Cognitive and psychological problems after total joint replacement in older adults.
Julia Erin Scott November 2016
November 2016

This dissertation is submitted in fulfilment of the requirements for the degree

of Doctor of Philosophy in the Faculty of Health Sciences,

School of Psychology, at the University of Adelaide

1

Table of Contents

Table of Contents	
List of Tables fix	۰۰۰۰۰۰۰۰۰۰۰۰۰۰۰۷
List of figures fix	vi
Abstract	vii
Declaration	xi
Acknowledgements	xi\
Chapter 1. Cognitive and Psychological Problems in Patients who Undergo Tota Replacement 1	al Joint
Total Joint Replacement in an Ageing Population	1
Postoperative Cognitive Dysfunction	5
Potential causes of postoperative cognitive dysfunction after total joint replace	ement6
Impact of postoperative cognitive dysfunction on outcomes after surgery	8
Measurement of postoperative cognitive dysfunction following total joint replace	cement 8
Delirium	10
Delirium in hospitalised older adults	11
Delirium after total joint replacement	13
Sources of variation in reported rates of delirium	14
Depression and Anxiety after Total Joint Replacement	16
Causes of depression and anxiety in patients who undergo total joint replacer	nent18
Depression, anxiety, and postoperative outcomes	20
The impact of total joint replacement surgery on depression and anxiety	21
References	23
Chapter 2. Postoperative Cognitive Dysfunction and Cognitive Reserve	45
Brain and Cognitive Reserve	46
The Relationship between Cognitive Reserve and Cognitive Decline	48
Cognitive Reserve and Postoperative Cognitive Dysfunction after Total Joint Replacement	49
Overview, Aims and Thesis Structure	52
Deferences	57

Chapter 3. Study 1	66
Statement of Authorship	6
Preface	68
Abstract	69
Methods	75
Search strategy and selection criteria	75
Research design and data preparation	75
Effect size calculations and analyses	77
Results	80
Participants	80
Early postoperative outcomes	82
Longer-term postoperative outcomes	82
Discussion	87
References	92
Appendices	100
Preface	
Abstract	
Method	
Search strategy and research design	
Effect size calculations and analyses	
Results	
Discussion	121
References	
Appendices	127
	127
	127
·	127
Statement of Authorship	127 137 139 140
Statement of Authorship Preface	127 137 139 140
Statement of Authorship Preface Abstract	
Statement of Authorship Preface	

Effect size calculation and analyses	147
Results	150
Search results	150
Research designs and data preparation	151
Participants	153
Prevalence of clinically significant levels of depression and anxiety	155
Changes on the severity of depression and anxiety symptoms pre- to pos	st-surgery157
Discussion	161
References	167
Appendices	180
Chapter 6. Study 4	185
Statement of Authorship	186
Preface	188
Abstract	192
Methods	196
Participants	196
Procedure	197
Measures	198
Statistical Analysis	201
Results	202
Participant details	202
Standardised regression-based analyses	206
Predictors of pre- to postoperative cognitive change	212
Discussion	213
References	218
Appendices	227
Chapter 7. Discussion	228
Summary of Findings, Strengths and Limitations	228
Study 1	228
Study 2	232
Study 3	234
Study 4	237

Clinical Implications and Future Research Recommendations	
Cognitive outcomes after total joint replacement	240
Psychological outcomes of total joint replacement	245
Summary	247
References	249

List of Tables

Chapter 3
Table 3-1: Summary demographic and surgery data for the total joint replacement and
control groups81
Table 3-2: Pre-discharge cognitive outcomes after total joint replacement surgery83
Table 3-3: 3-6 month cognitive outcomes after total joint replacement surgery85
Chapter 4
Table 4-1: Summary of demographic and surgical details for total joint replacement
patients113
Table 4-2: Incidence of delirium during hospital admission for total joint replacement120
Chapter 5
Table 5-1: Summary demographic and surgery data for the total joint replacement and
control groups
Table 5-2: Prevalence of depression and anxiety in total joint replacement patients156
Table 5-3: Change in symptoms of depression before and after total joint replacement .159
Table 5-4: Change in symptoms of anxiety before and after total joint replacement160
Appendices
Table 5-A: Individual study characteristics
Chapter 6
Table 6-1: Summary of details of the cognitive, physical, and psychological measures200
Table 6-2: Baseline total joint replacement and healthy control group characteristics204
Table 6-3: Control participant regression equations for predicting neuropsychological
follow-up scores
Table 6-4: Proportion of total joint replacement patients and controls who experienced
cognitive decline at follow-up
Table 6-5: Mean pre- to post-surgery change in cognitive scores among total joint
replacement patients and controls
Appendices

