THE EFFECT OF CHEMOTHERAPY ON COGNITION IN PATIENTS WITH AND SURVIVORS OF COLORECTAL CANCER

Kristy Diane Giles (née Hodgson)

School of Psychology

University of Adelaide, SA, Australia

October, 2013

TABLE OF CONTENTS

ABST	ΓRACT	v
DEC	KNOWLEDGMENTS ix APTER 1 1 roduction Preamble Chemotherapy-Related Cognitive Impairment: An Overview Confounding Factors in CRCI Interventions for CRCI Limitations of Existing CRCI Research Detailed Review of the CRCI Literature 1.5.1 Background 1.5.2 Objectively-Measured Versus Self-Reported CRCI 1.5.3 Factors that Contribute to CRCI and the Severity of its Symptoms 1.5.4 Personality and CRCI Colorectal Cancer Summary and Aims Chapter Summary and Future Directions APTER 2	viii
ACK	NOWLEDGMENTS	ix
СНА	PTER 1	1
Intro	duction	1
1.0	Preamble	1
1.1	Chemotherapy-Related Cognitive Impairment: An Overview	1
1.2	Confounding Factors in CRCI	4
1.3	Interventions for CRCI	9
1.4	Limitations of Existing CRCI Research	14
1.5	Detailed Review of the CRCI Literature	16
	1.5.1 Background	16
	1.5.2 Objectively-Measured Versus Self-Reported CRCI	20
	1.5.3 Factors that Contribute to CRCI and the Severity of its Symptoms	22
	1.5.4 Personality and CRCI	25
1.6	Colorectal Cancer	29
1.7	Summary and Aims	30
1.8	Chapter Summary and Future Directions	33
СНА	PTER 2	
A Me	ta-Analysis of the Effects of Chemotherapy on Cognition in Patients with	th
Canc	er (Study 1)	
2.0	Preface	35
2.1	Chapter Summary and Future Direction	68

CHAPTER 3

The Effect of Chemotherapy on Cognition in Patients treated for Colorect	al
Cancer (Study 2)	
3.0 Preface	72
3.1 Chapter Summary and Future Directions	95
CHAPTER 4	
Self-Reported Cognitive Function in Patients with Colorectal Cancer (Stu	dy 3)
4.0 Preface	98
4.1 Chapter Summary and Future Directions	124
CHAPTER 5	
The Effect of Optimism and Locus of Control on Memories of Psychologic	al
Wellbeing and Cognitive Functioning during Treatment in Colorectal Car	ıcer
Survivors (Study 4)	
5.0 Preface	126
CHAPTER 6	
Conclusions	
6.1 Overview of Thesis	151
6.1.1 Meta-Analysis	153
6.1.2 Primary Study of the Effect of Chemotherapy on Cognition in Pa	tients
with Colorectal Cancer	156
6.1.3 Colorectal Cancer Literature	160
6.1.4 Primary Study on the Relationship between Objectively-Measure	d and
Self-Reported Cognitive Functioning	162
6.1.5 Optimism and Locus of Control Study	164
6.1.6 Conclusions	167

6.2 Limitations and Difficulties Associated with this Research	
6.3 Future Research	171
6.5 Final Comments	172
Appendices	
Appendix A. Published manuscript of study 1 and author contribution statements	174
Appendix B. Published manuscript of study 2 and author contribution statements	183
Appendix C. Longitudinal follow-up of study 2	198
Appendix D. Example question from the Everyday Problems Test from study 3	206
Appendix E. Table of correlations from study 3	207
Appendix F. Study 3 author contribution statements	209
Appendix G. Correlation matrix for all measures in Study 4	211
Appendix H. Correlation matrix for cancer survivors and their spouses for all	
measures in Study 4	212
Appendix I. Study 4 author contribution statements	
References	215

ABSTRACT

This thesis has explored the phenomenon that has been described as chemotherapy-related cognitive impairment (CRCI), both in the wider cancer patient population, as well as looking specifically at patients being treated for colorectal cancer. CRCI refers to the situation in which treatment with chemotherapy for cancer leads to a subsequent decline in the cognitive functioning of affected patients, evident in both self-report data and the results of psychological testing.

