The Impact of Deep Brain Stimulation on Personality, Self and Relationships: A Qualitative Exploration in a Neurological and Psychiatric Population

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Abbreviations

ALIC: anterior limb of the internal capsule

BoN: burden of normality

BNST: bed nucleus of the stria terminalis

COMT: catechol-O-methyltransferase

COREQ: Consolidated Criteria for Reporting Qualitative Research

CT: computed tomography

DBS: deep brain stimulation

DRT: dopamine replacement therapy

ECT: electroconvulsive therapy

ET: essential tremor

FDA: Food and Drug Administration

FLOPS: Frontal Lobe Personality Scale

FrSBe: Frontal Systems Behavior Scale

GPi: globus pallidus internus

ICD: impulse control disorder

IPG: implantable pulse generator

IRSPC: Iowa Rating Scales of Personality Change

LH: lateral habenula

MDD: major depressive disorder

MFB: medial forebrain bundle

MRI: magnetic resonance imaging

NA: nucleus accumbens

OCD: obsessive-compulsive disorder

PIAAAS: personality, identity, agency, authenticity, autonomy and self

PD: Parkinson's disease

RCT: randomised control trial

SAC: subgenual anterior cingulate

STN: subthalamic nucleus

SN: substantia nigra

TCI: Temperament and Character Inventory

TMS: transcranial magnetic stimulation

TRD: treatment-resistant depression

USD: United States dollar

VC/VS: ventral capsule/ventral striatum

VIM: ventral intermediate nucleus

Abstract

The potential for DBS-related changes in personality, self and interpersonal relationships are significant issues facing patients who undergo DBS and their families and has been a topic of interest for scientific and non-scientific communities in recent years. The ethical and philosophical literature on the topic often holds a theoretical and speculative stance that discounts the growing neuropsychiatric, psychological and social scientific literature. This thesis attempts to bridge this gap by exploring the narrative accounts of DBS patients, caregivers and clinicians. Experiences across both an established (Parkinson's disease) and experimental (treatment-resistant depression) DBS indication were investigated. A qualitative approach was taken to allow nuanced clinical data to be captured that cannot be assessed using quantitative psychometric measures alone. This thesis aims were to prospectively examine the impact of DBS on patient personality, self and interpersonal relationships, in an established neurological (PD) and emerging psychiatric (TRD) indication. Multiple perspectives on these issues were obtained by qualitatively investigating the views of patients, caregivers and DBS clinicians. This is the first study to investigate patient and caregiver experiences pre- and post-surgery in both a neurological and psychiatric population. The thesis consists of three empirical studies based on semi-structured interviews that were analysed using iterative thematic analysis. In Study 1, interviews were conducted with 16 DBS clinicians from various disciplines (e.g., neurology, nursing, neuropsychology). Interviews explored clinicians' experiences of unanticipated psychosocial issues in patients following DBS and approaches to management. Clinicians working in Parkinson's disease (PD) described a variety of personality changes following DBS, including irritability, impulsivity and impaired decision-making. Multiple factors were considered as contributing to post-DBS changes. Stimulation-related changes where typically transient, but could have a significant impact on patients and families. Clinicians working in treatment-resistant depression (TRD) described a restoration of pre-morbid personality associated with alleviated illness. In Studies 2 and 3, small groups of DBS patient/caregiver dyads were recruited (PD: 11 patients/11 caregivers; TRD: 6 patients/5 caregivers). Caregivers included spouses, parents and children. Participants were interviewed individually both before and approximately 9-months after DBS. Pre-surgery interviews explored participants' expectations for DBS, including what impact

they felt DBS may have upon the patient's personality, their sense of self and the functioning of their relationship. Post-surgery interviews explored DBS outcomes, including how the patients' personality or identity had been impacted, and the implications for their relationship. In Study 2, prior to DBS, negative personality changes related to either PD or medication were reported. After DBS, both positive and negative personality changes were described, with some, but not all, attributed to the stimulation. Patients with a positive clinical outcome experienced a restoration of their 'old self'. Similarly, patients in Study 3 who experienced a meaningful reduction in depression felt reconnected with their pre-morbid self; however, the process of regaining wellness created new challenges that involved considerable adjustment for patients and caregivers. The findings from the three studies and the different participant perspectives are compared and contrasted. Implications for future DBS clinical care and management, experimental clinical research, and bioethics and neuroethics discourse are discussed.

Publications, Conference Proceedings, Awards & Prizes During Candidature

The thesis contains manuscripts published by or submitted to journals:

Thomson, C.J., Segrave, R.A., & Carter, A. (2019). Changes in personality associated with deep brain stimulation: A qualitative evaluation of clinician perspectives. *Neuroethics*, 1-16. doi:10.1007/s12152-019-09419-2

Thomson, C.J., Segrave, R.A., Racine, E., Warren, N., Thyagarajan, D., & Carter, A. (2020). 'He's back so I'm not alone': The impact of deep brain stimulation on personality, self, and relationships in Parkinson's disease. *Qualitative Health Research, 30*(14), 2217-2233. doi:10.1177/1049732320951144

Thomson, C.J., Segrave, R.A., Fitzgerald, P.B, Richardson, K.A., Racine, E., & Carter, A. (2020). Illness, self-concept and device embodiment: Patient and caregivers lived experiences of deep brain stimulation for treatment-resistant depression. *Journal of Affective Disorders.* Manuscript submitted for publication.

The following manuscripts related to the thesis were published or accepted for publication during candidature and are included in Appendices B to D:

Thomson, C., & Segrave, R. (2017). "I miss you too": More voices needed to examine the phenomenological effects of deep brain stimulation. *AJOB Neuroscience*, *8*(2), 122-123. doi:10.1080/21507740.2017.1320321

Thomson, C., Segrave, R., Gardner, J., & Carter, A. (2018). Patients' weighing of the long-term risks and consequences associated with deep brain stimulation in treatment-resistant depression. *AJOB Neuroscience*, *9*(4), 243-245. doi:10.1080/21507740.2018.1561542

Thomson, C., & Carter, A. (2020). Ethical issues in experimental treatments for psychiatric disorders: Lessons from deep brain stimulation. *Translational Issues in Psychological Science*, *6*(3), 240-246. doi:10.1037/tps0000267

Additional research output during candidature (08/02/2016 – 04/08/2020)

Lee, S., Chung, S.W., Rogasch, N.C., **Thomson, C.J.**, Worsley, R.N., Kulkarni, J., Thomson, R.H., Fitzgerald, P.B., Segrave, R.A. (2018). The influence of endogenous estrogen on transcranial

direct current stimulation: A preliminary study. *European Journal of Neuroscience, 48*(4), 2001-2012. doi:10.1111/ejn.14085

Chung, S.W., **Thomson, C.J.**, Lee, S., Worsley, R.N., Rogasch, N.C., Kulkarni, J., Thomson, R.H., Fitzgerald, P.B., & Segrave, R.A. (2019). The influence of endogenous estrogen on high-frequency prefrontal transcranial magnetic stimulation. *Brain stimulation*, *12*(5), 1271-1279. doi:10.1016/j.brs.2019.05.007

Parts of the thesis were presented at the following conferences and events:

Thomson, C., Carter, A., & Segrave, R. (2017, September). The impact of deep brain stimulation on personality, identity and interpersonal relationships in neurological and psychiatric populations. *Poster presentation at the 1st Neuroscience and Society Conference: Sydney, Australia.*

Thomson, C. (2017, November). Investigating changes in personality, identity and interpersonal relationships following deep brain stimulation for Parkinson's disease. *Oral presentation at the Monash Dementia & Neurodegeneration Research Symposium: Melbourne, Australia.*

Thomson, C. (2018, February). The impact of deep brain stimulation on quality of life in neurological and psychiatric populations. *Oral presentation at the Academic Medical Centre: Amsterdam, The Netherlands.*

Thomson, C., Carter, A., & Segrave, R. (2018, February). Optimising psychosocial outcomes following deep brain stimulation: Evaluating an established and emerging indication. *Oral and poster presentation at the Herrenhausen Conference: Hannover, Germany.*

Thomson, C., Carter, A., & Segrave, R. (2018, August). Deep brain stimulation and changes in personality and identity: A qualitative evaluation of clinician perspectives. *Oral presentation at the 2nd Neuroscience and Society Conference: Sydney, Australia.*

Thomson, C., Carter, A., & Segrave, R. (2018, November). Deep brain stimulation and changes in personality and identity: Qualitative perspectives from Parkinson's clinicians. *Oral presentation at the 17th National Conference of Emerging Researchers in Ageing: Melbourne, Australia.*

Thomson, C., Segrave, R., Racine, E. & Carter, A. (February, 2019). The impact of deep brain stimulation on personality, identity, and relationships in neurological and psychiatric conditions. *Poster presentation at the 3rd International Brain Stimulation Conference: Vancouver, Canada.*

Thomson, C., Segrave, R., Racine, E. & Carter, A. (October, 2019). Impact of deep brain stimulation on personality, identity and relationships: Patient, caregiver and clinician perspectives. *Poster presentation at the 1st Medtech: Into the Future Symposium: Melbourne, Australia.*

Thomson, C. (November, 2019). Changes in personality following deep brain stimulation: Patient and caregiver perspectives. *Oral Presentation at the APS College of Clinical Neuropsychologists Conference: Barossa Valley, Australia.*

Thomson, C., Segrave, R., Racine, E. & Carter, A. (November, 2019). The impact of deep brain stimulation on personality, identity and relationships. *Poster presentation at the Inaugural Monash Neuroscience Symposium: Melbourne, Australia.*

Thomson, C., Segrave, R., Racine, E. & Carter, A. (November, 2019). Deep brain stimulation and changes in personality, identity and relationships: Patient, caregiver and clinician perspectives. *Oral presentation at the 2019 Society for Mental Health Research Conference: Melbourne, Australia.*

Thomson, C. (January, 2020). Deep brain stimulation and personality change in Parkinson's disease. *Oral presentation at the Ageing and Neurodegeneration Research Program Lunchtime Lectures, Monash University: Melbourne, Australia.*

Thomson, C., Segrave, R., Fitzgerald, P., Richardson, K., Racine, E. & Carter, A. (October, 2020). 'I'll wear this as a badge of honour because it's made me better': Illness, self-concept and device embodiment in DBS for treatment-resistant depression. *Oral presentation at the International Neuroethics Society Annual Meeting, virtual conference.*

Thomson, C., Segrave, R., Racine, E., Warren, N., Thyagarajan, D., & Carter, A. (November, 2020). 'He's back so I'm not alone': The impact of deep brain stimulation on personality, identity and relationships. *Oral presentation at the Parkinson's Australia National Symposium 'Prosper' 2020, virtual conference.*

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Monash Graduate Education Postgraduate Travel Award to attend the *3rd International Brain Stimulation Conference: Vancouver, Canada, 2019*

Poster Award for Most Outstanding Clinical Research at the *Inaugural Monash Neurosciences Symposium: Melbourne, Australia, 2019*

Best Abstract Award at the *International Neuroethics Society Annual Meeting: virtual conference, 2020*

General Declaration

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 two original paper published in peer reviewed journals and one submitted publication. The core theme of the thesis is the impact of deep brain stimulation on patient personality, self and their relationships. The ideas, development and writing up of all the papers in the thesis were the principal responsibility of myself, the student, working within the Turner Institute for Brain and Mental Health and School of Psychological Sciences under the supervision of A/Prof Adrian Carter and Dr. Rebecca Segrave.

The inclusion of co-authors reflects the fact that the work came from active collaboration between researchers and acknowledges input into team-based research. No co-authors are Monash University students. In the case of chapters four, five and six my contribution to the work involved the following:

Thesis Chapter	Publication Title	Status	Nature and % of student contribution	Co-author name(s) Nature and % of Co-author's contribution
4	Changes in personality associated with deep brain stimulation: A qualitative evaluation of clinician perspectives	Published	90% Primary development of study design, participant recruitment, data collection, analysis and interpretation, manuscript synthesis and preparation.	1) Rebecca Segrave, supervision of study design, manuscript input 5% 2) Adrian Carter, supervision of study design, data analysis interpretation, manuscript input 5%
5	'He's back so I'm not alone': The impact of deep brain stimulation on personality, self, and relationships in Parkinson's disease	Published	80% Primary development of study design, participant recruitment, data collection, analysis and interpretation, manuscript synthesis and preparation.	1) Rebecca Segrave, supervision of study design, data analysis interpretation, manuscript input 5% 2) Eric Racine, assistance with study design, manuscript input 5% 3) Narelle Warren, data analysis assistance, manuscript input 2.5% 4) Dominic Thyagarajan, recruitment assistance, manuscript 2.5% 5) Adrian Carter, supervision of study design, analysis interpretation, manuscript input 5%
6	Illness, self-concept and device embodiment: Patient and caregiver lived experiences of deep brain stimulation for treatment-resistant depression	Submitted	83% Primary development of study design, participant recruitment, data collection, analysis and interpretation, manuscript synthesis and preparation.	1) Rebecca Segrave, supervision of study design, data analysis interpretation, manuscript input 5% 2) Paul Fitzgerald, recruitment assistance, manuscript input 2.5% 3) Karyn Richardson, recruitment assistance, manuscript input 2.5% 4) Eric Racine, manuscript input 2% 5) Adrian Carter, supervision of study design, data analysis interpretation, manuscript input 5%

I have formatted articles for consistent presentation; however, none of the content was changed.

Student name: Cassandra Thomson

Student signature:  **Date:** 4 August 2020

I hereby certify that the above declaration correctly reflects the nature and extent of the student's and co-authors' contributions to this work. In instances where I am not the responsible author, I have consulted with the responsible author to agree on the respective contributions of the authors.

Main Supervisor name: Adrian Carter

Main Supervisor signature:  **Date:** 4 August 2020

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CHAPTER ONE

INTRODUCTION AND THESIS OVERVIEW

Chapter One – Introduction and Thesis Overview

Background and the Research Problem

Deep brain stimulation (DBS) is a neurosurgical procedure used in the treatment of movement disorders, primarily Parkinson's disease (PD), and is being trialled in a range of psychiatric conditions, including treatment-resistant depression (TRD), obsessive-compulsive disorder and addiction. Over 175,000 individuals have been implanted with DBS devices worldwide (Medtronic, 2019). DBS has been shown to significantly improve the motor symptoms associated with PD, such as bradykinesia, tremor and freezing (Deuschl et al., 2006; Schüpbach et al., 2013). Adverse effects associated with DBS are well-documented and tend to be categorised as surgery-related (stroke, seizure, intracerebral haemorrhage), device-related (infection, device dysfunction) or stimulation-related (dysarthria, insomnia, mania) (Silberstein et al., 2009). DBS has also been associated with adverse effects related to personal and interpersonal experiences following surgery. These include changes in personality, altered experiences of self, and increased conflict within spousal relationships (Agid et al., 2006; Gilbert, Goddard, Viaña, Carter, & Horne, 2017; Lewis, Maier, Horstkotter, Eggers, et al., 2015; Lewis, Maier, Horstkotter, Zywczok, et al., 2015). Despite growing recognition amongst clinicians and researchers, these unanticipated psychosocial outcomes remain under investigated and form the focus of the following thesis.

There has been growing ethical and philosophical debate in recent years about the impact of DBS on identity and personhood (Gisquet, 2008; Schechtman, 2010; Witt, Kuhn, Timmermann, Zurowski, & Woopen, 2013), but few studies have investigated these issues directly with the patients and caregivers themselves. Clinicians working in DBS are responsible for educating, treating and monitoring patients. Importantly, the knowledge, understanding and experiences of clinicians in managing these changes is yet to be examined. Standard psychometric measures typically used in clinical trials (such as those assessing personality, quality of life, social adjustment) were not designed to detect critical changes in complex concepts such as sense of self and identity, which form around an individual's memories, experiences, values and relationships (Gilbert, Viaña, & Ineichen, 2018; Kubu et al., 2019; Lewis, Maier, Horstkotter, Zywczok, et al., 2015). Qualitative interviews ensure

that these subtle, yet pertinent changes, are elucidated, and reveal the personal meaning and significance they hold for patients and caregivers.

Clinical trials have demonstrated that DBS has the potential to substantially alleviate symptoms of depression (Fenoy et al., 2016; Mayberg et al., 2005); however, results have been inconsistent and mostly reliant upon small samples. Research efforts remain ongoing to determine the optimal implantation site, patient characteristics and stimulation parameters (Fitzgerald & Segrave, 2015). While ethical concerns have been raised about the potential for DBS to result in personality change (Glannon, 2009), some argue this is the procedure's intended outcome in TRD (Synofzik & Schlaepfer, 2008). Few studies have investigated patients' subjective experience of DBS and how it is perceived to impact their personality or sense of self (de Haan, Rietveld, Stokhof, & Denys, 2017; Klein et al., 2016). To-date, no published TRD studies have included caregivers. This is despite their unique position to provide an additional perspective on the impact of DBS on their loved-one and its potential to significantly impact their own lives. Caregivers are also critical partners in the intervention procedures and as such can have a significant impact on its potential success. Narrative accounts of both pre- and post-surgical experiences from both patients and caregivers are essential to fully capture and understand the psychosocial impact of DBS. Such knowledge and understanding would help inform clinical practice and ethical discussions surrounding DBS, as well as assist in minimising negative and unintended effects. The current work is the first study to conduct a prospective, qualitative investigation of patient and caregiver perspectives in both a neurological and psychiatric DBS population.

The thesis considers important psychosocial factors on which there is limited research to-date in what is often considered a neurobiological treatment. The examination and triangulation (methodological approach discussed in Ch. 3) of DBS clinician, patient and caregiver voices and perspectives informs our understanding of changes in personality, sense of self, and relationships that occur in the context of DBS.

Research Aims

The primary aim of this thesis was to prospectively examine the impact of DBS on patient personality, self and interpersonal relationships, in an established neurological (PD) and emerging psychiatric (TRD) indication. To do so, I obtained multiple perspectives on these issues by qualitatively investigating the views of patients, caregivers and DBS clinicians. Three empirical studies involving semi-structured interviews with clinicians, DBS recipients (for PD or TRD) and their caregivers were conducted. Over 80 interviews were conducted and the content of these were analysed using an iterative thematic analysis approach (see Ch. 3).

Thesis Outline

The thesis comprises seven chapters, including three empirical papers that have been published or submitted for publication in peer-reviewed scientific journals. Consequently, there is some repetition of concepts. Following the current chapter, a literature review is presented in *Chapter 2*, including the history and development of DBS in clinical research and practice and its application in movement and psychiatric disorders, with a specific focus on PD and TRD. An overview of existing research reporting unanticipated psychosocial outcomes following DBS (personality change, altered perceptions of self and relationship discord) is described. The absence of research examining key stakeholder perspectives (patients, caregivers and clinicians) and lived experiences of DBS is highlighted, providing the rationale for the current thesis. In *Chapter 3,* I provide an overview of the methodology that was applied across the empirical work of the thesis and expand on various methodological considerations, such as epistemological position, analysis approach and establishing qualitative rigour. *Chapter 4* presents the first empirical paper, the content of which is based on qualitative interviews with DBS clinicians, including neurologists, psychiatrists and nurses. *Chapter 5* contains the second empirical paper, which involved qualitative interviews with patients undergoing DBS for PD and their caregivers. Interviews were conducted both before and after surgery and patients and caregivers were interviewed separately. *Chapter 6* is the final empirical paper of the thesis and presents findings from qualitative interviews with patients involved in a clinical trial of DBS for TRD and their caregivers both before and after surgery. In *Chapter 7,* I conduct an integrated

discussion of the empirical findings with implications across two broad areas; those relating to DBS clinical practice and research, and those relevant to the ongoing philosophical and ethical discussions regarding DBS iatrogenic effects.

Beyond the core narrative of the thesis (personality, self and relationships), the interviews also covered a range of conceptually associated topics. Specifically, topics such as informed consent, decision-making process and capacity, DBS procedural processes and care, and expectations and outcomes were also examined. Although these topics were not central to the research questions at hand, and are therefore not discussed extensively within the thesis, they are explored where relevant as certain aspects were linked to the core discussions of personality, self and relationships. Furthermore, coverage of these additional topics in presented in *Appendices C* and *D*.

CHAPTER TWO

LITERATURE REVIEW

Chapter Two – Literature Review

History and Development of Deep Brain Stimulation

Early Electrical Brain Stimulation and Stereotactic Neurosurgery

The modern neurosurgical deep brain stimulation (DBS) procedure evolved from the early practices of electrical brain stimulation and the development of stereotactic neurosurgery (Valenstein, 1973). During the 1930s intraoperative cortical electrical stimulation was used to investigate and treat epilepsy (Gardner, 2013). The emergence of a stereotactic apparatus in the 1940s enabled accurate targeting of specific neuroanatomical regions, leading to a rapid growth in ablative procedures and substantial improvement in neurosurgery mortality (Gildenberg, 2000). Stereotactic surgery also enabled more precise stimulation of subcortical regions. Surgical lesioning was used across a range of intractable conditions, including thalamotomies and pallidotomies in movement disorders, and cingulotomies and lobotomies in psychiatric disorders (Valenstein, 1986). These remained commonplace until the 1960s when effective psychopharmaceutical treatments became available (e.g., levodopa for PD; antipsychotics for schizophrenia, tricyclics for depression) (Wichmann & Delong, 2006). Ethical concerns related to the widespread use of crude irreversible lobotomy procedures and belated recognition of the significant cognitive harms they caused (e.g., impairment in executive control and social regulation) led to a rapid decline in psychosurgery (Valenstein, 1986).

For movement disorders, clinical research efforts turned to developing a surgical procedure that could mimic the effects of stereotactic lesioning, but with the use of an adjustable continuous source of electrical stimulation. In the late 1980s, high-frequency electrical DBS was trialled in the treatment of essential tremor (ET) and later PD (Benabid, Pollak, Louveau, Henry, & de Rougemont, 1987). Although stimulation methods had been trialled earlier, the application of high-frequency stimulation dramatically increased efficacy. With greater reversibility and control over treatment effects, DBS quickly became the preferred option to surgical lesioning (Benabid, Benazzous, & Pollak, 2002; Wichmann & Delong, 2006). DBS has since received Food and Drug Administration (FDA) approval as a treatment for PD, ET and dystonia, with over 175,000 devices implanted worldwide (Medtronic, 2019). The success of DBS in treating movement disorders fuelled efforts to

determine if similar success could be achieved in psychiatric disorders. This was based on knowledge gained from psychosurgical procedures (e.g., anterior capsulotomy, subcaudate tractotomy, limbic leucotomy) and the increased understanding of the neural circuitry involved in common disorders, such as depression and obsessive-compulsive disorder (OCD) (Fitzgerald & Segrave, 2015; Gabriels, Cosyns, Nuttin, Demeulemeester, & Gybels, 2003; Mayberg, 1997; Mayberg et al., 2005). In clinical research, DBS has been trialled in a range of conditions, most commonly for treatment-resistant OCD (under an FDA humanitarian device exemption granted in 2009) and treatment-resistant depression (TRD), and to a lesser extent for anorexia nervosa and addiction. DBS is not, however, an established treatment for any psychiatric indications (Hendriks et al., 2019).

DBS Surgery and Post-Implantation Stimulation Procedures

The DBS neurosurgical procedure involves two stages. First, a small opening is created in the skull through which the electrodes are implanted in the brain. Magnetic resonance imaging (MRI), computed tomography (CT) and microelectrode recording are used to precisely implant the electrodes in the target brain region (Hasegawa, Samuel, Douiri, & Ashkan, 2014). DBS can be unilateral or bilateral with electrodes inserted into one or both hemispheres. Second, a neurostimulator is surgically implanted in the chest or abdomen. This device is connected to the electrodes via a subcutaneous extension lead that supplies electrical impulses into the brain. Most neurostimulators implanted today are rechargeable via a remote induction charging device (Jakobs et al., 2019; Mitchell et al., 2019). This increases device longevity and reduces the frequency of surgeries required to replace batteries. The stimulation settings are adjustable using an external electromagnetic programmer (Silberstein et al., 2009). Various stimulation parameters can be adjusted to try and alleviate symptoms including voltage, pulse width and frequency (Fitzgerald, 2012). Despite over 30 years of research and hundreds of thousands of surgeries, the precise mechanism of action in DBS (inhibition, excitation or disruption of neural activity) remains unresolved (Benabid et al., 2002; Benabid, Chabardes, Mitrofanis, & Pollak, 2009; Chiken & Nambu, 2016). While the exact mechanism remains unknown, DBS appears to modulate and normalise dysfunctional circuits associated with pathology (Mayberg, 2009; van Westen, Rietveld, Figee, & Denys, 2015).

The Application of DBS in Parkinson's Disease

Parkinson's Disease

PD is the second most common neurodegenerative disorder following Alzheimer's disease and is estimated to affect over 7 million people worldwide (de Lau & Breteler, 2006). PD is characterised by classic motor features, including: resting tremor, slowness of movement (bradykinesia), muscular rigidity, postural instability and impairment of gait (Shulman, De Jager, & Feany, 2011). These motor manifestations, known collectively as parkinsonism, were first described in 1817 by British physician James Parkinson in his text *An Essay on the Shaking Palsy* (Parkinson, 1817). The pathology of motor symptoms is associated with the progressive loss of dopaminergic neurons and presence of Lewy bodies in the midbrain, specifically the substantia nigra (Kalia & Lang, 2015). It is now recognised that multiple neurotransmitters, neuroanatomical regions (subthalamic nucleus, substantia nigra) and neural networks are implicated in the disease, and its symptoms are not strictly limited to motor functions (Wichmann, DeLong, Guridi, & Obeso, 2011). Common clinically significant non-motor features in PD are: neuropsychiatric symptoms (depression, anxiety, dementia, psychosis, apathy), cognitive impairment (slowed information processing, high level attentional impairment, executive dysfunctions), sleep disorders, autonomic dysfunction, sensory dysfunction (olfactory impairment, pain, paraesthesia) and fatigue (Weintraub, Comella, & Horn, 2008).

Figure 1. Illustration of PD from 'A Manual of Diseases of the Nervous System' by William Gowers (1886)

The greatest risk factor for PD is advancing age and it occurs more frequently in males and individuals of European ancestry (Shulman et al., 2011). The aetiology of PD appears to be a complex

combination of genetic and environmental factors. There are, however, a subset of patients whose onset of the disease appears clearly driven by either genetic or environmental factors (Kalia & Lang, 2015). The diverse range of nature and nurture interactions that can lead to PD may contribute to the substantial inter-individual variability in symptoms that patients experience. There is currently no reliable biomarker available to facilitate early detection (Kalia & Lang, 2015), although a number of promising technologies (wearables, sensors, brain imaging) that use machine learning to predict the future onset of PD are being developed (Lonini et al., 2018). Typically, it is not until significant visually identifiable symptoms are present that diagnosis is initially made, which is subsequently confirmed by the successful reduction of motor symptoms secondary to prescription of a dopaminergic medication. Symptomatic treatments include: oral or infusion-based dopamine replacement therapies (DRTs) (levodopa, dopamine agonists), infusion therapies (apomorphine, Duodopa) and surgery (lesional or DBS). These treatments primarily assist in managing the debilitating motor symptoms of PD. Though there is controversy about whether certain medications or when they are commenced altering the disease course (e.g., delays the neurodegenerative process), no definitive answer has been reached.

DBS for Parkinson's Disease

Progression of the disease. In the natural history of PD, a patient's motor symptoms are typically well managed and controlled using DRTs combined with other medications (e.g., amantadine, catechol-O-methyltransferase (COMT) inhibitors) for a number of years. While the rate of disease progression varies considerably between individuals, treatment milestones are similar (Wichmann et al., 2011). Over time patients will develop motor fluctuations with reduced *on* periods (where mobility is well controlled) and increasing *off* periods (where symptoms such as tremor and bradykinesia emerge). Over time, medication becomes less effective in addressing motor symptoms and increasing levodopa dosages can detrimentally result in dyskinesia (excessive and involuntary movements). Another common pharmacological side-effect of dopamine agonists is impulse control disorders (ICDs), which affect approximately one in six patients (Eisinger et al., 2019). These include pathological gambling, compulsive shopping, compulsive eating, hypersexuality, punding (repetitive, purposeless behaviours) and addiction to DRTs (dopamine dysregulation syndrome). Withdrawal

from DRTs can induce dopamine agonist withdrawal syndrome, which is characterised by anxiety, apathy, dysphoria, irritability, pain, fatigue and sleep disturbance (Rabinak & Nirenberg, 2010). The numerous neurocognitive and neurobehavioural side-effects of pharmacological treatments for PD can be particularly disabling and distressing for patients and families (Carter, Ambermoon, & Hall, 2011; Colosimo et al., 2010; Weintraub, David, Evans, Grant, & Stacy, 2015). As the disease advances, *off* periods become inconsistent and unpredictable (see Figure 3). This stage in which oral medication inevitability fails, motivated the search for other therapies to provide symptomatic relief. This led to the development of advanced therapies, including DBS and infusion therapies (inserted devices providing continuous medication delivery).

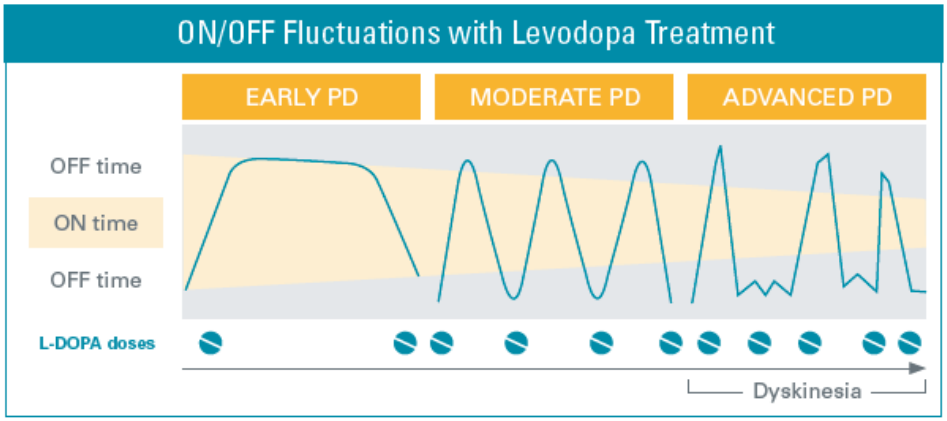

Figure 3. Development of motor fluctuations over the progression of PD. Source: Boston Scientific 'Parkinson's Treatment' (2020)

DBS targets. The subcortical stimulation target for PD can be one of several regions to alleviate motor symptoms. The subthalamic nucleus (STN) is the most common target, followed by the globus pallidus internus (GPi) and ventral intermediate nucleus (VIM) of the thalamus (see Figure 2) (Silberstein et al., 2009). The pedunculopontine nucleus is another proposed target, but its clinical efficacy remains under investigation (Thevathasan et al., 2018). In PD, neural activity in these regions appears abnormal (overactive or irregular) and continuous high-frequency stimulation has a local inhibitory effect (Benabid et al., 2002; Wichmann & Delong, 2006). The stimulation target is selected on an individual basis with symptom profile, medication response and co-morbidities factored into the decision. STN is the preferred target and is associated with reduced post-operative DRT requirements,

but neuropsychiatric side-effects occur more frequently at this location (possibly due to inadvertent stimulation of limbic circuits) (Kleiner-Fisman et al., 2006; Smeding, Speelman, Huizenga, Schuurman, & Schmand, 2011; Voon, Kubu, Krack, Houeto, & Troster, 2006). There is, however, ongoing debate as to whether the difference in adverse event profiles between STN and GPi is clinically significant (Williams et al., 2017).