Table 6-A: Baseline data for total joint replacement patients who completed the stu	dy and
those lost to attrition	227

List of Figures

Chapter 4	
Figure 4-1: Individual study and mean incidence of delirium after total joint replaceme	nt
	115
Figure 4-2: Funnel plot of observed and imputed individual logit effect size	
Appendices	
Figure 4-A: Outcomes of the database searches	116
Chapter 5	
Appendices	
Figure 5-A: Flow chart detailing the outcomes of the database searches, and applicat	tion of
the inclusion/exclusion criteria	182

Abstract

Total joint replacement (TJR) of the hip or knee is a major elective procedure that is frequently performed in older adults to treat end-stage osteoarthritis. It is generally considered to be a highly successful procedure because it significantly reduces the pain and disability caused by severe arthritis, and allows people to resume many of their everyday activities. However, there is also research to suggest that older patients may be susceptible to cognitive and psychological problems following TJR.

Research investigating cognitive and psychological outcomes following TJR has provided mixed results, making it difficult to draw conclusions to inform clinical practice. While some studies have reported evidence of postoperative cognitive dysfunction (POCD) after TJR, others have not. Similarly, the reported rates of delirium after TJR have varied enormously (0% to 82%). In addition, estimates of the prevalence of clinically significant cases of depression and anxiety among TJR patients range from very high (i.e., 85-95%) to rates that are comparable to the general population. It is also unclear whether TJR has an impact on the levels of depression and anxiety that are reported by patients.

The current thesis examined the cognitive and psychological outcomes of persons undergoing TJR surgery in order to clarify the risk of these problems in this patient population. To this end, three meta-analyses (Chapters 3-5) were conducted to evaluate the risk of cognitive and psychological problems following TJR: one examined POCD, another delirium, and one depression and anxiety. Lastly, a clinical study was conducted (Chapter 6) to address the outstanding issues within the POCD literature revealed by these reviews.

Study 1 meta-analysed research that examined cognition pre- and post TJR. Data were categorised according to the cognitive domain that was assessed (e.g. memory, attention, executive function), follow-up interval (pre-discharge, 3 to 6 months post-

surgery) and study design (single TJR group repeated measures, TJR and Control group repeated measures). Unfortunately, the incidence of POCD could not be determined because the studies did not use comparable definitions of POCD. Furthermore, limited conclusions could be drawn, largely because practice effects were generally not adequately controlled for. Overall, this meta-analysis revealed the need for methodologically rigorous research that controls for repeat testing confounds and uses a theoretically and statistically defensible definition of cognitive decline to investigate the incidence and severity of POCD after TJR.

The second meta-analysis (Study 2) investigated the incidence of delirium after TJR, and whether differences in sample characteristics (e.g. hip vs knee, general vs regional anaesthesia) and study methodology (e.g. measure, assessment interval) contributed to the variability in the incidence rates reported by different studies. Delirium was found to occur in approximately one in six patients following TJR, but the variability in findings proved difficult to explain.

Study 3 meta-analysed the research that examined depression and anxiety symptoms pre- and post-TJR. This study examined the prevalence of clinically significant levels of depression and anxiety in TJR patients, and changes in these symptoms pre- to post-surgery. Data were grouped and analysed according to the length follow-up interval. Although only limited data were available, a high proportion of TJR patients appeared to experience clinically significant levels of depression and anxiety pre- and early post-surgery. Modest decreases in symptoms were observed after surgery, but were unlikely to reflect clinically significant change. Once again, this study highlighted the fact that few studies have used a control group.

