified keyboard key if the letter was X or Z or a different key for other letters (easy). For the hard level, there were 4 target letters (X, Z, O, Y). Concurrently, participants repeated 4 (easy) or 5 (hard) digits in the same order. For the complex choice RT, participants viewed 4 X 4 matrices of Xs and Os, and indicated whether four Xs (easy) *or* four Xs or four Os (hard) appeared in a row. Concurrently, participants repeated 3 (easy) or 4 (hard) digits in backward order.

Results showed that in the simple choice RT tasks, older adults were significantly slower than, but as accurate as younger adults. In the complex choice RT tasks, older adults were significantly less accurate, but as fast as younger adults. RT decreased and error rates increased with greater task difficulty for both age groups and both dual task sets. Older adults had greater dual task costs for error rates in the simple choice RT, whereas in the complex choice RT, it was the younger group that had greater dual task costs. Overall, these findings suggest that different age groups may adopt differential behavioural strategies, which emphasise either speed or accuracy, depending on both the complexity and difficulty of dual tasks.

The second study, as presented in Chapters 4 and 5, was conducted with participants in the early stages of HD and healthy controls. Similarly to Chapter 2, Chapter 4 describes a study that used circle tracing with serial subtraction (see description of tasks earlier in this section). Results showed that HD participants were significantly slower and less accurate than controls, and their performance was more compromised in the hard circle tracing condition, suggesting that different difficulty levels may affect differentially dual tasking in HD. Despite this, we found no group differences in dual task costs. Surprisingly, accuracy increased from single to dual tasks for both groups. Finally, unlike controls, we found that HD participants were not susceptible to speed-accuracy trade-offs. Overall, the key finding of this study is that although HD participants differ from controls in dual task performance, we did not find evidence suggesting that HD is associated with greater susceptibility to dual task interference.

Chapter 5 presented a study with HD participants that compared the two dual task sets described earlier in this section: simple choice RT with digit forward and complex

choice RT with digit backward. For this study however, the complex choice RT task was modified because findings from the ageing study indicated that older adults committed a large number of errors, suggesting the task would be too difficult for HD participants. To simplify the task, the stimuli that were used in the HD study were 3 X 3 matrices of Xs and Os instead of 4 X 4 matrices that were used in the ageing study. In addition, participants had to indicate whether four Xs (easy) *or* fours Xs and four Os appeared in a row either horizontally or vertically, unlike the ageing study in which rows of Xs and Os appeared diagonally as well. Results suggested that HD participants were overall slower than controls. In terms of accuracy, there were no group differences in the simple choice RT task; however, HD participants were more compromised in the complex choice RT task compared with controls. Furthermore, HD participants were more susceptible to speed-accuracy trade-offs. Despite this, we found no dual task cost differences between the two groups. These findings suggest that speed and accuracy may be affected differently by complexity and difficulty of dual tasks in HD.

In summary, we found that HD participants differ from healthy controls in dual task performance (Chapters 4 and 5), and similarly, older adults differ from younger adults in dual task performance (Chapters 2 and 3). Our findings suggest that distinct measures (i.e., speed and accuracy) may be affected differently during dual task performance. They also suggest that particular groups may adopt different strategies depending on both the difficulty and complexity of dual tasks. For the first time, this thesis examined dual task performance in HD and in different age groups by using a battery of dual task sets at different difficulty and complexity levels. Our findings showed that the type of concurrent task does matter in dual task performance in both HD and ageing.

6.2. Implications of Findings

Dual tasking poses a pervasive challenge in contemporary life. Modern adults are constantly faced with numerous demands that, often, have to be satisfied within a restricted timeframe. Our overall findings supported past research that has found HD participants to be more compromised during dual task performance compared with healthy controls (Delval et al., 2008; Müller et al., 2002; Sprengelmeyer, Lange, & Hömberg, 1995), and older adults to be more compromised compared with younger adults (Crossley & Hiscock, 1992; McPhee, Scialfa, Dennis, Ho, & Caird, 2004; Verhaeghen, Steitz, Sliwinski, & Cerella, 2003).

From a practical perspective, understanding dual task differences in HD and in healthy ageing may provide insights into functional attentional abilities. For example, studies have shown that changes in dual task performance are significantly correlated with risk of falls in older adults (Beauchet et al., 2009; Verghese et al., 2002). In addition, HD participants have been found to have difficulty walking while performing concurrent cognitive tasks (Delval et al., 2008), and thus, are at greater risk of falls compared with the general population. Dual tasking is important for independent living; therefore, our findings stress the significance of empirical work on this topic, as they may inform the development of approaches that compensate for weaknesses in dual tasking due to HD or older age. Further research may provide insight regarding increased dual task deficits in these populations, and if identified early, could enable timely intervention programs that will enhance the quality of life of people living with HD and of older adults.

From a clinical perspective, it is generally agreed upon that attentional changes are an early feature of HD. Thus, because they are a means of taxing attentional processes,

dual task tests may provide a useful means for assessing, diagnosing and monitoring disease progression. Our second study (Chapters 4 and 5) clearly showed that dual tasks can discriminate between HD and healthy controls. Research is essential for the development of tests that will be well-suited for clinical use, and may contribute to diagnosis early in the course of the disease. In addition, it may allow implementation of interventions and treatments. Functional decline in HD may partially be attributed to underperformance when faced with complex sets of environmental demands, pointing to the need to consider how to modify environments and demands to keep functioning at its best levels. Currently, the sensitivity of dual tasking to disease severity and progression compared with other cognitive deficits is unknown. Therefore, it may be useful to investigate dual tasking in conjunction with other tasks. From a pharmacological standpoint, because these tasks have a large need for attentional resources and strategic allocation of attention, it may be possible that improvements can be made with treatments that affect attention. For instance, galantamine has been used to treat Alzheimer's disease (Kavanagh, Van Baelen, & Schauble, 2011), has neuroprotective effects (Egea et al., 2012), and there is some evidence that can attenuate neurodegeneration in HD (Park, Lee, Im, Chu, & Kim, 2008; Petrikis, Andreou, Piachas, Bozikas, & Karavatos, 2004).

6.3. Theoretical Implications

We found that people with HD as well as older adults are less able to attend to two tasks simultaneously as compared with healthy age-matched participants and younger adults, respectively. These declines in performance in HD and older adults may be due to pathological changes in the frontal regions of the brain that regulate working memory processes, a possibility that provides some support for the Posner and Petersen (1990) model of attention. The Posner model posits that an anterior attention system, involving the prefrontal cortex and the anterior cingulate, is activated when individuals have to attend to simultaneous tasks. This system is more sensitive to the effects of older age and possibly also to the effects of HD, since the prefrontal cortex has been implicated in both.

The current thesis addressed the issue of Unitary versus Multiple Resources theories in HD and ageing. Contrary to the predictions of the Multiple Resources Theory, which states that attention has separate resource pools that can be divided among concurrent tasks (Wickens, 2008), overall, our results showed evidence of resource sharing between tasks with seemingly different inputs and outputs, suggesting that the visual and auditory modalities and the manual and vocal responses are not totally separate. Consistent with the predictions of the Unitary Resource Theory, which states that attention is a single limited capacity resource that can be allocated to a single task or divided between tasks (Kahneman, 1973), for most task combinations, performance of participants deteriorated with increased task difficulty. However, for some task combinations, participants' performance was similar across easier and harder conditions. For example, as described in Chapter 2, we found no age-related differences in accuracy of circle tracing performance with increased task difficulty. Furthermore, accuracy in circle tracing increased from single to dual tasks in both HD participants and healthy controls (Chapter 4). Therefore, our results only partially supported the unitary resource framework.

Although our data do not support the Multiple Resources Theory, we cannot be conclusive as we did not match the tasks that made up each dual task set for difficulty. Due to the nature of our dual task sets, one could argue that participants did not process them in parallel (i.e., processing tasks simultaneously), but rather switched their attention between the two tasks. For instance, several participants struggled to complete complex choice RT concurrently with digit backward. In some cases we observed participants gazing up to rehearse the digits and consequently missing out on the complex choice RT task. In all probability, our participants may have varied in the strategies they used to complete these tasks, including parallel and serial processing (i.e., processing one task at a time). A speculative suggestion that has been endorsed by previous investigators (Müller et al., 2002; Sprengelmeyer et al., 1995) is that attention is a multidimensional system comprising related but otherwise semi-independent processes. Therefore, there is some support for a composite theory that incorporates aspects of both unitary and multiple resources theories.

Our findings also have implications for the Processing-Speed Theory as they indicate that age-related differences cannot be explained entirely by processing speed. The Processing-Speed Theory predicts that age-related differences are likely to be underpinned by processing speed changes, and should be more pronounced in more cognitively demanding tasks (Salthouse, 2002). Chapter 4 showed that age-related differences are best demonstrated by both speed and accuracy, with the relationships between these measures and ageing varying with task difficulty levels. Specifically, we found older adults to be slower than, but as accurate with younger adults in simple processing tasks; however, in more complex processing tasks, older adults were as quick as, but less accurate than younger adults. These findings support previous research that also found differential effects on processing speed and processing accuracy (Brébion, 2001). Furthermore, Chapter 5 presents a HD study that showed that although HD participants were overall slower, they maintained similar levels of accuracy in simple processing tasks with controls, but their accuracy decreased in more complex processing tasks relative to controls. Overall, our findings suggest that it is important to characterise dual task performance using different measures of performance (i.e., speed and accuracy) as people seem to share resources between various factors, including processing speed and processing accuracy. In addition, several conditions that span an array of difficulty levels should be included, as our results suggest that different groups may employ different strategies depending on the difficulty and complexity of dual tasks.

6.4. Limitations and Future Research Directions

The results presented in this thesis must be considered in light of some limitations. We did not counterbalance the administration order of our tasks. Counterbalancing was deemed impractical due to the large number of conditions and our small sample sizes. Although our sample sizes were adequate to allow us detect significant differences between group comparisons, future research should attempt to replicate our findings in studies using larger samples that will allow better permutation of the different conditions for the various dual task sets.