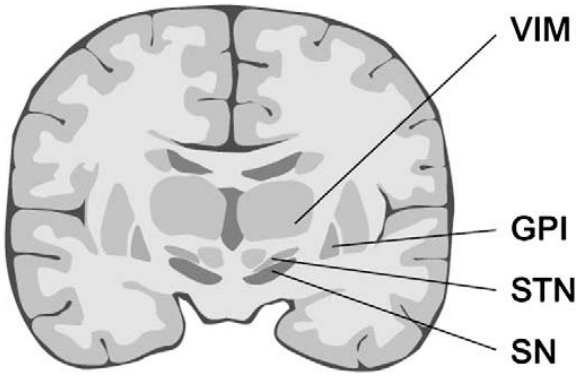

Figure 2. Coronal section with main DBS targets for PD. GPi: globus pallidus internus; SN: substantia nigra; STN: subthalamic nucleus; VIM: ventral intermediate nucleus. Source: Silberstein et al. (2009).

New thinking on the timing of DBS. The DBS procedure was originally proposed as a late-stage therapy to be applied in patients with advanced PD and severe levodopa-induced motor complications. More recent studies, however, have shown that early intervention with DBS provides better health outcomes and should be considered early in the course of the disease, as soon as medical therapies fail to provide satisfactory motor control (Schüpbach et al., 2014; Silberstein et al., 2009; Williams et al., 2017). DBS is not a suitable treatment option for all patients with PD. Typical contraindications include: substantial cognitive impairment, refractory psychiatric disorder or significant medical co-morbidity (Silberstein et al., 2009). While age must be considered, it should not serve as an absolute contraindication for DBS. General health and any age-related comorbidities such as cognitive dysfunction, gait disorders and levodopa-resistant symptoms (dysarthria, dysphagia and postural instability) may be more important than a patient's chronological age (Lang et al., 2006). The decision to undergo DBS is a significant one, in which a number of well-established benefits and risks must be considered.

Benefits and risks. DBS is extremely effective in reducing the motor symptoms of PD, such as bradykinesia, tremor and rigidity. The procedure achieves motor effects comparable to medication, with patients generally achieving 75 to 80% of their best medication response (Deuschl et al., 2006; Schüpbach et al., 2013). A meta-analysis of 22 studies examining STN-DBS revealed average reductions in DRT of 56% and DRT-related dyskinesia of 69% (Kleiner-Fisman et al., 2006). DBS provides patients with greater stability and consistency with their symptoms, with increased daily *on* periods and reduced daily *off* periods. DBS can reduce non-motor fluctuations in hyperdopaminergic (e.g., elevated, disinhibited) and hypodopaminergic (e.g., lethargic, flat) behaviours (Castrioto, Lhommée, Moro, & Krack, 2014), and reduce DRT-related ICDs. Conversely, it should be noted some studies suggest that DBS can induce or exacerbate ICDs (Averbeck, O'Sullivan, & Djamshidian, 2014). Smoother motor movements and suppressed tremor significantly benefit mobility and performance of activities of daily living. Quality of life typically improves following DBS, with benefits observed mostly in motor and physical domains (Benabid et al., 2009; Spottke et al., 2002). An additional benefit of the treatment is that stimulation adjustments can continue to be made until optimal individualised parameters are established.

DBS-related adverse events are well-documented and categorised as either surgical complications (death, intracerebral haemorrhage, pulmonary embolism – rare <5%), device-related complications (infection, subcutaneous seroma, skin erosion – infrequent 5-10%), or post-surgical stimulation-related complications (balance and gait problems, depression, dysarthria, dyskinesia increased, freezing/worsening of mobility, pain and weight gain – relatively frequency >10%) (Odin et al., 2015). Overall, the procedure involves a myriad of risks, ranging in severity from mildly troublesome to life-threatening, and duration form transient to permanent. Each potential DBS patient's case requires careful examination to balance the likelihood of prospective adverse events with the likelihood of prospective therapeutic effects.

Recent scientific developments have improved the accuracy, safety and efficacy of DBS. These advancements include: new software programs to guide the route of insertion and localisation of electrodes during neurosurgery (Horn & Kuhn, 2015), current steering to direct stimulation spread (Pollo et al., 2014), and closed-loop stimulation systems that continuously measure neural activity and

modulate stimulation output in response to it, although this has not become standard clinical practice (Krack, Volkmann, Tinkhauser, & Deuschl, 2019). These developments are relevant across all DBS indications and not limited to PD.

The Application of DBS in Treatment-Resistant Depression

Treatment-Resistant Depression

Depression is a psychiatric disorder that is estimated to affect 264 million individuals globally. It is the leading cause of disability worldwide resulting in 800,000 deaths by suicide each year (James et al., 2018). Depression emerges from a complex interaction of biological, psychological and social factors. A 'major depressive disorder' diagnosis can be characterised by depressed mood (sad, hopeless, irritable), anhedonia (diminished interest and pleasure), somatic features (weight changes, sleep disturbance, fatigue and lethargy, psychomotor retard/agitation), cognitive issues (difficulty concentrating, indecisiveness), feelings of guilt and worthlessness, and suicidal ideation (American Psychiatric Association, 2013). For most, depression is alleviated through evidence-based treatments, such as antidepressants, psychotherapy or both, or it resolves over time without intervention. For one-fifth, however, their depression fails to respond to multiple trials of the range of standard treatment approaches (Mayberg et al., 2005).

TRD is a severely debilitating disorder characterised by immense personal suffering, functional impairment and care burden for families (Fitzgerald & Segrave, 2015). What constitutes 'treatment resistance' varies considerably and formal staged criteria outlines its sequential levels (Thase & Rush, 1995). The lowest end of the spectrum can be a failure to respond to an adequate trial of a single antidepressant, while the higher end can include the failure to respond to all classes of antidepressants and combination therapies, evidence-based psychotherapy with a qualified therapist (e.g., cognitive behavioural therapy) and little-to-no benefit from ECT (Berlim & Turecki, 2007; Dandekar, Fenoy, Carvalho, Soares, & Quevedo, 2018). The criteria applied across DBS clinical trials has differed considerably (see Loo et al. (2010) for discussion of medico-legal factors that dictate this in Australia). This variability is one of the factors that makes comparing clinical trial outcomes challenging.

DBS in Treatment-Resistant Depression

Rationale and targets. The pressing need for novel effective treatment for depression is clear; with a failure of existing therapies to provide benefit to a substantial proportion of individuals and an absence of innovations in psychopharmaceutical development over recent decades (Trivedi et al., 2006; van Gerven & Cohen, 2011). Like DBS for movement disorders, investigators were curious if similar outcomes to psychosurgical procedures could be achieved using a non-ablative form of stimulation that was both adjustable (allowing treatment response to be maximised and side-effects minimised) and reversible (i.e., stimulation could be ceased or device explanted) (Greenberg et al., 2003; Nuttin et al., 2003). In addition, a growing body of neuroimaging research has led to an increased understanding of depression pathophysiology and the maladaptive neural networks associated with the experience of major depression (Fitzgerald & Segrave, 2015; Mayberg, 2009), providing further rationale for the exploration of DBS in individuals with intractable depression. The initial DBS stimulation target for TRD investigated in a proof-of-concept study was the white matter tracts adjacent to the subgenual anterior cingulate (SAC) (Mayberg et al., 2005). Functional imaging studies have shown that this area is hyperactive in depressed patients and normalised in those who have responded to treatment (Cleary, Ozpinar, Raslan, & Ko, 2015). Patients who initially underwent DBS at this site reported acute intraoperative effects including a "sudden calmness or lightness" and "disappearance of the void" (p.652); four out of six achieved remission within 6-months (Mayberg et al., 2005). Subsequent long-term data from 20 patients demonstrated an average response rate of 64.3% over three years (with response defined as >50% reduction in Hamilton Depression Rating Scale score), reflecting a persistent antidepressant effect with continuous stimulation (Kennedy et al., 2011). A second major DBS target is the anterior limb of the internal capsule (ALIC) and ventral capsule/ventral striatum (VC/VS), due to antidepressant effect observed in OCD patients when the structure was stimulated (Fitzgerald & Segrave, 2015; Kisely, Li, Warren, & Siskind, 2018). An initial study of a small patient group implanted in the VC/VS demonstrated a response rate of 53% at the final follow-up (Malone et al., 2009). Other targets investigated include the medial forebrain bundle (MFB) (Bewernick et al., 2017; Schlaepfer, Bewernick, Kayser, Madler, & Coenen, 2013), the nucleus accumbens (NA) (Bewernick et al., 2010; Bewernick, Kayser, Sturm, & Schlaepfer, 2012),

and the lateral habenula (LH) (see Figure 4) (Sartorius et al., 2010). Current perspectives on the mechanism of DBS in depression include an inhibition or functional override of hyperactivity in limbic-cortical connections (Kisely et al., 2018). It is worth noting DBS is rarely conceptualised as a standalone or complete treatment for TRD. Many acknowledge the need for additional therapies such as recovery-oriented psychotherapy to optimise DBS outcomes and help manage the disorder (Fitzgerald & Segrave, 2015; Holtzheimer & Mayberg, 2010; Nuttin et al., 2014).

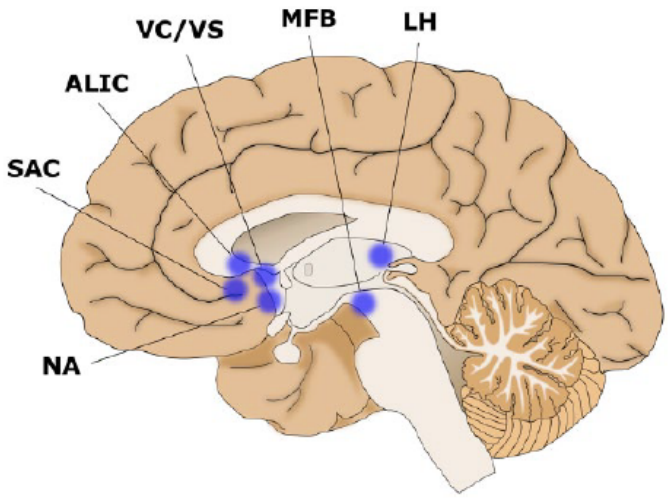

Figure 4. Implantation targets for DBS in TRD. ALIC: anterior limb of the internal capsule; LA: lateral habenula (LH); MFB: medial forebrain bundle; NA: nucleus accumbens; SAC: subgenual anterior cingulate; VC/VS: ventral capsule/ventral striatum. Source: Fitzgerald and Segrave (2015)

Efficacy and safety. Despite promising early results, DBS for TRD remains an experimental treatment (Kisely et al., 2018). While responder rates trend towards 50%, the outcomes reported across different trials vary considerably (Fitzgerald & Segrave, 2015). Factors influencing this variability include differences in research protocol, such as implantation site, participant inclusion criteria, patient clinical characteristics, stimulation parameters, and programming and follow-up procedures (Fins et al., 2017; Fitzgerald, 2012). Meta-analyses and systematic reviews of the TRD literature highlight that the majority of clinical outcome data comes from small samples, exploratory pilot studies or case series, with few double-blind randomised control trials (RCT) (Dandekar et al., 2018; Zhou et al., 2018). DBS for TRD is an expensive, resource-heavy intervention that requires substantial financial and clinical support, making large-scale RCTs difficult to conduct. Results from

two of the largest RCTs did not support observations of significant antidepressant effects reported in earlier open label investigations (Malone et al., 2009; Mayberg et al., 2005). The largest RCT of DBS, a multi-centre trial targeting the SAC was halted following a 6-month futility analysis (Holtzheimer et al., 2017). A trial targeting the VC/VS reported no significant difference between active and control conditions during the controlled phase of the study (Dougherty et al., 2015). The reasons behind the disparate open label versus RCT outcomes has been the focus of numerous commentaries and articles (Dobbs, 2018; Fins et al., 2017; Fitzgerald, 2016; Frieden, 2017; Schlaepfer, 2015). The structure and design of the RCTs, while appropriate for the needs of pharmaceutical trials, are considered incompatible with the complex needs of DBS trials (e.g., optimisation of individual participant outcomes; long-term follow-up to detect late effects). Blinding participants or delivering sham stimulation is another particularly difficult and problematic challenge (Fitzgerald, 2016). Different trial structures have been proposed that draw on knowledge derived from both responders and non-responders, to iteratively apply this knowledge in an attempt to maximise outcomes for all (Fins et al., 2017). Mining knowledge from scarce resources in this manner would maximise the procedure's efficacy and provide important information on depression phenotypes to guide future patient selection (Mayberg, 2009).

Surgery and device-related adverse events in TRD are similar to those associated with PD; however, the type and frequency of stimulation-related complications differ. The target site can influence what stimulation-related adverse effects emerge, but transient hypomania, agitation and sleep disturbance are common across TRD samples (Dougherty et al., 2015; Malone et al., 2009). Other reported adverse events include: anxiety, irritability, nausea, headache and labile mood (Dandekar et al., 2018; Kisely et al., 2018; Lozano et al., 2008). A number of attempted and completed suicides have been reported following DBS for TRD (Bewernick et al., 2012; Dougherty et al., 2015; Kennedy et al., 2011). Determining the precise causal role of DBS in a patient group with a high pre-existing suicide risk is challenging, but the potential for stimulation to induce suicidal ideation and/or impulsive behaviour cannot be discounted (Carter & Hall, 2013). Patients may feel suicide is their only option if DBS does not alleviate the severity of their depression. Suicide risk is

therefore a particularly important and complex issue for clinical research teams to monitor and manage (Appleby, 2013; Mosley, Marsh, & Carter, 2015).

Assessing treatment outcomes. The primary outcomes used to determine treatment response to DBS are the Hamilton Rating Scale for Depression (Hamilton, 1960) or the Montgomery–Åsberg Depression Rating Scale (Montgomery & Asberg, 1979). Both provide an assessment of depression symptom severity, frequency and intensity, but some question whether these are adequate for comprehensively gauging the treatment's benefit, particularly in cases of complex and chronic depression (Mayberg, 2018). What is a 'success' or what is 'well' is highly specific to the individual (Fins et al., 2017). Inclusion of more patient-centred outcome measures based on personalised goals have been recommended in PD as an indicator of DBS success, rather than symptom severity measures alone (Kubu et al., 2017; Kubu & Ford, 2012; Kubu et al., 2018; Liddle, Beazley, Gustafsson, & Silburn, 2019; Liddle, Phillips, Gustafsson, & Silburn, 2018; Schüpbach et al., 2006). Standard quantitative measures were not designed to capture patient's subjective wellbeing or experiences of post-operative distress that can emerge during adjustment from chronic illness (Wilson, Bladin, & Saling, 2001); therefore, they should be supplemented with richer, more person-centred outcome assessments.

Unanticipated Psychosocial Outcomes for Patients and Caregivers Following DBS

Over the past two decades, a small but increasing number of studies have reported a variety of unanticipated psychosocial outcomes for patients with PD following DBS (Agid et al., 2006; Gilbert et al., 2017). These have included changes in personality (Houeto et al., 2002), experience of self (Schüpbach et al., 2006), and relationship dynamics with negative implications for caregivers (Mosley et al., 2019). Features of this existing literature are discussed in detail within subsequent empirical chapters; therefore, key findings are presented here with relative brevity to avoid excessive repetition.

Personality Changes Following DBS

Personality is a concept that theorists have long struggled to define, in part because of its use across a wide range of disciplines with different epistemic aims. Modern psychological definitions broadly understand personality as an individual's enduring qualities and predictable patterns of

thinking, feeling and behaving (American Psychiatric Association, 2013); however, within clinical research uncertainty remains in how best to define, operationalise and reliably measure personality (Ineichen, Baumann-Vogel, & Christen, 2016). This is reflected in the varied approaches researchers have taken to investigate personality change after DBS (discussed in the following sections). Attempts have been made to quantify the issue of personality change following DBS for PD. A systematic review of roughly 1400 STN-DBS patients reported that personality changes were observed in less than 0.5% of patients (Temel et al., 2006). Patients from only two studies contributed to this figure. In one study, anecdotal changes consisting of "intermittent disinhibited or childlike behavior" (p.853) were reported by a patient's family (Kumar et al., 1998). In the second study, undesirable or "aggravated" personality changes in a subset of patients were reported according to a measure of frontal lobe disturbance (Houeto et al., 2002). A 2007 meta-analysis of 546 articles reporting on 10,339 DBS patients (primarily STN or GPi for PD) found low instances of psychiatric adverse events (Appleby, Duggan, Regenberg, & Rabins, 2007). Specific adverse events included: postoperative delirium/confusion (4-8%), depression (2-4%), mania/hypomania (0.9-1.7%), suicidality (0.3-0.7%), anxiety (0.3-0.6%), behavioural change (0.2-0.5%), hypersexuality (0.2-0.5%) and emotional change (0.1-0.2%). These were reported as psychiatric adverse events rather than personality changes, but provide some indication of the types of changes that can emerge after DBS and their relative frequency. Subsequent individual studies have reported on personality change specifically; however, according to different conceptual definitions. A brief summary of the key approaches taken to-date is presented here.

Psychological trait theory and mental disorders. Taking a traditional psychological trait theory perspective of personality, Boel et al. (2016) examined differences in outcomes between STN-DBS and GPi-DBS patients (n = 128) using a variant measure of the dominant *Five-Factor Model* – the Five-Factor Personality Inventory (Hendriks, Hofstee, & Raad, 1999). Results from the self-report measure revealed that the STN group had significantly lower scores on Autonomy (factor capturing dominance, leadership) and the GPi group significantly lower scores on Extraversion and Agreeableness after DBS. Taking an alternative psychopathological view of personality, Castelli et al. (2006; 2008) investigated changes in *personality disorder* traits (e.g., borderline, antisocial

personality disorder) using the Structured Clinical Interview for the DSM-III-R Axis II Disorders. Findings from two studies (n = 72, n = 25) revealed significantly lower obsessive-compulsive traits in patients after STN-DBS.

Frontal systems disturbance. Other researchers have considered personality from the perspective of *frontal lobe disturbance*. Houeto et al. (2002) used the Iowa Rating Scales of Personality Change (IRSPC) to assess STN-DBS patients (n = 24). The IRSPC is typically used to detect changes following frontal lobe injury and assesses emotional functioning, behavioural control, social and interpersonal behaviour, and higher-order cognitive abilities (Barrash, Tranel, & Anderson, 2000). The IRSPC relies purely on family observations. Characteristics revealed to have worsened after DBS were lack of initiative, perseveration, lack of persistence, lack of planning, apathy and vulnerability to pressure. Saint-Cyr et al. (2000) and Denheyer et al. (2009) also investigated frontal lobe dysfunction using the Frontal Lobe Personality Scale (FLOPS) and the Frontal Systems Behaviour Scale (FrSBe) respectively (Stout, Ready, Grace, Malloy, & Paulsen, 2003). These measures are designed to quantify three frontal lobe behaviour syndromes associated with distinct frontal subcortical circuits – apathy, disinhibition and executive dysfunction. Both measures include patient and caregiver ratings. In the Saint-Cyr et al. sample (n = 11), mild score elevations (indicating increased endorsement of frontal symptomology) were reported by caregivers at 3 – 6 months and significantly elevated scores by 9 – 12 months. These score elevations were not reported by patients themselves, which the researchers attributed to a lack of personal insight. In comparison, Denheyer et al. (n = 16) reported high levels of item agreement between patients and caregivers for post-DBS ratings; however, this was not the case for retrospective pre-DBS ratings. The researchers attributed this to reduced accuracy in participants' recall and therefore encouraged the use of prospective ratings in future research.

Psychobiological model. A number of researchers have applied Cloninger's *psychobiological model* (Cloninger, Svrakic, & Przybeck, 1993) that proposes a relationship between neurotransmitter systems (dopaminergic, serotonergic, noradrenergic) and personality (framed to consist of temperament and character dimensions). The studies that applied Cloninger's Temperament and Character Inventory (TCI) possessed considerable methodological differences, which may partly

explain their varied findings. Houeto et al. (2006) found no change in the sample's TCI-R (n = 20) (revised version) scores at 24-months after STN-DBS when compared with pre-surgery. In a matched-control study (with a 'PD with no DBS' and healthy control group), Fassino et al. (2010) reported TCI data collected 6-months post-surgery. Higher scores were reported on two novelty-seeking subscales in the STN-DBS group (n = 22), but lower rigidity and non-impulsiveness scores than the 'PD with no DBS' group. In their STN-DBS sample (n = 40), Pham et al. (2015) revealed significant declines in the TCI-125 temperament dimension Persistence and character dimension Self-Transcendence 3-months post-surgery. Individuals that score low on Persistence are characterised as giving up easily when faced with frustration and demonstrate low level perseverance in response to intermittent reward, while individuals low on Self-Transcendence tend to be more self-centred and less self-conscious. Lhommée et al. (2017) assessed 73 participants 12-month after STN-DBS. Results from the Tridimensional Personality Questionnaire (Cloninger, Przybeck, & Svrakic, 1991) revealed a significant increase in the temperament dimension Harm Avoidance and in particular subdomains anticipatory worry, shyness and fatigability. Unlike previous studies, the researchers highlighted the influence of drastic reductions in DRT (on average 67%). Variability in individuals' DRT requirements after DBS may make it difficult to generalise personality change outcomes according to the psychobiological model.

Limitations of personality investigations. These existing investigations into personality change possess a number of methodological limitations (e.g., small sample sizes, lack of control condition, retrospective ratings, data collected at inconsistent time-points, limited rationale for personality approach and instrument used). Yet what is lacking most is any evidentiary insight into the real significance or meaning of the findings for patients and families; whether they are experienced to be subjectively relevant or even being detected by the people most impacted by such outcomes. Although the existing studies give some preliminary indication of population trends in personality change, what these mean to an individual could differ widely. For instance, a decrease in extraversion could be considered beneficial by one patient, while for another it could be incredibly devastating with negative implications for their familial and social relationships. Another potential

limitation is that the measures used in these studies do not detect all the relevant changes, which may include subtle, but yet important changes for patients and their family.

Subjective and personal approaches to personality. To address some of these limitations, Lewis et al. (2015) conducted a prospective, mixed-methods investigation of personality and mood after STN-DBS from the perspective of both patients and caregivers. The sample included 27 patients and their caregivers who were assessed before and 12-months after DBS. Patients completed a battery of mood, neuropsychiatric and quality of life measures. The only personality scale administered was the Hypomanic Personality Scale (Eckblad & Chapman, 1986), which the authors chose due to previous reports of hypomania following STN-DBS. Both patients and caregivers completed semi-structured interviews after DBS where they were asked if the patient's mood and personality had changed. Results revealed 22% of patients perceived personality changes with descriptions varying from "more fun, more laughing" to "more brooding; quieter". Of the caregivers, 44% reported personality changes, with "selfish", "aggressive", "apathetic" and "overestimates self" frequent terms. One caregiver used the phrase "behaves like a teenager" – a telling description and one could wonder if or how this would emerge from a psychometric scale. It is therefore unsurprising that the authors found standard measures did not accurately reflect or align with participants' subjectively perceived changes. What the participants reported, however, was clearly meaningful and important to them, with potential to impact familial and social relationships (either positively or negatively). These findings demonstrate the value of collecting qualitative data, not only from individuals themselves, but caregivers as well, as they can both detect and be affected by the changes. While Lewis et al.'s inclusion of the caregiver perspective is a significant advancement on previous studies, they acknowledge that gaining the perspectives of medical professionals would also be highly informative. This was discussed by the authors in the context of the role such professionals hold in increasing patient and caregiver preparedness for experiencing personality changes and the need for postoperative support. The inclusion of a medical professional perspective would therefore have provided insight into current practices regarding this preparation and support.

Personality Change Following DBS for TRD

Investigations into personality changes following DBS for TRD have been limited. This may be due to the fact that active and intentional attempts are made to alter a patient's psyche, therefore, a change in personality is not considered an unanticipated or ethically problematic outcome (Cyron, 2016). It may also reflect the fact that DBS for TRD is an experimental procedure that has only been used in a small number of trials. One TRD study reported personality measure outcomes after DBS of the supero-lateral branch of the MFB. Bewernick et al. (2018) used the NEO Five-Factor Inventory (Borkenau & Ostendorf, 2008) to assess personality and found no difference in Five-Factor scales at 6-months (n = 21), 2 years (n = 17) or 5 years (n = 11) after DBS, despite patients obtaining an antidepressant response. The authors suggest this may reflect a 'scar effect' – a long-term, irreversible change in personality due to lengthy depressive episodes. Clearly, the addition of a qualitative component with patients and families would have provided greater understanding of whether subjective personality change was considered to have occurred and what the meaning of this change was in the context of their debilitating psychiatric condition.

Identity and Self

Qualitative investigations conducted with patients following DBS have also revealed insights into how the procedure and implanted device may impact a person's sense of self and self-image. The most notable of these being Schüpbach and colleagues' (2006) key paper '*Neurosurgery in Parkinson disease: A distressed mind in a repaired body?*'. A subset of patients demonstrated "several kinds of problems with social adjustment […] affecting the patients' perception of themselves and their body, marital situation, and professional life" (p. 406). These problems sat in paradox with improved motor function and were marked by spousal, familial and professional conflicts. Some patients experienced feelings of strangeness in terms of who they felt they were and their purpose in life without their illness. Others experienced an alteration in body-image by virtue of having an implanted electronic device. A range of standard measures were collected (motor disability, quality of life, social adjustment), which provided some indication of poor psychosocial outcomes. The semi-structured interviews, however, were central to understanding the personal and interpersonal dissatisfaction present for patients and partners. DBS knowledge and clinical practice has advanced greatly since the Schüpbach et al. (2006) study was conducted, but due to the limited number of studies since that have

directly examined patients' personal experiences it is difficult to assess whether these types of psychosocial difficulties remain common or relevant experiences for patients and families. Some recent examples from Gilbert et al. (2017) and Mosley et al. (2019) should be noted for their in-depth qualitative investigations of unanticipated outcomes after DBS. These articles are discussed at length within the empirical papers (Ch. 4 and 5) and will not be summarised here.

Within DBS for TRD research, few studies have examined patients' lived experience with the device or how it has impacted their identity and sense of self. Klein et al. (2016) conducted interviews and focus groups with individuals who had a DBS device for either TRD or OCD. The purpose was to investigate their attitude towards closed-loop stimulation systems (next-generation DBS). Within the participants' perspectives on future devices, some insight into their experience with existing DBS devices was revealed. Some participants indicated that through lifting them out of depression, DBS allowed their true self to re-emerge or had allowed them the freedom to construct a new self. Participants also commented upon how DBS centred within interpersonal disagreements. For example, if patients were experiencing any negative emotion (sadness, frustration), family would put this down to the device and suggest they have the stimulator adjusted. This *easy solution* for family did not necessarily align with patients' own views of what underlay their unhappiness or frustration. These findings indicate the importance of assessing and understanding how DBS influences the broader family system and not just the DBS recipient.

Impact on Relationships and Caregivers

Some of the literature discussed so far has provided preliminary indications of the unanticipated implications DBS can have for relationships with caregivers (typically spouses or family). Agid et al. (2006) found that 65% of patients with a partner experienced a conjugal crisis in the two years following surgery. In many cases there had been pre-existing relationship issues, but DBS appeared to exacerbate these. Some suggestions of how DBS contributed to these crises included: the stress of undergoing surgery, changes in the relationship dynamics (with the patient becoming more or less dependent), the neurobiological impact of the stimulation on personality (patient more outgoing, apathetic or disengaged), or the failure of the intervention to meet patient and caregiver expectations.

In an exploratory, mixed methods study, Lewis et al. (2015) revealed over 50% of their caregiver sample (n = 25) reported negative subjective wellbeing 12-months after DBS. Issues commonly cited as contributing to this were increased conflict with the patient, more anxiety regarding the patient's welfare and less personal freedom. In the qualitative component, caregivers described needing to manage the patient's "unreasonable troubling behaviour" (p.342) such as secretive gambling. They also mentioned how the patient's apathetic behaviour and "loss of interest in life" negatively impacted their personal wellbeing. In some cases, DBS was considered as contributing to these changes, resulting in negative attitudes towards DBS.

A recent example of increased caregiver burden and relationship strain following the emergence of stimulation-induced behavioural changes is reported in Mosley et al. (2019). This article will be explored within in *Chapters 4* and *5*. As mentioned, there are no existing studies that have specifically considered the impact of DBS on patient relationships or caregivers in a TRD sample. This will be the first study to do so.

The Current Thesis

Rationale

Unanticipated psychosocial outcomes following DBS include personality changes, alterations in self, and disturbances in relationships. These are prominent ethical and clinical issues with potentially significant implications for patients and caregivers. Important aspects of these issues have not been investigated thoroughly with those directly involved in the procedure (i.e., clinicians, patients and caregivers). As such, there is limited understanding of patients and caregivers' awareness of unanticipated outcomes, the personal meaning and significance of these experiences, how they are individually affected, how these issues are related to the DBS, and what support is available to help them manage. Qualitative investigations can provide broader insight into an intervention's outcomes beyond standard psychometric measures, which have increasingly been shown to be inadequate. Caregivers have been absent from the majority of investigations, but the limited existing studies indicate DBS can substantially impact their lives in ways they are often unprepared to manage. Understanding the full picture of DBS experiences will ensure prospective patients and caregivers can

be comprehensively informed of all potential outcomes. These findings can help shape and optimise future clinical practice and research through understanding how unanticipated outcomes can be minimised and managed.

While there has been extensive ethical and philosophical discussion speculating on the effects of DBS on patient personality, identity and self (see *Chapter 4*), there is limited existing empirical data directly assessing these issues with lived experience experts. Increased understanding of these personal experiences is required in order for more relevant and informed ethical discussions.

Thesis Aim and Research Questions

The primary aim of this thesis was to prospectively examine the impact of DBS on patient personality, self and interpersonal relationships, in an established neurological (PD) and emerging psychiatric (TRD) indication. To do so, I obtained multiple perspectives on these issues by qualitatively investigating the views of DBS clinicians, patients and caregivers. The thesis findings focus predominantly on personality and personality change, but the topics of self (and related concepts identity, self-concept) and patient-caregiver relationships are also examined. No specific models or theories of personality or self were applied in order to allow participants' own language and meaning attached to these concepts to emerge and drive the subsequent themes. Six research questions were posed:

1) What awareness or knowledge of DBS-related personality changes do patients and caregivers have prior to DBS?

2) What, if any, were participants' experiences of personality change following DBS?

3) How does DBS impact patients' identity and sense of self?

4) What is the perceived cause of these changes?

5) What impact do these changes have upon patients, caregivers and their relationship?

6) How are any unanticipated outcomes managed clinically?

Three Empirical Studies

In order to address the thesis aim and research questions, three empirical studies were conducted, which are presented in the following order across *Chapters 4* to *6*:

1. DBS clinicians: single interview with each clinician who worked in DBS for either movement disorders, psychiatric disorders or both.
2. PD DBS patients and caregivers: separate interviews with each participant before and 9-months post-surgery.
3. TRD DBS patients and caregivers enrolled in an experimental clinical trial: separate interviews with each participant before and 9-months after stimulation initiation.

In the next chapter, I outline the research methodology underpinning these studies.