Lastly, a clinical study (Study 4) was designed to overcome the limitations in previous research identified in Study 1 by including a control group and using standardised regression-based statistical methodology to reduce the confounding effects of repeat testing (practice effects, measurement error and regression to the mean) and to provide a statistically defensible definition of POCD. In addition, this study investigated whether POCD was related to cognitive reserve, which refers to individual differences in cognitive abilities that may protective against brain damage. Cognitive reserve has often been used to explain the lack of a clear relationship between brain pathology and the resulting symptoms, but has not yet been investigated in the context of POCD after TJR.

TJR and matched healthy control groups were recruited, and cognitive functioning was assessed using a battery of tests both pre- and post-surgery (6 months). Other variables that may have affected cognitive performance were also assessed (e.g. demographics, medical history, pain, psychological distress). This study found minimal evidence of POCD six months after TJR, with patients only experiencing significant decline in their performance on a single test. Although preliminary, this suggests that patients who undergo TJR have good cognitive outcomes post-surgery. Although at odds with the findings of many previous studies, it highlights the importance of controlling for repeated testing by using a control group and appropriate statistical techniques (standardised regression-based statistics).

Whether cognitive reserve was protective against POCD could only be explored to a limited degree because TJR patients only showed greater pre- to post-surgery decline on one task when compared to controls. Although cognitive reserve and performance on this task were not related, reserve predicted cognitive change among those TJR patients achieved the greatest improvement and greatest decline pre- to post-surgery, suggesting that cognitive reserve is related to better cognitive recovery post-surgery among a subset

of patients. It remains to be seen whether cognitive reserve would better predict POCD in a sample with more pronounced cognitive dysfunction.

Overall, this thesis provides a summary of the literature to date on cognitive and psychological outcomes after TJR in the elderly. In addition, this thesis has addressed some outstanding questions that remain regarding POCD. The clinical implications of these findings for patients who undergo TJR are discussed, and recommendations for future research are made.

Declaration

I, Julia Scott, certify that this work contains no material which has been accepted for the award of any other degree or diploma in my name, in any university or other tertiary institution 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 Search and also through web search engines, unless permission has been granted by the University to restrict access for a period of time.

Published works

Chapter 3: Study 1

Scott, J. E., Mathias, J. L., & Kneebone, A. C. (2014). Postoperative cognitive dysfunction after total joint arthroplasty in the elderly: A meta-analysis. Journal of Arthroplasty, 29, 261-267. doi:10.1016/j.arth.2013.06.007.

Chapter 4: Study 2

Scott, J. E., Mathias, J. L., & Kneebone, A. C. (2015). Incidence of delirium following total joint replacement in older adults: A meta-analysis. *General Hospital Psychiatry*, 37, 223-229. doi:10.1016/j.genhosppsych.2015.02.004.

Chapter 5: Study 3

Scott, J. E., Mathias, J. L., & Kneebone, A. C. (2016). Depression and anxiety after total joint replacement among older adults: a meta-analysis. *Aging and Mental Health, 20*, 1243-1242. doi:10.1080/13607863.2015.1072801.

Chapter 6: Study 4

Scott, J. E., Mathias, J. L., Kneebone, A. C., & Krishnan, J. (2016). Postoperative cognitive dysfunction and its relationship to cognitive reserve in elderly total joint replacement patients. *Journal of Clinical and Experimental Neuropsychology, In Press.* doi:10.1080/13803395.2016.1233940.

Julia Scott		
Signed:	Date:	

Acknowledgements

I am indebted to the following people, who made this PhD possible:

To my supervisor, Professor Jane Mathias, whose patience, advice, encouragement, and commitment has been unwavering and invaluable in my development as a researcher.

To my supervisor, Dr Tony Kneebone, whose insight, clinical expertise, support, and good humour has inspired, reassured, and helped to overcome many obstacles.

To Professor Jegan Krishnan, who gave generously his time and vast knowledge to this project and worked tirelessly in setting up patient recruitment and assessment without which this study would not have been possible. In addition, to the International Musculoskeletal Research Institute, in particular to Anneka Bowman and Nicholas Kerrison or their ongoing support, and efforts in patient recruitment.

To my family, in particular my parents, for their ongoing encouragement and to Andrew, for putting up with me these last few years.

Finally, to the study participants who gave so much time and effort towards the study. Their enthusiasm, interest, and kindness made data collection a delight, and I feel very privileged by their involvement