Participants were instructed to perform tasks as quickly and as accurately as possible. However, for some dual task sets we found that there may have been an ageing (Chapter 2) or HD (Chapter 5) effect on the balance between the competing goals of speed and accuracy. Participants may have intentionally or unintentionally emphasised either speed or accuracy, and this tendency may have been associated with the group to which the participant belonged. Our study, as well as the majority of studies reviewed in this thesis, employed laboratory dual tasks to investigate HD- and age-related differences in divided attention, and these are fairly artificial means of trying to understand what happens in dual tasking in everyday life. It is unknown and remains an important question whether these differences exist when notably pertinent to everyday functioning tasks are paired. Therefore, future studies should aim to employ more 'real world' dual tasks instead of laboratory tasks that simulate everyday processing requirements in divided attention. Similarly, it remains to be determined whether the different pattern of results across the simple and complex choice RT tasks (Chapters 3 and 5) is under conscious control, and whether the speed-accuracy trade-off effects that we observed were more a result of conscious than automatic processes.

6.5. Concluding Remarks

The overall aim of this thesis was to examine dual task performance in individuals with HD, and in neurologically healthy individuals across younger and older adulthood by using several dual task sets that varied in difficulty and complexity. To our knowledge, no study has used multiple dual tasks that varied in difficulty in HD or ageing research. Overall, we found that HD participants were slower and less accurate than healthy controls, and likewise, older adults were slower and less accurate than younger adults. Our results suggest that different groups may adopt different strategies (i.e., emphasise either speed or accuracy) depending on both the difficulty and complexity of dual tasks. In addition, different measures, such as speed and accuracy, may or may not be affected by HD and ageing. A key outcome of our findings, which we hope will inspire further investigation, is that the type of concurrent task does matter in both HD and ageing. We found that although HD participants were overall slower compared with controls, their

accuracy varied depending on the dual task combination. Specifically, HD participants were less accurate when performing circle tracing with serial subtraction and complex choice RT with digit backward dual task. However, their accuracy levels were similar to controls when performing simple choice RT with digit forward. In regards to our ageing research, older adults were overall slower, but as accurate as younger adults when performing more simple dual tasks (i.e., circle tracing with serial subtraction and simple choice RT with digit forward), but less accurate, and as fast as younger adults when performing more complex dual tasks (i.e., complex choice RT with digit backward).

This thesis has contributed to understanding the differences in dual task performance associated with HD and normal ageing. Our studies have important theoretical and practical implications with regard to attentional processes in HD and ageing, and also have clinical implications that may assist in the early identification and management of HD. Further research is warranted to promote our understanding of dual tasking in order to develop treatments that will improve the quality of lives in people living with HD and in the elderly.

References

- Abbruzzese, G., & Berardelli, A. (2003). Sensorimotor integration in movement disorders. *Movement Disorders*, 18, 231-240.
- Alberts, J. L., Voelcker-Rehage, C., Hallahan, K., Vitek, M., Bamzai, R., & Vitek, J. L. (2008). Bilateral subthalamic stimulation impairs cognitive-motor performance in Parkinson's disease patients. *Brain*, 131, 3348-3360.
- Alexander, G. E., DeLong, M. R., & Strick, P. L. (1986). Parallel organization of functionally segregated circuits linking basal ganglia and cortex. *Annual Review* of Neuroscience, 9, 357-381.
- Allport, D. A. (1980). Attention and performance. In G. L. Claxton (Ed.), New directions in cognitive psychology (pp. 112-153). London: Routledge & Kegan Paul.
- André, V. M., Cepeda, C., Fisher, Y. E., Huynh, M., Bardakjian, N., Singh, S., . . . Levine, M. S. (2011). Differential electrophysiological changes in striatal output neurons in Huntington's disease. *The Journal of Neuroscience*, 31, 1170-1182.
- Andresen, J. M., Gayán, J., Djoussé, L., Roberts, S., Brocklebank, D., Cherny, S. S., . .
 Wexler, N. S. (2006). The relationship between CAG repeat length and age of onset differs for Huntington's disease patients with juvenile onset or adult onset. *Annals of Human Genetics*, *71*, 295-301.
- Andrews, T. C., & Brooks, D. J. (1998). Advances in the understanding of early Huntington's disease using the functional imaging techniques of PET and SPET. *Molecular Medicine Today*, 4, 532-539.
- Anguera, J. A., Reuter-Lorenz, P. A., Willingham, D. T., & Seidler, R. D. (2011). Failure to engage spatial working memory contributes to age-related declines in visuomotor learning. *Journal of Cognitive Neuroscience*, 23, 11-25.

- Arango-Lasprilla, J. C., Rogers, H., Lengenfelder, J., DeLuca, J., Moreno, S., & Lopera,
 F. (2006). Cortical and subcortical diseases: Do true neuropsychological differences exist? *Archives of Clinical Neuropsychology*, 21, 29-40.
- Aretouli, E., & Brandt, J. (2010). Episodic memory in dementia: Characteristics of new learning that differentiate Alzheimer's, Huntington's, and Parkinson's diseases. *Archives of Clinical Neuropsychology*, 25, 396-409.
- Armieri, A., Holmes, J. D., Spaulding, S. J., Jenkins, M. E., & Johnson, A. M. (2009).
 Dual task performance in a healthy young adult population: Results from a symmetric manipulation of task complexity and articulation. *Gait & Posture, 29*, 346-348.
- Aron, A. R., Schlaghecken, F., Fletcher, P. C., Bullmore, E. T., Eimer, M., Barker, R., .
 . Robbins, T. W. (2003). Inhibition of subliminally primed responses is mediated by the caudate and thalamus: Evidence from functional MRI and Huntington's disease. *Brain*, *126*, 713-723.
- Aron, A. R., Watkins, L., Sahakian, B. J., Monsell, S., Barker, R. A., & Robbins, T. W. (2003). Task-set switching deficits in early-stage Huntington's disease: Implications for basal ganglia function. *Journal of Cognitive Neuroscience*, 15, 629-642.
- Aviezer, H., Bentin, S., Hassin, R. R., Meschino, W. S., Kennedy, J., Grewal, S., . . . Moscovitch, M. (2009). Not on the face alone: Perception of contextualized face expressions in Huntingtons disease. *Brain*, 132, 1633-1644.
- Aylward, E. H., Codori, A. M., Barta, P. E., Pearlson, G. D., Harris, G. J., & Brandt, J. (1996). Basal ganglia volume and proximity to onset in presymptomatic Huntington disease. *Archives of Neurology*, *53*, 1293-1296.

- Aylward, E. H., Sparks, B. F., Field, K. M., Yallapragada, V., Shpritz, B. D., Rosenblatt, A., . . . Ross, C. A. (2004). Onset and rate of striatal atrophy in preclical Huntington disease. *Neurology*, 63, 66-72.
- Azouvi, P., Couillet, J., Leclercq, M., Martin, Y., Asloun, S., & Rousseaux, M. (2004).
 Divided attention and mental effort after severe traumatic brain injury.
 Neuropsychologia, 42, 1260-1268.
- Bachoud-Levi, A. C., Maison, P., Bartolomeo, P., Boisse, M. F., Dalla Barba, G., Ergis,A. M., . . . Peschanski, M. (2001). Retest effects and cognitive decline in longitudinal follow-up of patients with early HD. *Neurology*, 56, 1052-1058.
- Bäckman, L., Robins-Wahlin, T. B., Lundin, A., Ginovart, N., & Farde, L. (1997). Cognitive deficits in Huntington's disease are predicted by dopaminergic PET markers and brain volumes. *Brain*, 120, 2207-2217.
- Baddeley, A. (1990). Human memory: Theory and practice. Hove, London: Erlbaum.
- Baddeley, A. D. (2001). Is working memory still working? *American Psychologist*, 56, 851-864.
- Baddeley, A. D. (2003). Working memory: Looking back and looking forward. Nature Reviews Neuroscience, 4, 829-839.
- Bates, G., Harper, P., & Jones, L. (2002). *Huntington's disease* (3rd ed.). Oxford: Oxford University Press.
- Beauchet, O., Annweiler, C., Dubost, V., Allali, G., Kressig, R. W., Bridenbaugh, G. B.,. . . Herrmann, F. R. (2009). Stops walking when talking: A predictor of falls in older adults? *European Journal of Neurology*, *16*, 786-795.
- Beauchet, O., Dubost, V., Aminian, K., Gonthier, R., & Kressig, R. W. (2005). Dualtask-related gait changes in the elderly: Does the type of cognitive task matter? *Journal of Motor Behavior*, 37, 259-264.

- Ben-Shakhar, G., & Sheffer, L. (2001). The relationship between the ability to divide attention and standard measures of general cognitive abilities. *Intelligence*, 29, 293-306.
- Berardelli, A., Noth, J., Thompson, P. D., Bollen, E. L. E. M., Currà, A., Deuschl, G., .
 . . Roos, R. A. C. (1999). Pathophysiology of chorea and bradykinesia in Huntington's disease. *Movement Disorders*, 14, 398-403.
- Beste, C., Saft, C., Güntürkün, O., & Falkenstein, M. (2008). Increased cognitive functioning in symptomatic Huntington's disease as revealed by behavioral and event-related potential indices of auditory sensory memory and attention. *The Journal of Neuroscience*, 28, 11695-11702.
- Bherer, L., Kramer, A. F., Peterson, M. S., Colcombe, S., Erickson, K., & Becic, E. (2008). Transfer effects in task-set cost and dual-task cost after dual-task training in older and younger adults: Further evidence for cognitive plasticity in attentional control in late adulthood. *Experimental Aging Research*, 34, 188-219.
- Bilney, B., Morris, M. E., & Denisenko, S. (2003). Physiotherapy for people with movement disorders arising from basal ganglia dysfunction. NJ Journal of Physiotherapy, 31, 94-100.
- Bilney, B., Morris, M. E., & Perry, A. (2003). Effectiveness of physiotherapy, occupational therapy, and speech pathology for people with Huntington's disease:A systematic review. *Neurorehabilitation & Neural Repair*, 17, 12-24.
- Bohanna, I., Georgiou-Karistianis, N., Hannan, A. J., & Egan, G. F. (2008). Magnetic resonance imaging as an approach towards identifying neuropathological biomarkers for Huntington's disease. *Brain Research Reviews*, 58, 209-225.
- Bonelli, R. M., & Cummings, J. L. (2007). Frontal-subcortical circuitry and behavior. *Dialogues in Clinical Neuroscience*, 9, 141-151.