CHAPTER THREE

METHODS OVERVIEW

Chapter Three – Methods Overview

In this chapter, I overview the methodological framework applied across the empirical components of the thesis contained within *Chapters 4* to *6*. Given these chapters provide detailed design and method information, I will minimise repetition and focus instead here on exploring methodological considerations, such as epistemological position, research reflexivity and establishing qualitative rigour, to provide depth beyond that required for manuscript submission.

The Purpose and Merits of Qualitative Research

Qualitative research encompasses a broad range of distinct methodologies, but is broadly defined as:

> *An emergent, inductive, interpretive and naturalistic approach to the study of people, cases, phenomena, social situations and processes in their natural settings in order to reveal in descriptive terms the meaning people attach to their experiences of the world* (Yilmaz, 2013 p. 312).

Qualitative methods are a powerful tool for exploratory research questions where limited empirical information exists. Qualitative research promotes the development of hypotheses and construction of theories to be tested by quantitative means (Morse & Field, 1996). Due to the inherent complexity of certain phenomenon, some are better suited to qualitative exploration (at least initially). Qualitative approaches are also useful for understanding the lived experience of a phenomenon or event. In these cases, participants are the experts in what it is like to experience the phenomenon and what factors were relevant in their decisions (e.g., to undergo DBS). Answers to these sorts of questions are important for ensuring the products of research are rapidly translated into practice in a patient-centred manner, with minimal harm and optimal efficacy. The Institute of Medicine considers qualitative approaches necessary for 'crossing the quality chasm' and overcoming the failure of many treatments to translate into practice (Institute of Medicine, 2001). In this way, qualitative research is valuable for identifying phenomenon missed by quantitative means.

Unlike quantitative research, which is concerned with numerical representations of a phenomenon (e.g., amount, intensity, frequency), qualitative research focuses on the nature and

meaning of the phenomenon. Rather than asking questions of 'how many', qualitative research methods aim to answer questions of 'how', 'what' and 'why' (Boeije, 2010; Yilmaz, 2013). Qualitative research can uncover reasons, motivations and outcomes that hide behind quantitative representations. Multiple participants may score the same on a quantitative scale, but have very different reasons and experiences that led to these scores. Without such understanding of participant experiences, the full benefits or harms of an intervention remain unclear. This may have critical implications in the clinical treatment and management of patients, particularly those experiencing a debilitating psychiatric disorder and undergoing an experimental neurosurgical procedure with uncertain and complex effects.

Qualitative research aims to identify a comprehensive account of the various views and experiences within a defined population relevant to the research question. Purposeful sampling of a diverse participant group with a range of experiences is often used to achieve this (Creswell, 2014). The intention is not to determine how representative these views are or to quantify them, rather the aim is to obtain a wide range of views or experiences. Sample size in qualitative research is often determined by the point at which all representative views are captured, often described as a saturation of themes or 'data saturation'. The sample size is influenced by the heterogeneity of the sample, the research questions, and diversity of experiences. While there are no hard rules about how many participants are necessary to achieve data saturation, six to 12 participants have been shown to be sufficient in largely homogenous samples (Fusch & Ness, 2015; Guest, Bunce, & Johnson, 2006). Saturation is often achieved in samples smaller than those common in quantitative research, which must be sufficiently powered to demonstrate a finding is a true result (i.e., statistically significant) and may be true of the broader population the sample is thought to represent.

These sampling processes and sample sizes limit the generalisability of qualitative findings, but the intention is to produce nuanced and in-depth findings that are highly context, participant and researcher dependent (Yilmaz, 2013). As such, the final report or presentation from a qualitative study should contain the following: the researcher/s' reflexivity (their orientation, predispositions, biases), the participants' voices, a complex description and interpretation of the phenomenon or problem, and an acknowledgement of its contribution to the literature and/or its implications for society (Creswell

& Poth, 2018). These key components are discussed below and within each empirical chapter (Ch. 4 to 6), followed by a summary of their combined contributions and implications for change in the integrated discussion (Ch.7).

Epistemological and Ontological Foundation

A qualitative research framework is defined by the basic principles of epistemology, methodology and method (Carter & Little, 2007). Regarding epistemological position, I conducted the thesis from a realist position through a psychological lens. Basic assumptions held in this position include: the existence of movement and psychiatric disorders (i.e., as opposed to social constructions), recognition that their pathology has a neurobiological basis (e.g., neurogenerative process, dysfunctional neurocircuitry), while acknowledging the critical role of psychological and social factors in how they present and are managed. This aligns with the *biopsychosocial model* commonly used in psychology to conceptualise health and mental illness and guide treatments (Lehman, David, & Gruber, 2017). The application of this framework was realised in the research in the following ways: I held an openness to the possibility that changes in personality or behaviour after DBS could be driven primarily or in equal parts by biological (e.g., stimulation-induced, medication-related, pathology-based), psychological (e.g., undiagnosed mood disorder, response to treatment) or social factors (e.g., re-negotiating relationship dynamics). This framework likely influenced the nature of the interviews (e.g., by enquiring about factors participants may not have considered) and subsequent analysis. However, as a realist paradigm assumes a direct relationship between language and meaning or experiences, where participants' language represents the reality of their life and reflects the meaning they have assigned to their experiences (Braun & Clarke, 2006), I was mindful not to re-interpret the meaning of participants' language.

Thesis Methodology

A consistent methodological framework was applied across all three studies with minor variations in participants, procedure and analysis. An overview of the study methods is presented in Table 1.

Table 1. Summary of Study Method

	Participants	Sampling and Recruitment	Data Collection	Data Analysis
Study 1. DBS Clinicians	- 16 clinicians working in Australian DBS clinical practice. Average length = 11 years (range: 1.5 – 25 years). - From various disciplines: neurology = 4, nursing = 4, neuropsychology = 4, neuro-/psychiatry = 4. - Specialisations: movement disorders = 10, psychiatric disorders = 4, and both = 2.	- Purposive sampling used to recruit clinicians actively involved in the treatment of individuals undergoing DBS. - Expert nominations, snowballing and searches of DBS services used to identify and recruit suitable participants. - No DBS neurosurgeons approached chose to participate.	- Single semi-structured interviews conducted with each participant, either in-person or via video-/teleconference. - Average length = 39 mins (range: 17 – 74 mins). Audio-recorded and transcribed by professional service. - Transcripts reviewed for accuracy and de-identified (applies to all studies).	- An iterative thematic analysis approach used (Braun and Clarke, 2006). - Data imported and analysed in NVivo 12 software. Cross-coding conducted on three transcripts [CT, AC]. - Results presented in paper (Ch. 4) and at conferences.
Study 2. PD-DBS Patients and Caregivers	- 11 patients with PD enrolled for DBS (M_{age} = 62.5; M = 7, F = 4), plus 11 respective caregivers (spouses, family members) (M_{age} = 60.5; M = 2, F =9). - 1 patient who completed an initial interview ultimately chose not to proceed with DBS. - Target site: STN = 9, GPi = 1.	- Purposive sampling used to recruit patients with PD enrolled for DBS. - Recruited via neurologists specialising in DBS for PD in Melbourne, Victoria. - All patients underwent DBS through the private health system. Attempts to include public patients were hindered by project timeline.	- Semi-structured interviews with patients and caregivers individually, either in-person or via video-/teleconference. - Interviews conducted both pre-surgery and approx. 9-months post-surgery. - Average length = 41 mins (range: 24 – 121 mins).	- Thematic analysis (as above). - Transcripts analysed manually (handwritten margin notes and case summaries) and charting in Word document. Cross-coding on data from three pairs [CT, AC, RS]. - Results presented in paper (Ch. 5) and at conferences.
Study 3. TRD-DBS Patients and Caregivers	- 6 patients with TRD enrolled in a DBS clinical trial (M_{age} = 52; M = 1, F = 5), plus 5 respective caregivers (spouses, family) (M_{age} = 59.5; M = 3, F = 2). - 1 patient participated independently (no caregiver). - Target site: BNST for all.	- Consecutive sampling used to recruit individuals actively enrolled in a Melbourne-based clinical trial of DBS for TRD. - Individuals who met clinical trial criteria, including diagnosis of severe TRD invited to participate. - All patients and caregivers approached opted to participate.	- Semi-structured interviews with patients and caregivers individually, either in-person or via video-/teleconference. - Interviews conducted pre-surgery and approx. 9-months post-stimulation initiation. - Average length = 50.5 mins (range: 34 -86 mins).	- Thematic analysis (as above). - Data imported and analysed in NVivo 12 software. Cross-coding conducted on six transcripts [CT, AC, RS]. - Results present in paper (Ch. 6) and at conferences.

Note. Research ethics approval for all three studies obtained from the Monash University Human Research Ethics Committee (CF16/1888-2016000963) – see appendix.
PD: Parkinson's disease; TRD: treatment-resistant depression; STN: subthalamic nucleus; GPi: globus pallidus; BNST: bed nucleus of the stria terminalis.

Semi-Structured Interviews

All studies utilised semi-structured interviews, the format of which allows an agenda of pre-set questions addressing the research aims to be asked and discussed in detail, while also enabling novel topics to be explored as they arise (Rhodes & Coomber, 2010). I developed the initial interview schedules which were refined with input from an interdisciplinary research team (neurologist, psychiatrist, neuropsychologist, anthropologist, social scientist and ethicist) ensuring a range of relevant issues and perspectives were considered (see *Appendices E* to *G*). After completing training in qualitative interviewing and analysis, I conducted all interviews across the three studies

A single semi-structured schedule of interview questions was conducted with the DBS clinicians in Study 1. These interviews covered a broad range of topics including clinicians' experiences of unanticipated outcomes following DBS (e.g., personality changes, behavioural issues), as well as managing patient expectations, informed consent and maximising patient quality of life.

Studies 2 (PD) and 3 (TRD) examined participants' lived experiences of undergoing and living with DBS and the meaning they attached to this experience (Creswell & Poth, 2018). Semi-structured interviews were conducted before and after surgery. The intention for pre-surgery interviews was to conduct them when participants were prepared for the surgery, but not so close that the interview were dominated by anticipatory anxiety. In the TRD study, two patients completed pre-surgery interviews before their surgeries were delayed for unforeseen reasons by a couple of months. In the PD study, follow-up interviews were scheduled nine-months after surgery. The intention with this timing was to capture reasonably recent recollections of post-operative experiences (e.g., surgical recovery, optimising stimulation, emerging side-effects), while allowing time for a stable therapeutic response to be achieved. In the TRD study, they were nine-months after *stimulation-initiation*, which for the current sample occurred between one to three-months post-implantation. It was anticipated patients in the TRD study would not be as advanced in the optimisation of settings as the PD patients, as the TRD clinical trial protocol includes a five-month period of pseudo-randomised stimulation parameters before attempting to personally optimise settings.

Thematic Analysis

Thematic analysis was the chosen analytic approach applied across all studies. Thematic analysis involves identifying patterns of meaning within data, but can be used to highlight similarities, differences and inconsistencies both within and across interviews (e.g., within participants' own interviews and when compared with others') (Braun & Clarke, 2006). This is useful for exploring the same phenomenon from different perspectives (patient and caregiver) and at different points in time (before and after surgery). Thematic analysis also lends itself to psychological interpretations, which was considered appropriate with my academic background, epistemological posture, psychological lens and the project aims.

While thematic analysis is a widely used and commonly reported qualitative research method, it can be poorly demarcated. Braun and Clarke's (2006) approach provides a clear, transparent and rigorous method for thematic analysis which was applied in all three studies. The approach involves a six-phase process, presented in Figure 1.

Phase	Description of the process
1. Familiarizing yourself with your data:	Transcribing data (if necessary), reading and re-reading the data, noting down initial ideas.
2. Generating initial codes:	Coding interesting features of the data in a systematic fashion across the entire data set, collating data relevant to each code.
3. Searching for themes:	Collating codes into potential themes, gathering all data relevant to each potential theme.
4. Reviewing themes:	Checking if the themes work in relation to the coded extracts (Level 1) and the entire data set (Level 2), generating a thematic 'map' of the analysis.
5. Defining and naming themes:	Ongoing analysis to refine the specifics of each theme, and the overall story the analysis tells, generating clear definitions and names for each theme.
6. Producing the report:	The final opportunity for analysis. Selection of vivid, compelling extract examples, final analysis of selected extracts, relating back of the analysis to the research question and literature, producing a scholarly report of the analysis.

Figure 1. 'Phases of thematic analysis'. Source Braun and Clarke (2006, p. 87)

These phases are not linear, but recursive, involving a cyclical process of comparison between the data, coding ideas, themes and the final write-up (Carter & Little, 2007). In the current work, the coding frameworks were developed in a ground-up, inductive manner, that strongly linked the emergent themes to the data, including *in vivo* codes (e.g., participant quotes used as labels) (Braun & Clarke, 2006). Despite employing an inductive approach, it is not uncommon for themes to reflect the topic guides informed by project aims and research questions. This can be because participants are directly responding to the questions posed to them, and therefore are likely to use convergent phrasing

(Rhodes & Coomber, 2010). An overall analysis was conducted on the data corpus (entire body of collected data), followed by detailed and refined analyses on data sets (aspects of the data considered relevant to the research questions).

Maximising Qualitative Rigour

As the nature of knowledge in quantitative (or rationalistic) paradigms differs from qualitative (or naturalistic) paradigms, so does the meaning of language used for assessing qualitative rigour (Morse, Barrett, Mayan, Olson, & Spiers, 2002). In qualitative research, validity involves determining the accuracy of findings from a researcher, participant and reader perspective and employing procedures throughout the research process to regularly assess accuracy (Creswell, 2014). A range of terms are discussed and debated when addressing validity, including *trustworthiness*, *authenticity* and *credibility* (Creswell & Miller, 2000). Here I describe the *validity strategies* used during the research process and how they relate to the concept of rigour.

Qualitative checklists. Established checklists are one approach for establishing rigour in qualitative research, in particular increasing the transferability of findings. Braun and Clarke (2006) provide a 15-point checklist specifically for their thematic analysis approach. I referred to this and reflected upon it during various stages of analysis to ensure a thorough analysis was completed. Additionally, the Consolidated Criteria for Reporting Qualitative Research (COREQ) was used to support comprehensive and transparent reporting in empirical papers (Tong, Sainsbury, & Craig, 2007).

Triangulation. Two types of triangulation were present in the current project: 1) analyst and 2) source triangulation. For all studies, following my initial coding of the transcripts, independent coding was conducted on a subset of transcripts by members of the research team experienced in qualitative research. Comparison and discussion of coding approaches led to the development of coding frameworks. By incorporating multiple perspectives during this process, a deeper understanding of the data in relation to the research questions was achieved. Another strength of the project was the gathering of information from multiple sources, including participant sources (patients, caregivers and clinicians) and data sources (multiple interviews, field notes, and demographic and psychometric information). Field notes consisting of brief written summaries were

completed after interviews that conveyed my impressions, observations and initial thoughts. These notes contained non-verbal information, expressions and contextual details absent from transcripts. This practice also promoted researcher reflexivity during the data collection process (Fossey, Harvey, McDermott, & Davidson, 2002). Some demographic and psychometric information was collected from patients and caregivers at each interview. The purpose of this information was to help characterise the samples and provide myself with a deeper understanding of each individual and the patient-caregiver relationship at that specific time-point. These measures were not collected for the purpose of statistical analysis and scores were not included in empirical papers.

Three potential outcomes when applying triangulation in research are convergence, inconsistency and contradiction (Denzin & Lincoln, 2005). All of these outcomes contribute to a deeper understanding and superior explanation of the research issue (Yilmaz, 2013).

Peer debriefing. Peer debriefing was performed in two ways. Firstly, it was performed in the form of regular meetings with the research team [CT, AC, RS] where interview impressions, coding ideas and analysis interpretations were discussed. These discussions allowed the interviewer and research team to reflect on their preconceptions, biases and interests informed by professional and personal experiences (Barbour, 1998). Secondly, peer debriefing was conducted by having fellow researchers with experience and understanding of the research topic review preliminary interpretations, study findings and the final written report to provide feedback and comment on their resonance (Yilmaz, 2013). This process is considered important for increasing the credibility of the research (Creswell & Miller, 2000).

Member checking. Member checking is an important strategy for increasing credibility in qualitative research; however, its value is regularly questioned and there is on-going debate as to how it impacts research validity (Birt, Scott, Cavers, Campbell, & Walter, 2016; McConnell-Henry, Chapman, & Francis, 2011; Morse et al., 2002). In light of this contention, we chose not to conduct member checking due to the nature of our research protocols. Specifically, one form of member checking traditionally involves returning transcript copies to individual participants to have them review and verify the content. For Study 2 and 3, patient-caregiver dyads participated together, but were interviewed separately to allow open and honest discussion. Returning transcripts to participants

who share a physical residence and in some cases email account runs the risk that confidential and sensitive information could inadvertently be revealed to the other party. Another form of member checking involves providing all participants with the same summary of themes and coding descriptions. This approach is problematic as the synthesised and decontextualised summary does not contain information recognisable for any individual, leaving participants unable to identify and verify their own perspectives (Morse et al., 2002).

A recommended alternative to member checking, particularly when examining peoples' lived experiences, is to seek clarification during the co-construction of data (i.e., during interview). I applied interviewing techniques recommended by McConnell-Henry and colleagues (2011) to explore participants' lived experiences and seek clarification in the moment. These included: 1) giving participants space to fully consider their thoughts, including allowing for silence; 2) providing participants enough time to say all they need and not rushing the interview or being bound tightly to time; 3) using probing follow-up questions when I felt I had not fully grasped what the participant has said or intended and wanted to clarify my understanding; 4) judicious use of paraphrasing to demonstrate active listening, but also to ensure that my interpretation of information is correct; and 5) using open-ended questions so that participants can contribute perspectives in their own words, as well as opportunities to add any extra experiences that lie outside the direct line of questioning.

Researcher Reflexivity

An essential component of the research process and qualitative reporting is researcher reflexivity. It involves the researcher reflecting upon their own role and how it shapes and influences the research. This can include assumptions, biases, interests, and personal and professional experiences (Barbour, 1998). Due to the subjective nature of qualitative research, contextual transparency such as researcher reflexivity is required when reporting findings. Here reflexivity is expanded on in greater detail than within each empirical paper, in part due to limited space, but so that commentary on reflexivity relating to the thesis as a whole can be provided.

A number of professional and personal experiences shaped my approach to the thesis, including an academic background in psychology, concurrent clinical training and a previous role as a research

co-ordinator at a psychiatric research centre conducting brain stimulation clinical trials. The analysis and interpretation were conducted with a psychological lens, although the process of peer debriefing allowed for input and discussion from other perspectives (e.g., neuroethics, social science, neuropsychology). As mentioned, one assumption from a psychological lens is that human experiences, whether they be behaviours, feelings or cognitions, are influenced by a complex range of biological, psychological and social factors. Therefore, a change in these human experiences after DBS (e.g., behaviour, mood, relationships) may be influenced by one or multiple factors. This open approach and tendency to explore various contributing factors would have influenced the types of questions asked of participants and possibly encouraged them to consider their situation more broadly. While I may have possessed an independent perspective on factors contributing to an experience or phenomenon reported by participants (e.g., abrupt change in patient behaviour), ultimately, participants' own beliefs and perceptions were primary and guided analysis.

Study 3 involved candidates enrolled in an experimental trial of DBS for TRD. My research supervisor [RS] previously co-ordinated this particular clinical trial (prior to the current study) and I previously co-ordinated a non-invasive brain stimulation clinical trial in TRD (electroconvulsive therapy vs. magnetic seizure therapy) in the same research centre. These experiences were relevant to the current study and undoubtedly influenced the approach taken (i.e., a clinical research lens). This intimate knowledge of the clinical trial's internal processes and exposure to participants and families experiencing similar circumstances provided important contextual understanding leading to a fully informed analysis. These previous experiences also contributed to my initial interest in the current study and a desire to voice both patient and caregiver experiences.

I also have personal experience providing support to a family member with refractory depression and their caregiver. While this is not considered to have influenced the analysis or interpretation of data from the TRD study, it contributed to a deeper sense of empathy and shared understanding with participants during interviews.

CHAPTER FOUR

CHANGES IN PERSONALITY ASSOCIATED WITH DEEP BRAIN STIMULATION: A QUALITATIVE EVALUATION OF CLINICIAN PERSPECTIVES

Chapter Four – Changes in Personality Associated with Deep Brain Stimulation: A Qualitative Evaluation of Clinician Perspectives

Preamble to Paper One

The empirical papers are presented in the order in which studies were completed. As Study 1 involved only single interviews with participants, it was completed and published first. Some of the clinicians who participated were involved in the care of patients included in Studies 2 and 3 or worked at institutions associated with their DBS surgeries; however, specific patients were not discussed during these interviews. Rather clinicians spoke generally about their experiences working with patients over the course of their DBS careers. The intention was to recruit Australian clinicians working in the disorders represented in Studies 2 (PD) and 3 (TRD). Due to small numbers working in TRD, clinicians working in OCD were also invited to participate. It was anticipated some similarities would be shared across the two specialties, given the experimental nature of psychiatric DBS, its relative infancy in Australia and the legislative procedures associated with performing psychosurgery. Clinicians were asked how they felt DBS impacted patients' identity and how patients viewed themselves, but these questions had limited relevance. Clinicians either had little to contribute on the topic, felt unable to comment on patients' behalf or had found their own questions posed to patients on this topic had mostly been met with confusion. For this reason, the paper focuses primarily on personality change as it was a clinically relevant topic discussed extensively in the majority of interviews.

This original research article was first published online in the journal *Neuroethics* in July 2019 and will be included in a forthcoming special issue on the topic of ethics hype and controversial evidence in DBS. Contributions to the issue were made in response to an article from Gilbert and colleagues (2018) entitled '*Deflating the "Deep brain stimulation causes personality changes" bubble?*'. The authors highlighted the limited empirical evidence corroborating the link between DBS and post-operative changes in personality (and other related concepts), suggesting much of the neuroethics literature debating the issue either ignored the conclusions from empirical studies, distorted the findings or incorrectly cited secondary accounts. The intention with this paper was to

contribute to the empirical research on the topic by examining the perspectives of those directly involved in patient care, who have expertise in the area and exposure to numerous patients and clinical outcomes.

While *treatment-resistant depression* (TRD) is used elsewhere in the thesis and is how participants in Study 3 were classified, here, the more general diagnostic term *major depressive disorder* (MDD) was used.

The supplementary material referred to in this paper consists of the interview schedule that can be found in *Appendix E*.

Abstract

Gilbert et al. argue that the neuroethics literature discussing the putative effects of Deep Brain Stimulation on personality largely ignores the scientific evidence and presents distorted claims that personality change is induced by the DBS stimulation. This study contributes to the first-hand primary research on the topic exploring DBS clinicians' views on post-DBS personality change among their patients and its underlying cause. Semi-structured interviews were conducted with sixteen clinicians from various disciplines working in Australian DBS practice for movement disorders and/or psychiatric conditions. Thematic analysis of the interviews revealed five primary themes: 1) types, frequency and duration of personality change, 2) causes of personality change, 3) impact on patient and family, 4) communication, comprehension and awareness, and 5) management. Clinicians described a variety of personality changes in Parkinson's disease following DBS including irritability, impulsivity and impaired decision-making. The frequency of personality change seen in patients varied amongst clinicians, but changes were overwhelmingly transient. Clinicians considered both DBS stimulation and additional factors (response to treatment, disease pathology, pharmacological changes) as inducing personality change. For DBS patients with major depressive disorder, a restoration of pre-morbid personality was associated with alleviation of illness. Considerations for future research of personality change following DBS include selecting suitable tools for quantitative examination and developing a common language between the scientific and ethics communities. Clinical implications including recommendations for the informed consent process for patients and families and clinicians' management of personality change are discussed.

Keywords: deep brain stimulation; personality; identity; self; neuroethics; surgical trials

Introduction

The paper from Gilbert et al. (2018) prompts a necessary reflection on the "unchallenged narrative" (p. 1) within the neuroethics discourse that deep brain stimulation (DBS) induces changes in personality, identity, agency, authenticity, autonomy and self (PIAAAS). The authors highlight the limited use of empirical studies in many theoretical neuroethics articles and suggest that these have led to a speculative neuroethics bubble. The authors' examination of changes in PIAAAS following DBS led to four primary findings: 1) claims made within the neuroethics literature did not match the conclusions from first-hand primary research data (post-DBS changes were ascribed to DBS technology rather than psychosocial or pathology factors), 2) extensive conceptual discussions from neuroethicists and philosophers were based on a few quotes, heavily derived from a single sample (Agid et al., 2006; Schüpbach et al., 2006), 3) post-DBS outcomes were related to disease-specific pathology rather than the DBS technology itself, and 4) common assumptions about the putative effects of DBS on PIAAAS were made without reference to first-hand primary research. Concerns such as the presentation of generalised conclusions or claims based on limited quotes from few patients have been raised previously (Bittlinger, 2017; Müller, Bittlinger, & Walter, 2017), including in response to previous studies from Gilbert et al. (2017). In addition to acknowledging the inconsistent and distorted claims within the DBS neuroethics literature, there is growing consensus on the need for more empirical research to provide a more accurate and robust picture of the impact of DBS on PIAAAS (Christen, Bittlinger, Walter, Brugger, & Müller, 2012). Our study is a contribution to the body of PIAAAS first-hand primary research and will be evaluated in light of Gilbert et al.'s key findings.

Personality and the impact of DBS upon it, has received the most attention of all the PIAAAS concepts across both the neuroethics (Glannon, 2009; Synofzik, 2007; Synofzik & Schlaepfer, 2008) and scientific literature (Fassino et al., 2010; Lewis, Maier, Horstkotter, Zywczok, et al., 2015; Lhommee et al., 2017; Pham et al., 2015). However, the issue of personality change following DBS has rarely been explored with the clinicians and researchers directly involved in the treatment. Exceptions include a global survey of DBS experts (n = 113), predominantly neurosurgeons and neurologists (Christen, Ineichen, Bittlinger, Bothe, & Müller, 2014). Responses indicated that experts

considered personality change a relevant DBS risk, with 26.5% believing personality changes occur within at least 5% of patients. For 43.4%, stimulation was believed to be the main cause of personality changes. Types of changes commonly described by experts were characterised as alterations in patient mood e.g., (hypo)mania, euphoria, depression, apathy. Bell et al. (2011a) conducted a qualitative investigation of Canadian healthcare providers' perspectives of social and ethical challenges related to DBS for movement disorders. Healthcare providers identified post-surgery psychiatric and behavioural complications as a safety concern and the monitoring of behavioural side-effects as an important responsibility for patients and family during the device programming process. A recommendation from the investigation was for patients and families to have access to postoperative psychological counselling or social work services to assist them in the monitoring and management of psychiatric and behavioural side-effects. Although healthcare providers considered psychiatric or behavioural complications a social and ethical challenge, it was not considered as crucial as issues such as patient screening and selection criteria, and public understanding and awareness of DBS risks and benefits.

In regards to DBS for psychiatric conditions, health care trainees have provided perspectives on the potential impact of DBS upon personality (Bell & Racine, 2013). The health care trainees, who had no direct experience working within DBS, felt that DBS could impact patient personality, but that these changes were considered acceptable. Gaining feedback from patients and family was suggested as a way to evaluate whether the personality change was desirable or not. These are speculative considerations from trainees with no clinical experience with DBS. A more informed understanding of the issue can be established through evaluating the personal accounts of clinicians directly working with DBS for psychiatric conditions.

The benefits of seeking first-hand accounts from clinicians in the field include: 1) exposure to high numbers of patients with varying presentations and circumstances, 2) expertise in detecting, managing and appreciating the aetiology of personality change, and 3) a comprehensive understanding on the impact of DBS on personality by gathering perspectives from clinicians across various disciplines (e.g., neurology, psychiatry, nursing) and treating patients of different populations

(e.g., movement disorders, psychiatric conditions). A qualitative approach also allows for an in-depth exploration of these issues not possible with psychometric measures.

The issue of personality change following DBS has been heavily explored within the neuroethics and bioethics literature, but rarely has it been investigated with those involved directly in DBS clinical practice. This study sought to explore clinicians' experiences of personality change in patients following DBS, and extend upon Gilbert et al.'s (2018) first key finding – that the neuroethics claims of technology-driven post-DBS changes did not match the conclusions of empirical studies – by investigating clinicians' beliefs about the perceived cause of personality change. We conclude by discussing the ethical and clinical implications of their views, including the impact of personality changes upon patients and families and clinicians' approaches to managing them.

Methods

Sample and Recruitment

Clinicians actively involved in the treatment of individuals undergoing DBS within Australia were recruited using expert nominations, snowballing, and searches of academic publications and Australian DBS services. Thirty-four clinicians were invited to participate via email, of whom 16 (47%) were willing to participate. The sample consisted of clinicians from various disciplines, including: neurology (n = 4), nursing (n = 4), psychiatry (n = 3), neuropsychology (n = 4), and neuropsychiatry (n = 1). Clinicians from neurosurgery were approached, but none agreed to participate. The majority of the sample specialised in DBS for movement disorders (n = 10), primarily Parkinson's disease, with some experience across dystonia, essential tremor, and Tourette syndrome. A smaller group were involved in DBS for psychiatric disorders (n = 4), specifically obsessive-compulsive disorder (OCD) and major depressive disorder (MDD). Two clinicians had experience across both movement and psychiatric disorders (n = 2). The level of experience within the sample is outlined in Table 1.

Table 1. Participant Demographic Information

Characteristics	Descriptive statistics (n = 16)	
Gender	8 (50%) Female	
Movement disorders specialisation	12 (75%)	
Discipline	4 = Neurology 4 = Nursing 3 = Neuropsychology 1 = Neuropsychiatry	
	Mean (SD)	Range
Years working in DBS	11.04 (6.44)	1.5 – 25
Approx. number of DBS patients treated	311.08 (372.15)	40 – 1215
DBS surgeries performed at site per year	41.8 (26.27)	25 – 100
Psychiatric disorders specialisation	6 (37.5%) *	
Discipline	3 = Psychiatry 3 = Neuropsychology	
	Mean (SD)	Range
Years working in DBS	6.25 (2.99)	2.5 – 10
Approx. number of DBS patients treated	9.2 (3.27)	6 – 14
DBS surgeries performed at site per year	1.6 (2.31)	1 – 3

Note. * Two participants dually coded in both movement and psychiatric groups.

Movement disorder clinicians tended to have a high level of experience, with 67% having either >10 years' experience in DBS or having treated >100 patients who have undergone DBS. Clinicians working in psychiatric disorders reported fewer years' experience working in DBS and had notably smaller numbers of patients. However, this reflects the experimental nature and relative infancy of psychiatric DBS clinical trials in Australia. Despite these small numbers, the degree and length of therapeutic engagement between clinicians and individuals seeking DBS for OCD or MDD was reportedly high, often commencing 6 to 12 months before surgery and continuing beyond the individual's involvement in the clinical trial. The sample were involved in various aspects of care including the assessment, selection, education, treatment planning, programming and support of DBS patients and families. Clinicians worked in varied settings across multiple states, including: private practice, public and private metropolitan hospitals, research facilities, and consumer advocacy and

education organisations. The majority of the sample were involved in DBS-related research projects. Research ethics approval was obtained from the Monash University Human Research Ethics Committee (CF16/1888–2016000963) prior to conducting this study and informed consent was received from all clinicians prior to their participation.