Four studies have been completed. The first study was a meta-analysis of the literature published up until 2010, which investigated the effect of treatment with chemotherapy on cognitive functioning across a number of different types of cancer. This study found that, although CRCI has been well documented as occurring in patients treated with chemotherapy for breast cancer, research is lacking in relation to other types of cancer, in particular colorectal cancer. This outcome justified the research that followed; the specific focus of which was to evaluate the effect of chemotherapy on cognition in patients with colorectal cancer.

Following the meta-analysis, a primary research study was conducted to assess the effect of chemotherapy on cognition in patients treated for colorectal cancer. This study comprised four sample groups, all of whom, with the exception of healthy, agematched controls (n=20), had been diagnosed with colorectal cancer: participants who have been treated with chemotherapy (n=19), participants who received treatment with the anti-vascular drug Avastin (n=12) and participants who have received only surgery (n=10). Results supported previous reports that cognitive impairment may occur in patients treated for cancer, however suggestions that chemotherapy impacts cognition more than other forms of treatment was not

supported by the results, with the surgery patients being the only group to be significantly different in their cognitive performance from the healthy controls.

The next study (Study 3) investigated the relationship between subjective and objective measures of cognitive functioning in colorectal cancer patients. In general, the results revealed that patient perception of cognitive functioning was not significantly related to performance on objective cognitive tests, with the possible exception being tests of memory, indicating that a discrepancy may exist between objectively and subjectively measured CRCI. Depression and anxiety were negatively related and emotional wellbeing positively related to subjective reports of CRCI.

Study 4 (Chapter 5) aimed to assess whether locus of control, optimism / pessimism and depression influence recall of cognitive functioning after cancer treatment among colorectal cancer survivors. Two different groups were included in the sample: survivors of colorectal cancer (n = 88) and their spouses (n = 40). Recall of cognitive difficulties after cancer treatment was validated through significant correlation with recall of the participants' cognition after treatment, provided by their partners. Significant positive relationships were established between internal locus of control, optimism and perceived cognitive functioning and a negative relationship for depression. Regression analyses revealed that after controlling for depression, internal locus of control and optimism/pessimism contributed very little to the survivors' recall of cognitive functioning after cancer treatment. However, it was proposed that depression may moderate the relationship between internal locus of control and recall of cognitive functioning; hence if depression were to be treated, it is possible that internal locus of control would significantly contribute to recall of cognition after treatment. This was not the case for optimism/pessimism. These results were discussed in terms of their importance for researchers and clinicians alike. The

treatment experience of cancer patients and survivors must be considered in light of their level of depression and the extent to which they demonstrate an internal locus of control. Where depression is high, recall of cognitive impairment associated with treatment may be impacted.

DECLARATION

I certify that this work contains no material which has been accepted for the

award of any other degree or diploma in any university or other tertiary institution in

my name and, to the best of my knowledge and belief, contains no material previously

published or written by another person, except where due reference has been made in

the text. In addition, I certify that no part of this work will, in the future, be used in a

submission in my name, for any other degree or diploma in any university or other

tertiary institution without the prior approval of the University of Adelaide and where

applicable, any partner institution responsible for the joint award of this degree.

I give consent to this copy of my thesis when deposited in the University

Library, being made available for loan and photocopying, subject to the provisions of

the Copyright Act 1968.

The author acknowledges that copyright of published works contained within

this thesis resides with the copyright holder(s) of those works.

I also give permission for the digital version of my thesis to be made available

on the web, via the university's digital research repository, the Library catalogue and

also through web search engines, unless permission has been granted by the

University to restrict access for a period of time.

Kristy Giles

October, 2013.

viii

ACKNOWLEDGMENTS

I would like to start off by thanking my three supervisors, Carlene, Ted and Amanda for all of their help and invaluable advice throughout my PhD candidature. Thankyou also to Dr Ganessan Kichenadasse for assisting with referral of patients to the studies; this would not have been possible without your help.

Thank you to my friends Amy, Lizzie, Megan and Tanya for taking an interest and giving me an opportunity to talk about my research. I would also like to thank my fellow PhD candidates Adella, Emma and Nadja for providing support from the beginning. Our catch-ups reassured me that I was not alone in both the good and bad times of my candidature.

I would also like to thank Mum, Dad and Amanda for their ongoing love and support both during my PhD and always. You pushed me when I needed motivation and encouraged me to take a break when I was stressed. For that, I am grateful.

Finally to Trent, you are my best friend and have given me so much support over the last few years. You have experienced all of the ups and downs with me; I love you and am so lucky to have you.