- Brandt, J., Leroi, I., O'Hearn, E., Rosenblatt, A., & Margolis, R. L. (2004). Cognitive impairments in cerebellar degeneration: A comparison with Huntington's disease. *Journal of Neuropsychiatry and Clinical Neurosciences*, 16, 176-184.
- Brandt, J., Shpritz, B., Codori, A. M., Margolis, R., & Rosenblatt, A. (2002). Neuropsychological manifestations of the genetic mutation for Huntington's disease in presymptomatic individuals. *Journal of the International Neuropsychological Society*, 8, 918-924.
- Brandt, J., Shpritz, B., Munro, C. A., Marsh, L., & Rosenblatt, A. (2005). Differential impairment of spatial location memory in Huntington's disease. *Journal of Neurology, Neurosurgery, & Psychiatry*, 76, 1516-1519.
- Brébion, G. (2001). Language processing, slowing and speed/accuracy trade-off in the elderly. *Experimental Aging Research*, 27, 137-150.
- Brown, R. G., Jahanshahi, M., & Marsden, C. D. (1993). The execution of bimanual movements in patients with Parkinson's, Huntington's and cerebellar disease. *Journal of Neurology, Neurosurgery, & Psychiatry, 56*, 295-297.
- Brunenberg, E. J. L., Moeskops, P., Backes, W. H., Pollo, C., Cammoun, L., Vilanova, A., . . . Platel, B. (2012). Structural and resting state functional connectivity of the subthalamic nucleus: Identification of motor STN parts and the hyperdirect pathway. *PLoS ONE*, *7*, e39061.
- Burns, A., Folstein, S., Brandt, J., & Folstein, M. (1990). Clinical assessment of irritability, aggression, and apathy in Huntington and Alzheimer disease. *Journal* of Nervous and Mental Disease, 178, 20-26.

- Chatterjee, A., Anderson, K. E., Moskowitz, C. B., Hauser, W. A., & Marder, K. S. (2005). A comparison of self- report and caregiver assessment of depression, apathy, and irritability in Huntington's disease. *Journal of Neuropsychiatry & Clinical Neurosciences*, 17, 378-383.
- Chen, C. M., Wu, Y. R., Cheng, M. L., Liu, J. L., Lee, Y. M., Lee, P. W., . . . Chiu, D. T. Y. (2007). Increased oxidative damage and mitochondrial abnormalities in the peripheral blood of Huntington's disease patients. *Biochemical and Biophysical Research Communications*, 359, 335-340.
- Cho, C.-Y., Gilchrist, L., & White, S. (2008). A comparison between young and old adults in their ability to rapidly sidestep during gait when attention is divided. *Gerontology*, 54, 120-127.
- Ciarmiello, A., Cannella, M., Lastoria, S., Simonelli, M., Frati, L., Rubinsztein, D. C., & Squitieri, F. (2006). Brain white-matter volume loss and glucose hypometabolism precede the clinical symptoms of Huntington's disease. *Journal* of Nuclear Medicine, 47, 215-222.
- Clark, V. P., Lai, S., & Deckel, A. W. (2002). Altered functional MRI responses in Huntington's disease. *Neuroreport*, *13*, 703-706.
- Como, P. G. (2006). Huntington's disease. In R. Kurlan (Ed.), *Handbook of secondary dementias* (pp. 151-178). New York: Taylor & Francis.
- Conway, A. R. A., Kane, M. J., Bunting, M. F., Hambrick, D. Z., Wilhelm, O., & Engle,
 R. W. (2005). Working memory span tasks: A methodological review and user's guide. *Psychonomic Bulletin & Review*, 12, 769-786.

- Corbetta, M., Miezin, F. M., Dobmeyer, S., Shulman, G. L., & Petersen, S. E. (1991). Selective and divided attention during visual discrimination of shape, color, and speed: Functional anatomy by positron emission tomography. *The Journal of Neuroscience*, 11, 2383-2402.
- Couette, M., Bachoud-Levi, A.-C., Brugieres, P., Sieroff, E., & Bartolomeo, P. (2008). Orienting of spatial attention in Huntington's disease. *Neuropsychologia*, 46, 1391-1400.
- Craik, F. I. M., & Lockhart, R. S. (1979). Levels of processing: A framework for memory research. *Journal of Verbal Learning and Learning Behavior*, 11, 671-684.
- Crossley, M., & Hiscock, M. (1992). Age-related differences in concurrent-task performance of normal adults: Evidence for a decline in processing resources. *Psychology and Aging*, 7, 499-506.
- D'Esposito, M., Aguirre, G. K., Zarahn, E., Ballard, D., Shin, R. K., & Lease, J. (1998). Functional MRI studies of spatial and nonspatial working memory. *Cognitive Brain Research*, 7, 1-13.
- D'Esposito, M., Postle, B. R., & Rypma, B. (2000). Prefrontal cortical contributions to working memory: Evidence from event-related fMRI studies. *Experimental Brain Research, 133*, 3-11.
- Dannhauser, T. M., Walker, Z., Stevens, T., Lee, L., Seal, M., & Shergill, S. S. (2005). The functional anatomy of divided attention in amnestic mild cognitive impairment. *Brain*, 128, 1418-1427.
- Davis, J. D., Filoteo, J. V., & Kesner, R. P. (2007). Is short-term memory for discrete arm movements impaired in Huntington's disease? *Cortex*, *43*, 255-263.

- De Diego-Balaguer, R., Couette, M., Dolbeau, G., Dürr, A., Youssov, K., & Bachoud-Lévi, A.-C. (2008). Striatal degeneration impairs language learning: Evidence from Huntington's disease. *Brain*, 131, 2870-2881.
- de Ribaupierre, A., & Ludwig, C. (2003). Age differences and divided attention: Is there a general deficit? *Experimental Aging Research*, 29, 79-105.
- Deckel, A. W., Weiner, R., Szigeti, D., Clark, V., & Vento, J. (2000). Altered patterns of regional cerebral blood flow in patients with Huntington's disease: A SPECT study during rest and cognitive or motor activation. *The Journal of Nuclear Medicine*, 41, 773-780.
- Decruyenaere, M., Evers-Kiebooms, G., Cloostermans, T., Boogaerts, A., Demyttenaere, K., Dom, R., & Fryns, J. P. (2003). Psychological distress in the 5year period after predictive testing for Huntington's disease. *European Journal of Human Genetics*, 11, 30-38.
- Delis, D. C., Massman, P. J., Butters, N., & Salmon, D. P. (1991). Profiles of demented and amnesic patients on the California Verbal Learning Test: Implications for the assessment of memory disorders. *Psychological Assessment: A Journal of Consulting and Clinical Psychology*, 3, 19-26.
- Della Sala, S., Foley, J. A., Beschin, N., Allerhand, M., & Logie, R. H. (2010). Assessing dual-task performance using a paper-and-pencil test: Normative data. Archives of Clinical Neuropsychology, 25, 410-419.
- DeLong, M. R., & Wichmann, T. (2007). Circuits and circuit disorders of the basal ganglia. Archives of Neurology, 64, 20-24.
- Delval, A., Krystkowiak, P., Delliaux, M., Dujardin, K., Blatt, J.-L., Destée, A., . . . Defebvre, L. (2008). Role of attentional resources on gait performance in Huntington's disease. *Movement Disorders*, 23, 684-689.

- Douaud, G., Behrens, T. E., Poupon, C., Cointepas, Y., Jbabdi, S., Gaura, V., ... Remy,
 P. (2009). In vivo evidence for the selective subcortical degeneration in Huntington's disease. *Neuroimage*, 46, 958-966.
- Douaud, G., Gaura, V., Ribeiro, M. J., Lethimonnier, F., Maroy, R., Verny, C., . . . Remy, P. (2006). Distribution of grey matter atrophy in Huntington's disease patients: A combined ROI-based and voxel-based morphometric study. *Neuroimage*, 32, 1562-1575.
- Dranias, M. R., Ju, H., Rajaram, E., & VanDongen, A. M. (2013). Short-term memory in networks of dissociated cortical neurons. *The Journal of Neuroscience*, *33*, 1940-1953.
- Duff, K., Paulsen, J. S., Beglinger, L. J., Langbehn, D. R., Stout, J. C., & Predict-HD investigators of the Huntington Study Group. (2007). Psychiatric symptoms in Huntington's disease before diagnosis: The Predict-HD study. *Biological Psychiatry*, 62, 1341-1346.
- Dumas, E. M., van den Bogaard, S. J. A., Ruber, M. E., Reilmann, R., Stout, J. C., Craufurd, D., . . . Roos, R. A. C. (2012). Early changes in white matter pathways of the sensorimotor cortex in premanifest Huntington's disease. *Human Brain Mapping*, 33, 203-212.
- Eddy, C. M., & Rickards, H. E. (2012). Moral judgment and decision making in Huntington's disease. *Basal Ganglia*, *2*, 139-142.
- Egea, J., Martín-de-Saavedra, M. D., Parada, E., Romero, A., Del Barrio, L., Rosa, A. O., . . . López, M. G. (2012). Galantamine elicits neuroprotection by inhibiting iNOS, NADPH oxidase and ROS in hippocampal slices stressed with anoxia/reoxygenation. *Neuropharmacology*, 62, 1082-1090.