Qualitative Interviews and Analysis

Participants took part in audio-recorded semi-structured interviews between June 2017 and August 2018. All interviews were conducted by the first author [CT] who is a female provisional psychologist with training in qualitative methods and experience interviewing DBS patients and caregivers. Interviews were conducted via telephone (n = 4), videoconference (n = 3), or face-to-face (n = 9) at participant's workplace or home. The average interview length was 39 minutes (range = 17 to 74 minutes). An interview schedule was used, containing open-ended questions exploring clinicians' perspectives on a range of topics, including: patient selection, consenting process, patient and caregiver expectations, personality and identity change following DBS, impact upon relationships, and post-surgery support (refer to Supplementary Material for full interview schedule). Additional probing questions were asked to increase depth of information and responses were reflected back to participants to ensure interviewer understanding. Field notes were kept and regular debriefing was conducted with co-authors, whose backgrounds in neuropsychology [RS] and neuroethics and qualitative research [AC] influenced these discussions. This paper reports on a subset of themes related to personality change only.

All interviews were transcribed verbatim by a professional transcription service and reviewed by the first author to ensure transcription accuracy. An iterative thematic analysis approach within an essentialist/realist paradigm was used, whereby it is assumed participants' language reflects the reality of their experiences and meanings (Braun & Clarke, 2006). Data was imported and organised using NVivo 12 software (QSR International Pty Ltd., Doncaster, Australia). A subset (3) of transcripts were independently coded by two members of the research team [CT, AC]. These codes were discussed and compared before developing a final coding structure that reflected the primary themes emerging from the transcript data. Subsequent interviews were coded by one researcher [CT] applying the same structure, with codes created or revised as required following discussion with the

team. Data coded within each primary theme was revised and secondary themes identified. For movement disorder-related interviews, data saturation was reached at participant 11 (of 12). Data saturation was unable to be reached within the number of psychiatric disorders-related interviews conducted (n = 6). Additional interviews were not able to be conducted due to the small pool of psychiatric DBS clinicians in Australia.

Results

The thematic analysis revealed five primary themes (see Table 2). Comments presented below refer primarily to clinicians' experiences working within DBS for Parkinson's disease (PD), unless stated otherwise.

Table 2. Primary and Secondary Themes Emerging from the Analysis

Primary themes	Secondary themes
1. Types, frequency and duration of personality change	Characteristic personality changes Impulse-control disorder-related changes Mood, cognitive and psychiatric changes Rates of personality change Transient and persistent changes
2. Causes of personality change	Stimulation-dependent changes Complexities in determining cause Exacerbation of underlying traits Relationship between illness and personality
3. Impact of personality change on patient and family	Emotional impact on caregiver and family Negative relationship and societal consequences Adjustment period Accommodating in content of ongoing illness
4. Communication, comprehension and awareness of potential personality change	Informed consent Reduced patient insight and awareness Eliciting patient and caregiver feedback
5. Management	Early detection and intervention Specialist DBS clinical care Hypothesis-testing approach

Types, Frequency and Duration of Personality Change

Clinicians described a wide variety of personality changes within their patients following deep brain stimulation, including disinhibition (*n* = 4), irritability (*n* = 6, one discussing an OCD case), aggression (*n* = 3), violent behaviour (*n* = 2), loss of empathy (*n* = 1), excessive laughter (*n* = 2), increased energy or drive (*n* = 2) and changes in sexual behaviour or fetishism (*n* = 3) (examples displayed in Table 3). A pool of common experiences included increased impulsivity (n = 7) and impaired decision-making (n = 3), with specific reference to impulse control disorders (*n* = 4) and associated behaviours such as gambling (*n* = 3), over-eating (*n* = 1), hobbyism (*n* = 1), excessive shopping (*n* = 2), and hypersexuality (*n* = 3).

Other responses clinicians provided to changes in patient personality included heightened anxiety (*n* = 1), apathy (*n* = 3), amotivation (*n* = 2), low mood and sadness (*n* = 6), psychotic symptoms (*n* = 2), subtle cognitive changes (*n* = 3), and hypomanic and manic episodes (*n* = 5, two discussing PD cases, three discussing OCD cases). One clinician highlighted improvements in anxiety, depression and irritability in their PD patients. Although some of the above would not be classified as personality changes according to current psychological models (a distinction that some clinicians noted), it appears that clinicians took a broad view of patients' personality that encompassed their cognitions, feelings, and behaviours when providing responses to questions about personality change.

Views on the frequency of personality change varied significantly amongst the sample. Some said that it was not something they encountered much in their practice (*n* = 3), but they were aware of it being reported in the DBS literature.

We know from the literature it does happen, but yeah, it's very rare. (Neuropsychologist 6, PD)

These kinds of responses came from clinicians with lower levels of DBS experience (<10 years or <100 patients) and who tended to have shorter therapeutic relationships with patients (e.g., pre and post assessments). Clinicians with high levels of experience and often lengthier therapeutic relationships noted that it was something they encountered fairly regularly, with some offering a figure of how common they believed personality changes were in DBS patients (*n* = 3).

Table 3. Example Responses Regarding Personality Change Following DBS

	Characteristic personality changes
Disinhibition	*We've had some people who've had some minor personality change, which tends to be often a bit of stripping back of some of the social veneer…some of the social etiquette is just rubbed away.* Nurse 5, PD
Irritability	*The patient or partner or caregiver is seeing this slight irritable change that can be just something hard to put a finger on.* Neurologist 7, PD
Aggression and violent behaviour	*I've seen one case…when we did turn a patient on, they became violent and aggressive…but that's the only one case I've seen.* Nurse 5, PD
Excessive laughter	*To get people with pathological laughter or crying as a side effect of stimulation is rare…I've seen mild versions of that where somebody comes in and says: 'I get a bit giggly.' Is everything else going alright? Because we can make some changes. 'No, that's not as good, I'm stiffer and speech isn't so good.' Say well, do you want to go back to the old setting where you were a bit giggly and your kids used to tease you? 'Yeah, I'd prefer that.' There are worse things in life.* Neurologist 1, PD
Increased energy or drive	*I guess the more common ones you're seeing someone who's a bit energised and more impulsive and having to adjust stimulation and medications around that.* Neurologist 11, PD
Sexual behaviour or fetishism	*[It] can be as pronounced as a substantial change in sexual behaviour or fetishism.* Neurologist 7, PD
	Impulse-control disorder-related changes
Impulsivity	*I guess it's more they crave their independence again. They're probably a bit impulsive…so, impulsivity is a problem.* DBS Nurse 4, PD
Impaired decision-making	*You can become a little manic, a bit impulsive, a bit too rapid in your decision-making, not considering things properly and generally too fast of thought.* Neurologist 7, PD
Impulse-control disorders	*We see a characteristic syndrome…it is characterised by impulsive decision-making, recklessness, disinhibition, loss of empathy. That can manifest itself in florid impulse control disorders, but it's often more attenuated than that and is more manifested in interpersonal style, which is often described as a change in personality.* Neuropsychiatrist 2, PD
	Mood, cognitive and psychiatric changes
Heightened anxiety	*In the patient I'm thinking of…she was incredibly anxious after the surgery…she had quite a negative psychological reaction, so she went from sort of mild trait anxiety to being quite severe.* Neuropsychologist 9, PD
Apathy	*[We have] people who have a bit more apathy and maybe their wife or husband is more impressed by the motor change, but the patient hasn't noticed how good their improvement is.* Neurologist 11, PD
Low mood and sadness	*Down the track getting into the three-month period, you can see once their elevation has gone, they tend to be a little bit the opposite, depressive.* DBS Nurse 4, PD *Many times, they would be depressed because of their motor symptoms that had been persisting quite a long time, so usually that had improved almost always afterwards.* Neuropsychologist 10, PD
Subtle cognitive changes	*One of the things is where there's subtle cognitive changes that are a nuisance…a little bit more word finding difficulty or more distractibility, or that they're losing a little bit more forward planning and they're getting a bit more passive.* Neurologist 1, PD

One in 10, one in 10, yep. (DBS Nurse 4, PD)

Yes, I'd say quite often, about 30 percent of the time…say if the rate of impulse control problems with dopamine agonists…runs at about 15 percent overall, it would run a bit higher in this group. (Neurologist 1, PD)

The 90 percent of our cases that do really well post-operatively, I don't really have much to do with. I'm involved when things are not going well. (Neuropsychiatrist 2, PD)

The tendency for personality changes to emerge in the months following surgery was also noted (n = 3).

The temporary behavioural changes…are probably a little more likely in that period of time after an operation than when you are going through those once, two or three times a year medication changes. (Neurologist 7, PD)

Developments in DBS clinical practice, including increasing use of DBS in younger patients with reduced disease duration or severity (Schüpbach et al., 2013), was believed to be associated with decreased instances of personality change (n = 2).

Certainly, you don't often see the marked personality changes as much with early stimulation as you do with later stimulation. (Nurse 5, PD)

Increasing appreciation of the potential for personality change was also believed to have reduced the incidence of personality change (n = 1).

It was when we had lesser of an understanding about the consequences. We just don't see it as much as we used to…back in the day people were much more impulsive I think after the operation. (Neurologist 11, PD)

Personality changes were commonly described as transient or temporary, and easily addressed through clinical intervention (n = 4). Reports of persistent personality change were extremely rare and were attributed to previously undisclosed or undiagnosed psychiatric conditions or vulnerabilities (n = 2).

Often you can get around [personality change] with using different electrodes in your programming and so on. It's not something that you are not going to be able to fix generally

speaking…So, yes you can see some personality change, but I've not seen one that's permanent. (DBS Nurse 8, PD)

Causes of Personality Change

Due to this transient nature and time-dependent relationship with stimulation adjustments, clinicians attributed most personality changes directly to the stimulation effect (n = 6).

If I turn someone's stimulation up and they start going a bit mental in here…then I will turn down the stimulation, simple as that…That's a normal stimulation-induced side effect. If I turn it up high enough, I'm going to cause that in most people. I avoid doing that as much as possible by turning things up slowly. (Neurologist 7, PD)

However, some acknowledged that the process of determining the cause of the changes was more complex than just the stimulation effect itself (n = 5), with adjustment to treatment outcome, medication adjustment, disease progression and psychosocial changes all playing a potential role.

[Personality change] can be for multi-fold reasons. One is obviously adjusting to the change that's happened after DBS. One is…the time adjusting their DBS stimulator because that can actually affect their cognition and mood. The other is there's often a concomitant adjustment in their medication. So, making sure that you're not reducing something, like, they're having withdrawal from dopamine agonist…you need to balance that all up. (Neurologist 11, PD)

Some clinicians noted the rarity of marked or extreme personality changes, acknowledging that an exacerbation or magnification of pre-existing personality traits was more common (n = 4).

I don't think it's common where it's really out of the blue and it's…changed their personality…it's usually an exacerbation of an underlying situation. (Neurologist 3, PD)

In some cases, alleviated motor symptoms were described as increasing patient and caregiver focus on other negative features that had likely developed with the disease (n = 1).

[DBS] unmasks their frustration with…the negative features as you might say, the apathy, amotivation features of the Parkinson's to remove some of the motor features. (Neurologist 1, PD)

Conversely, others noted that alleviated motor symptoms often led to positive personality changes (n = 2).

The most common outcomes I've seen is that sort of irritability or that frustration that came beforehand with the illness and not being able to do things…is lessened because their symptoms have improved. (Neuropsychologist 9, PD)

Unlike clinicians working in PD, clinicians working within psychiatric conditions did not describe changes in patient personality following DBS. For example, transient hypomania (n = 1) and mania (n = 2) were reported in patients with OCD following DBS, but these were conceptualised as adverse events rather than personality change. In patients with MDD that had received benefit from DBS, clinicians felt what they observed was a restoration of patients' premorbid personality, revealed through the alleviation of their depression. When asked whether they had witnessed any personality changes in their psychiatric patients, clinicians responded:

No…Certainly a restoration of their personality, but not a change in a way that I would say that it's bringing out different personality characteristics that weren't either there as part of the way they were when they were well or unwell before…Their depression going away is obviously a very profound impact on all those things…so the changes in the way they interact with people around them and the world around them changes quite profoundly…I'm not trying to conceptualise that as personality change. I think I'd just conceptualise it as them being fundamentally different people well than they were when they were unwell. (Psychiatrist 15, MDD)

Not personality, no. With response, they've had improvements in their depression, which has changed the way they interact with people…I'd say that's removing an illness, not changing their personality, but depends on the nuance that you mean by personality…It just allows their personality to show really…there have been patients who haven't looked me in the eye, haven't smiled, haven't asked a question, haven't really spoken anything more than the very bare minimum and when they've had relief from their depression, they've smiled, they've looked at me, they've asked how I'm going, they've told me stories about their family…I guess the way I describe it is more of, not necessarily a change of personality, but just letting their personality actually show because they have been quite significantly depressed and haven't been able to engage at all. (Neuropsychologist 16, MDD)

The tendency for severe psychiatric illness to obscure personality was noted by others, with a likelihood of illness-specific personality profile features dominating.

> *I think it's very hard to get a sense of somebody's personality when they're very unwell with any sort of psychiatric disorder. And I think it can exacerbate personality vulnerabilities as well if you're very unwell.* (Psychiatrist 14, OCD)

Unlike MDD where response to DBS was associated with a restoration of premorbid personality, clinicians working in OCD noted how regardless of response there was a persistence of a personality established early in their life and engrained with the illness (n = 2).

> *The majority of [DBS OCD patients] have had onset of their illness in their teens or earlier in some cases. Their entire personality structure, their entire life, has really revolved around their illness and around the OCD, and what it means to be a person with OCD, and what it means to be a person who is sick and disabled.* (Neuropsychologist 9, OCD)

This was compared with PD, an illness that emerges later in life.

> *In Parkinson's…their symptoms develop later in life. They've had a life, they've had a chance to develop an intact personality, an intact structure.* (Neuropsychologist 9, PD)

Impact on Patient and Family

Clinicians described the significant impact personality changes associated with DBS had on caregivers and family. A common reflection was that personality changes were considered stressful, distressing and concerning for families (n = 5), especially if impulsive, aggressive or ICD changes were involved.

> *It can be very stressful for the family…if there is a change in behaviour in this way, say hypomania or impulsivity, it can be very distressing.* (Neurologist 7, PD)

Caregivers' frustration with apathetic or motivational changes was also noted (n = 2), along with the devastation of feeling as though their once attentive and engaged partner or parent has been lost.

> *I see it quite frequently that those apathetic motivational things are a carer stress, it's frustrating. Every so often somebody…will break down crying and say 'I've lost my man, he used to be so on the ball and always doing things and having ideas, and [now] he just sits there and only speaks when spoken to'.* (Neurologist 1, PD)

In addition to these emotional experiences, personality changes were identified as having substantive consequences for patients, including their intimate and social relationships (n = 3). Clinicians indicated both directly (n = 2) and indirectly through common use of male pronouns that often the issues arose from changes in men.

> *It's often a case the patient has changed his behaviour in some way and that is impacting the marital relationships, whether it be through verbal irritability or loss of affection…it can be really harmful for their spouse or relationship in particular.* (Neuropsychiatrist 2, PD)

Behaviours with notable financial, legal and ethical implications were described also.

> *We've had people gamble away the family savings, we've had people try to open nightclubs…when they're cognitively impaired. We've had people buy expensive sports cars on auction sites, we've had people assault police officers and be charged, we've had all sorts of weird, sexual fetishistic behaviour from dress up dolls to sex toys to cross-dressing to your more boring prostitutes…it's really out there for some people.* (Neuropsychiatrist 2, PD)

Clinicians described a period of adjustment revolving around personality changes that emerge following DBS and how this could contribute to a persistence, rather than reduction, in caregiver burden.

> *I think it's not really true that [caregivers] have to do a whole heap less. You still have Parkinson's, it's just a different sort of Parkinson's. I think sometimes they have more adjustment to the patient's change in energy, personality, mood, and those sorts of things rather than just their motor function, or their role.* (Neurologist 11, PD)

Conversely, some clinicians acknowledged the capacity of caregivers to easily accommodate personality changes (n = 2), especially in the context of disease and medication-related changes already experienced.

> *I think people have the great capacity to be accommodating for change and being quite comfortable thinking 'oh, it's just this'. He's still Bob or she's still Mary, but it's just this other little change that you just get on with it.* (Nurse 5, PD)

Communication, Comprehension and Awareness

Most clinicians reported discussing the risk of personality change with patients and caregivers during the informed consent process. The purpose of this was to increase patient and caregiver awareness and understanding, sometimes using a physiological framework or metaphors, to promote vigilance of changes, and to reduce stress and provide reassurance when changes emerge.

> *They would have been well consented about the possibility of these after an operation. So, it's not usual that they just were wandering around not knowing what was happening. They knew that this was a potential to happen, so they usually seek medical advice, and then we adjust their treatment accordingly. Sometimes just having a structured framework around the symptoms is better than just sort of not knowing, or not appreciating that there has been change in the person with the operation. So, appreciating that difference.* (Neurologist 11, PD)

A number of clinicians noted a common lack of patient insight into their personality changes (n = 4). For this reason, some clinicians described seeking an advance directive from the patients during the consent process regarding future stimulation adjustments (n = 2).

> *Usually, the patient resists adjustment of the stimulation because typically they lack insight unfortunately is the characteristic phenomenon. What we are very careful to do is when we take consent for this procedure, we make sure that we documented that they're aware of these stimulation-dependent changes. We ask them to tell us would they like us to intervene if we or their family believe that their behaviour was changed for the worse following this operation. We've always been able to say to people, 'Remember this conversation we've had? I think this is happening, we need to adjust your stimulation'. Typically, when we do that the changes remit almost immediately.* (Neuropsychiatrist 2, PD)

This characteristic lack of insight in patients was one reason that most recommended caregivers or family attend consultations (n = 4).

> *To have a reference body is incredibly important, because often a person who's experiencing some of those behaviours is oblivious to them…Most individuals are not so aware that there's been some change…it's one of those things where people often assimilate that into normal life.* (Nurse 5, PD)

One clinician felt that patients were often aware of the changes, but may consider them a positive consequence of the intervention.

> *Many times, the patient recognises it themselves, it's not something that they don't recognise. It's just that they may not be the first person to mention it because they may actually think it's a bit of a benefit from the operation. But they may have just some difficulty judging whether it's actually a true benefit, or whether actually it's a side effect that is maybe going to put a dent on their relationships and their social circumstances if you know they've become a little bit too energised or too, too…driven.* (Neurologist 11, PD)

Some clinicians noted that patients and caregivers may not raise certain changes, especially when they're of a sexual nature, due to discomfort or embarrassment and may downplay them as a trade-off for improved motor symptoms. Clinicians described their approaches for eliciting this information, both directly and indirectly.

> *The partners and the patients might not be so readily to talk about that, saying 'It's not really a problem, it's just a little bit of a change'. That comes back to the skill of the clinician to actually ask the questions that draws out that sort of information, so that's hidden as little as possible…I actively try and draw it out in the right situation…On the topic I might get out there and say 'Well, has the sexual behaviour changed?'…but, subtle indicators like 'Well, what time do you go to bed?' If someone used to go to bed at 10 o'clock and now they are up playing games on the internet at two o'clock in the morning, that's a big change…that gives me a clue that maybe we are driving the engine a bit more.* (Neurologist 7, PD)

DBS nurses (n = 2) reported that they are often approached by patients and caregivers first about personality change rather than the treating neurologist, due to easier accessibility (direct-line phone call), and being perceived as more approachable and less busy.

> *They will be in the [consultation] rooms and they won't tell us…and the next day I'll get a phone call if there is a problem…That is not uncommon…people still have doctors on a pedestal…particularly in older people.* (DBS Nurse 8, PD)

Management

Clinicians described signs that helped them determine whether patients were experiencing a change in personality, including the presence of behaviours not observed preoperatively.

> *Usually that they're too good to be true. The smiling, there's probably just an air of aggression comparatively to preoperatively, the stressed caregiver. There's a lot of…'I'm not allowed to tell you' or 'I'm going to tell you something but don't tell them' and 'I feel like my old self again'…They're disinhibited, it's quite obvious and people like that are quite likeable. If you have a nice happy person that's got a positive attitude sitting in front of you as a health professional, you'd much rather deal with that person than someone who is all grumpy and negative. So, that in itself is an alarm bell. If you know this person preoperatively, they were just a bit quiet or reserved and now they're out there giving everyone a hug and a kiss…you think 'yeah…we might just re-evaluate that'. So, you get all hands on deck, talk to those around them and just say 'yeah, they've been doing some weird stuff'. You can address that.* (DBS Nurse 4, PD)

Some clinicians emphasised the importance of early detection and intervention, due to potential negative long-term consequences associated with increased impulsivity or disinhibition.

> *Managing [personality change] and being able to pick it up quickly and act on it without it destroying…the person's reputation, their standing, where they stand in their little societal group. You've got to be very careful that that doesn't snowball.* (DBS Nurse 4, PD)

Stimulation-induced changes, including increased impulsivity or impaired decision-making, were perceived by some as problematic and unacceptable side effects of DBS.

> *It will most often be change in decision-making and impulsivity…They are things that patients are warned about, we talk about. They would be the most common things and again completely expected side effects and one that we would adjust the stimulation for…in a way that it's unacceptable to have someone moving too quickly with their feet and wriggling around the place, it's unacceptable to have someone moving too quickly in their thoughts and behaviour.* (Neurologist 7, PD)

The importance of specialist DBS clinical care and the limited knowledge of most health care professionals about DBS was raised (n = 4), with examples of inappropriate management and response to personality change.

> *I've had more experience with taking over other patients' management who have been stimulated or programmed by other doctors who in some cases have been in nursing homes from being so spaced out and personality change. A guy I saw yesterday, and I've been managing for seven years now, he's still driving a car, living independently in a flat, 43 years into Parkinson's disease. But when I met him, he was in a nursing home and completely psychotic and completely behaviourally intolerable for any nursing staff. Now he is independent…seven years down the track.* (Neurologist 7, PD)

Clinicians described being approached by patients or families with concerns about undesirable changes in the patient and their process for evaluating potential influential factors, including unmet expectations, a previously undisclosed psychiatric history, or stimulation or medication-related effects.

> *The first thing…I would be trying to do is just decide whether this was a matter of unrealistic or unrealised expectations or an affective state that I wasn't really aware of beforehand. Or whether in fact, it was really just simply due to the medications and stimulator settings and therefore could be fixed pharmacologically or therapeutically.* (Neurologist 3, PD)

Clinicians described having initial hypotheses about the underlying cause of the change and attempts to confirm or disconfirm these, while addressing the changes. These attempts often involved an ongoing process of stimulation adjustment (including reducing or stopping stimulation), medication review, neuropsychological testing, psychological counselling and feedback from patient and family. The following is one such example:

> *One of the patients I saw today, she's probably a year and a bit down the track [post-DBS] and her partner is concerned about her cognitive performance being off. Sure enough, after repeating the cognitive testing…she is a bit flatter in some of her cognitive processes. It may have been related to the DBS – that was one of the thoughts. Earlier, maybe two months ago when she came in, she was making some reasonably personal comments…This seemed unusual, a bit like you*

might expect from a manic person. On the basis of the cognitive changes and what I perceived or understood to be a little bit of impulsivity and disinhibition we sort to turn down the stimulation to try and reduce those side effects and improve the cognition and change in behaviour. In fact, seeing her today she is actually worse with it all turned down. The cognitive changes are just normal progression of Parkinson's disease. The disinhibition, well, in fact on reflection the partner says 'I wouldn't entirely expect her not to say that'. (Neurologist 7, PD)

Discussion

This study provides important empirical insights into personality changes from clinicians with expert knowledge in DBS for both neurological and psychiatric conditions. According to the clinicians we interviewed, personality change following DBS for PD is a significant phenomenon they encounter and are required to manage. The types of changes they see are consistent with those reported in the literature, including increased aggression (Lewis, Maier, Horstkotter, Zywczok, et al., 2015), disinhibition (Kumar et al., 1998), apathy (Funkiewiez, 2004; Houeto et al., 2002; Lewis, Maier, Horstkotter, Zywczok, et al., 2015), hypersexuality (Krause et al., 2001; Romito et al., 2002), mirthful laughter (Krack et al., 2001), reduced empathy (Mosley et al., 2018), hasty decision-making and impulsivity (Mosley et al., 2018; Pham et al., 2015), and episodes of hypomania and mania (Herzog et al., 2003; Krack et al., 2003; Romito et al., 2002). In the literature, changes in depression, anxiety and impulse-control disorders following DBS for PD are mixed (some indicate overall improvements within samples, others declines) (Voon et al., 2006), and these divergent outcomes were reflected in the clinicians' comments. Instances of increased irritability (de Haan, Rietveld, Stokhof, & Denys, 2015) and transient episodes of mania (Haq et al., 2010) and hypomania (Mallet et al., 2008) described by our sample of clinicians working in OCD, have also been reported in OCD DBS literature. The nature and prevalence of personality change differed substantially according to treatment indications (e.g., PD, MDD and OCD). This finding supports Gilbert et al.'s third key observation that post-DBS outcomes must be considered in the context of their disease-specific pathology. The clinicians we interviewed also emphasised the transience of personality change. This is consistent with the literature which shows that changes are primarily identified during the first three

months post-surgery (Voon et al., 2006). This is an important finding as personality change is often discussed within the neuroethics literature as a lasting or enduring change. Rare cases of persistent post-DBS changes were attributed to undisclosed or unmasked psychiatric disorders or features, which aligns with conclusions from previous PD samples (Houeto et al., 2002).

Evaluations of the Cause and Nature of Personality Changes

Gilbert et al. (2018) noted how the neuroethics literature commonly ascribed post-DBS changes in personality to the DBS device, ignoring other potential psychosocial or pathological factors described in first-hand primary studies. In contrast, the majority of clinicians we interviewed believed that changes in personality were attributable to a variety of causes, including the DBS, as well as psychosocial, pathological and pharmacological factors. In certain circumstances, particular types of changes were more or less likely to be attributed to a specific cause. For example, in PD changes where the patient appeared more impulsive, manic-like or "driven" were often attributed to the stimulation, a view that was confirmed via their amenability to stimulation adjustment. Low mood or apathetic changes were sometimes attributed to post-DBS reductions in dopamine replacement medications and confirmed when improvements were seen following a review of medication dosage. However, clinicians displayed an openness and acknowledgement of a confluence of factors potentially playing a role (e.g., medication changes, adjusting to alleviation of chronic illness, disease progression, unmet expectations). A benefit of using qualitative interviews was that clinicians were able to discuss the neurobiological and psychosocial complexity of this issue and were not limited to pre-determined responses, as it were in the previous clinician survey (Christen et al., 2014). Definitively determining the mechanism by which personality change occurs is extremely difficult, and attempts to design a study to address this question would involve various theoretical, logistical and ethical challenges (e.g., differentiating between direct versus indirect effects, deciding what form a control condition should take, delaying patients with PD timely access to an effective and established treatment) (Pugh, Pycroft, Maslen, Aziz, & Savulescu, 2018; Schüpbach et al., 2014). In the absence of study methodologies capable of determining the mechanism of change, it is understandable that clinicians rely on temporal causation. For example, impulsivity that emerges

during stimulation titration, then remits following adjustment, is likely de novo, while cognitive changes that emerge 18-months post-DBS with no recent adjustments are likely neuropathological.

Considerations for Future Research of Post-DBS Personality Change

Gilbert et al. (2018) called for further first-hand primary research on post-DBS personality change to better characterise the issue and to provide more accurate prevalence rates. This information would reduce the level of speculation within the neuroethics literature and assist prospective patients and caregivers evaluate DBS-related risk. The reported prevalence of personality change in the current sample of clinicians was extremely variable, but the majority had witnessed or experienced transient personality changes following DBS within their own or others' patients. A number of factors may contribute to this variability, including: 1) length of career in DBS and overall number of DBS patients (as noted, higher instances were reported by clinicians with greater experience), 2) role within the medical team, typical length of patient-clinician relationship, and amount of post-DBS contact with patient (e.g., a neuropsychologist conducting pre and post assessments only may be less likely to observe changes than a neurologist who has treated a patient for 10 years or a DBS nurse who has extensive contact with patients and families in the months following surgery), and 3) individual differences in clinical practice, such as thresholds for candidate selection (age cut-off, timing of DBS) and approaches to manipulating stimulation (e.g., conservative titration, frequency of adjustments). Each clinician and DBS site will function differently, so a degree of variation is to be expected. The research literature documents variable figures of personality and behavioural changes following STN-DBS (0.5% - 40%), some of which are attributed to differences in criteria (Christen et al., 2014; Mosley et al., 2018; Voon et al., 2006). As some participants suggested, rates of personality change may be decreasing with improvements in practice. This rationale was used to explain lower rates of personality change provided by surveyed clinicians when compared with figures from ageing studies (Christen et al., 2014).

In order to gain a wider and more accurate indication of current rates and types of personality change following DBS, further research using quantitative methods is required. With the exception of a personality scale used in an OCD clinical trial, clinicians in the current study rarely administered personality scales to their DBS patients. Behaviour rating scales have been recommended for

neuropsychological follow-up with DBS patients (Pillon, 2002), including the Frontal Systems Behavior Scale (FrSBe; formerly the FLOPS) (Denheyer et al., 2009; Stout et al., 2003) or the Iowa Rating Scales of Personality Change (IRSPC) (Barrash et al., 2000). The FrSBe assesses behaviour disturbances associated with damage to frontal-subcortical brain circuits in the form of three frontal syndromes: apathy, disinhibition, and executive dysfunction – each of which were mentioned and described by the current clinicians. Self, family and clinician versions of the FrSBe allow for a comprehensive evaluation of patient behaviour. Similarly, a number of characteristics assessed by the IRSPC were described by the current clinicians, including: irritability, impulsivity, obsessiveness, lack of insight, social inappropriateness, apathy, depression, and anxiety. Such measures would be sensitive to these changes, regardless of the underlying cause (neurodegenerative process, stimulation effect, medication-related side effects, or unmet post-DBS expectations) and more appropriate for assessing individuals with neurological disorders than traditional psychological personality inventories (e.g., NEO Personality Inventory; Minnesota Multiphasic Personality Inventory). Routine pre- and post-surgery administration of these measures would have benefits in both research and clinical capacities. In research, administering at regular timepoints (e.g., 3-, 6-, 12-months and longer post-surgery) could provide more accurate information about patterns of personality change following DBS including the types, frequency, timing and duration of changes – all important information for prospective patients and caregivers. Clinically, it could be used as a tool to support consultation discussions and clinical impression, through either confirming or disconfirming clinician's suspicions or providing hints about areas missed by the clinician that require further investigation.

Many of the post-DBS patient changes observed by clinicians do not align with folk notions of personality or traditional psychology models e.g., the five-factor model of personality containing dimensions of extraversion, agreeableness, conscientiousness, neuroticism, and openness to experience. This likely explains why when responding to specific questions about *personality change,* clinicians would often instead proceed using terms such as "behavioural issues", "subtle cognitive changes", "mood or psychiatric changes", or "impulse-control problems", or use them interchangeably with "personality change". If taking a modern definition of personality, such as the "psychological qualities that contribute to an individual's enduring and distinctive patterns of feeling,

thinking, and behaviour" (p. 7) (Cervone & Pervin, 2015), the majority of the post-DBS changes described do fall within this broad and inclusive concept, with one exception. As noted by the participants, provided changes are promptly detected and treated, they are transient, not enduring, hence why they are inclined to consider them as side effects of the intervention. In previous interviews with clinicians, similar terminology such as "behavioural" or "psychiatric complications" or "side-effects" was preferred (Bell et al., 2011a) and clinical trials that have included personality measures have flexibly incorporated them into broader examinations of 'neuropsychological consequences' (Saint-Cyr et al., 2000) or 'psychiatric and social outcomes' (Boel et al., 2016). Gilbert et al. (2018) acknowledge the grounding of the PIAAAS terms in philosophical, rather than scientific, discourse and use of these search terms likely restricted their selection of first-hand primary research exploring personality and patient change. This highlights a disconnect in the language used in clinical and scientific communities compared with the neuroethics and bioethics fields, warranting a need for greater interdisciplinary collaboration. An extensive body of empirical literature capturing these issues exists, but is described using broad and flexible terminology, that is incongruent with the highly specific PIAAAS terms. This signifies a need for a common language for the scientific and ethics communities to be able to communicate on these issues. Such a language could be informed by the phenomenological experiences of patients and families involved in DBS or stem from broader use of a descriptive tool such as the FrSBe.