- Faulkner, K. A., Redfern, M. S., Rosano, C., Landsittel, D. P., Studenski, S. A., Cauley,J. A., . . . Newman, A. B. (2006). Reciprocal influence of concurrent walking and cognitive testing on performance in older adults. *Gait & Posture*, 24, 182-189.
- Fennema-Notestine, C., Archibald, S. L., Jacobson, M. W., Corey-Bloom, J., Paulsen, J. S., Peavy, G. M., . . Jernigan, T. L. (2004). In vivo evidence of cerebellar atrophy and cerebral white matter loss in Huntington disease. *Neurology*, 63, 989-995.
- Fenney, A., Jog, M. S., & Duval, C. (2008). Bradykinesia is not a "systematic" feature of adult-onset Huntington's disease; Implications for basal ganglia pathophysiology. *Brain Research*, 1193, 67-75.
- Ferreira, I. L., Nascimento, M. V., Ribeiro, M., Almeida, S., Cardoso, S. M., Grazina, M., . . . Rego, A. C. (2010). Mitochondrial-dependent apoptosis in Huntington's disease human cybrids. *Experimental Neurology*, 222, 243-255.
- Filoteo, J. V., Delis, D. C., Roman, M. J., Demadura, T., Ford, E., Butters, N., . . .
 Swerdlow, N. (1995). Visual attention and perception in patients with Huntington's disease: Comparisons with other subcortical and cortical dementias. *Journal of Clinical and Experimental Neuropsychology*, 17, 654 - 667.
- Fine, E. M., Delis, D. C., Wetter, S. R., Jacobson, M. W., Hamilton, J. M., Peavy, G., . .
 Salmon, D. P. (2008). Identifying the 'source' of recognition memory deficits in patients with Huntington's disease or Alzheimer's disease: Evidence from the CVLT-II. *Journal of Clinical and Experimental Neuropsychology*, *30*, 463-470.
- Finke, K., Schneider, W. X., Redel, P., Dose, M., Kerkhoff, G., Müller, H. J., & Bublak,P. (2007). The capacity of attention and simultaneous perception of objects: A group study of Huntington's disease patients. *Neuropsychologia*, 45, 3272-3284.

- Galletly, R., & Brauer, S. G. (2005). Does the type of concurrent task affect preferred and cued gait in people with Parkinson's disease? *Australian Journal of Physiotherapy*, 51, 175-180.
- Georgiou-Karistianis, N. (2009). A peek inside the Huntington's brain: Will functional imaging take us one step closer in solving the puzzle? *Experimental Neurology*, 220, 5-8.
- Georgiou-Karistianis, N., Churchyard, A., Chiu, E., & Bradshaw, J. L. (2002). Reorientation in attention in Huntington's disease. *Neuropsychiatry, Neuropsychology, and Behavioral Neurology, 15*, 225-231.
- Georgiou-Karistianis, N., Farrow, M., Wilson-Ching, M., Churchyard, A., Bradshaw, J.
 L., & Sheppard, D. M. (2012). Deficits in selective attention in symptomatic
 Huntington disease: Assessment using an attentional blink paradigm. *Cognitive & Behavioral Neurology*, 25, 1-6.
- Georgiou-Karistianis, N., Sritharan, A., Farrow, M., Cunnington, R., Stout, J., Bradshaw, J., . . . Egan, G. (2007). Increased cortical recruitment in Huntington's disease using a Simon task. *Neuropsychologia*, 45, 1791-1800.
- Georgiou-Karistianis, N., Stout, C. J., Dominquez, J. F., Carron, S. P., Ando, A., Churchyard, A., . . . Egan, G. F. (2013). Functional magnetic resonance imaging of working memory in Huntington's disease: Cross-sectional data from the IMAGE-HD study. *Human Brain Mapping, in press 12 March 2013*.
- Georgiou, N., Bradshaw, J. L., Phillips, J. G., Chiu, E., & Bradshaw, J. A. (1995). Reliance on advance information and movement sequencing in Huntington's disease. *Movement Disorders*, 10, 472-481.

- Georgiou, N., Bradshaw, J. L., Phillips, J. G., Bradshaw, J. A., & Chiu, E. (1995). The Simon effect and attention deficits in Gilles de la Tourette's syndrome and Huntington's disease. *Brain*, *118*, 1305-1318.
- Georgiou, N., Bradshaw, J. L., Phillips, J. G., & Chiu, E. (1996). The effect of Huntington's disease and Gilles de la Tourette's syndrome on the ability to hold and shift attention. *Neuropsychologia*, 34, 843-851.
- Georgiou, N., Bradshaw, J. L., Phillips, J. G., & Chiu, E. (1997). Effect of directed attention in Huntington' s disease. *Journal of Clinical and Experimental Neuropsychology*, 19, 367-377.
- Georgiou, N., Phillips, J. G., Bradshaw, J. L., Cunnington, R., & Chiu, E. (1997). Impairments of movement kinematics in patients with Huntington's disease: A comparison with and without a concurrent task. *Movement Disorders, 12*, 386-396.
- Gil, J. M., & Rego, A. C. (2008). Mechanisms of neurodegeneration in Huntington's disease. *European Journal of Neuroscience*, 27, 2803-2820.
- Girotti, F., Marano, R., Soliveri, P., Geminiani, G., & Scigliano, G. (1988). Relationship between motor and cognitive disorders in Huntington's disease. *Journal of Neurology*, 235, 454-457.
- Gómez-Tortosa, E., del Barrio, A., Barroso, T., & García Ruiz, P. J. (1996). Visual processing disorders in patients with Huntington's disease and asymptomatic carriers. *Journal of Neurology*, 243, 286-292.
- Göthe, K., Oberauer, K., & Kliegl, R. (2007). Age differences in dual-task performance after practice. *Psychology and Aging*, 22, 596-606.

- Grabli, D., McCairn, K., Hirsch, E. C., Agid, Y., Féger, J., François, C., & Tremblay, L. (2004). Behavioural disorders induced by external globus pallidus dysfunction in primates: I. Behavioural study. *Brain*, 127, 2039-2054.
- Gray, M. A., Egan, G. F., Ando, A., Churchyard, A., Chua, P., Stout, J. C., & Georgiou-Karistianis, N. (2013). Prefrontal activity in Huntington's disease reflects cognitive and neuropsychiatric disturbances: The IMAGE-HD study. *Experimental Neurology*, 239, 218-228.
- Grégoire, J., & Van der Linden, M. (1997). Effect of age on forward and backward digit spans. *Aging, Neuropsychology, and Cognition, 4*, 140-149.
- Groen, J. L., de Bie, R. M. A., Foncke, E. M. J., Roos, R. A. C., Leenders, K. L., & Tijssen, M. A. J. (2010). Late-onset Huntington disease with intermediate CAG repeats: True or false? *Journal of Neurology, Neurosurgery, & Psychiatry, 81*, 228-230.
- Gusella, J. F, Wexler, N. S., Conneally, P. M., Naylor, S. L., Anderson, M. A., Tanzi, R.E, . . . Martin, J. B. (1983). A polymorphic DNA marker genetically linked to Huntington's disease. *Nature*, 306, 234-238.
- Gutekunst, C.-A., Li, S.-H., Yi, H., Mulroy, J. S., Kuemmerle, S., Jones, R., . . . Li, X.-J. (1999). Nuclear and neuropil aggregates in Huntington's disease: Relationship to neuropathology. *The Journal of Neuroscience*, 19, 2522-2534.
- Gutekunst, C.-A., Norflus, F., & Hersch, S. M. (2002). *Huntington's disease* (3rd ed.). Oxford: Oxford University Press.
- Halliday, G. M., McRitchie, D. A., Macdonald, V., Double, K. L., Trent, R. J., & McCusker, E. (1998). Regional specificity of brain atrophy in Huntington's disease. *Experimental Neurology*, 154, 663-672.

- Harris, M. K., Shneyder, N., Borazanci, A., Korniychuk, E., Kelley, R. E., & Minagar,A. (2009). Movement disorders. *Medical Clinics of North America*, 93, 371-388.
- Hartley, A. A., Maquestiaux, F., & Silverman Butts, N. (2011). A demonstration of dual-task performance without interference in some older adults. *Psychology and Aging*, 26, 181-187.
- Hawkins, H. L., Kramer, A. F., & Capaldi, D. (1992). Aging, exercise, and attention. *Psychology and Aging*, 7, 643-653.
- Hayward, P. (2004). Genes, environment, and the onset of Huntington's disease. *Lancet Neurology*, *3*, 199.
- Hein, G., & Schubert, T. (2004). Aging and input processing in dual-task situations. *Psychology and Aging, 19*, 416-432.
- Heinsen, H., Rüb, U., Bauer, M., Ulmar, G., Bethke, B., Schüler, M.,. . . Schmitz, C. (1999). Nerve cell loss in the thalamic mediodorsal nucleus in Huntington's disease. *Acta Neuropathologica*, 97, 613-622.
- Hester, R. L., Kinsella, G. J., & Ong, B. (2004). Effect of age on forward and backward span tasks. *Journal of the International Neuropsychological Society*, *10*, 475-481.
- Hinton, S. C., Paulsen, J. S., Hoffmann, R. G., Reynolds, N. C., Zimbelman, J. L., & Rao, S. M. (2007). Motor timing variability increases in preclinical Huntington's disease patients as estimated onset of motor symptoms approaches. *Journal of the International Neuropsychological Society*, 13, 539-543.
- Ho, A. K., Nestor, P. J., Williams, G. B., Bradshaw, J. L., Sahakian, B. J., . . . Barker,
 R. A. (2004). Pseudo-neglect in Huntington's disease correlates with decreased angular gyrus density. *Brain Imaging*, 15, 1061-1064.

- Ho, A. K., Sahakian, B. J., Brown, R. G., Barker, R. A., Hodges, J. R., Ané, M.-N., . . .
 Bodner, T. (2003). Profile of cognitive progression in early Huntington's disease. *Neurology*, *61*, 1702-1706.
- Ho, A. K., Sahakian, B. J., Robbins, T. W., Barber, R. A., Rosser, A. E., & Hodges, J.
 R. (2002). Verbal fluency in Huntington's disease: A longitudinal analysis of phonemic and semantic clustering and switching. *Neuropsychologia*, 40, 1277-1284.
- Hobbs, N. Z., Pedrick, A. V., Say, M. J., Frost, C., Dar Santos, R., Coleman, A., . . . Scahill, R. I. (2011). The structural involvement of the cingulate cortex in premanifest and early Huntington's disease. *Movement Disorders*, 26, 1684-1690.
- Hoth, K. F., Paulsen, J. S., Moser, D. J., Tranel, D., Clark, L. A., & Bechara, A. (2007). Patients with Huntington's disease have impaired awareness of cognitive, emotional and functional abilities. *Journal of Clinical and Experimental Neuropsychology*, 29, 365-376.
- Huntington Study Group. (1996). The Unified Huntington's Disease Rating Scale: Reliability and consistency. *Movement Disorders*, 11, 136-142.
- Jahanshahi, M., Brown, R. G., & Marsden, C. D. (1993). A comparative study of simple and choice reaction time in Parkinson's, Huntington's and cerebellar disease. *Journal of Neurology, Neurosurgery, & Psychiatry, 56*, 1169-1177.
- Jahfari, S., Waldorp, L., van den Wildenberg, W. P. M., Scholte, H. S., Ridderinkhof,
 K. R., & Forstmann, B. U. (2011). Effective connectivity reveals important roles
 for both the hyperdirect (fronto-subthalamic) and the indirect (fronto-striatalpallidal) fronto-basal ganglia pathways during response inhibition. *The Journal of Neuroscience*, *31*, 6891-6899.

- Jensen, P., Fenger, K., Bolwig, T. G., & Sørensen, S. A. (1998). Crime in Huntington's disease: A study of registered offences among patients, relatives, and controls. *Journal of Neurology, Neurosurgery, & Psychiatry*, 65, 467-471.
- Joel, D. (2001). Open interconnected model of basal ganglia-thalamocortical circuitry and its relevance to the clinical syndrome of Huntington's disease. *Movement Disorders*, 16, 407-423.
- Johnson, A., & Proctor, R. W. (2004). *Attention: Theory and practice*. California: Sage Publications.
- Julien, C. L., Thompson, J. C., Wild, S., Yardumian, P., Snowden, J. S., Turner, G., & Craufurd, D. (2007). Psychiatric disorders in preclinical Huntington's disease. *Journal of Neurology, Neurosurgery, & Psychiatry*, 78, 939-943.
- Kahneman, D. (1973). Attention and effort. New Jersey: Prentice-Hall.
- Kassubek, J., Juengling, F. D., Ecker, D., & Landwehrmeyer, G. B. (2005). Thalamic atrophy in Huntington's disease co-varies with cognitive performance: A morphometric MRI analysis. *Cerebral Cortex*, 15, 846-853.
- Kassubek, J., Juengling, F. D., Kioschies, T., Henkel, K., Karitzky, J., Kramer, B., ...
 Landwehrmeyer, G. B. (2004). Topography of cerebral atrophy in early
 Huntington's disease: A voxel based morphometric MRI study. *Journal of Neurology, Neurosurgery, & Psychiatry, 75*, 213-220.
- Kavanagh, S., Van Baelen, B., & Schauble, B. (2011). Long-term effects of galantamine on cognitive function in Alzheimer's disease: a large-scale international retrospective study. *Journal of Alzheimer's Disease*, 27, 521-530.
- Kemper, S., Herman, R. E., & Lian, C. H. T. (2003). The costs of doing two things at once for young and older adults: Talking while walking, finger tapping, and ignoring speech or noise. *Psychology and Aging*, 18, 181-192.

- Kemper, S., Schmalzried, R., Herman, R., Leedahl, S., & Mohankumar, D. (2009). The effects of aging and dual task demands on language production. *Aging, Neuropsychology, and Cognition, 16*, 241-259.
- Kim, J.-S., Reading, S. A. J., Brashers-Krug, T., Calhoun, V. D., Ross, C. A., & Pearlson, G. D. (2004). Functional MRI study of a serial reaction time task in Huntington's disease. *Psychiatry Research*, 131, 23-30.
- Kirkwood, S. C., Siemers, E., Hodes, M. E., Conneally, P. M., Christian, J. C., & Foroud, T. (2000). Subtle changes among presymptomatic carriers of the Huntington's disease gene. *Journal of Neurology, Neurosurgery, & Psychiatry*, 69, 773-779.
- Klöppel, S., Henley, S. M., Hobbs, N. Z., Wolf, R. C., Kassubek, J., Tabrizi, S. J., & Frackowiak, R. S. J. (2009). Magnetic resonance imaging of Huntington's disease: Preparing for clinical trials. *Neuroscience*, *164*, 205-219.
- Knopman, D., & Nissen, M. J. (1991). Procedural learning is impaired in Huntingtonsdisease: Evidence from the serial reaction-time-task. *Neuropsychologia*, 29, 245-254.
- Koechlin, E., Basso, G., Pietrini, P., Panzer, S., & Grafman, J. (1999). The role of the anterior prefrontal cortex in human cognition. *Nature*, *399*, 148-151.
- Kremer, H. P. H., Roos, R. A. C, Dingian, G. M., Bots, G. Th. A. M., Bruyn, G. W., & Hofman, M. A. (1991). The hypothalamic lateral tuberal nucleus and the characteristics of neuronal loss in Huntington's disease. *Neuroscience Letters*, 132, 101-104.
- Krobitsch, S., & Kazantsev, A. G. (2011). Huntington's disease: From molecular basis to therapeutic advances. *The International Journal of Biochemistry and Cell Biology*, 43, 20-24.

- Langbehn, D. R., Brinkman, R. R., Falush, D., Paulsen, J. S., Hayden, M. R. (2004). A new model for prediction of the age of onset and penetrance for Huntington's disease based on CAG length. *Clinical Genetics*, 65, 267-277.
- Larsson, M. U., Almkvist, O., Luszcz, M. A., & Wahlin, T. B. R. (2008). Phonemic fluency deficits in asymptomatic gene carriers for Huntington's disease. *Neuropsychology*, 22, 596-605.
- Lawrence, A. D., Hodges, J. R., Rosser, A. E., Kershaw, A., ffrench-Constant, C., Rubinsztein, D. C., . . . Sahakian, B. J. (1998). Evidence for specific cognitive deficits in preclinical Huntington's disease. *Brain*, 121, 1329-1341.
- Lawrence, A. D., Sahakian, B. J., Hodges, J. R., Rosser, A. E., Lange, K. W., & Robbins, T. W. (1996). Executive and mnemonic functions in early Huntington's disease. *Brain*, 119, 1633-1645.
- Lawrence, A. D., Watkins, L. H. A., Sahakian, B. J., Hodges, J. R., & Robbins, T. W. (2000). Visual object and visuospatial cognition in Huntington's disease:
 Implications for information processing in corticostriatal circuits. *Brain*, 123, 1349-1364.
- Lemay, M., Fimbel, E., Beuter, A., & Chouinard, S. (2005). Sensorimotor mapping affects movement correction deficits in early Huntington's disease. *Experimental Brain Research*, 165, 454-460.
- Lemiere, J., Decruyenaere, M., Evers-Kiebooms, G., Vandenbussche, E., & Dom, R. (2002). Longitudinal study evaluating neuropsychological changes in so-called asymptomatic carriers of the Huntington's disease mutation after 1 year. Acta Neurologica Scandinavica, 106, 131-141.

- Lemiere, J., Decruyenaere, M., Evers-Kiebooms, G., Vandenbussche, E., & Dom, R. (2004). Cognitive changes in patients with Huntington's disease (HD) and asymptomatic carriers of the HD mutation - A longitudinal follow-up study. *Journal of Neurology*, 251, 935-942.
- Lepron, E., Péran, P., Cardebat, D., & Démonet, J.-F. (2009). A PET study of word generation in Huntington's disease: Effects of lexical competition and verb/noun category. *Brain and Language*, 110, 49-60.
- Lineweaver, T. T., Salmon, D. P., Bondi, M. W., & Corey-Bloom, J. (2005). Differential effects of Alzheimer's disease and Huntington's disease on the performance of mental rotation. *Journal of the International Neuropsychological Society*, 11, 30-39.
- Longworth, C. E., Keenan, S. E., Barker, R. A., Marslen-Wilson, W. D., & Tyler, L. K. (2005). The basal ganglia and rule-governed language use: Evidence from vascular and degenerative conditions. *Brain*, *128*, 584-596.
- Loose, R., Kaufmann, C., Auer, D. P., & Lange, K. W. (2003). Human prefrontal and sensory cortical activity during divided attention tasks. *Human Brain Mapping*, 18, 249-259.
- Lundervold, A. J., Reinvang, I., & Lundervold, A. (1994). Characteristic patterns of verbal memory function in patients with Huntington's disease. *Scandinavian Journal of Psychology*, 35, 38-47.
- Macdonald, V., & Halliday, G. (2002). Pyramidal cell loss in motor cortices in Huntington's disease. *Neurobiology of Disease, 10*, 378-386.
- Majerová, V., Kalinčík, T., Laczó, J., Vyhnálek, M., Hort, J., Bojar, M., . . . Roth, J. (2012). Disturbance of real space navigation in moderately advanced but not in early Huntington's disease. *Journal of the Neurological Sciences*, *312*, 86-91.

- Mann, D. M. A., Oliver, R., & Snowden, J. S. (1993). The topographic distribution of brain atrophy in Huntington's disease and progressive supranuclear palsy. *Acta Neuropathologica*, 85, 553-559.
- Maroof, D. A., Gross, A. L., & Brandt, J. (2011). Modeling longitudinal change in motor and cognitive processing speed in presymptomatic Huntington's disease. *Journal of Clinical and Experimental Neuropsychology*, 33, 901-909.
- Martinez-Vicente, M., Talloczy, Z., Wong, E., Tang, G., Koga, H., Kaushik, S., . . . Cuervo, A. M. (2010). Cargo recognition failure is responsible for inefficient autophagy in Huntington's disease. *Nature Neuroscience*, 13, 567-578.
- Mayes, A. (1998). Memory in neurodegenerative disease: What has been learned about the organization of memory? In A. I. Tröster (Ed.), *Memory in neurodegenerative disease: Biological, cognitive, and clinical perspectives*. Cambridge: Cambridge University Press.
- Mazzoni, P., & Wexler, N. S. (2009). Parallel explicit and implici control of reaching. *PLoS ONE*, *4*, e7557.
- McDowd, J. M., & Craik, F. I. M. (1988). Effects of aging and task difficulty on divided attention performance. *Journal of Experimental Psychology: Human Perception* and Performance, 14, 267-280.
- McDowd, J. M. (1986). The effect of age and extended practice on divided attention performance. *Journal of Gerontology*, *41*, 764-769.
- McLeod, P. (1977). Dual task response modality effect Support for multiprocessor models of attention. *Quarterly Journal of Experimental Psychology*, 29, 651-667.
- McPhee, L. C., Scialfa, C. T., Dennis, W. M., Ho, G., & Caird, J. K. (2004). Age differences in visual search for traffic signs during a simulated conversation. *Human Factors*, 46, 674-685.