Implications for the Clinical Management of DBS

Irrespective of whether their aetiology is technology, pathology or psychology, it is apparent that personality changes do emerge following DBS. Given their potential for significant negative outcomes (e.g., recklessness financial decisions, marital conflict) this raises important ethical questions about how such changes are managed. The potential for post-DBS personality change was a risk most clinicians conveyed to patients and family during the informed consent process. However, there was minimal indication of the manner in which information was conveyed, how comprehension of risk was assessed, and whether patients and caregivers retained this information. Normative judgements whereby clinicians assumed that information discussed preoperatively was fully understood and would be retained post-operatively were apparent. DBS is a complex intervention that

is often offered at a time of great upheaval that can impair a prospective patient's ability to take in and appreciate the various risks that it raises (Bell et al., 2011a). It is understandable that the risk of personality change is overshadowed by more dire and immediate concerns related to surgery (e.g., cerebral haemorrhage, seizure etc.) (Christen et al., 2014; Mosley et al., 2019; Thomson, Segrave, Gardner, & Carter, 2019) or simply forgotten amongst the dense information that a patient and family must comprehend. The cognitive and emotional features associated with disorders such as PD, MDD and OCD also need to be considered in terms of how information is delivered (e.g., small information loads across multiple meetings, written information, recall checks) as they can impact comprehension and retainment. Post-DBS for PD, the issue can be further complicated by lack of patient insight into personality and behavioural changes noted here and elsewhere in the literature (Mosley et al., 2018; Saint-Cyr et al., 2000); although this certainly does not apply to all patients (Denheyer et al., 2009). The routine inclusion of a partner, family member or close-other during medical consultations is integral, with both DBS and other medical treatments such as dopamine agonists. This is not only to increase caregiver awareness and understanding of what might occur, but so that they can provide informed observations if the patient experiences personality change that may impair their insight or decision-making. Clinicians could also employ some form of corrected feedback during the consent process (i.e., assessment of the patient and caregiver's comprehension of the potential risk of personality change) to ensure that they have fully understood the information presented to them (Festinger, Dugosh, Croft, Arabia, & Marlowe, 2010). The advance directive approach discussed by some participants has been examined and debated within the neuroethics literature, with pragmatists suggesting advance directives, specifically Ulysses contracts, allow patients to exercise autonomy while promoting beneficence (Müller et al., 2017). In a Ulysses contract, a patient requests a future course of action related to their treatment should their decision-making capacity be later impacted (e.g., during DBS-induced mania where patient is against adjustment). This process would ideally strengthen patient and family comprehension about the risks of personality change, while allowing them to make an informed and valid judgement about their future treatment. A Moral Case Deliberation protocol has also been reported as an approach to managing discrepant perceptions of post-DBS changes between patients and families. This involves as highly consultative process

between the patient, family and a multidisciplinary team where the patient's autonomy and authenticity are reviewed and evaluated. However, this approach has only been described briefly with a case of a DBS patient with depression and requires further investigation (Widdershoven, Meynen, Hartman, & Denys, 2014). The benefits of a multidisciplinary DBS team (e.g., neurology, neurosurgery, neuropsychology, psychiatry, nursing) for the prevention, identification and treatment of transient personality changes has been frequently noted (Bell, Maxwell, McAndrews, Sadikot, & Racine, 2011b; Christen et al., 2014; Kubu & Ford, 2012; Mosley et al., 2018). In addition to specialised skill sets, participant comments indicate that time-constraints and approachability of different team members influences communication with DBS patients and families. The extent to which clinicians discuss and elicit information about personality change during post-operative consultations with patients and caregivers varied significantly in our sample. The potential for patients and caregivers to consider this information embarrassing or as a trade-off for other improvements highlights the importance of clinicians regularly creating opportunities to openly discuss such changes. Creating regular opportunities to discuss and explore possible changes appears vital, given the importance of early detection in ensuring that changes in the patient's thinking, behaviour or mood do not result in negative outcomes with long-term consequences.

Conclusion

This study responds to the speculative neuroethics bubble proposed by Gilbert et al. (2018) that asserts DBS causes personality change, by exploring DBS clinicians' experiences of personality change and their beliefs about how the intervention influences patient personality. Based on clinicians' various descriptions of personality changes in patients with PD, it appears that this is a legitimate post-DBS phenomenon that many experience and are required to manage. Direct brain stimulation was only one of a confluence of factors clinicians believed to be involved in postoperative personality change. Stimulation-related personality changes were mostly evaluated as unacceptable and problematic side-effects, due to their potentially negative impact upon patients and families. However, the risk of transient personality change should be weighed against the common benefits of DBS and considered in the context of personality changes that occur as a result of the disease and as

side-effects of pharmacological treatments (Christen et al., 2012; Mosley et al., 2019). In psychiatric conditions, restoration of personality through alleviation of illness was considered desirable. Further research using quantitative methods is required to provide a more accurate indication of current rates, durations and types of personality change following DBS. Clinicians often used broad and inclusive terminology to discuss personality change, and this clinically-informed language is often incongruous with the dialogue surrounding patient change favoured in the neuroethics and bioethics literature. The umbrella term 'personality change' is unlikely to be shirked entirely, but needs to be regularly caveated by the words 'transient' or 'reversible', to reflect that changes should be temporary provided they are appropriately managed. The potential for personality changes following DBS appeared a key component of most clinicians' informed consent process; however, normative judgements about how this information is comprehended by patients and caregivers and retained post-operatively was demonstrated. Patient and caregivers' awareness and understanding of the risk of personality change following DBS is an area of ethical importance requiring further exploration. Due to the characteristic lack of patient insight into personality and behavioural changes described here and reported elsewhere in the literature, the following recommendations informed by clinicians' experiences are made: 1) routine inclusion of caregivers, family or close-others in both pre- and post-operative consultations, 2) tailoring the delivery of information to the cognitive and emotional profile of the patient 3) wider practice of advance directives from patients regarding future adjustments to stimulation, and 4) routine discussion and assessment of personality changes during clinical consultations. These recommendations should result in reduced instances of personality changes involving negative and potentially long-term consequences, and allow for a more ethical, clinical response to personality change associated with DBS.

CHAPTER FIVE

‘HE’S BACK SO I’M NOT ALONE’: THE IMPACT OF DEEP BRAIN STIMULATION ON PERSONALITY, SELF AND RELATIONSHIPS IN PARKINSON’S DISEASE

Chapter Five – 'He's Back so I'm not Alone': The Impact of Deep Brain Stimulation on Personality, Self, and Relationships in Parkinson's Disease

Preamble to Paper Two

The following chapter presents an original research article first published online in the journal *Qualitative Health Research* in August 2020. This chapter extends upon the previous discussion of clinician perspectives and experiences of personality change in patients following DBS by exploring the actual experiences of patients and caregivers themselves. The paper reports on the findings from interviews conducted with eleven patient-caregiver pairs prior to and following DBS for PD. The aim of the study was to prospectively examine the meaning and significance of DBS-related changes in personality and self for patients and their caregivers. So as not to exclude individuals without spouses, individuals with a non-spousal patient-caregiver relationship also participated (parent/child relationships represented in sample). In line with journal guidelines, participant pseudonyms or identifying numbers were not included in the manuscript. Instead, the main text is used to highlight important comparisons in perspective or experience across pairs or time points. These findings reflect the complexity of these experiences and need to consider them in each patient's individual context, including their adjustment to chronic illness, existing relationship quality, history of undesirable changes associated illness or treatments, and the outcome of their procedure. The results are followed by a discussion of the impact of DBS on patient personality and its role in patients' experience of self. Clinical practice implications for patients are caregivers are also explored.

The supplementary material referred to in this paper includes participant demographic information, interview schedules and an overview of the identified themes with example quotes. These can be found in *Appendix F*.

Abstract

Deep brain stimulation (DBS) for Parkinson's disease successfully alleviates motor symptoms, but unanticipated changes in personality, self and relationships can occur. Little is known about how these non-motor outcomes impact patients and families. We prospectively examined the experience and meaning of DBS-related changes in personality and self for patients and caregivers. In-depth, semi-structured interviews were conducted with 22 participants (11 patient-caregiver dyads) before and 9-months after DBS and analyzed using thematic analysis. We identified three themes present prior to DBS that reflected a time of *anticipation*, while three themes present after DBS reflected a process of *adjustment*. Participants noted both positive and negative personality changes, with some, but not all, attributing them to the stimulation. The risk of stimulation-related personality change should be weighed against the procedure's motor benefits and considered in the context of disease and medication-related personality changes. Clinical implications including perioperative education and follow-up management are discussed.

Keywords: Parkinson's disease; neurology; neurological disorders; caregivers; caretaking; self; experiences; illness and disease; qualitative; agency

Introduction

Deep brain stimulation (DBS) is a neurosurgical procedure used to treat severe movement disorders, primarily Parkinson's disease (PD). DBS received Food and Drug Administration approval for PD in 2002 and over 150,000 patients have since been implanted with devices (Medtronic, 2019). DBS can significantly improve motor symptoms associated with PD, such as bradykinesia, tremor, freezing and increase functional independence (Deuschl et al., 2006). However, a variety of unanticipated psychosocial changes have been reported in some patients, including aggression, disinhibition, hypomania, hypersexuality, apathy and impulsivity (Lewis, Maier, Horstkotter, Zywczok, et al., 2015; Pham et al., 2015; Romito et al., 2002). The terminology used to describe such changes in patients after DBS varies across research and clinical practice, including: neuropsychiatric symptoms, neuropsychological consequences, psychiatric complications, behavioural issues and adverse events (Thomson, Segrave, & Carter, 2019). To best explore a broad and inclusive range of patient experiences (i.e., in thinking, feeling and behaving), we have chosen to examine *personality change*.

Patients have also experienced changes in how they perceive themselves and their body after DBS. Some feel "dehumanized" by the device and see it as an alien entity, while others accept it as part of their body and who they are (Agid et al., 2006; Gilbert et al., 2017). Cases of poor psychosocial adjustment following DBS have been documented, whereby patients struggle to adapt from being chronically ill to suddenly well (Baertschi, Flores Alves Dos Santos, et al., 2019; Bell et al., 2011b). This is often referred to as the *burden of normality* (Wilson et al., 2001). Researchers have speculated on the potential for personality change and poor postoperative adjustment to negatively impact interpersonal relationships, particularly with spouses (Agid et al., 2006; Schüpbach et al., 2006). However, there is limited research on patient and caregiver perspectives on the causes of these outcomes and their significance.

Reports of undesirable personality changes and feelings of self-estrangement following DBS have prompted significant interest in the field of neuroethics. These changes have been widely debated according to various philosophical interpretations of identity and self (e.g., personal identity, autonomy, authenticity) (Baylis, 2013; Glannon, 2009; Kraemer, 2013a). Some neuroethicists and

clinicians have raised concerns about the potential sensationalising and inflating of the putative effects of DBS on personality and related concepts (Gilbert et al., 2018). These include the tendency for articles to ignore, distort or misrepresent empirical findings and that the alarmist discourse could produce unjustified fears that deter patients and families from pursuing a potentially beneficial treatment (Kubu et al., 2019). To address this sensationalism, first-hand empirical studies investigating the meaning and significance of DBS-related changes for patients and families are required. The role of related issues in the presentation of personality changes also need to be considered (e.g., prolonged impact of illness, expectations for DBS, adjustment to treatment outcome).

To achieve this, a prospective, in-depth qualitative approach involving both patients and caregivers is required. Standard psychometric personality measures are not designed to detect the types of changes associated with DBS and there are limited reliable measures that examine complex concepts such as self and identity (Kubu et al., 2019; Lewis, Maier, Horstkotter, Zywczok, et al., 2015). Personality changes associated with DBS can be transient, remitting with stimulation reprogramming, and therefore, may not be present at the exact time of assessment. Crucially, the meaning of what a given change in personality represents to a person, its impact on a person's life narrative and sense of self is best understood using an open-ended, qualitative and narrative-oriented approach. This has the advantage of reflecting the relational aspects of personal identity, as well as the limits of self-awareness and insight into one's own behaviour (Barclay, 2000; Mead, 1934). Relational dynamics, including with spouses and close relatives, are generally self-shaping relationships (Overall, Fletcher, & Simpson, 2010) and have been shown to be affected following DBS (Agid et al., 2006). Patients can have limited insight into their changed behaviour, with caregivers noticing changes patients themselves are unaware of or unconcerned with (Pham et al., 2015). Caregivers are also directly affected by the changed behaviour, so their perspective provides additional insight into DBS' broader relational and social impact (Haahr, Kirkevold, Hall, & Ostergaard, 2013). With the exception of a phenomenological case study (Eatough & Shaw, 2017), qualitative research thus far has been primarily retrospective. This requires patients and caregivers to reflect on their preoperative and premorbid states months after surgery. Retrospective recall can be

biased by current circumstances and interim events, leading to an inaccurate reflection of an individual's actual experience (Schacter, Chiao, & Mitchell, 2003). In taking a prospective, longitudinal approach, a nuanced psychosocial picture of the patient-caregiver dyad prior to DBS can be created and contrasted with post-DBS outcomes. Capturing patient and family voices highlights personal needs that can guide more patient-centred approaches to DBS clinical care (Eatough & Shaw, 2017; Hariz, Limousin, & Hamberg, 2016).

The purpose of the current study was to examine the significance and meaning of DBS-related changes in personality and self for patients and caregivers. In doing so, we addressed the following research questions: 1) To what extent are patients and caregivers aware of the risk of DBS-related personality change?; 2) What, if any, changes in patient personality or sense of self are experienced following DBS?; 3) What do patients and caregivers consider the cause of such changes?; 4) What impact do these changes have on patients and caregivers?; and 5) How is unintended personality change managed clinically?. This is the first study to conduct a *prospective*, qualitative analysis of both DBS patients with PD *and* their caregivers that addresses these issues.

Methods

A prospective qualitative study design was used to explore participants' perspectives, expectations, and experiences of DBS at significant time points (pre- and post-surgery), with a particular focus on patients' personality and self. The term personality is often understood differently between psychological and sociological disciplines. Rather than restricting participants' responses, and our qualitative interpretation of them, to one framework or definition we purposefully adopted the participants' own understanding of personality. Research ethics approval was obtained from Monash University Human Research Ethics Committee (CF16/1888-2016000963) prior to conducting the study and written informed consent was received from all participants.

Participants

Purposive sampling was used to recruit individuals with PD preparing for DBS in the Melbourne, Victoria region via neurologists specializing in movement disorders. Participants were eligible if they: 1) had a diagnosis of PD; 2) were scheduled for DBS surgery; 3) were aged between

18-75 years; 4) were able to provide informed consent; and 5) had a caregiver (spouse, family member providing daily support) who was willing to participate. Exclusion criteria for patients included: dementia, severe psychiatric or additional neurological disorders (typical DBS contraindications assessed by the medical team during the selection process). Eleven patient-caregiver dyads preparing for DBS agreed to participate. Patients were seven men and four women, ranging 45 to 73 years of age. Six were employed and five had retired. Time since PD diagnosis ranged from 3 to 12 years. Caregivers were two men and nine women, ranging 51 to 69 years of age. They included spouses (n = 9), parents (n = 1) and children (n = 1) and had known the patient for 29 to 51 years (additional demographic information in Supplemental File). Two patient-caregiver dyads did not complete follow-up interviews; one due to the patient ultimately deciding not to undergo DBS and the second due to health issues. One dyad completed two follow-up interviews; the first 9-months after an initially unsuccessful surgery due to infection and the second 9-months after a subsequent successful re-implantation. The subthalamic nucleus (STN) was the implantation site for all patients, except one with globus pallidus. Small samples are suited to longitudinal interview-based studies of this kind, as they require the fostering of positive, on-going relationships with participants and produce an abundance of rich, complex data (Crouch & McKenzie, 2006). Data saturation was achieved at each time point, which suggests that the sample size was appropriate.

Procedure

Audio-recorded, semi-structured interviews were conducted with participants between May 2017 and January 2019. Pilot-tested interview schedules were used, one for each participant type (patient/caregiver) and time point (pre-/post-surgery) (see Supplemental File). All interviews were conducted by Cassandra Thomson. Separate interviews were conducted with patients and caregivers to allow for open discussion and discrepant perspectives (Mellor, Slaymaker, & Cleland, 2013). Pre-surgery interviews were conducted 3-25 days (M = 13) prior to surgery. Follow-up interviews were conducted approximately 9-months post-surgery. Interviews were conducted in-person or via telephone/video-conference for participants who lived remotely or interstate. Interviews ranged in length from 30 to 120 minutes (M = 42), with a total of 30 hours recorded data collected. The interviewer maintained field notes and regularly debriefed with co-authors. These discussions were

influenced by backgrounds in neuropsychology, psychology, qualitative research and neuroethics. Audio-recordings were transcribed verbatim by a professional transcription service and reviewed for accuracy by the research team. Transcripts were not returned to participants for corrections or comments.

Data Analysis

Interviews were analysed using a thematic analysis approach whereby patterns of meaning are examined and identified inductively within the data (Braun & Clarke, 2006). This approach is suited to studies that aim to elucidate participants' perceptions, feelings and experiences. Thematic analysis also allows similarities and differences across participant groups and time points to be highlighted (e.g., patients/caregivers, before/after surgery). The analysis was conducted within a realist paradigm that assumes the language used by participants reflects the reality of their experiences and meanings (Braun & Clarke, 2006). The analysis process commenced with data immersion involving listening to audio-recordings and reading transcripts several times. Initial reflections were recorded in margin notes. An initial list of codes was continually revised, condensed and arranged into meaningful groups that reflected the emerging primary and secondary themes. Summaries for each interview from every dyad were also created, highlighting similarities and differences in perspectives across participants and time points. Cross-coding was conducted on three sets of patient-caregiver interviews. The coders compared coding approaches and minor disagreements were discussed until a consensus was reached and final coding structure developed. This structure was then applied across all interviews, with minor adjustments made following feedback from co-authors.

Results

Themes identified prior to surgery reflected a time of *anticipation*. These interviews contained a mixture of hope, anxiety, fear ("*I'm scared*"), and eagerness ("*bring it on!*") centred around the impending surgery. Overarching this was a sense of uncertainty for the outcomes of this key event and its implications for the future. Following DBS, participants had moved beyond the surgical event and were now in a process of *adjustment*, to the DBS itself, but within the broader context of ongoing adjustment to chronic illness. Interview questions focused on participants'

experience with DBS, but responses were considered in this broader context of psychological, social and physical adjustment to chronic illness (Moss-Morris, 2013) for both patients and caregivers. As questions surrounding personality change were guided by participants' own interpretations, responses included non-traditional aspects, such as changes in day-to-day routine, mood, self-confidence and bodily functioning. Results focus primarily on personality change, as this topic held relevance for participants and produced the most responses. Themes identified during the time of anticipation and process of adjustment are displayed in Figure 1.

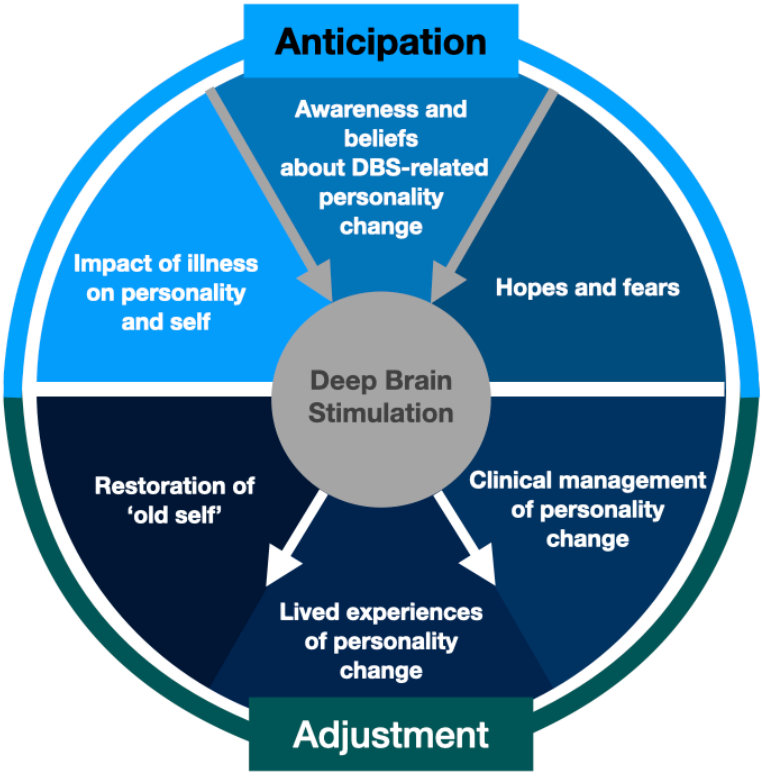

Figure 1. Thematic analysis visualization

Anticipation Themes

Impact of illness on personality and self. Throughout the interviews, participants described how the patient's personality and sense of self had been impacted or changed by their illness. Many felt that PD sat incongruently to important features of their self-concept and inhibited their ability to express their true personality. Examples include: an active, adventurous person being hampered by

fatigue and amotivation; a highly social person becoming withdrawn and apathetic; and a fiercely independent person having to rely and depend on others for support.

How PD affected expression of the patient's personality and self were varied, with physical, mobility, cognitive and speech deficits all impacting. Participants commonly stated that the illness had diminished the patient's self-confidence and that they regularly experienced feelings of anxiety, angst and embarrassment, especially in social settings.

> *I find that Parkinson's in particular undermines your self-belief and personal confidence. All those sorts of things. The Parkinson's runs sort of counter to that… people see me sort of shuffling around and knocking over the bloody water jug in restaurants and not being able to open doors.* (Patient [P])

This reduced self-confidence appeared linked to patients' perceived lack of personal control over their symptoms (e.g., freezing, excessive sweating, motor fluctuations, becoming dyskinetic) and concerns about how others may perceive and misinterpret their symptoms (e.g., due to alcoholism or a stroke, or are "*cuckoo*").

Patients and caregivers discussed problematic changes that had occurred since developing PD, either as a result of medication or the disease itself. These included the development of depression, anxiety, apathy, amotivation, impulsiveness, cautiousness, impaired decision-making and impulse-control disorders (ICDs) (e.g., compulsive gambling, shopping, eating, hypersexuality and hobbyism). The emotional impact of these changes spanned from minor inconveniences that participants stoically took in their stride to more frightening and distressing transformations. For patients who had experienced notable cognitive or neuropsychiatric changes (e.g., ICDs, medication-induced psychosis), spouses conveyed feelings of estrangement from the person they had married and known for decades:

> *This man, this personality change he's gone through, it's crazy. It's not – he's not the man I married. He's definitely not the man I married. He's changed so much. If that's just part and parcel of Parkinson's, I guess?* (Caregiver [C], discussing ICDs)
>
> *I had a whole range of behavioural problems…a whole raft of really, really odd stuff… [spouse] tells me I was really scary. That really sort of upset me to think that we've been married…a long*

time and when someone tells you that you've scared them…She said that often I've got the capacity to – only since the Parkinson's stuff – to scare people. (P, discussing medication-induced psychosis)

Participants off-set these undesirable changes by highlighting positive aspects of the patient that were robust and unwavering despite their illness, such as their positive attitude, strong character and kind "*do anything for you*" nature.

Awareness and beliefs about DBS-related personality change. Many participants reported they were unaware of the risk of potential changes in personality, mood or behaviour following DBS. For the few who were, the kinds of changes they described included depression, compulsivity, increased emotion, decreased empathy/compassion and generally "*wanting to do things differently*". Awareness of these changes had occasionally come through information provided by their DBS team, but more often other sources, such as internet pages, journal articles or other DBS patients' personal experiences e.g., losing "*your sense of empathy*" (P). A few participants were aware of some PD medications being associated with certain changes, including increased interest in gambling and alcohol, but were unaware of a relationship with DBS.

Certainly tablet-related. They talked about things to look out for in terms of drinking, gambling, and things…but yeah, not particularly after the surgery. (P)

When participants were asked if they thought DBS could change who they are/who the patient is, a few reflected it could, given the mystery surrounding how the brain functions and multiple brain regions possibly being affected. Some patients described the effects of medication on their thinking and feeling, leading them to believe another form of treatment could temporarily change who they are.

I've always been amazed that these tiny drugs can affect – have cognitive effects as well as physical. You can break a tiny one in half…and it can make a difference. (P)

Most patients (n = 9) had undergone psychiatric and neuropsychological assessments as part of the procedure screening process. Based on assessment feedback, some patients understood themselves to be in good cognitive and psychological health (i.e., cognitively intact with an absence of depression or problem gambling). This feedback encouraged a sense of self-efficacy in these patients who felt they were unlikely to experience any future personality change. A stable demeanour, "*strong*

personality" and positive outlook were also suggested as reasons for a reduced risk of personality change. One caregiver felt DBS would not change their spouse's personality, as that was not the intended purpose of the procedure:

> *[DBS is] there to stimulate for [in place of] drugs, not to stimulate his personality or change him into a monster or anything. So, no, I don't think anything about him is going to change except what it's meant to do.* (C)

When asked about how long they believed a change in personality could last, many expressed uncertainty. Others felt it would be fixable and could be addressed by their treating doctor adjusting the stimulator or changes to medication (e.g., treating low mood with an antidepressant). Turning the device off completely was considered a means by which any undesirable changes could be ceased and a reassurance. Others felt proceeding with the procedure could have more permanent consequences, depending on whether the intervention was successful or not.

> *That's one of the concerns that [spouse] has…once we go down this path, you can't go back. In fact, [neurologist] said that. He said…'you'll change, whether it's for better or worse', he said 'you won't be the same person'.* (P)

Hopes and fears. Undesirable changes in patient personality following DBS was a concern for some, particularly those who had already experienced significant personality changes as a result of disease pathology or medication (e.g., ICDs, medication-induced psychosis). These participants, particularly caregivers, expressed fears that these behaviours could be exacerbated or would re-emerge following DBS.

> *When you read up on the deep brain stimulation, it says it can actually make them [ICDs] worse. I'm thinking, oh my God, how much worse can it get?!* (C)

In cases where these fears had been fully discussed with the DBS team, they were sufficiently allayed for the pair to feel comfortable proceeding with the procedure.

Participants were asked what aspects of themselves/their close-other they were unwilling to lose or exchange for improvements in motor symptoms. Patients reflected on their socially desirable qualities, such as being caring, positive, reliable and trustworthy. They also considered the negative

consequences that could arise if these were to change, such as becoming isolated from their family and friends or disrupting their successful relationships with workplace colleagues and clients.

> *It's just me and how I treat the people around me. They're all very fond of me…I don't want to lose that. I have so many friends around me because I'm a caring person.* (P)

Caregivers expressed concerns their close-other could lose their defining characteristics (e.g., willingness to "*take life in both hands*" or "*very placid*" temperament). The extent of the change was also important, as some felt they could accept and adjust to minor negative changes, but not dramatic or serious changes (e.g., becoming violent).

> *I wouldn't want to see any kind of change that was too dramatic…if he was to become really outgoing or really inward or really selfish or – I wouldn't want any of those in exchange for his physical capabilities.* (C)

While undesirable personality changes were a concern, perioperative issues tended to be more pressing. These included anxiety about ceasing medication prior to surgery, adverse events occurring during surgery, uncertainty about postoperative care (e.g., changing bandages), aesthetic concerns (e.g., shaving hair, scarring on scalp) and ultimately whether the procedure would be successful or not.

With these concerns came hopes for desirable personality change with DBS, specifically a restoration of qualities lost through the disease or to simply go "*back to normal*". Some hoped DBS would give them the "*freedom and energy*" to express their true self and act in the world in a way they value. Particular areas participants hoped to see change were mood (be a "*happy person*" not "*miserable*"), demeanour ("*fun-loving*" not "*easily frustrated*") and social engagement and connection with others (take "*more of the world in*" not just focus on illness).

Adjustment Themes

Restoration of the 'old self'. Following surgery, several patients did experience a restored sense of premorbid self post-surgery, that was often referred to as their "*old self*". Improvements in energy, mood, motivation, cognition and mobility contributed to the restoration. This allowed them to express their true self in ways the illness had hindered. This sense of a restored *"old self"* was exclusive to patients who experienced good clinical outcomes with DBS. One patient who had their

DBS removed due to infection was able to reflect and contrast their experiences of being with and without the device, including the certainty and control DBS provided:

> *I certainly was a different person [with DBS], like going back – it was the old me rather than what we've got now…yeah, I just had more energy, more up and go, not tied down to a timeline so to speak, because I know at certain times during the day I go into an off period, so therefore I alter my life around that.* (P)

Caregivers of patients who felt their 'old self' had been restored shared this perspective, including how their mood, motivation and behaviour reflected the person they had known prior to PD. Feeling the patient was back "*to normal*" led one caregiver to refer to the disease in the past-tense, despite knowledge of its ongoing presence:

> *When she had the Parkinson's – she used to worry a lot. She used to be really down. Now she's sort of the old [spouse] I know. She laughs at my jokes, even how corny they are…yeah so, no, she's a much happier person.* (C)

These couples appeared to return to a more equitable relationship dynamic. Caregiver burden was reduced, with increased freedom to enjoy activities independently and security leaving their loved one alone overnight. Restoration of the 'old self' was associated with a sense of relief for family and friends and re-established unity for spouses.

> *Any work colleagues or friends of his [say], 'it's great to see the old [patient name] back, we were really worried there for a little while'…now I feel like I'm not totally, you know, he's back so I'm not alone again. So that's good.* (C)

Caregivers focused more on external features, such as the patient's physicality and regained facial animation. Patients tended to only become aware of these improvements from observer comments. While positive comments were mostly well-received by patients, one expressed frustration that these often did not reflect their internal experience:

> *When you see people, they go 'oh gee, you're looking well'. Yeah okay, I might be looking well, but I…don't feel that well. So, I wish people wouldn't say that…sometimes that doesn't necessarily match who you are or what you are or how you feel at that particular time…because, as you know, Parkinson's doesn't only affect movement, it affects other parts of the body.* (P)

The alleviation of debilitating symptoms provided patients with a restored sense of self-confidence. Alleviated tremor or dyskinesia were associated with reduced feelings of anxiety and embarrassment (for both patients and caregivers), leading to greater socialisation.

> *[DBS] gives me my self-confidence. If you don't feel confident, because you got shakes…because you think people think you're an alcoholic or something, it knocks you about a bit. So that, having that cleared up makes a big difference.* (P)

For a few, increased self-confidence emerged from an internal experience of improved cognitive clarity and alertness, facilitating better engagement and connection with others.

Increased certainty and symptom control, compared to medication alone, was noted as allowing patients confidence to be more independent and perform activities aligned with their values and prior selves (e.g., attending music concerts, hosting dinner parties). In contrast, those with less favourable outcomes reported a sustained experience of negative self-confidence. A key feature of these experiences were problems with speech (slurring, rapid speech, low volume, articulation difficulty and stuttering).

> *I've never had a stutter in my entire life, ever. It was only post-operation… Basically, my self-confidence has gone out the window and a lot of it is due to the bloody Parkinson's, the – this, having the stammer.* (P)

While some participants were uncertain, others were confident speech issues were an unintended stimulation side-effect due to their immediate onset post-surgery or responsiveness to stimulation adjustment. The development of postoperative issues with mobility, balance and mood also impacted confidence.

> *It would be good to know [be close to] some of my great grandkids…now I daren't. You know, I don't feel confident enough like I did before.* (P)

Lived experiences of personality change. In the nine patients followed-up after DBS, personality changes experienced varied from positive mood changes (n = 4) (e.g., being happier, more light-hearted, more euphoric), to negative mood changes (e.g., more depressed (n = 2), angry, frustrated, grumpy, irritable (n = 5)), changes in thinking and cognition (alert, quicker, clearer (n = 2); more confused, slower, forgetful (n = 3)), and changes in behaviour and interpersonal style (e.g., more

assertive, forthright (*n* = 2), fixated, obsessive (*n* = 2), impulsive, impatient (*n* = 3), demanding, disinhibited, insensitive (*n* = 1) and withdrawn (*n* = 3). Patients described exactly how they felt different from their "*normal*" or usual self.

> *At the moment, [I'm] slightly more euphoric than normal. That was one of the side effects of…one of the changes.* (P)
>
> *I'm probably more angry than I used to…I get a bit agro towards [spouse]…just suddenly started – when I can't move – bang! I get cranky quick, agro.* (P)
>
> *I've always been quite patient, but now…there are times when I've been really stubborn and times when I want to do something…then I have to go now; I have to do it now.* (P)

Participants identified a wide variety of potential causes for the changes experienced, including: 1) the direct effect of stimulation within the brain; 2) the indirect effect of stimulation through alleviating debilitating symptoms or new side-effects; 3) medication adjustments; 4) frustration with residual symptoms and unmet expectations; 5) comorbidities and additional medical procedures, and; 6) the ongoing progression of PD. Participants displayed a nuanced understanding of the potential influence of one or multiple factors and occasionally attributed different changes to different causes.

> *She was always a bit feisty beforehand, but now…she does get very defensive very quickly…It could be a mixture I think, of the DBS and muddling with her brain, and the fact that her Parkinson's has progressed, and the [cancer related] operation.* (C)
>
> *Whether [the cognitive changes] were just marred by the movement prior to and you concentrate just on one thing and forget about the others…because we concentrated so much on the movement and trying to help with that.* (C)

Pairs could describe the same observed change, but draw different causal conclusions, with patients more likely to consider the stimulation effect of DBS as the causal factor.

> *I think I fly off the handle probably a bit more than I used to…I put it down to the DBS, because it's more abrupt. Parkinson's is very gradual, well with me anyway, very gradual, takes six months for something to develop.* (P)
>
> *He gets very frustrated and exasperated. It's not like [him], he was very placid beforehand…I'm not used to him being like that and being so expressive… It could be the Parkinson's too, I think.*

Because it's still in the background…I know [another person with PD]…he was a very placid person too. He got very exasperated…So, I think that's something that probably happens. It's not necessarily the DBS. (C)

Participants described transient personality or behavioural changes that had occurred during the previous 9-months and since resolved. Two patients experienced postoperative confusion and disorientation that manifested in anxiety, emotional lability, hallucinations, vivid dreams, disturbed sleep, neediness and dependency on caregiver. These resolved with time and were attributed to the anaesthetic or the implant.

I thought it might have been…the fact that, you know, there's a foreign object in my brain. I was thinking that maybe that just disturbed things a bit. (P)

Two other patients experienced a postoperative 'high' where they were elated with their surgical outcome, while caregivers shared a more modest view. One patient was able to reflect on this period as a "*false high*", while the other struggled to come to terms with never being as good as they were in hospital. Some transient changes were considered stimulation-dependent due to their responsiveness to adjustment of stimulation parameters and included uncontrollable laughter and erratic, impulsive behaviour.

He talked incessantly, non-stop and just kept swapping from topic to topic to topic…He'd just ring people up and go, 'oh, I'll pick you up in 10 minutes'…but the neurologist just changed channels or whatever and that disappeared…Apparently, he was on a high with it. It was like being on drugs and stuff. (C)

Participants also described more sustained changes they had noticed in the months following the surgery and had continued until the time of interview. Sustained changes were often attributed to PD-related cognitive decline (e.g., poor engagement in conversation, verbal disinhibition). However, a few patients felt changes were associated with the stimulation effect (e.g., irritability, assertiveness), but had not attempted to address them as they were not considered overly problematic or were seen as a trade-off for improvements in other areas.

There was high consistency in the types of changes described within dyads (e.g., irritability, low self-confidence, positive or negative mood changes), although some caregivers reported changes

their loved one did not. Caregiver comments suggest this was due to the patient having limited insight into their behaviour, either in the context of a brief stimulation-related episode (n = 1) or progressive cognitive decline (n = 2). One patient described past behaviours where they appeared to have poor insight at the time, but following discussion with their caregiver, came to recognize it as uncharacteristic or unusual.

> *I look back on some of the things that I suggested and said, and they were ridiculous! Like buy heaters when we don't need heaters [laughs].* (P)

When exploring the impact of personality changes following DBS, transient experiences such as postoperative confusion and erratic, impulsive behaviours were particularly concerning for caregivers and raised momentary doubts about the decision to undergo DBS.

> *It was actually quite scary, his behaviour and stuff was quite erratic…[I'm] thinking is this what the future basically is with this person? Have we done the right thing?...because he was a little bit awkward to live with for a little while there.* (C)

In such instances, a resolution of the changed behaviour was a relief for the caregiver and family, but this was not always the patient's experience.

> *Whereas for him, he said it was terrible, because it was like being pulled off your medication…and being withdrawn from it, because he felt great.* (C)

The patient did not raise this particular experience in the interview and it is uncertain whether this was due to limited recall or insight, or due to feelings of shame or embarrassment. Another patient who experienced more persistent, yet minor changes (e.g., increased assertiveness, stubbornness) expressed some embarrassment when reflecting on their changed behaviour in a social community setting:

> *[In] a committee of 12, when I'd say 'well, come on, what are we going to do?' We'll go around the table and everyone says 'no' [laughs] and [I say] 'yes'. Okay…work that out…I suppose a degree of carelessness in that role, and also a degree of self - focused…not conducive to having discussions about things.* (P)

This was particularly noticeable when contrasted with comments from the same patient's previous interview where a comparable scenario was described, but with the patient playing a more passive role:

I'm chairman of the committee, so I can let everybody else make the decisions, I just sit back and say 'okay then, that's great, go with it'. We have a great committee who always produce a really good result. That's really good for me. It makes me feel great when it happens. (P)

The three reported instances of presumed stimulation-related personality change appeared to have brief or minor social implications, with the caregiver relationship mostly impacted. In response, some caregivers demonstrated capacity to accept and integrate minor changes into their lives. For example, one adjusted to an increase in compulsiveness by indulging their spouse's innocuous desires (e.g., getting an ice-cream), while being firmer and taking more time to discuss unreasonable requests (e.g., taking a spontaneous overseas holiday).

We just have more discussions I think about why or why not, particularly with money…it's probably just explaining things a little bit more to him. (C)

Caregivers were also able to adapt to changes they had initially feared (e.g., spouse no longer being placid). Other persistent changes, such as apathy and social withdrawal, could be more difficult for spouses who wanted to share activities and experiences as a couple, especially as they enter retirement. Irritability, frustration and anger were also a challenge, but how caregivers responded differed and appeared influenced by their pre-existing relationship.

I wouldn't say adjusted to [laughs]. I just tell him 'don't speak to me like that!'. Not in a nasty way…joke in a way. Because I know he doesn't mean it, he just gets a bit frustrated with himself because he gets aches and pains. (C)

I argue back, don't worry about that. I argue right back at him, I think just because you've got Parkinson's disease, you're not getting away with this. (C)

For one pair, ICDs were a pre-DBS relationship stressor with the caregiver expressing concern DBS could exacerbate them. After DBS, the caregiver felt there had been no increase, nor had DBS produced significant treatment effects beyond medication reduction.

I don't think it's made it any better or worse, I really don't think it's changed anything, to be honest, except his meds are down…but as far as the personality and [his] behaviours, they haven't changed. (C)

Notable cognitive changes, whether neuropathological or stimulation-related, had a more pronounced negative relational impact. Cognitive decline signalled a progressive loss of who the patient was and grief for family and friends. The nature of these relationships also tended to change, with caregivers taking on more of a nurse role. Caregiver burden was higher in these instances and compounded by the fact caregivers themselves were experiencing serious medical issues. While some personality changes were considered frightening or challenging, they tended to be low on participants' list of concerns. Issues such as balance and falls were a higher priority and associated with greater levels of anxiety, particularly for caregivers.

Overall, questions about personality change were easily answered by participants, with most able to identify and describe various changes. Participants occasionally had difficulty articulating exactly what they observed or experienced, and sometimes made contradictory statements about whether personality change had occurred:

> *[It] hasn't changed his personality…but he's now got a little bit more assertiveness…or – not argumentative [pause]. There is a change and I can't quite pinpoint how I would verbalise it…Stand up for himself is not right either…he's always been pretty passive so it's quite funny when he'll just say 'no, I don't think that's right'…yeah, so there is a slight, you might actually say personality change* (C)

In comparison to questions about personality change, questions about whether the patient felt like themselves after DBS were met with much sparser and hesitant responses. Most indicated that they did feel like themselves, despite previous discussion around the ways in which they or their personality had changed. Some participants felt they or their loved one were only partially themselves now, but what they had lost was largely attributed to PD, not DBS.

Clinical management of personality changes. There was significant variability in participants' reporting of clinician enquiry about changes in mood, personality or behaviour after DBS. There appeared no link between participants' responses and the clinicians involved in their care or where surgery was performed. Those who reported not being asked about it felt they could raise it with their treating team or contact them if needed. Some participants vaguely recalled conversations about personality change, but were uncertain who initiated it. In these cases, no attempts were made to

address the changes as either the pair considered them "*nothing major*" or the clinician attributed them to PD rather than DBS.

> *We probably told them [DBS clinicians], but it doesn't ever seem to be much of a problem. Like it's not that it's not taken seriously, but it's like 'oh well, that's Parkinson's', that's one of the Parkinson's things and it's like 'move on'…no, they're only concerned if there's something big or real or something they can change.* (C)

For patients living far from medical specialists, the number of consultations and degree of clinical contact they had appeared limited compared with metropolitan patients. Limited clinical contact and time-pressured appointments were reasons given for their specialist not raising the topic of personality change.

> *He [neurologist] hasn't asked anything really…most of the appointment takes up getting the meds sorted and getting the machine sorted.* (C)

Caregivers felt their feedback was generally encouraged in appointments, but could not always attend due to full-time work or other commitments. One caregiver noted the importance of attending so they could respond to clinician enquiries and had reported impulsive-compulsive type changes they had witnessed that their spouse did not raise:

> *That's why I do like to go to the appointments with him when I can, because…then you give your point of view. That's how this popped up the first time, because he would have said 'no, I'm fine. I'm fine'. I said 'well, actually…' [laughs], you know? Because otherwise – yeah, he [neurologist] would have never have known.* (C)

In this case, the behaviours swiftly ameliorated following stimulation adjustment. The experience left the caregiver confident they could detect uncharacteristic behaviour in the future and gave them a sense of relief that such behaviour would be transient. Still, a desire for more preoperative information around these types of changes was expressed. It was believed that this information would better prepare the caregivers for potential personality change, provide an explanation for any changes, and provide a rationale for clinicians' line of questioning during appointments.

> Interviewer: *Are there things you would have liked to have known beforehand, before the surgery or maybe had emphasized more?*

Definitely the behaviour side of it…because that was really quite scary…he would just go!...whatever he'd thought he'd just go and do it…We had no understanding that could just be changed by changing the controls…So I think they need to tell people that, because if it had gone on and just let him do whatever…Well, I wondered why – every time you go to a neurologist appointment, they'd ask you 'oh, is there any change in behaviour?'… gambling, sort of, alcohol-type behaviour...I'm going 'no'…then when that happened…'oh, now I know why you ask that all the time!' (C)

For caregivers of patients with cognitive issues, allied health professionals assisted them with communication of corrective feedback that was often challenging due to patient personality changes, such as impulsivity or stubbornness.

Interviewer: *Has it been helpful going to the movement disorders clinic?*

It was, because it wasn't just me saying it to [her], this is how you're supposed to be getting in and out of a chair. It was someone else, and she was just reiterating and giving more hints. (C)

Caregivers of patients with cognitive issues and poor DBS outcomes experienced increased burden. These individuals highlighted the value of family and social support to manage these demands (e.g., overnight stays, getting to appointments) and importance of respite services to focus on their own health concerns. For patients experiencing depression or disappointment with their DBS outcome, opportunities to talk with other individuals with PD or DBS helped them feel connected and understood, even if their experiences differed. These connections were often facilitated through PD community groups.

Discussion

Little is known about the significance of personality change following DBS for patients and families, nor their understanding of these potential changes prior to surgery. How the procedure impacts patients' sense of self has been widely debated in the philosophical neuroethics literature (Gilbert et al., 2018), but few studies have directly investigated the meaning and importance of such changes for the patients themselves. This prospective examination of the DBS lived experience

provides unique insights into these issues and raises a number of important points for consideration in DBS clinical practice.

Significance and Meaning of DBS-related Personality Change

Before exploring the effects of DBS on patient personality and sense of self, it is necessary to consider the preceding and ongoing impact of illness. Across interviews, both prior and following DBS, PD was generally perceived as having a negative impact on patient personality and self-concept. Although some patients found positives from their illness (e.g., spending more time with family), none felt it had positively influenced their personality. This aligns with preliminary findings of another PD sample of DBS patients, where many reported significant, largely negative, personality changes due to their illness (Kubu et al., 2019). When reflecting on their most-valued personality characteristics, patients expressed a diminution of these over the course of their illness (Kubu et al., 2019). Patients reported fewer changes in personality after DBS, and those they reported were largely positive. Similarly, the current sample reported a mix of positive and negative personality changes after DBS, while illness-related changes appeared to have a greater, more pervasive and distressing impact. This does not suggest that significant and distressing changes related to DBS do not occur, as these have been reported elsewhere (Mosley et al., 2019; Romito et al., 2002). Rather it highlights features of the DBS experience often overlooked in the conceptual neuroethics literature. That is, patients and families are entering it from a pre-existing context of illness-related change and that DBS can positively impact patients' personality and self-concept. We found that a positive impact on personality and self was highly connected with a good clinical outcome. Rates of positive clinical outcomes should continue to improve with promising developments in DBS such as: the identification of target-specific biomarkers (Sinclair et al., 2019), improved prediction of neuropsychiatric outcomes with lead location (Mosley et al., 2018), and closed-loop DBS systems (Krack et al., 2019).

Participants identified numerous ways they believed DBS had contributed to personality change, either in a transient or sustained sense. These changes did not result in the patient feeling they were now an entirely different person, but were incorporated into their self-concept. In another qualitative study, patients with PD reported no change in identity after STN-DBS, despite experiencing significant neuropsychiatric symptoms (Mosley et al., 2019). Once recovered, these

radical changes appeared integrated into patients' autobiographical narrative. The authors suggested participant comments reflected an essentialist core self that PD had suppressed and which DBS had released to varying degrees. Much like the restored "old self", others have noted patients feeling more like their authentic "true self" after DBS (Schüpbach & Agid, 2008). In contrast, some have felt unlike themselves after DBS and these experiences have been described in terms of alienation and self-estrangement. When discussing authenticity and alienation, Kraemer (2013a) described two outcomes following DBS. First, that "DBS could threaten authenticity" (p. 484) with the patient feeling and acting unlike themselves, or second, that PD could be seen as a time of alienation, with DBS bringing them closer to authenticity. The latter resonates with our sample's experiences, with neuropathological changes and/or medication side-effects leading patients to feel and act unlike themselves, potentially to the degree their caregiver feels they no longer recognise them (Toms, Quinn, Anderson, & Clare, 2015). Differential abilities of patients to integrate changes (positive or negative) into their self-concept could be explained by varying levels of coping, resilience, and ability to adjust narrative to existential changes, as well as support to do so.

Self-estrangement, autonomy and control. The notion of self-estrangement can be applied to patients' relationship with their illness, although it has typically been used to describe patients' postoperative experiences. In the current sample, illness-related self-estrangement appeared to be buffered in those displaying cognitive and behavioural factors associated with adaptive adjustment to chronic illness (e.g., benefit finding, optimism, problem-focused strategies and engaging in good health behaviours) (Gardenhire, Mullet, & Fife, 2019). On the other hand, it was exacerbated in those who displayed maladaptive approaches (e.g., wishful thinking, helplessness, coping through avoidance) (Dekker & de Groot, 2016; Moss-Morris, 2013). The introduction of DBS appeared to play either a restorative or deteriorative role in levels of self-estrangement. The direction of this role was influenced by the perceived success of the procedure and the development of unanticipated side-effects (e.g., speech, balance issues). This direction also had the potential to shift depending on health status and treatment decisions (e.g., adjustments to stimulation parameters and medication, implant removal/re-implantation, microlesion 'honeymoon' effect). Gilbert et al. (2017) previously described the qualitative nature of self-estrangement after DBS as restorative and deteriorative, with restorative

reports characterised by an excessive perception of capacity (e.g., physical capabilities) and deteriorative characterised by a perceived loss of control. In the present study, restorative changes were largely perceived as a return to equilibrium disrupted by illness, rather than an excessive perception of capacity. In a deteriorative sense, some patients may have perceived personality changes and uncharacteristic behaviour as a loss of control, but equally, perceived improved physical capabilities as regained control. These multifaceted responses to treatment, in addition to patients only experiencing minor or transient stimulation-related personality changes, may explain why none felt DBS had fundamentally changed them.

Perceived control was relevant to patients both prior to and after DBS and was important for determining how much they felt like their 'true self'. This is unsurprising given the fundamental role of autonomy in the construction of one's identity (Ryan & Deci, 2000). PD had only a diminutive effect on patients' feelings of control, while DBS had the potential to both increase control (e.g., through greater predictability and flexibility managing motor symptoms) or *further* decrease control (e.g., through poor speech production, unstable balance and uncharacteristic behaviour), echoing the pattern seen with personality. Improvements in perceived control have been documented in other PD DBS samples. Kubu et al. (2017) asked patients prior to DBS to identify their personal top symptom and behavioural goal, with a subjective rating of their perceived control over these. DBS significantly improved control over these personally identified symptoms and goals (e.g., with relationships, hobbies and work particularly important) and patients' perception of control also improved. Mixed experiences have been reported in other samples. In their sample of STN-DBS patients, Mosley et al. (2019) described variable perceptions of control in relation to significant neuropsychiatric symptoms patients experienced (e.g., ICDs, irritability, aggression, dangerous driving). Some felt a loss of autonomy, due to their actions being out of keeping with their usual behaviour and values. Others actively sought to change their mood with higher stimulation levels, thereby using DBS as a tool to exert control albeit in a way others deemed problematic. Mosley and colleagues' sample was selected for their significant neuropsychiatric side-effects and represent the "most severe end of the spectrum" (p.13). In selecting patients preoperatively, our sample experienced less dramatic side-effects (speech, balance, cognitive issues) that resulted in reduced levels of autonomy and control. These findings

support previous studies which have shown how physical control impacts sense of self-efficacy, autonomy and control (Racine, Lariviere-Bastien, Bell, Majnemer, & Shevell, 2013). From an experiential perspective, autonomy (as self-governance) is not clearly separated from physical independence and mobility. In standard PD care, promoting self-efficacy, control and mastery is crucial, whether it be through adopting a healthy lifestyle, engaging in therapies (physio, speech, music) or developing hobbies (Gardenhire et al., 2019). Physical and sensory integrating activities in particular are recommended for the process of *preserving self* in PD (Vann-Ward, Morse, & Charmaz, 2017).

Individual and relationship adjustment. Self-efficacy and control are important features of patient care and adjustment to any chronic illness (Moss-Morris, 2013). Given the complexity of symptoms and treatment outcomes in PD, multidisciplinary input is often recommended to support both the patient and family system (Hodgson, Garcia, & Tyndall, 2004) and promote positive psychosocial adjustment (Baertschi, Flores Alves Dos Santos, et al., 2019). DBS is only able to address a limited selection of the diverse symptoms experienced by patients with PD. As a result, patients will generally be left with unresolved symptoms following DBS, in addition to any undesirable side-effects. For this reason, the 'burden of normality' (BoN) phenomenon may not apply to PD DBS patients as previously proposed (Gilbert, 2012). BoN was originally used to describe the poor psychosocial adjustment witnessed in patients relieved of chronic epilepsy following temporal lobectomy (Wilson et al., 2001). Despite being effectively cured, these patients experienced difficulty with social and vocational reintegration, to the dismay of those around them. In the current sample, one pair reflected on how the patient's post-DBS experience failed to match the perceptions of those around them (family, friends, and doctor), sharing some similarities with a BoN response to treatment. The patient, however, emphasised the on-going impact of symptoms unaddressed by DBS that leaves it far from a cure. Others have recognised that the progressive nature of PD leaves it difficult to determine what underlies postoperative maladjustment (Baertschi, Flores Alves Dos Santos, et al., 2019). Despite differences in aetiology and symptomatology, the multidisciplinary rehabilitation approach advocated for in the case of temporal lobectomy is also relevant to patients' psychosocial adjustment following DBS.

Concerns about the negative impact of DBS in spousal relationships have been raised ever since Agid and colleagues (2006) reported 65% of their patients with partners experienced a conjugal crisis within two years of undergoing DBS. Stimulation-related personality changes were considered one possible contributing factor, in addition to changes in relationship dynamics, the stress of undergoing neurosurgery, and the intervention's failure to meet expectations. Here it appeared pre-existing relationship issues were exacerbated by the procedure. In our prospective study, we found relationship quality tended to remain fairly consistent longitudinally, regardless of whether undesirable personality changes developed.

A poor clinical outcome and progressive cognitive decline were more challenging aspects for pairs, regardless of relationship type (spousal, parent/child). In a previous qualitative investigation of cognitive impairment in PD, two prominent grieving themes were described: a *loss of sense of self* for patients and a *loss of partner* for spouses (Lawson, Collerton, Taylor, Burn, & Brittain, 2018). While patients attempt to maintain a sense of self and valued identity, spouses process the progressive loss of their partner and relationship (Toms et al., 2015). Advanced cognitive impairment in PD is associated with troubling personality changes and poor caregiver quality of life, with spouses struggling to maintain at-home care (Davis et al., 2014; Lawson et al., 2017). Psychological input, social support (formal or informal), self-care opportunities and respite are suggested to improve caregiver wellbeing and manage this grieving process (Mastel-Smith & Stanley-Hermanns, 2012; Toms et al., 2015). Our findings strongly support these recommendations.

Clinical Practice Implications

Education and communication of risk. DBS is a complex intervention involving substantial preoperative medical information for patients and families to digest. Desperation to undergo surgery, disease-related cognitive issues and surgery-related anxiety can all impact patients' comprehension and recall of information. No clinical guidelines specifically outline the informed consent process for DBS in PD and there is high variability in how preoperative procedures are conducted across individual clinicians, hospitals and geographic locations. There has been very little research on patient comprehension of complex DBS risk information and ways to facilitate this. The current study

highlights particular areas in the communication of DBS-related risks and outcomes that require consideration, while keeping these inherent challenges in mind.

The language and labels clinicians use to describe changes to patients and families will vary according to personal preference and how they conceptualise them. A drawback for using *personality change* is its confronting nature and potential to discourage prospective patients. In our preoperative interviews, however, only some were concerned about potential personality change and none sufficiently so to dissuade them from their decision. A benefit of using *personality change* is that it holds meaning for patients and families and manages to encompass a variety of potential changes in patient mood, behaviour and cognition. Clinicians may need to explore this meaning with patients and caregivers, including what they value most about the patient's personality. This would provide an opportunity to clarify and reassure patients and caregivers of what is unlikely (e.g., become a monster) and what is possible (e.g., irritable, impulsive, impatient).

The transience of stimulation-related personality changes is a particularly important aspect to reiterate with patients and families. In a comprehensive review of neuropsychiatric symptoms associated with DBS for PD, Voon et al. (2006) proclaim the majority are "transient, treatable and potentially preventable" (p. S305). Emphasising the *transient* nature of personality change will likely reduce patient and family apprehension and initiate an understanding that treating them depends on communication and feedback between the clinician and themselves. This does not preclude DBS from potential long-term effects. Even after amelioration through stimulation reprogramming, a patient's uncharacteristic and problematic behaviour can have lasting repercussions for the caregiver and spousal relationship (Mosley et al., 2019). Our results reflect how disappointment with the procedure outcome and stimulation-related side-effects (e.g., speech, balance issues) can have an indirect lasting effect, particularly on mood and self-confidence. These findings support the need for providing nuanced and contextualised information to patients (Bell, Maxwell, McAndrews, Sadikot, & Racine, 2010).

Participants' awareness of ICDs and compulsive behaviours as a DBS side-effect was limited. It is possible this information was provided by the clinical team, but not retained and recalled by our participants. It is also possible it was not discussed due to time constraints, the need to prioritise

surgical information, the assumption another team member addressed it or due to a clinical decision that it was not relevant to the patient. Educating patients and families on this matter is made difficult by conflicting clinical trial results. DBS has been reported as worsening existing ICDs and producing de novo cases, while also being reported as improving existing ICDs and producing only few, transient de novo cases (Averbeck et al., 2014; Eisinger et al., 2019; Kim et al., 2018). The relationship is particularly complex with multiple factors involved, including lead placement, implantation site, levodopa dosage, neuropsychiatric history and stimulation programming. For patients with an existing history of ICDs, nuanced clinical discussions are required to explain these potential outcomes (e.g., reduced levodopa may improve ICDs, but DBS could exacerbate), intentions for managing it (e.g., taking a cautious stimulation approach) and the implications for procedure outcome (e.g., possible reduced clinical benefit). In the current sample, some patients and caregivers required greater clinical reassurance around these particular issues. Conversely, those without existing ICDs or psychiatric history were confident they would go unchanged by DBS. Although statistically at a reduced risk, cases of de novo ICDs and behavioural changes have been reported in patients with no history, so should not be discounted as a potential outcome (Mosley et al., 2019; Voon et al., 2006).

Participants' limited awareness of post-DBS personality change and expressed desire for more preoperative information suggests clinical communication on this topic requires improvement. Direct education from clinicians to patients and caregivers does not guarantee information is retained or ensure preparedness to manage changes (Mosley et al., 2019). More experiential information that uses the words and language of other PD patients and families has been suggested for improving comprehension and setting realistic expectations (Liddle et al., 2019). Our interviews demonstrated personal experiences from other DBS patients and families were well-retained by participants and influential in establishing their expectations. Exposing prospective patients and families to a selection of patient experiences and outcomes could assist comprehension and increase preparedness to manage post-DBS difficulties (not just personality change, but balance and falls, speech and communication). Vignettes with patient experiences could be shared via multimedia presentation. An existing psychoeducation program developed to target psychosocial maladjustment after DBS has incorporated

multimedia into their education, using videos to demonstrate potential outcomes (e.g., patient displaying apathy) (Flores Alves Dos Santos et al., 2017). Encouraging long-term results for patients in this program have been reported, albeit from a small sample, particularly across social adjustment and psychological health domains. Other program features that benefit comprehension is the spread of information across seven sessions, some prior to DBS and some following. Each session has a particular focus: neurosurgery, social or couple-related content, with appropriate disciplinary input as required (neurosurgery, neurology, psychology, psychiatry). The separation of surgery-focused and psychosocial-focused information likely aids comprehension of each and delivering at a relevant time increases its practicality. Programs of this type ensure timely education is provided (e.g., information on lesion effect, postoperative confusion prior to surgery), that concerns can be raised and addressed (e.g., process for ceasing medication prior to surgery), and opportunities exist for clinicians to assess comprehension, correct inaccurate beliefs (e.g., DBS causing problem-drinking) and address unrealistic expectations. This program was designed for both patients and caregivers. Involving caregivers in the informed consent and education process is essential (Haahr et al., 2013), with preparedness shown to temper caregiver strain and assist coping (Carter, Lyons, Stewart, Archbold, & Scobee, 2010; Mastel-Smith & Stanley-Hermanns, 2012).

Follow-up clinical care. In addition to DBS education and preparation, postoperative support and clinical care also requires consideration. The psychoeducation program evaluated by Flores et al. (2017) included postoperative sessions to assist the transition from DBS preparation to management and adjustment. This provided patients and caregivers with practical psychosocial support in the months immediately following surgery. The format of DBS postoperative care in clinical settings more broadly is incredibly variable. Ongoing neurology consultations are standard treatment, but follow-up neuropsychiatric assessments are not always routine, despite being recommended for detection and management of mood and behavioural changes (Voon et al., 2006). Neurologists, who typically are familiar with their patients and existing personalities, often detect changes or enquire about them, but face the challenge of time-constraint (Thomson, Segrave, & Carter, 2019). Access to a multidisciplinary team (e.g., PD nurse, general practitioner, social worker, psychologist or psychiatrist) gives patients and families increased opportunities and time to discuss psychosocial

issues and receive relevant support. Nurse specialists in particular are recommended as they can assist with device practicalities while assisting emotional adjustment (Haahr et al., 2020). They can also provide continuity of care across the patient's wider illness and treatment trajectory (Eatough & Shaw, 2017; Vann-Ward et al., 2017). In the case of ICDs, some may prefer disclosing to a nurse rather than a specialist doctor (Thomson, Segrave, & Carter, 2019). However, disclosing can also be impacted by poor insight, shame, embarrassment or seeing them as a trade-off for other improvements. Patients and caregivers may feel more comfortable disclosing on a validated questionnaire, such as the Questionnaire for Impulsive-Compulsive Disorders in Parkinson's Disease (Weintraub et al., 2009) or Frontal Systems Behavior Scale (Stout et al., 2003). These can serve as screening tools to prompt sensitive conversations. These questionnaires need to be considered in the context of the patient's premorbid personality with verbal feedback from patient and caregiver. Hypervigilance to de novo changes could result in typical behaviour being pathologized. If a mild personality change comes with improvements in other symptoms, a discussion between patient, caregiver and clinician needs to occur to establish the acceptability of this trade-off.

Strengths and Limitations

The design of the present study possessed important strengths. The patient-caregiver dyads allowed multiple perspectives on the patient experience and insight into the broader impact on the caregiver and their relationship. The prospective approach ensured participants' expectations, knowledge and concerns accurately reflected current circumstances, which were then contrasted with actual outcomes and experiences. Semi-structured interviews and open-ended questions allowed for ambiguity, contradiction and complexity in responses, reflecting the true nature of human narratives and meaning-making. This avoids issues of restriction associated with binary (yes/no) or predetermined response methods (de Haan et al., 2017; Hariz et al., 2016).