- Medina, F. J., & Tunez, I. (2010). Huntington's disease: The value of transcranial meganetic stimulation. *Current Medicinal Chemistry*, *17*, 2482-2491.
- Michell, A. W., Goodman, A. O. G., Silva, A. H. D., Lazic, S. E., Morton, A. J., & Barker, R. A. (2008). Hand tapping: A simple, reproducible, objective marker of motor dysfunction in Huntington's disease. *Journal of Neurology*, 255, 1145-1152.
- Middleton, F. A., & Strick, P. L. (2000). Basal ganglia and cerebellar loops: Motor and cognitive circuits. *Brain Research Reviews*, *31*, 236-250.
- Mohr, E., Brouwers, P., Claus, J. J., Mann, U. M., Fedio, P., & Chase, T. N. (1991). Visuospatial cognition in Huntington's disease. *Movement Disorders*, *6*, 127-132.
- Montoya, A., Pelletier, M., Menear, M., Duplessis, E., Richer, F., & Lepage, M. (2006).
 Episodic memory impairment in Huntington's disease: A meta-analysis. *Neuropsychologia*, 4, 1984-1994.
- Montoya, A., Price, B. H., Menear, M., & Lepage, M. (2006). Brain imaging and cognitive dysfunctions in Huntington's disease. *Journal of Psychiatry & Neuroscience 31*, 21-29.
- Mühlau, M., Gaser, C., Wohlschläger, A. M., Weindl, A., Städtler, M., Valet, M., . . . Peinemann, A. (2007). Striatal gray matter loss in Huntington's disease is leftward biased. *Movement Disorders*, 22, 1169-1201.
- Mühlau, M., Weindl, A., Wohlschlager, A. M., Gaser, C., Stadtler, M., Valet, M., . . . Peinemann, A. (2007). Voxel-based morphometry indicates relative preservation of the limbic prefrontal cortex in early Huntington disease. *Journal of Neural Transmission, 114*, 367-372.

- Müller, S. V., Jung, A., Preinfalk, J., Kolbe, H., Ridao-Alonso, M., Dengler, R., & Münte, T. F. (2002). Disturbance of "extrinsic alertness" in Huntingtons disease. *Journal of Clinical and Experimental Neuropsychology*, 24, 517-526.
- Murray, L. L. (2000). Spoken language production in Huntington's and Parkinson's diseases. *Journal of Speech, Language and Hearing Research, 43*, 1350-1366.
- Murray, L. L., & Lenz, L. P. (2001). Productive syntax abilities in Huntington's and Parkinson's diseases. *Brain and Cognition*, *46*, 213--219.
- Murray, L. L., & Stout, J. C. (1999). Discourse comprehension in Huntington's and Parkinson's diseases. American Journal of Speech-Language Pathology, 8, 137-148.
- Mutter, S. A., & Goedert, K. M. (1997). Frequency discrimination vs frequency estimation: Adult age differences and the effect of divided attention. *The Journals of Gerontology*, *52B*, P319-P328.
- Naarding, P., Janzing, J. G. E., Eling, P., van der Werf, S., & Kremer, B. (2009). Apathy is not depression in Huntington's disease. *Journal of Neuropsychiatry and Clinical Neurosciences*, 21, 266-270.
- Nairne, J. S., & Healy, A. F. (1983). Counting backwards produces systematic errors. Journal of Experimental Psychology: General, 112, 37-40.
- Navon, D., & Gopher, D. (1979). On the economy of the human processing system. *Psychological Review*, 86, 214-255.
- Nehl, C., Ready, R. E., Hamilton, J., & Paulsen, J. S. (2001). Effects of depression on working memory in presymptomatic Huntington's disease. *Journal of Neuropsychiatry & Clinical Neurosciences*, 13, 342-346.

- Nopoulos, P., Magnotta, V. A., Mikos, A., Paulson, H., Andreasen, N. C., & Paulsen, J. S. (2007). Morphology of the cerebral cortex in preclinical Huntington's disease. *American Journal of Psychiatry*, 164, 1428-1434.
- Norman, D. A., & Shallice, T. (1980). Attention to action: Willed and automatic control of behaviour. In M. S. Gazzaniga (Ed.), *Cognitive neuroscience: A reader*. Oxford: Blackwell.
- O'Donnell, B. F., Blekher, T. M., Weaver, M., White, K. M., Marshall, J., Beristain, X.,
 . . . Foroud, T. (2008). Visual perception in prediagnostic and early stage Huntington's disease. *Journal of the International Neuropsychological Society*, 14, 446-453.
- O'Donnell, B. F., Wilt, M. A., Hake, A. M., Stout, J. C., Kirkwood, S. C., & Foroud, T. (2003). Visual function in Huntington's disease patients and presymptomatic gene carriers. *Movement Disorders*, 18, 1027-1034.
- Orth, M., Schippling, S., Schneider, S. A., Bhatia, K. P., Talelli, P., Tabrizi, S. J., & Rothwell, J. C. (2010). Abnormal motor cortex plasticity in premanifest and very early manifest Huntington disease. *Journal of Neurology, Neurosurgery, & Psychiatry*, 81, 267-270.
- Owen, A. M., Evans, A. C., & Petrides, M. (1996). Evidence for a two-stage model of spatial working memory processing within the lateral frontal cortex: A positron emission tomography study. *Cerebral Cortex*, 6, 31-38.
- Owen, A. M., Herrod, N. J., Menon, D. K., Clark, J. C., Downey, S. P. M. J., Carpenter, T. A., . . . Pickard, J. D. (1999). Redefining the functional organization of working memory processes within human lateral prefrontal cortex. *European Journal of Neuroscience*, 11, 567-574.

- Panegyres, P. K., & Goh, J. G. S. (2011). The neurology and natural history of patients with indeterminate CAG repeat length mutations of the Huntington disease gene. *Journal of the Neurological Sciences*, 301, 14-20.
- Paré, N., Rabin, L. A., Fogel, J., & Pépin, M. (2009). Mild traumatic brain injury and its sequelae: Characterisation of divided attention deficits. *Neuropsychological rehabilitation 19*, 110-137.
- Park, J. E., Lee, S. T., Im, W. S., Chu, K., & Kim, M. (2008). Galantamine reduces striatal degeneration in 3-nitropropionic acid model of Huntington's disease. *Neuroscience Letters*, 448, 143-150.
- Paulsen, J. S. (2009). Functional imaging in Huntington's disease. Experimental Neurology, 216, 272-277.
- Paulsen, J. S., Hayden, M., Stout, J. C., Langbehn, D. R., Aylward, E. H., Ross, C. A., .
 . Predict-HD Investigators of the Huntington Study Group. (2006). Preparing for preventive clinical trials: The Predict-HD study. *Achives of Neurology*, *63*, 883-890.
- Paulsen, J. S., Nehl, C., Hoth, K. F., Kanz, J. E., Benjamin, M., Conybeare, R., . . . Turner, B. (2005). Depression and stages of Huntington's disease. *Journal of Neuropsychiatry and Clinical Neurosciences*, 17, 496-502.
- Paulsen, J. S., Ready, R. E., Hamilton, J. M., Mega, M. S., & Cummings, J. L. (2001). Neuropsychiatric aspects of Huntington's disease. *Journal of Neurology*, *Neurosurgery*, & *Psychiatry*, 71, 310-314.
- Paulsen, J. S., Zimbelman, J. L., Hinton, S. C., Langbehn, D. R., Leveroni, C. L., Benjamin, M. L., . . . Rao, S. M. (2004). fMRI biomarker of early neuronal dysfunction in presymptomatic Huntington's Disease. *American Journal of Neuroradiology*, 25, 1715-1721.

- Pavese, N., Andrews, T. C., Brooks, D. J., Ho, A. K., Rosser, A. E., Barker, R. A., . . . Piccini, P. (2003). Progressive striatal and cortical dopamine receptor dysfunction in Huntington's disease: A PET study. *Brain*, *126*, 1127-1135.
- Peavy, G. M., Jacobson, M. W., Goldstein, J. L., Hamilton, J. M., Kane, A., Gamst, A. C., . . . Corey-Bloom, J. (2010). Cognitive and functional decline in Huntington's disease: Dementia criteria revisited. *Movement Disorders*, 25, 1163-1169.
- Peinemann, A., Schuller, S., Pohl, C., Jahn, T., Weindl, A., & Kassubek, J. (2005). Executive dysfunction in early stages of Huntington's disease is associated with striatal and insular atrophy: A neuropsychological and voxel-based morphometric study. *Journal of the Neurological Sciences*, 239, 11-19.
- Pellecchia, G. L. (2003). Postural sway increases with attentional demands of concurrent cognitive task. *Gait & Posture*, 18, 29-34.
- Péran, P., Démonet, J.-F., Pernet, C., & Cardebat, D. (2003). Verb and noun generation tasks in Huntington's disease. *Movement Disorders, 19*, 565-571.
- Petrides, M. (1994). Frontal lobes and working memory: Evidence from investigations of the effects of cortical excisions in nonhuman primates. In F. Boller & J. Grafman (Eds.), *Handbook of neuropsychology* (pp. 59-84). Amsterdam: Elsevier Science.
- Petrikis, P., Andreou, C., Piachas, A., Bozikas, V. P., & Karavatos, A. (2004). Treatment of Huntington's disease with galantamine. *International Clinical Psychopharmacology*, 19, 49-50.
- Pillon, B., Deweer, B., Agid, Y., & Dubois, B. (1993). Explicit memory in Alzeheimer's, Huntington's and Parkinson's diseases. Archives of Neurology, 50, 374-379.

Ponsford, J., & Kinsella, G. (1992). The use of a rating scale of attentional behaviour. *Neuropsychological Rehabilitation*, *1*, 241-257.

Posner, M. I. (1966). Components of skilled performance. Science, 152, 1712-1718.

- Posner, M. I., & Petersen, S. E. (1990). The attention system of the human brain. Annual Review of Neuroscience, 13, 25-42.
- Reading, S. A. J., Dziorny, A. C., Peroutka, L. A., Schreiber, M., Gourley, L. M., Yallapragada, V., . . . Ross, C. A. (2004). Functional brain changes in presymptomatic Huntington's disease. *Annals of Neurology*, 55, 879-883.
- Reedeker, N., Van Der Mast, R. C., Giltay, E. J., Van Duijn, E., & Roos, R. A. C. (2010). Hypokinesia in Huntington's disease co-occurs with cognitive and global dysfunctioning. *Movement Disorders*, 25, 1612-1618.
- Reilmann, R., Bohlen, S., Kirsten, F., Ringelstein, E. B., & Lange, H. W. (2011). Assessment of involuntary choreatic movements in Huntington's disease - Toward objective and quantitative measures. *Movement Disorders*, 26, 2267-2273.
- Rodrigues, G. R., Souza, C. P., Cetlin, R. S., de Oliveira, D. S., Pena-Pereira, M., Ujikawa, L. T., . . . Tumas, V. (2009). Use of the frontal assessment battery in evaluating executive dysfunction in patients with Huntington's disease. *Journal of Neurology*, 256, 1809-1815.
- Rosas, H. D., & Goldstein, J. M. (2004). Evidence for more widespread cerebral pathology in early HD: An MRI-based morphometric analysis - Reply. *Neurology*, 62, 524-524.
- Rosas, H. D., Hevelone, N. D., Zaleta, A. K., Greve, D. N., Salat, D. H., & Fischl, B. (2005). Regional cortical thinning in preclinical Huntington disease and its relationship to cognition. *Neurology*, 65, 745-747.

- Rosas, H. D., Koroshetz, W. J., Chen, Y. I., Skeuse, C., Vangel, M., Cudkowicz, M. E.,
 . . . Goldstein, J. M. (2003). Evidence for more widespread cerebral pathology in early HD: An MRI-based morphometric analysis. *Neurology*, 60, 1615-1620.
- Rosas, H. D., Liu, A. K., Hersch, S., Glessner, M., Ferrante, R. J., Salat, D. H., . . . Fischl, B. (2002). Regional and progressive thinning of the cortical ribbon in Huntington's disease. *Neurology*, 58, 695-701.
- Rosas, H. D., Salat, D. H., Lee, S. Y., Zaleta, A. K., Hevelone, N., & Hersch, S. M. (2008). Complexity and heterogeneity: What drives the ever-changing brain in Huntington's disease? *Annals of the New York Academy of Sciences*, 1147, 196-205.
- Rosas, H. D., Salat, D. H., Lee, S. Y., Zaleta, A. K., Pappu, V., Fischl, B., . . . Hersch,
 S. M. (2008). Cerebral cortex and the clinical expression of Huntington's disease:
 Complexity and heterogeneity. *Brain*, *131*, 1057-1068.
- Rosas, H. D., Tuch, D. S., Hevelone, N. D., Zaleta, A. K., Vangel, M., Hersch, S. M., & Salat, D. H. (2006). Diffusion tensor imaging in presymptomatic and early Huntington's disease: Selective white matter pathology and its relationship to clinical measures. *Movement Disorders*, 21, 1317-1325.
- Rumbaugh, D. M., & Washburn, D. A. (1996). Attention and memory in relation to learning: A comparative adaptation perspective. In G. R. Lyon & N. A. Krasnegor (Eds.), *Attention, memory and executive function*. Baltimore: Paul H. Brookes Publishing.
- Ruocco, H. H., Bonilha, L., Li, L. M., Lopes-Cendes, I., & Cendes, F. (2008).
 Longitudinal analysis of regional grey matter loss in Huntington disease: Effects of the length of the expanded CAG repeat. *Journal of Neurology, Neurosurgery,* & *Psychiatry*, 79, 130-135.

- Rupp, J., Dzemidzic, M., Blekher, T., Bragulat, V., West, J., Jackson, J., . . . Foroud, T. (2011). Abnormal error-related antisaccade activation in premanifest and early manifest Huntington disease. *Neuropsychology*, 25, 306-318.
- Sack, A. T. (2010). Using non-invasive brain interference as a tool for mimicking spatial neglect in healthy volunteers. *Restorative Neurology and Neuroscience*, 28, 485-497.
- Saft, C., Schuttke, A., Beste, C., Andrich, J., Heindel, W., & Pfleiderer, B. (2008). fMRI reveals altered auditory processing in manifest and premanifest Huntington's disease. *Neuropsychologia*, 46, 1279-1289.
- Saint-Cyr, J. A. (2003). Frontal-striatal circuit functions: Context, sequence, and consequence. Journal of the International Neuropsychological Society, 9, 103-128.
- Saldert, C., Fors, A., Ströberg, S., & Hartelius, L. (2010). Comprehension of complex discourse in different stages of Huntington's disease. *International Journal of Language and Communication Disorders*, 45, 656-669.
- Salthouse, T. A. (1985). A theory of cognitive aging. Amsterdam: North Holland.
- Salthouse, T. A. (1996). The processing-speed theory of adult age differences in cognition. *Psychological Review*, 103, 403-428.
- Salthouse, T. A. (2000). Aging and measures of processing speed. *Biological Psychology*, 54, 35-54.
- Sarter, M., & Turchi, J. (2002). Age- and dementia-associated impairments in divided attention: Psychological constructs, animal models, and underlying neuronal mechanisms. *Dementia and Geriatric Cognitive Disorders*, 13, 46-58.

- Say, M. J., Jones, R., Scahill, R. I., Dumas, E. M., Coleman, A., Dar Santos, R. C., . . .TRACK-HD Investigators. (2011). Visuomotor integration deficits precede clinical onset in Huntington's disease. *Neuropsychologia*, 49, 264-270.
- Schmidtke, K., Manner, H., Kaufmann, R., & Schmolck, H. (2002). Cognitive procedural learning in patients with fronto-striatal lesions. *Learning and Memory*, 9, 419-429.
- Sebastian, M. V., Menor, J., & Elosua, M. R. (2006). Attentional dysfunction of the central executive in AD: Evidence from dual task and perseveration errors. *Cortex*, 42, 1015-1020.
- Selemon, L. D., Rajkowska, G., & Goldman-Rakic, P. S. (2004). Evidence for progression in frontal cortical pathology in late-stage Huntington's disease. *The Journal of Comparative Neurology*, 468, 190-204.
- Seong, I. S., Ivanova, E., Lee, J.-M., Choo, Y. S., Fossale, E., Anderson, M.,. . . MacDonald, M. E. (2005). HD CAG repeat implicates a dominant property of huntingtin in mitochondrial energy metabolism. *Human Molecular Genetics*, 14, 2871-2880.
- Sheridan, P. L., Solomont, J., Kowall, N., & Hausdorff, J. M. (2003). Influence of executive function on locomotor function: Divided attention increases gait variability in Alzheimer's disease. JAGS, 51, 1633-1637.
- Sitek, E. J., Sołtan, W., Wieczorek, D., Schinwelski, M., Robowski, P., Harciarek, M., .
 Sławek, J. (2013). Self-awareness of executive dysfunction in Huntington's disease: Comparison with Parkinson's disease and cervical dystonia. *Psychiatry and Clinical Neurosciences*, 67, 59-62.
- Smith, G. A., & Brewer, N.. (1995). Slowness and age: Speed-accuracy mechanisms. Psychology and Aging, 10, 238-247.

- Smith, M. A., Brandt, J., & Shadmehr, R. (2000). Motor disorder in Huntington's disease begins as a dysfunction in error feedback control. *Nature*, 403, 544-549.
- Snowden, J. S., Craufurd, D., Griffiths, H., Thompson, J., & Neary, D. (2001). Longitudinal evaluation of cognitive disorder in Huntington's disease. *Journal of the International Neuropsychological Society*, 7, 33-44.
- Snowden, J. S., Craufurd, D., Thompson, J., & Neary, D. (2002). Psychomotor, executive, and memory function in preclinical Huntington's disease. *Journal of Clinical and Experimental Neuropsychology*, 24, 133-145.
- Soliveri, P., Monza, D., Piacentini, S., Paridi, D., Nespolo, C., Gellera, C., . . . Girotti,
 F. (2002). Cognitive and psychiatric characterization of patients with Huntington's disease and their at-risk relatives. *Neurological Sciences*, 23, S105-S106.
- Solomon, A. C., Stout, J. C., Johnson, S. A., Langbehn, D. R., Aylward, E. H., Brandt, J., . . . Paulsen, J. S. (2007). Verbal episodic memory declines prior to diagnosis in Huntington's disease. *Neuropsychologia*, 45, 1767-1776.
- Spargo, E., Everall, I. P., & Lantos, P. (1993). Neuronal loss in the hippocampus in Huntington's disease: A comparison with HIV infection. *Journal of Neurology*, *Neurosurgery*, & *Psychiatry*, 56, 487-491.
- Sprengelmeyer, R., Lange, H., & Hömberg, V. (1995). The pattern of attentional deficits in Huntington's disease. *Brain*, *118*, 145-152.
- Stout, J. C., & Johnson, S. A. (2005). Cognitive impairment and dementia in basal ganglia disorders. *Current Neurology and Neuroscience Reports*, 25, 355-363.
- Stout, J. C., Jones, R., Labuschagne, I., O'Regan, A. M., Say, M. J., Dumas, E. M., . . . Frost, C. (2012). Evaluation of longitudinal 12 and 24 month cognitive outcomes in premanifest and early Huntington's disease. *Journal of Neurology, Neurosurgery, & Psychiatry, 83*, 687-694.