These results reflect the experiences of a subset of patients and families from a particular region and may not generalise to patients and families elsewhere. However, great diversity in DBS clinical practice exists regardless of physical location, leaving generalisability of results an on-going research issue. Although our interest rested in the common experience of undergoing DBS, purposive sampling ensured diverse experiences were captured (e.g., in age, disease length, symptoms profile,

implantation site, treating clinicians). Regrettably, only patients undergoing DBS through the private health care system were included. Attempts were made to include patients in the public system, but lengthy and uncertain surgery waitlists impacted opportunities for participation.

Conclusions

Post-DBS changes in personality were experienced by participants in this study. The stimulation was considered to be only one of many causes for the observed changes and in each of these cases the effects were either transient or minor. Personality changes directly impacted caregivers and were most pronounced when they were associated with disease progression. The negative influence of illness on patients' personality and sense of self was apparent. For some, DBS facilitated a restoration of the patient's premorbid self. Perceptions of control were also relevant to patients and future research should consider approaches for optimising this across both standard PD and DBS care.

Patient and caregiver awareness of personality change as a post-DBS risk appeared limited, suggesting education and communication around these issues could be improved. Further studies are required to evaluate the benefit of perioperative psychoeducation programs for this purpose. With exceptions in obsessive-compulsive disorder (de Haan et al., 2017), how DBS impacts personality and selfhood in psychiatric conditions has rarely been explored. As psychiatric indications for DBS emerge and develop, so should our understanding of the intervention's broader psychosocial impact.

CHAPTER SIX

ILLNESS, SELF-CONCEPT AND DEVICE EMBODIMENT: PATIENT AND CAREGIVER LIVED EXPERIENCES OF DEEP BRAIN STIMULATION FOR TREATMENT-RESISTANT DEPRESSION

Chapter Six – Illness, Self-Concept and Device Embodiment: Patient and Caregiver Lived Experiences of Deep Brain Stimulation for Treatment-Resistant Depression

Preamble to Paper Three

The following chapter presents an original research article submitted to the *Journal of Affective Disorders* in August 2020, currently under peer-review. This chapter extends upon the previous investigation of changes in personality and self following DBS for an established neurological indication (PD), by exploring these same concepts with a sample undergoing DBS as an experimental psychiatric treatment (for TRD). The paper reports on the findings from interviews conducted with six candidates enrolled in a clinical trial of DBS for TRD and five of their respective caregivers (a candidate with no caregiver participated independently). Details of the clinical trial in which participants were enrolled are described in the paper methods. The aim of the current study was to qualitatively examine how DBS for TRD impacts patient personality, self-concept and relationships, from the perspectives of both patients and caregivers. Patients with a non-spousal caregiver also participated in the study (one child/parent relationship represented in sample). Unlike in the previous empirical paper, participant pseudonyms as well as numeric identifiers corresponding to dyads (e.g., Patient 2, Caregiver 2) are used. These findings reflect distinct perceptions of self that exist within an individual's states of illness and wellness. The complex and at times challenging process of recovery from chronic mental illness was apparent for both parties. Implications for future DBS clinical research in psychiatric conditions are discussed within.

The supplementary materials referred to in this paper (interview schedules) can be found in *Appendix G*.

Abstract

Background: Numerous research trials of deep brain stimulation (DBS) for treatment-resistant depression (TRD) have been conducted. However, studies investigating patient and their families lived experiences remain absent. This study examined patient and caregiver perspectives and experiences as they prepared for and adjusted to life with DBS. **Methods:** A prospective qualitative design was used. Participants were six patients and five caregivers (spouses, family). Patients were enrolled in a clinical trial of DBS of the bed nucleus of the stria terminalis. Semi-structured interviews were conducted with participants before DBS-implantation and 9-months after stimulation initiation. The 21 interviews were thematically analysed. **Results:** Three primary themes identified during analysis were: (a) *impact of mental illness and treatment on self-concept;* (b) *device embodiment*, and (c) *relationships and connection*. Severe refractory depression had profoundly impacted who patients were, how they viewed themselves, and the quality and functioning of their relationships. Patients who benefited from DBS felt reconnected with their premorbid self, yet still far from their ideal self. Caregivers reported familiar elements of their loved-one re-emerging, but noted a persistence of qualities established during mental illness. While reductions in depression were broadly beneficial for relationships, the process of adjusting relationship dynamics created new challenges. All patients reported recharging difficulties and challenges accommodating the device. **Limitations:** The sample was small and reflects the limited number of patients undergoing DBS for TRD. **Conclusions:** Therapeutic response to DBS is a gradual and complex process that involves an evolving self-concept, adjusting relationship dynamics, and growing connection between body and device.

Keywords: deep brain stimulation; depression; caregivers; self; identity; relationships

Introduction

Deep brain stimulation (DBS) is a neurosurgical procedure being trialled in individuals with treatment-resistant depression (TRD). The procedure involves implanting microelectrodes in specific brain regions thought to be associated with depression psychopathology. Continuous electrical pulses are sent from a battery (implantable pulse generator; IPG) located in the patient's chest to the brain via subcutaneous leads. A range of target regions have been trialled for TRD, including the subcallosal cingulate gyrus (Kennedy et al., 2011; Lozano et al., 2008), ventral capsule/ventral striatum (Dougherty et al., 2015; Malone et al., 2009), medial forebrain bundle (Bewernick et al., 2017; Fenoy et al., 2016) and nucleus accumbens (Bewernick et al., 2010; Millet et al., 2014). The bed nucleus of the stria terminalis (BNST) has been a recent target of interest (Fitzgerald et al., 2018; Raymaekers, Luyten, Bervoets, Gabriels, & Nuttin, 2017) and is the implantation site for the present sample. DBS has demonstrated capacity to significantly and effectively alleviate depressive symptoms (Zhou et al., 2018). However, response and remission rates vary considerably across studies and optimal patient characteristics, stimulation parameters, and implantation sites remain under investigation (Fitzgerald & Segrave, 2015).

While the efficacy and safety of DBS for TRD continues to be investigated via clinical trials, with mixed results (Mosley et al., 2015), there have been no studies investigating patients' experience of DBS and their perspectives on the changes they undergo. The experience and impact of DBS on caregivers and family has also been under investigated, from both a quantitative and qualitative perspective. Qualitative studies involving DBS candidates with TRD have been limited to questions of decision-making, capacity to consent (Christopher et al., 2012; Fisher et al., 2012; Leykin et al., 2011) and attitudes towards developing closed-loop systems (Klein et al., 2016). These are important ethical issues to consider, particularly when offering an experimental treatment to vulnerable individuals (Bell, Leger, Sankar, & Racine, 2016; Thomson, Segrave, Gardner, et al., 2019). But they do not provide insight into the lived experience of DBS or its broader psychosocial implications. Qualitative studies with patients who have undergone DBS for other clinical indications, such as Parkinson's disease, have revealed important insights using this methodological approach.

In Parkinson's disease (PD), patients and caregivers describe both positive and negative changes in patient personality emerging after DBS (e.g., more fun, open, talkative; more aggressive, selfish, quiet) (Lewis, Maier, Horstkotter, Zywczok, et al., 2015). With improved PD symptoms, patients and caregivers can feel the patient's *old self* has been restored (Thomson et al., in press). However, when patients experience unintended side-effects (e.g., irritability, compulsive behaviours) spouses can feel they are no longer married to the same person (Mosley et al., 2019). Some patients report difficulty psychologically accepting the implanted electrical device and experience altered body image, while caregivers can feel "lost" when their partner no longer depends on them (Schüpbach et al., 2006). In obsessive-compulsive disorder (OCD), patients describe post-DBS changes as being more or less aligned with their perceived true self and needing to *get used to* how they are now or needing to *find out* who they are without OCD (de Haan et al., 2017).

These complex and highly nuanced psychosocial experiences are not captured by quantitative psychopathology and functional scales used in clinical trials. However, they can have substantial implications for patient and caregiver wellbeing. Therefore, the aim of this study was to qualitatively examine how DBS for TRD impacts patient personality, self-concept and relationships from the perspectives of both patients and caregivers as they prepare and adjust to life with DBS. Patient and caregiver narrative accounts reflect their needs and priorities and this information can be used to guide more patient-centred approaches to DBS clinical interventions.

Method

This exploratory study used a prospective qualitative design. Methods are reported according to COREQ guidelines for qualitative research (Tong et al., 2007). Ethics approval was obtained from Monash University Human Research Ethics Committee (CF16/1888-2016000963) and all participants provided written informed consent.

Participants

Consecutive sampling was used to recruit individuals actively enrolled in the *Deep Brain Stimulation for the Treatment of Major Depressive Disorder* clinical trial conducted at the Monash Alfred Psychiatry Research Centre and Alfred Hospital (Australian New Zealand Clinical Trials

Registry: ACTRN12613000412730). Participants were recruited by the first-author after permission to be contacted was granted via the clinical trial co-ordinator. Verbal and written study information was provided to the candidates and their respective caregivers. All who were approached chose to participate, including: six DBS candidates (5 women, 1 man, M_{age} = 52 years, age range = 26-73 years) and five caregivers (4 spouses, 1 parent, 2 women, 3 men, M_{age} = 59.5 years, age range = 45-75 years). One candidate lived alone and chose to participate independently. One candidate who completed a preoperative interview did not complete a postoperative interview as it was deemed too burdensome. The current sample represents the majority, but not complete clinical trial sample, as the current study commenced after the trial began. DBS candidates had a long history of TRD (time since diagnosis: *M* = 18 years, range = 8-42 years) and met Stage V criteria of the Thase and Rush (1995) classification for TRD. This is the most severe classification with patients failing to respond to adequate courses of all evidence-based therapies, including pharmacotherapy (all antidepressant classes and combination/augmentation strategies), psychotherapy (cognitive behavioural therapy with a registered psychologist) and non-invasive brain stimulation (bilateral electroconvulsive therapy, transcranial magnetic stimulation). None of the DBS candidates were engaged in paid employment.

Procedure

One-on-one, semi-structured interviews were conducted between 2016 and 2019 with the first-author, a female provisional psychologist with training in qualitative methods and experience interviewing DBS patients, families and clinicians. Interviews were conducted face-to-face (at participants' home, research centre) or via telephone or video-conference for participants living interstate. Interviews were conducted separately with patients and caregivers to allow open discussion. Pre-surgery interviews occurred 3 to 15-weeks prior to surgery (*M* = 46 minutes, range = 34-58 minutes) and explored participants' knowledge of DBS and anticipated procedure outcomes (see Supplementary Material for interview schedules). Participants then underwent DBS surgery, with electrodes implanted in the BNST. After a recovery period, a pseudorandomised schedule of active or sham (control condition) stimulation commenced, with participants blinded. Over five months, five stimulation settings were trialled: one inactive, two low-level (2 volts), and two moderate-level (4 volts). Following this, stimulation continued in an open-label manner, with parameters optimised

according to individual responses. Post-surgery interviews occurred 9 to 11-months after stimulation initiation (M = 55 minutes, range = 36-86 minutes), roughly 3-months into the optimisation phase. These explored experiences living with DBS and the perceived personal and relational impact. Field notes were maintained during the interview process. Audio-recordings were transcribed verbatim by a professional transcription service, then reviewed for accuracy (by CT) and de-identified using pseudonyms.

Data Analysis

Interview transcripts were entered into NVivo 12 software (QSR International) and analysed using thematic analysis (Braun & Clarke, 2006). This is an iterative and inductive process that allows novel themes and patterns of meaning to emerge from the data. Data was analysed according to the six-step process outlined by Braun and Clarke (2006), involving: familiarisation through repeated listening and reading of interviews, initial generation of codes, searching for themes, reviewing and refining themes, defining and naming themes, and reporting using representative quotes with pseudonyms to protect confidentiality. All interviews were coded by CT. Data saturation, the stage at which no novel themes were evident, was reached in analyses of both pre- and post-surgery data. Approaches to increase the quality and credibility of the results included cross-coding a subset (6) of interviews with the research team [AC, RS] to ensure consistency in coding. Any disagreements in coding were discussed until a consensus was reached. Triangulation, where a phenomenon is examined from different perspectives, was achieved by inclusion of a diverse research team (clinical psychology, neuropsychology, neuroethics, social science).

Results

Thematic analysis revealed three primary themes relevant to the current paper. Primary themes developed longitudinally, with secondary themes reflective of specific time points (before/after surgery). Themes are illustrated using representative quotes. Both patient and caregiver perspectives are represented across all themes.

Impact of Mental Illness and Treatment on Self-Concept

Prior to DBS, participants expressed how severe and chronic depression had obscured defining aspects of the patient's self and personality. These included traits such as being outgoing, confident, and a "bit of a joker". Three patients had previously enjoyed fulfilling careers in health care. These caring professions were integral to patients' identities and their inability to perform them due to mental illness was a significant loss. Patients' interest and ability to engage in meaningful and rewarding activities, such as intellectual and creative pursuits, were profoundly impaired and detrimental to self-worth.

Years of depression had created a sense of an absent person and life, with patients merely existing. This was pronounced in patients receiving regular ECT, which caregivers characterised as a means of keeping the patient alive rather than a treatment that remediated their depression. When asked if they thought DBS could change the patient's personality, most participants did not expect or were unconcerned that it would. Some hoped regained wellness would restore their premorbid personality. Others expressed concern DBS may alter personality in an undesirable way, but felt comfortable adjusting or ceasing stimulation would resolve this, or otherwise they would simply "have to cope". These concerns were minor compared with participants' primary preoccupation: would the intervention be effective and how would they cope if it wasn't?

Caregivers expressed hope that the person they had known prior to depression would be restored, but acknowledged that after years of mental illness they were unlikely to be exactly the same. Caregivers also identified qualities they valued in their loved-one that they hoped would remain after DBS, such as being a loyal partner and parent, a gentle and caring person, and sharing a close bond. However, some were willing to lose these if it meant the patient could achieve relief from depression and an improved quality of life. When imagining an ideal picture of their future self or loved one, participants desired normality and the ability to simply "do things". Some patients envisaged achieving professional goals or travelling to specific destinations, while others wished to feel more confident and at ease amongst people.

With DBS, patients' perspectives of themselves were greatly influenced by the procedure's perceived benefit. Those who experienced a subjectively meaningful antidepressant benefit that

sustained over multiple months leading up to the time of interview conveyed a sense of restored self (n = 2). Those with more modest effects or transient benefits recognised encouraging moments of their prior self (e.g., increased curiosity, interest in work activities). Caregivers recognised aspects of their loved one previously, but were less emphatic about this restoration, noting the persistence of qualities that had been established through depression (e.g., sympathy seeking, self-focused).

Decreased depression was accompanied by some transformation of self-concept; however, patients remained aware of the substantial distance between their idealised self (in terms of physical appearance, having friends, working etc.) and actual self. Novel qualities, including irritability and anger (n = 3) were reported by patients and caregivers. These were considered reactions to either the challenges of social reintegration, the procedure's perceived lack of effect, or a particular stimulation setting side-effect.

Patients who experienced no benefit felt fundamentally unchanged by DBS (n = 2), but transient experiences of acting uncharacteristically and feeling unlike oneself were reported in the context of stimulation-induced manic episodes (n = 1).

Table 1. Impact of Mental Illness and Treatment on Self-Concept

Pre-DBS
Defining aspects of self and identity inhibited
Caregiver 2: *She was very independent and very free spirited and quite fiery as well [laughs], but that's all changed. She's just very passive, doesn't make decisions.*
Caregiver 4: *She was confident, she was uplifting and energetic…but for quite some time now that's just not there.*
Caregiver 5: Yeah, she used to be fantastic in the work she did and she just lost all that confidence and it's just been a waste of her life for her and that's…been very hard to take.
Chronic depression creates an absence of person and life
Patient 3: *It's not just impacted on my ability to work; it's impacted on my ability to be a person.*
Patient 5: *[I hope] to be able to live my life rather than existing because that's all I feel I'm doing now, just existing and not living it.*
Caregiver 2*: [ECT] doesn't really lift her up…it's just existing.*
Caregiver 3: *[With ECT] she ended up pretty much like a zombie…like the walking dead, it was horrible.*
Potential impact of DBS on personality and self
Patient 1: *Depression itself kind of changes who you are so I suppose logically…that might also be a consequence but that's really to do with, that would be to do with resolving the depression, not with the surgery itself, the procedure itself.*
Caregiver 2: *After such a long period of time it's hard to remember what that personality was. I think it certainly will change her personality compared to what it is now…well the hope is it actually restores what it was.*
Patient 3: *No, I'm not concerned that it's going to change my personality. That's, again, one of the very common misnomers, that people say when you take antidepressants it alters who you are as a person or your personality traits…It might make you feel better or worse…but it's not changing who you are, that's a response to a symptom.*

Patient 6*: I could come out the other side like Jekyll and Hyde…This thought occurred to me yesterday. What happens if…I come out the other side and I'm not the same person? I don't have the same values...How are we going to cope with that? We'll just have to cope…we'll just have to…work it out.*

Ideal picture of future self/loved one

Patient 3: *I'd just really like a chance at being…what everyone takes for granted. Just being a regular person with a regular job.*

Caregiver 3: *I suppose just being able to live some form of a normal life and a happy life, or a happier life…[for her] to not have that terrible empty feeling all the time…Yeah, just to have somebody who is not always on the verge of suicide.*

Caregiver 2: *I don't want her to be dependent on anyone. I don't want her to depend on me. I want her to be a fully independent person, making her own money, doing her own things. She doesn't have any of that. That would be good but that's the Holy Grail.*

Caregiver 6: *I would love to have a bit of my old Christopher back [laughs]. I mean, look, I'll go for 100 per cent, I'll settle for 50, even 25. I mean, just so we go home and enjoy life together.*

Post-DBS

Experiences of former self and personality

Caregiver 2: *She's more interactive and more content and happy with things, so the kind of behaviours I'm seeing are what I tend to remember she was like before she had the depression…So, she's back, more back to her old self, I guess…[She's] started to feel more independent and wanting to do her own things, and plans for the future.*

Patient 4: *I don't think it's changed me, but there are little sparks of who I used to be coming back. Because I'm actually quite an outgoing person, so there's sparks of that coming back, instead of this awful person that would just sit…like [I] didn't even speak to people, I was so depressed. Couldn't look people in the eye, I couldn't even speak.*

Patient 6: *I'm back to where I was. No, I'm definitely back. I am the Christopher Daniels I was, dare I say it, 20 years ago. I'm not living in fear of being depressed. I'm not living in fear of being not in control, and being the victim…It's like looking in the mirror for the first time and seeing this person looking back at you. That person that you remember from 20 years ago.*

Transforming self-concept and associated adjustment difficulties

Patient 2: *Trying to describe what it felt like to be depressed and what it feels like now. There's no word for it…It feels like – the devil is when I was depressed, and I feel like an angel…I'd like to keep this personality, rather than being – I mean, I'm still nasty, angry at Doug [caregiver], because he's the only one that I'm usually in contact with, so if I have to take anything out, I usually take it out on him.*

Caregiver 2: *She's doing all these things, she's starting to feel better about herself, and she's hoping people see that and acknowledge that, and not everyone does. Everyone's involved in their own worlds as well, so she just has trouble expressing it, I guess.*

Caregiver 6: *He's different to how he was when he was grossly ill, but [he's] more like the Christopher that I had, just a little bit more self-centred…I think it's been all about him for so long…He has been ill a long time, and I assume it affects anybody, if you've been ill a long time…It's hard for him.*

Fundamentally unchanged, transient experiences

Caregiver 3: *I would say that there have been times where she's told me that she doesn't feel like herself, where she felt that she's done things that were out of character for her…There have been times where she has been experimenting with the DBS and those have led to the more manic episodes.*

Caregiver 5: *I think I've forgotten what the real Fiona is…it's not the real Fiona…That's not because of the DBS, but just in general*.

Device Embodiment

In preparation for DBS, patients considered the prospect of having an implanted device and how this may affect embodiment (i.e. sense of being in the body) or their view of themselves and their body. Most anticipated it having little impact and be easily adapted into their self-view. With the device encased within the body and not directly visible to others, most patients predicted being rarely

conscious of it. Many likened it to other implanted devices for medical conditions, such as pace-makers and insulin pumps. Unlike some of these static devices, one patient highlighted the dynamic relationship with DBS, requiring setting adjustments and battery recharging. Another patient expressed mild disgust imagining electrodes embedded in their brain and the IPG in their chest. They anticipated feeling physically self-conscious, especially while recovering with a shaved head and scarring. Whether the intervention was successful was considered likely to dictate how the device was viewed (i.e., with pride or disgust).

Participants had considered implications of having a DBS device, including not flying after surgery, navigating airport security scanners, and needing reliable access to electricity, none of which were considered particularly restrictive. Participants were expecting to receive a rechargeable battery (to increase battery longevity), but had not yet seen the recharging parts. Participants were aware of the need to regularly recharge and compared this process to charging a mobile phone – an everyday part of life. Those more comfortable with technology felt confident they could learn to manage the device independently, while some patients, particularly those characterised by low confidence, were fearful of "pressing the wrong button" and wanted control left in the professionals' hands. The need for device maintenance and specialist care in the distant future had played on some patients' minds.

After surgery, most patients felt conscious of their physical appearance (shaved head, bandages, scarring) and how others were perceiving them. For one patient, it was only once the stimulation was turned on and exerting some effect that they became conscious of their appearance. Patients tended to avoid discussing the procedure or its purpose with others unless asked directly ("I just don't want people to think I'm a freak"). Some experienced pain, discomfort, and tightness around their IPG and subcutaneous wiring in certain positions or postures. For some, comfort and freedom of movement came with time while others needed to make adaptations to alleviate device-related discomfort (sleeping on one side, cushioning pillows). Patients tended to see themselves no differently with DBS and had accepted the device as part of their body. For some, this acceptance had taken time and their perspective had been influenced by whether they considered DBS as having an effect.

One aspect all patients had struggled with to varying degrees was battery recharging. The recharging experience had been one of frustration and annoyance, even for those who considered themselves easy-going or tolerant. Frustration was associated with difficulty establishing a reliable connection, inconsistency in how long and often recharging was required, recharging taking longer than originally expected, and the growing need to prioritise recharging in daily life. Recharging requirements varied depending on each individuals' settings, with higher voltages associated with greater recharging burden. Some were still establishing an optimal recharging routine. Many had made contact with their device company representative to receive reassurance and guidance around recharging technique (e.g., understanding how body temperature, posture and tension influence connection).

Within the open-label phase, arrangements for adjustment of stimulation settings varied for each individual and were influenced by patient's geographical location, accessibility of support people (caregiver, psychiatrist), size of the adjustment being made, and the patient's preference. Patients' level of comfort controlling the device (adjusting settings within range, turning on/off) were consistent with their pre-DBS comments around technological confidence. Some preferred all adjustments be made by the DBS specialist, but this was not always possible or practical, due to geographical distance. This would occasionally require patients to make adjustments, with caregiver or psychiatrist support. One patient with no caregiver had all adjustments made while in hospital. They reflected on cognitive side-effects they experienced with one setting and how these effects would have impacted their ability to re-adjust the settings had they been alone. Outside the specialist clinical trial team, participants' experience with medical professionals broadly was that DBS, particularly for depression, was not well-understood. Device company representatives who provided patients with device education peri-operatively, were also engaged to guide medical professionals around appropriate device management during medical procedures unrelated to DBS.

Table 2. Device Embodiment

	Pre-DBS
Anticipations for implantation	
Interviewer: *How do you feel about the prospect of having a stimulator as part of you and as part of your body?*	

Patient 3: […] *It doesn't change how I identify myself. The only difference it will mean is, I have to go through a different line at the security - at the airport…If you break your arm and you get a plate put in, you don't suddenly think you're Iron Man and your whole sense of identity changes…I mean, for some things, yes, it does change you a bit. Like having a colostomy bag, that is a difficult change to adjust to and adapt. But because this is embedded in you and you can't see it – you might have to adjust it from time to time, but it's not going to cause discomfort or embarrassment. No one will know that you have one. It's really a non-issue.*

Patient 4: *Yeah, I feel that it's going to feel a bit creepy having it in my chest and knowing it's in my head. Especially until my hair grows back, I think I'm going to feel a bit yucky. Yeah. It's no different to having a cardiac pacemaker…I'm trying to think of it in those terms, but I wouldn't blindly say that I'm looking forward to having the stuff in my head and in my chest…I think maybe I'll look at that lump in my chest and…[if] I'm feeling much less depressed, I'm feeling happy again, I might look at it and go 'I think this is the best' – I'll wear this with pride and courage, wear this as a badge of honour because it's made me better. I think if I was mentally well, I would have a totally different view of this thing in my body, but the way I look at it now I go 'yuck', it's going to be a bit yucky.*

Interviewer: *Do you think…having the DBS, that it could change how Sarah views herself or sees herself?*

Caregiver 4: *Possibly, yeah, but I think that's part of the depression. I don't think it will change her and the way she sees herself as part of, well, I'm suddenly different now because I had DBS. I think it's more of I'm suddenly different now because I'm not ill anymore. No…we don't view the DBS as being any different to someone with a pacemaker. It's just another apparatus that helps you survive.*

Device management

Patient 1: *You have to have a reliable supply of electricity in order to continue to charge the stimulator which could have implications if you wanted to go and live in the Amazon for six months but I didn't weight that very heavily because it's not something in which I have any interest at all.*

Patient 4: *What happens in 30 years when all these doctors are dead and who's going to fix it then? I just have these thoughts about who's going to maintain me when these doctors retire?*

Patient 6: *I think I've got a reasonably technical…background to know where I draw the limit. I would certainly fully expect that I'd be trained over a period of time [to use it]…The only piece of equipment that I've seen were the stems with the two electrodes on the end…What I haven't seen is…the controller and the battery pack…Somehow you sort of wear a collar…It charges up – I don't know – 20, 30, 40 minutes and it holds the charge for three or four days. So, it's not really a great deal.*

Caregiver 4: *[The recharging] we've certainly been told…it's relatively simple. The recharger is only a little thing. You can hide it on your chest and it's an induction type recharge so we're not expecting anything unusual or unrealistic. In this modern era, we walk around with computers, phones and their chargers so it's almost part of current life.*

Post-DBS

Relationship between body and device

Interviewer: *Do you think you've adjusted to having the actual device as part of your body?*

Patient 4: *I'm finding it a pain with the charge up, because now it can take two or three hours every second night…I'm thinking is this going to be an absolute bind for the rest of my life, trying to get this charging right…It's becoming quite ugh this is going to be really tough. It's going to prioritise my life.*

Patient 2: *After DBS…before I had it turned on; I didn't care about what I looked like…after the surgery, I went to the shops with all the bandages on my head – and being bald and everything – and not worrying about what I looked like. Whereas, once it was turned on, I started to worry about what it actually looks like, and everyone – how they thought it looked like as well…but as my hair did grow, I felt a lot more comfortable.*

Patient 6: *Yeah, I did go through a stage. I felt I was a – what's the word [pause] I felt I was like a monstrosity with this thing. I went through a phase where – I've let my hair grow longer, but you can still see – when you look in the mirror it's very apparent to you that you've had this procedure. You've got this thing floating around in your chest, but I'm through that.*

Recharging experience

Interviewer: *Do you think that she's [patient] adjusted to having the device as part of her body?*

Caregiver 3: *Mostly…one of the things is that it's taking her a very, very long time to charge it, so that's very restrictive…so I think that side of it is frustrating. One of the hopes was that – obviously having ECT…you're having a general anaesthetic, you can't drive – it's affecting your lifestyle. So, the hope was with the DBS that it's…not having to go through all of that, but while you're having to be plugged*

into the wall for hours at a time, it does affect your lifestyle. So, I suppose from that side of things, she's not accepting it as part of her body because she's finding that part unacceptable.

Caregiver 2: *She was getting very frustrated with that [recharging] because sometimes it takes longer to charge than others…Yes, I guess the reality is always different to what you're expecting, but she's getting used to it. That will always be a little bit of a burden I guess because now everywhere we go she needs to take the stuff with her, and make sure she's got it with her. I guess it's just not that much different to people that take heart medication…So, if we were to go on a holiday somewhere, we have to make sure we've got power sources to charge it up, just things like that. It is an annoying factor, but considering what benefit it brings…*

Caregiver 4: Having the implant I don't think has really impacted it in terms of from a personality thing or from a view of herself. I think she is quite comfortable with that…It's just the physical bit; the recharge is quite a challenge and it's quite time consuming…Every other day it's a couple of hours…so if you don't do it for two days, its battery life is quite depleted…So that's her biggest challenge at the moment, but I think she is quite accepting of the fact that if I feel better and that's what I have to do, that's what I do. She says it's no different to someone having dialysis every other day or every third day. So, it's just an accepted part of the illness.

Device control

Patient 4: *I just feel nervous when I'm putting it up, because I'm scared I'm going to push the wrong button and switch it off or do something…I'd rather my husband did it, because I get nervous about doing it. I'm much more familiar with it now and I'm much better…[But], he's not so upset when he's doing it or nervous or depressed. He's in a good place.*

Caregiver 4: *No, the device is simple. No. Sarah has, and again, I think because of depression, she doesn't take it all in…[It's] relatively straight forward, [the DBS clinician] will say to us, 'you can go up a setting' or whatever the number is. It's quite easy. That's very easy to do…[And] not that Sarah ever wants to turn it off, but if you want to turn it off, you know how to. It's quite simple.*

Caregiver 5: *There was one episode…where she [patient]…just couldn't bear herself…Her anxiety about readjusting down was difficult for her, but she eventually…got to a stage that I had to do something so yeah, we turned it down and that reduced it down…I try to leave it for Fiona as much as I can, but …unfortunately [she] is not very good with technology and…having the depression all these years.*

Relationships and Connection

In pre-surgery interviewers, patients and caregivers discussed how their relationship with one another had been impacted by depression. Those in spousal relationships had experienced a shift in dynamics, with caregivers performing and identifying with the 'carer' role to varying degrees ("pseudo" to "full-time"). All expressed their commitment to and support of one another, but acknowledged their relationship was not reflective of what a true husband and wife relationship "should" be or had been previously. Couples described their inability to plan due to the uncertainty of the illness. Plans for socialising or holidays were avoided, with couples living a day-to-day existence and keeping their world small (family, close friends only). Caregivers noted they had freedom to do activities independently, but expressed their preference to share and enjoy these experiences with their partner. In addition to intense sadness and suicidal ideation, some patients experienced moments of aggression and intolerance, which were often directed at caregivers by virtue of them being around. A decrease in open, honest communication was described, with some caregivers "walking on eggshells"

and not wanting to rock the boat, while patients would withhold details about the depths of their depression or suicidal thoughts. In some cases, suicide attempts or completions had been prevented by caregivers, either in a physical sense or due to patients not wanting to cause them anguish. Despite the difficulties posed by depression, patients and caregivers maintained strong and meaningful bonds. For patients with children, discomfort was associated with their children seeing them unwell and patients avoided allowing them too much insight into their illness. Social relationships more broadly were considered effortful to maintain and the prospect of social interaction was anxiety-provoking for most patients.

Both patients and caregivers hoped aspects of their relationship with one another would change after DBS. Patients hoped caregivers would not have to regularly bear witness to their intense sadness or anger. Some felt highly indebted to their caregiver and hoped for a day they could repay them. Others desired greater physical intimacy with their spouse and hoped DBS would improve their sex drive. Caregivers hoped for a more equal relationship and to be able to enjoy "small things, but meaningful things" together (e.g., having a coffee, going for a walk). Many caregivers experienced worry and guilt when leaving the patient at home alone for fear of what they would return to and hoped DBS would alleviate this heavy burden. All participants wished for greater ease when interacting with others and that time spent with family and friends would be enjoyed rather than endured.