- Stout, J. C., Paulsen, J., Queller, S., Solomon, A. C., Whitlock, K. B, Campbell, C., . . . Aylward, E. H. (2011). Neurocognitive signs in prodromal Huntington disease. *Neuropsychology*, 25, 1-14.
- Stout, J. C., Rodawalt, W. C., & Siemers, E. R. (2001). Risky decision making in Huntington's disease. *Journal of International Neuropsychological Society* 7, 92-101.
- Stout, J. C., Weaver, M., Solomon, A. C., Queller, S., Hui, S., Johnson, S. A., . . .
 Foroud, T. (2007). Are cognitive changes progressive in prediagnostic HD? *Cognitive and Behavioral Neurology*, 20, 212-218.
- Swanenburg, J., de Bruin, E. D., Uebelhart, D., & Mulder, T. (2009). Compromising postural balance in the elderly. *Gerontology*, 55, 353-360.
- Szameitat, A. J., Schubert, T., Müller, K., & von Cramon, D. Y. (2002). Localization of executive functions in dual-task performance with fMRI. *Journal of Cognitive Neuroscience*, 14, 1184-1199.
- Tabrizi, S. J., Langbehn, D. R., Leavitt, B. R., Roos, R. A. C., Durr, A., Craufurd, D.,..
 The TRACK-HD Investigators. (2009). Biological and clinical manifestations of Huntington's disease in the longitudinal TRACK-HD study: Cross-sectional analysis of baseline data. *The Lancet Neurology*, *8*, 791-801.
- Tabrizi, S. J., Reilmann, R., Roos, R. A. C., Durr, A., Leavitt, B., Owen, G., . . . The TRACK-HD investigators. (2012). Potential endpoints for clinical trials in premanifest and early Huntington's disease in the TRACK-HD study: Analysis of 24 month observational data. *The Lancet*, 11, 1-12.

- Tabrizi, S. J., Scahill, R. I., Durr, A., Roos, R. A. C., Leavitt, B. R., Jones, R., . . . TRACK-HD Investigators. (2011). Biological and clinical changes in premanifest and early stage Huntington's disease in the TRACK-HD study: The 12-month longitudinal analysis. *The Lancet Neurology*, 10, 31-42.
- Teichmann, M., Darcy, I., Bachoud-Levi, A.-C., & Dupoux, E. (2009). The role of the striatum in phonological processing: Evidence from early stages of Huntington's disease. *Cortex*, 45, 839-849.
- Teichmann, M., Dupoux, E., Kouider, S., & Bachoud-Levi, A.-C. (2006). The role of the striatum in processing language rules: Evidence from word perception in Huntington's disease. *Journal of Cognitive Neuroscience*, 18, 1555-1569.
- Teichmann, M., Dupoux, E., Kouider, S., Brugières, P., Boissé, M.-F., Baudic, S., . . . Bachoud-Lévi, A.-C. (2005). The role of the striatum in rule application: The model of Huntington's disease at early stage. *Brain, 128*, 1155-1167.
- Teichmann, M., Gaura, V., Demonet, J.-F.Supiot, F., Delliaux, M., Verny, C., Renou,
 P., . . . Bachoud-Lévi, A.-C. (2008). Language processing within the striatum:
 Evidence from a PET correlation study in Huntington's disease. *Brain, 131*, 1046-1056.
- Teo, C. R. L., Wang, W., Law, H. Y., Lee, C. G., & Chong, S. S. (2008). Single-step scalable throughput molecular screening for Huntington disease. *Clinical Chemistry*, 54, 964-972.
- Thaut, M. H., Miltner, R., Lange, H. W., Hurt, C. P., & Hoemberg, V. (1999). Velocity modulation and rhythmic synchronization of gait in Huntington's disease. *Movement Disorders*, 14, 808-819.

- The Huntington's Disease Collaborative Research Group. (1993). A novel gene containing a trinucleotide repeat that is expanded and unstable on Huntington's disease chromosomes. *Cell*, 72, 971-983.
- Thieben, M. J., Duggins, A. J., Good, C. D., Gomes, L., Mahant, N., Richards, F., . . . Frackowiak, R. S. J. (2002). The distribution of structural neuropathology in preclinical Huntington's disease. *Brain*, 125, 1815-1828.
- Thiruvady, D. R., Georgiou-Karistianis, N., Egan, G. F., Ray, S., Sritharan, A., Farrow,
 M., . . . Cunnington, R. (2007). Functional connectivity of the prefrontal cortex in
 Huntington's disease. *Journal of Neurology, Neurosurgery, & Psychiatry*, 78, 127-133.
- Thompson, J. C., Poliakoff, E., Sollom, A. C., Howard, E., Craufurd, D., & Snowden, J. S. (2010). Automaticity and attention in Huntington's disease: When two hands are not better than one. *Neuropsychologia*, 48, 171-178.
- Thu, D. C. V., Oorschot, D. E., Tippett, L. J., Nana, A. L., Hogg, V. M., Synek, B. J., . . . Faull, R. L. M. (2010). Cell loss in the motor and cingulate cortex correlates with symptomatology in Huntington's disease. *Brain*, 133, 1094-1110.
- Tibben, A. (2007). Predictive testing for Huntington's disease. *Brain Research Bulletin*, 72, 165-171.
- Turner, C., & Schapira, A. H. V. (2010). Mitochondrial matters of the brain: The role in Huntington's disease. *Journal of Bioenergetics and Biomembranes*, 42, 193-198.
- van der Hiele, K., Jurgens, C. K., Vein, A. A., Reijntjes, R. H. A. M., Witjes-Ané, M.-N. W., Roos, R. A. C., . . . Middelkoop, H. A. M. (2007). Memory activation reveals abnormal EEG in preclinical Huntington's disease. *Movement Disorders*, 22, 690-695.

- van Zomeren, A. H., & Brouwer, W. H. (1994). *Clinical neuropsychology of attention*. Oxford: Oxford University Press.
- Vassos, E., Panas, M., Kladi, A., & Vassilopoulos, D. (2007). Higher levels of extroverted hostility detected in gene carriers at risk for Huntington's disease. *Biological Psychiatry*, 62, 1347-1352.
- Verghese, J., Buschke, H., Viola, L., Katz, M., Hall, C., Kuslansky, G., & Lipton, R. (2002). Validity of divided attention in predicting falls in older individuals: A preliminary study. *JAGS*, 50, 1572-1576.
- Verhaeghen, P., Steitz, D. W., Sliwinski, M. J., & Cerella, J. (2003). Aging and dualtask performance: A meta-analysis. *Psychology and Aging*, 18, 443-460.
- Walker, F. O. (2007). Huntington's disease. Lancet, 369, 218-228.
- Ward, J., Sheppard, J.-M., Shpritz, B., Margolis, R. L., Rosenblatt, Adam, & Brandt, Jason. (2006). A four-year prospective study of cognitive functioning in Huntington's disease. *Journal of the International Neuropsychological Society*, 12, 445-454.
- Watkins, L. H. A., Rogers, R. D., Lawrence, A. D., Sahakian, B. J., Rosser, A. E., & Robbins, T. W. (2000). Impaired planning but intact decision making in early Huntington's disease: Implications for specific fronto-striatal pathology. *Neuropsychologia*, 38, 1112-1125.
- Wechsler, D. (2009). Advanced clinical solutions for WAIS-IV and WMS-IV. San Antonio, TX: Pearson.
- West, R., & Bell, M. A. (1997). Stroop color-word interference and electroencephalogram activation: Evidence for age-related decline of the anterior attention system. *Neuropsychology*, 11, 421-427.

- Wichmann, T., & DeLong, M. R. (1996). Functional and pathophysiological models of the basal ganglia. *Current Opinion in Neurobiology*, 6, 751-758.
- Wickens, C. D. (2002). Multiple resources and performance prediction. *Theoretical Issues in Ergonomics Science*, 3, 159-177.
- Wickens, C. D. (2008). Multiple resources and mental workload. *Human Factors*, 50, 449-455.
- Wickens, C. D., & McCarley, J. S. (2008). Applied attention theory. Boca Raton: Taylor & Francis.
- Wild, E. J., & Tabrizi, S. J. (2007). The differential diagnosis of chorea. Practical Neurology, 7, 360-373.
- Witjes-Ané, M.-N., Mertens, B., van Vugt, J. P., Bachoud-Lévi, A.-C., van Ommen, G.-J. B., & Roos, R. A. C. (2007). Longitudinal evaluation of "presymptomatic" carriers of Huntington's disease. *Journal of Neuropsychiatry & Clinical Neurosciences*, 19, 310-317.
- Wolf, R. C., Sambataro, F., Vasic, N., Schönfeldt-Lecuona, C., Ecker, D., & Landwehrmeyer, B. (2008). Altered frontostriatal coupling in pre-manifest Huntington's disease: Effects of increasing cognitive load. *European Journal of Neurology*, 15, 1180-1190.
- Wolf, R. C., Sambataro, F., Vasic, N., Shönfeldt-Lecuona, C., Ecker, D., & Landwehrmeyer, B. (2008). Aberrant connectivity of lateral prefrontal networks in presymptomatic Huntington's disease. *Experimental Neurology*, 213, 137-144.
- Wolf, R. C., Vasic, N., Schönfeldt-Lecuona, C., Ecker, D., & Landwehrmeyer, G. B. (2009). Cortical dysfunction in patients with Huntington's disease during working memory performance. *Human Brain Mapping*, *30*, 327-339.

- Wolf, R. C., Vasic, N., Schönfeldt-Lecuona, C., Ecker, D., & Landwehrmeyer, G. B. (2008). Functional imaging of cognitive processes in Huntington's disease and its presymptomatic mutation carriers. *Nervenarzt*, 79, 408-420.
- Wolf, R. C., Vasic, N., Schönfeldt-Lecuona, C., Landwehrmeyer, B., & Ecker, D.
 (2007). Dorsolateral prefrontal cortex dysfunction in presymptomatic Huntington's disease: Evidence from event-related fMRI. *Brain*, 130, 2845-2857.
- Wolf, R. C., & Walter, H. (2005). Evaluation of a novel event-related parametric fMRI paradigm investigating prefrontal function. *Psychiatry Research: Neuroimaging*, 140, 73-83.
- Woollacott, M., & Shumway-Cook, A. (2002). Attention and the control of posture and gait: A review of an emerging area of research. *Gait and Posture*, 16, 1-14.
- Zakzanis, K. K. (1998). The subcortical dementia of Huntington's disease. *Journal of Clinical and Experimental Neuropsychology*, 20, 565-578.
- Zimbelman, J. L., Paulsen, J. S., Mikos, A., Reynolds, N. C., Hoffmann, R. G., & Rao,
 S. M. (2007). fMRI detection of early neural dysfunction in preclinical Huntington's disease. *Journal of the International Neuropsychological Society*, 13, 758-769.