Some participants reflected on how society tends to respond to individuals with mental illness. It was felt that people distance themselves when depression is involved and rarely show the same compassion and support to families as they would if their loved-one was suffering from a different illness, such as cancer. With the exception of close family and friends, a lack of support and community was apparent for some caregivers.

Post-DBS, those who had experienced notable benefits described how their relationships had both improved and become more complicated. Changing dynamics and re-negotiating roles occasionally let to increased conflict (e.g., patient more interactive and independent, caregiver needing to relinquish control). Despite improvements, some dynamics remained ingrained, such as a patient not contributing to housework or expecting to be waited on by a caregiver. Patients' increased

energy and motivation to do things was generally considered beneficial for the couple. However, caregivers occasionally tempered patients' impatience and enthusiasm to jump back into things too quickly (e.g., overseas travel, going back to work). These appeared driven by patients' desire to make up for lost time or re-establish their independence and identity. Caregivers felt more able to be open and expressive in their communication with the patient, although would still withhold or filter certain information. Patients' risk of self-harm had reduced, which was a considerable relief for caregivers. Relationships with family tended to improve, with patients more engaged and nurturing with children, and building rapport with grandchildren. Patients expressed interest in developing or re-establishing friendships, but were at the same time hesitant due to out-of-practice social skills and fear of judgement. Mental health support groups had been considered as avenues for building social connections.

For those who had experienced little-to-no benefit from DBS, their relationships remained mostly unchanged and functioned as before. However, the process of undergoing surgery and participating in the trial did result in some minor changes to relationship quality. For one patient, the energy and time they had available for others prior to DBS was depleted through the process of regularly travelling interstate for stimulation adjustments. This was difficult for some friends to understand and accept, resulting in more strained relationships. The tendency for some patients to display irritability after DBS led to caregivers becoming more irritable themselves. Instances of stimulation-related adverse events (e.g., mania, suicidal ideation), had been confronting experiences for caregivers and close-others and left lasting impressions. Caregivers discussed the difficulty they faced trying to cultivate a less dependent relationship with the patient, while also needing to be available when acute situations arose. Undergoing an experimental procedure for depression had prompted more discussion between patients and families (including children) about depression, but patients still avoided the topic so as not to burden others.

Caregivers discussed the relationships they had available to support their own wellbeing. Most caregivers had friends they could speak openly with or adult children they could seek support from. Some took antidepressant medication to help manage their daily stresses, but none were engaged in psychotherapy, although a number raised that perhaps they should be. The lack of support available to

carers of people with a mental illness, both in society generally and community services (e.g., support groups), was noted.

Table 3. Relationships and Connection

Pre-DBS
Impact of depression on relationships
Interviewer: *What changed for you in the way that you live since Deborah got depression?*
Caregiver 2: *Well it's very much multiple aspects, because from a relationship point of view that changes completely because you're not – well, you're still husband and wife but she just relies on me for everything to the point where she says she wouldn't be alive if I wasn't around [laughs] it's a pretty big responsibility. It's not something you really want. You're supposed to be there as a team and challenging each other and supporting each other but it's all very one sided. So, from that point of view it's a very different relationship than what we had before.*
Patient 1: *Depression itself is incredibly corrosive. Incredibly corrosive of relationships generally so I suppose were I to obtain some benefit, there might be some improvement in that area of my life…As things are right now, it's incredibly effortful to maintain relationships at all. It's really difficult if people ring me, just even to answer the phone…It's difficult to spend time with others, it's just exhausting. I would say certainly from the treatment at that level, it would just be a bit less effortful for me and I think that would have implications in terms of the quality of relationships as well.*
Caregiver 4: *You can look at yourself as a pseudo carer and just someone that's tagging along. We're there, we're together, but there's not really a proper relationship if you like…and that has to improve because it's not much of a life for either of us…There's still a commitment and you want to help someone get better but it's pretty tough for both of us…I think that's just where we want to go.*
Caregiver 6: *He loves his family…he loves but he can't show any warmth or affection…He's so preoccupied with…his illness and he's missing so much and he knows he is missing so much…It robs you of all these things.*
Hopes for future relationships
Interviewer: *How about yourself? How would you like your own picture to look in a year's time?*
Caregiver 4: *Oh, for me, I mean I'm just happy if – I'm happy when she's happy and I'm happy when I can walk out the door and know that she's safe…I'd like to do things together…but, at the moment we can't, we don't…So, for me it's just hoping to return to where we were…where we included our friends and we integrated more with people – and ourselves.*
Caregiver 2: *I just want to be in an open and honest relationship again – it's not a dishonest one now, you just have to filter what you say – and just communicate our wants and desires out of life. Just on a more equal footing in the relationship, that's what I'm expecting…Our relationship as husband and wife…how do we start re-engaging again? It might be hard for me to let go of making all the decisions or controlling everything. After ten years of it you start getting used to it, I suppose. Yeah, I guess we expect that…if she starts getting better our relationship will change again and we'll probably need some guidance for that to help us get through that. We'll see how we go.*
Patient 5: *I feel my [children], I'm not quite sure how to put this, see me as sick in some way, and I'd really like that to not be the case. I want them to see me as a fully functioning person, whereas, yes at the moment I just feel they see me as someone that's sick.*
Society and depression
Patient 3: *That's one of the biggest things that a lot of people don't seem to understand is that when you have depression it doesn't just impact you; it impacts the people who are close to you. It takes a huge toll on them…They seem to understand, okay, if someone is dying of cancer, that they're going through chemo – it's very emotional, it's very hard and they give the…carers a bit more love and empathy. But it's not the same with depression…They'll wait until that person has turned blue, and then suddenly all put on their little sympathy hats.*
Patient 4: *You get a lot of sympathy if you get cancer for eight years but when you've had depression for eight years people just are a bit sick of it really. If you've got cancer, they're having a fundraising ball for you but depression is actually probably worse than cancer because with cancer you live or die. Depression is a life sentence if you don't get rid of it.*
Caregiver 3: *Unfortunately, a lot of the times when people do have a mental illness, people do try, tend to treat you like you've got no brains, type thing.*

Post-DBS

Wellness and adjusting relationship dynamics

Interviewer: *Would you say that your relationship with Clementine [caregiver] has changed?*

Patient 6: *Oh yes. It has to have been. I've gone from – I've been a dead duck to – we're more involved in each other's lives now…I think last week we were out three times…I'm just looking forward to life being a hell of a lot better than what it has been…I'm glad to say my family have rolled with the punches. They've been there on the bad days and they're going to be there for the good days now…Let me put it this way, I feel I'm closer to my family than anything I've known for a long time, because there's just been so many occasions…I haven't been able to go because I've been too unwell.*

Interviewer: *Do you and Deborah feel like different people now?*

Caregiver 2: *I don't think so – well, no, yeah, she does definitely. Yeah, I don't know, it's a hard question that one. She definitely, for sure, and I guess I'm still trying to figure out where my place in all this is really, and still doing all the things that you do, but our relationship is obviously going to change as time goes on. We're getting there, but it doesn't come without its own set of drama.*

Interviewer: *If you were to describe your relationship since DBS, would you say things are better, easier, more strained, a bit more complex?*

Caregiver 2: *It's more complex actually, which is interesting, when you think it wouldn't be, but I think really when someone is so depressed and so low all the time you just get into that routine, and your interactions are pretty, day-by-day, the same…So, now she's become her own self, interactive and all that sort of stuff, so there's definitely more complexity to it for sure. I think some of…those roles that I was performing, which I need to let go of, these habits for me that I have to let go of. I'm not perfect, and sometimes I don't take that kind of feedback well [laughs]…[It's] definitely more complicated, but I think overall, she's certainly better…and she can express herself a bit better. Plus, I can express myself a bit more, which prior, it'll still be this way, but before I couldn't have a bad day…At least now there's a bit more scope to be able to share those own stresses that I have in my life. But it's still early days, and I still have to choose the amount information and the colour of it. But I think as time goes on it'll get – it'll all interact more freely like a couple should…We're certainly getting back more to that, and more of an equal relationship. It's not quick, it's going to take time.*

Caregiver 6: *Well, it's not just an improvement in his mental health, it's an improvement all around…I would have to say, because his mental health at the moment is pretty good, it [the relationship] has to be easier. I'm not saying it's perfect, but it has to be easier. Because – yes, I've got less worries of him trying to harm himself…He's very pedantic about things, and I don't see eye to eye with, but if I question it, I'm wrong. So, I'm learning somewhere along the line what to question and what to not.*

Impact of no benefit on relationships

Patient 4: *Parents are not meant to be depressed, they're meant to be your rock, and when that rock gets depressed and is sobbing in a corner, that's very challenging as a child I imagine.*

Patient 5: *I've probably said more to my [children]. Sometimes they'll say 'sometimes you say you're all right but you're not'. I suppose I have been a bit more open with them.*

Caregiver wellbeing and support

Caregiver 5: *I've got a couple of good mates, we talk things through and always checking in how things are going…So, that's been pretty good. I know I can talk to my [children] about it…but I haven't gone, haven't sought any professional help at this stage. Sometimes I think I should…Yeah, because I mean sometimes it does wear you down – then you think what she [patient] is going through, if I'm only going through this [laughs].*

Caregiver 6: *I belonged to a group once, where you used to meet up and talk, and that was fairly good, because you gave each other support on different things. That sort of petered and fell apart…I rang the council to see what they had…there isn't a lot, really, of support, I have to say. It's – there's a fair bit of stuff that the ill person can do, but the people who look after them, there isn't a lot. Which is sad. There must be so many people like me.*

Discussion

The aim of the current study was to qualitatively examine how DBS for TRD impacts patient personality, their identity and relationships, from both a patient and caregiver perspective. These narrative, first-hand accounts add to our understanding of DBS and provide valuable insights that are

typically not captured in randomised-controlled trials. We discuss these findings in light of existing DBS literature and consider their clinical implications.

Personality and Identity in Treatment-Resistant Depression

The onset of depression for most patients in the study was in adulthood (n = 5) after they had established identities and personalities distinct from those present during illness. Psychometric personality scales of depressed individuals often appear homogenous, with Five-Factor profiles characterised by high Neuroticism and low Extraversion, regardless of age (Weber et al., 2012). These profiles tend to reflect more the nature of the illness than the individual themselves. Concerns have been voiced about the potential for neurointerventions such as DBS to result in personality change (Glannon, 2009; Schechtman, 2010); however, in the case of psychiatric disorders this is the intended outcome. Synofzik and Schlaepfer (2008) suggest that if personality – that is "a dynamic and organised set of characteristics in a person that uniquely influences his or her cognitions, motivations, and behaviours in various situation" (p. 1514) – remain unchanged, the intervention has failed. The hope many have, including the participants, is that DBS will restore premorbid personality and self. This is a reasonable desire; however, it should not be expected that individuals who have endured years or decades of depression (as most patients had) will go completely unchanged by this experience and be restored unmarked (Johansson et al., 2011). In the present study, the degree to which patients felt their old personality or self had been restored was closely associated with the degree of benefit they had achieved. Still, even patients who felt much restored identified ways in which they were far from who they were previously, particularly regarding functional capacity to perform meaningful activities and roles (working, travelling, socialising). Similarly, caregivers recognised elements of their past loved-one, but continued to see persistent illness traits (e.g., sympathy-seeking, self-focus).

While an exact restoration of premorbid personality or self is improbable, if not impossible, they serve as helpful guideposts for recovery. The process is more complex where mental illness has emerged in adolescence during important stages of personality and identity development (Roberts, Caspi, & Moffitt, 2001; Waterman, 1982). This is often the case in OCD and regularly occurs in TRD. Following DBS, rather than attempting to pick up where one left off, these patients must attempt to

forge a new identity and personality that is not structured around mental illness (de Haan, Rietveld, Stokhof, & Denys, 2013; Thomson, Segrave, & Carter, 2019). The *burden of normality* concept has been used to describe identity challenges and poor psychosocial adjustment in neurological populations post-surgery (Baertschi, Favez, et al., 2019; Wilson et al., 2001), and has been applied in psychiatric DBS cases (Bosanac, Hamilton, Lucak, & Castle, 2018). This phenomenon where patients and caregivers experience difficulties transitioning from chronically ill to suddenly well, highlights the need for preparatory work and psychosocial rehabilitation in DBS to assist with regaining wellness and transitioning self-concept. Not all of the current patients were engaged in psychotherapy after DBS, but for one patient who gained benefit from DBS this support was vital for their psychosocial adjustment. Cognitive behavioural therapy has been recommended as a best-practice component for DBS recovery and shown to augment treatment effects (Mantione, Nieman, Figee, & Denys, 2014). DBS is only a starting point to living well, as the scaffolding around the patient will still reflect someone with chronic mental illness (e.g., limited social connections, ingrained dependency on caregiver).

Relational Adjustment

For patients who experienced therapeutic benefit, renegotiating the patient-caregiver relationship to a more egalitarian dynamic was a challenge. Even positive changes were difficult for caregivers at times as they broke predictable patterns (e.g., patient exerting independence, patient eager for daily outings). In De Haan and colleagues' (2015) OCD sample, patients reported that both they and their partners had to "get used to" the new them. As OCD had always been present in their relationship, couples had created lives that worked around the illness. With the current sample, caregivers had known patients well before depression onset. They possessed valuable knowledge and understanding of the patient and were well-positioned to provide observational feedback. This is one reason caregivers should routinely be involved in DBS patient's clinical care. Additionally, it is advantageous to include them in clinical research to assess the impact DBS has on their own lives. DBS can be a transformative experience (Agid et al., 2006; Bell et al., 2011b); therefore, a considerable period of adjustment is required for both parties. In PD, there is growing recognition of caregivers' essential role in patients' preparation for DBS, as well as the procedure's impact on their

lives and wellbeing. A lack of support to assist caregivers with the implications of DBS and psychosocial adjustment has been noted. A number of pilot studies have attempted to address this issue, including an 8-session psychoeducation program designed for patients and caregivers (Flores Alves Dos Santos et al., 2017), and an 8-session program of individual CBT therapy for caregivers post-DBS (Mosley et al., 2020). Although small samples, these results show promise and contribute to an area of unmet need. An absence of support for the current caregivers was apparent, both for assisting with relational adjustment and to focus on personal wellbeing. None had pursued formal psychotherapy, in part because the severity of their psychological needs was considered less than that of their loved-one. Given the unique challenges created by DBS, support programs designed specifically to meet these needs are recommended for caregiver wellbeing.

Device Embodiment and Acceptance

Patients did not experience sustained fundamental changes in self-perception or feel in anyway dehumanised by having an implanted electrical device, as has been reported in some DBS studies (Schüpbach et al., 2006). However, some factors had impacted patients' embodiment (i.e. sense of being in their body) and acceptance of the device. These included: the noticeability of scarring, intermittent pain associated with IPG and body positioning, DBS' perceived benefit (or lack of), and recharging needs and experiences. It was common for recharging to be difficult and frustrating. It is typical for an implanted device that functions well to go unnoticed and be easily incorporated into one's body schema (Slatman & Widdershoven, 2015). However, if it requires frequent attention and creates frustration (through regular, lengthy recharging), this can impact agency and may reinforce internalised feelings of defectiveness, particularly if no therapeutic benefit is gained. Patient satisfaction with rechargeable DBS products has been evaluated, but primarily in movement disorders (Jakobs et al., 2019; Mitchell et al., 2019). The recharging needs for individuals with psychiatric conditions differs from those with movement disorders, as does their psychological and cognitive profiles. In OCD, post-operative education has been shown to assist with device-related anxiety (De Vloo et al., 2018), but further investigation is needed. Notable memory difficulties, which the majority of current patients reported (n = 4), can affect retention of device-related information. For this reason, perioperative device education may require modification for TRD purposes. As DBS

for psychiatric indications progresses, so too should research evaluating patients' device-related needs (Klein et al., 2016).

Limitations

The patient sample (n = 6) included in the study was small, but it reflects the limited number of patients undergoing DBS for TRD in Australia. Samples of 6 have been shown to be sufficient for qualitative purposes and data saturation was achieved (Crouch & McKenzie, 2006; Guest et al., 2006). There is also a crucial obligation to learn as much as we can from these very few DBS for TRD cases (Fins et al., 2017). The triangulation of caregiver perspective, in addition to multiple time points, added to the richness and depth of the analysis. These patients were extreme in depression and treatment resistance in comparison with other patients who have undergone DBS for depression globally. It is also noteworthy that the majority of the patient sample were women (5 of 6). While this is not strictly a limitation, this gender imbalance is likely to have influenced the nature of the observed findings. Further, given the qualitative nature of the study and the specific context in which the results were derived, these findings will not be representative of all DBS for TRD patients' experiences. Few patients experienced sustained meaningful benefit at the time of follow-up (n = 2); therefore, our insights into the process of adjusting to wellness are from limited cases, although we have captured a broader range of experiences. Repeat interviews in subsequent years when patients have had the device longer would have been valuable to see how their experience evolved.

Conclusions

This is the first qualitative study of its kind to provide in-depth insight into the lived experience of DBS for TRD, including perspectives from patients and their closest supports who are vital throughout the preparation and recovery process. Change in self-concept was highly linked to therapeutic response and was part of a larger process of adjustment for patients, caregivers and their relationship. Caregiver-specific support is recommended for managing this challenging process. Patients' embodiment experience with the implanted device was marked by recharging challenges. Depression-specific research on patient satisfaction and user experience with rechargeable IPGs is required.

CHAPTER SEVEN

INTEGRATED DISCUSSION

Chapter Seven – Integrated Discussion

Review of the Research Problem and Thesis Aims

Prominent reports of PD patients experiencing changes in personality, self-perception and relationship quality following DBS implantation (Agid et al., 2006) created substantial interest amongst clinical, ethical and social science communities. Subsequent research, however, was unable to elucidate the perceived cause of these changes and their impact upon individuals and families. For example, quantitative assessment measures used in clinical trials were not designed to detect these unintended side-effects or complex lived experiences (Bluhm & Cabrera, 2018; Lewis, Maier, Horstkotter, Zywczok, et al., 2015). The research within conceptual and theoretical neuroethics speculated on how DBS can create alarming and ethically problematic changes in personality and identity; however, aspects of these discussions have been criticised for overinflating the risk of these changes and their relevance for most DBS patients questioned (Gilbert et al., 2018; Müller et al., 2017). Most significantly, the voices of those most equipped to discuss these issues were regularly absent; namely the patients – the DBS recipients – who undergo the intervention; the caregivers, who know patients intimately and observe them daily; and the clinicians, who provide medical care and manage patients' illness and treatment. The nature of these changes remained largely unknown, as has their impact on patients and families and how they manage them. By gaining the perspectives of these key stakeholders, we can begin to understand these complex issues. While the aim of DBS in psychiatric disorders differs from movement disorders (i.e., to intentionally alter mood, behaviour and thoughts, rather than improve motor function), the trialling of DBS for a growing number of psychiatric indications heightens the need for in-depth research investigating perspectives and lived experiences in these cases.

The primary aim of this thesis was to prospectively examine the impact of DBS on patient personality, self and interpersonal relationships, in an established neurological (PD) and emerging psychiatric (TRD) indication. To do so, I obtained multiple perspectives on these issues by qualitatively investigating the views of patients, caregivers and DBS clinicians. The thesis findings focused predominantly on personality and personality change, but the topics of self (and related

concepts identity, self-concept) and patient-caregiver relationships were also discussed. Six research questions were posed:

1) What awareness or knowledge of DBS-related personality changes do patients and caregivers have prior to DBS?

2) What, if any, were participants' experiences of personality change following DBS?

3) How does DBS impact patients' identity and sense of self?

4) What is the perceived cause of these changes?

5) What impact do these changes have upon patients, caregivers and their relationship?

6) How are any unanticipated outcomes managed clinically?

Here I present an integrated discussion of the study findings relating to these areas of investigation.

Awareness and Understanding of Personality Change

Clinicians working in PD (Ch. 4) discussed the risk of post-DBS personality changes (alternatively described as *behavioural*, *mood* or *psychiatric* changes) with patients and families during preoperative education. Exactly how this information was presented was unclear and no formal processes for assessing comprehension were discussed. Some clinicians demonstrated an assumption that information discussed preoperatively was understood and retained after DBS. Conversely, others described difficulties they faced with preoperative discussions not being recalled or understood post-DBS, particularly regarding the potential side-effects and goals for DBS ("[The patients] move the goalposts a little" PD Nurse 4). These issues were reflected in the interviews with PD patients and caregivers (Ch. 5). Few PD patients and caregivers were aware of the risk of personality change following DBS, either because it was not discussed or the information was not retained. Evidence of preoperative information no longer being recalled after DBS was also apparent. For example, in preoperative interviews some participants said they were aware speech may not improve or could decline with DBS. In postoperative interviews when speech issues had occurred, the same participants said they were unaware it was a potential outcome. This reflects the limitations of the contractual 'disclose and sign' informed consent process and supports previous recommendations for more iterative and ongoing discussions of patient and family goals, motivations and needs that is

accompanied by education and materials on the procedure's risks and benefits (Kubu et al., 2018; Liddle et al., 2019; Mosley et al., 2019). While advance directives might aid the informed consent process, they are not without complications and are a point of controversy within the bioethics literature (Glannon, 2009; Müller & Christen, 2011; Sankary et al., 2020).

Clinicians working in psychiatric disorders discussed the risk of stimulation-related *adverse events* (e.g., hypomania and mania) with patients and families, but not *personality changes*. Other unanticipated psychosocial outcomes were flagged, such as the challenges associated with adjusting from chronic mental illness and renegotiating familial and social roles. TRD participants' perspectives on whether DBS could result in changes in personality were shaped by personal opinion rather than any clinical discussions (Ch. 6). They commonly believed antidepressant effect would bring about a return of the patient's premorbid personality. Concerns that intervening directly within the brain could bring about a distinct and undesirable change (e.g., "like Jekyll and Hyde" Patient 6) were less common. Other unanticipated outcomes participants identified were stimulation-related side-effects (e.g., mania, sleep disturbance) and challenges altering deeply-ingrained relationship dynamics. However, awareness and understanding of surgical risks was considerably more thorough (see *Appendix C* and *D* for further discussion on informed consent and long-term risks).

Experiences of Personality Change

Clinicians working in PD (Ch. 4) had observed a wide range of personality changes over the course of their careers. These included some characteristic changes (disinhibition, irritability, increased energy and drive), impulse control issues (impulsivity, impaired decision-making and ICDs), plus mood, cognitive and psychiatric changes (anxiety, low mood, apathy and subtle cognitive changes). Some rare, but extreme outcomes were reported (violent behaviour, psychosis, mania). There was consistency in the types of changes described by these clinicians and the participants in the PD study (Ch. 5), in particular irritability, impulsivity, lowered mood and cognitive impairments. The patients and caregivers were more likely than clinicians to discuss positive and meaningful personality changes. This may reflect that *personality change* is understood as a pathology in clinical contexts. What the PD participants reported is consistent with general descriptions of personality and

behavioural changes described in clinical research (Houeto et al., 2002; Krack et al., 2001; Lewis, Maier, Horstkotter, Zywczok, et al., 2015; Pham et al., 2015; Saint-Cyr et al., 2000; Temel et al., 2006), but these subjective descriptions provide individual context, narrative and humanity to these experiences. Comments from clinicians and patient-caregiver dyads reflect how adept caregivers are at detecting subtle changes even if they are "hard to put a finger on" (PD Neurologist 7) and that their observations can be important for patients to also recognise the changes. This reflects caregivers' important role in detecting and reporting changes that may require careful clinical attention.

In contrast, clinicians working in TRD did not categorise what they observed in patients as a *change* in personality, rather a *restoration* or *unmasking* of premorbid personality in those who regained wellness. The connection between recovery and restored personality was also drawn by the TRD participants (Ch. 6). Notably, undesirable changes, such as hypomania, mania and intense irritability, were not considered personality changes, but stimulation side-effects. These were transient episodes, resolving with stimulation adjustment.

A number of factors may explain the different conceptualisations of changes observed in movement and psychiatric disorder populations. In TRD, patients, caregivers and clinical teams are highly attuned to mood, cognition and behaviour, with adjustments made to achieve optimum outcomes in these areas. These are certainly considered and monitored in PD; however, the primary aim of the intervention is reducing motor disability. Also, heightened attention to physical symptoms can come at the cost of psychological outcomes, particularly minor personality changes (e.g., impulsivity, irritability, impatience) that can be downplayed or considered a trade-off (see Ch. 4 and 5). In PD, characteristic compulsive behaviours (e.g., hypersexuality, compulsive gambling or shopping) related to both stimulation effects and dopaminergic medications can occur. These behaviours are often incongruent with the patient's values and usual character, to the point spouses can feel they are married to a different person (see Ch. 5 and Mosley et al. 2019). I suggest that this incongruent nature and the opportunity for changes to endure if overlooked or un-addressed contributes to their regular categorisation as *personality change* (Ch. 4).

Results from the thesis suggest that some pathology-focused models and measures of personality (e.g., FrSBe) are appropriate for detecting *certain* changes following DBS; however, a

more comprehensive model would be required to encompass the positive, as opposed to pathological, changes that were observed and reported. If changes were detected on the NEO Five-Factor Model traits, they could be speculated upon as being positive or desirable, but ultimately this is a personal judgment for individuals and their families to make. Responses from participants, particularly those in Chapter 5, included features not considered by traditional personality models (e.g., body functioning, facial expression) and demonstrated that each patient and their family valued specific aspects of their individual personality. This aligns with recommendations for more personalised, patient-centred approaches to assess outcomes, including personality, before and after DBS (Kubu et al., 2017; Kubu et al., 2019).

Impact on Self, Identity and Related Concepts

Although the topic of how DBS impacts patients' identity and sense of self was not reported within the published paper (Ch. 4), some comments from PD clinicians are worth noting in light of patient experiences (Ch. 5). A number of patients described feeling like their 'old self' after DBS. Interestingly, one clinician indicated that a patient saying "I feel like my old self again" (PD Nurse, 4) would alert them to possible *de novo* personality changes, in addition to being "disinhibited" or "too good to be true". Another clinician commented that if a patient had "suddenly become reborn" or felt like "a different person" after DBS, they would suspect "psychiatric overdrive" (Neurologist 7, PD) that was a result of stimulation. In the literature, a return to a "younger" self and personality has been connected to stimulation-related neuropsychiatric symptoms and distorted perceptions of enhanced capacities (Gilbert et al., 2017; Mosley et al., 2019). This raises an important question whether feeling like one's 'old self' is a return to equilibrium or an indicator of enhancement? Feedback from family may help to resolve this question. Caregivers commonly reported that patients were as they remembered and that their behaviour was not uncharacteristic, excessive or youth-like (Ch. 5). Rather than a stimulation side-effect, the experience of one's 'old self' appeared largely driven by the alleviation of debilitating symptoms and regained autonomy.

Despite PD patients reporting various changes in personality, none felt like they were a different person after DBS. In contrast, some TRD patients did feel like a different person, but in a

way that was linked to their prior 'well' selves. This creates some doubt about the clinical relevance of concerns that DBS is a *threat to identity* and carries a risk of *becoming another person* (Glannon, 2009; Schechtman, 2010; Witt et al., 2013). Previous studies have found that questions about such issues are not clearly understood by or relevant to patients (de Haan, 2017; Mosley et al., 2019), but issues of authenticity, autonomy and control do appear to hold greater clinical, and therefore, ethical salience (Goddard, 2017). Illness was considered by both PD and TRD patients as masking or hindering one's true self, with DBS allowing them to express or experience an authentic self, but only if the outcome of their procedure was successful (e.g., improved mobility, antidepressant effect) (Cabrera, Courchesne, et al., 2020; Klein et al., 2016). By the same token, DBS also had the ability to produce inauthentic experiences for patients, such as episodes of mania, hypomania and irritability, which felt "all way over the top" (Patient 6). There can be difficulties establishing what types of change reflect the most authentic or correct 'true self' (Johansson et al., 2011; Kraemer, 2013b). How the individual evaluates the change is important. For example, one patient may consider an increased libido after DBS to fit with their self, while for another it is "too much" (p. 12) (de Haan et al., 2017). The patient's evaluation should not be solely relied upon. In cases of hypomania or increased impulsivity, a patient may feel during these states that they are their authentic self, while their family and doctor disagree. From a pragmatic clinical perspective, relevant questions to consider according to De Haan and colleagues (2017), are: a) do the changes *fit* the patient (do they feel they are authentic)?, and b) are they problematic or causing any conflict with caregiver?. If so, are they a stimulation side-effect that requires adjustment or something enduring that would benefit from professional psychosocial support? Both before and after the intervention, PD and TRD patients' perception of control, over their mind, body and actions was also important in defining their sense of self and autonomy. For the most part, illness was accompanied by a sustained sense of impaired (and declining) control, while DBS restored it; however, transient stimulation-related episodes, persistent side-effects (e.g., speech, balance) or burdensome recharging commitments negatively impacted patients' perceived autonomy and control.

TRD patients that achieved meaningful benefit from DBS described distinct images of themselves that contrasted their ill and well selves: "The *devil* is when I was depressed and [now] I

feel like an *angel*" (Patient 2); "I'm not living in fear of not being in control and being the *victim"* (Patient 6) (emphasis added). This reflects a reconceptualisation of their identity and self-concept that is interlinked with their mental illness. As described by the *burden of normality* model of adjustment, this transition in self-concept is rarely straightforward and requires considerable psychosocial reorganisation (Wilson et al., 2001). There can also be intrapersonal and interpersonal expectations for the patient to function as a "normal" person after surgery. Aspects of the burden of normality outlined by Wilson et al. (2001) were present in the TRD study, including patients' urgency to return to work, make up for lost time, and caregiver frustration with the patient not performing housework. Aggression and hostility between patients and caregivers stemming from changing relationship dynamics was also present (e.g., caregiver needing to let go while patient exerts more control and independence). Fortunately, patients and caregivers were aware of these potential difficulties prior to surgery, which aligns with recommendations for psychosocial rehabilitation involving patients and family to commence before surgery (Wilson, Bladin, & Saling, 2007).

Perceived Causes of Observed Changes

While the qualitative method of inquiry used in the thesis cannot determine the causal roots of any iatrogenic harms (Bittlinger, 2017; Gilbert et al., 2018), it does demonstrate how patients, caregivers and clinicians make their own causal inferences and the meaning and implications they carry. Across all three studies and participant types (patients, clinicians and caregivers), a complex configuration of potential factors influencing changes in patient personality and experience of self were discussed. Clinicians working in PD identified a range of both neurobiological factors (stimulation titration and iterative adjustment, medication changes, disease progression) and psychosocial factors (response to treatment outcome, unmet expectations, alleviation of symptoms, and undisclosed or unmasked psychiatric disorders). It was important for clinicians to detect changes caused by stimulation (e.g., impulsivity, impaired decision-making) or medication adjustments (e.g., low mood), as these were significant and *fixable* side-effects. Some clinicians were clearly vigilant in monitoring undesirable *de novo* changes, with concerns they could negatively affect the patient's relationships and social reputation or that an abrupt drop in mood could pose a suicide risk. Minor

changes (e.g., tendency to giggle, slight irritability) were considered an acceptable trade-off following consultation with the patient and family.

An undesirable change that three TRD patients experienced was increased irritability, but the perceived cause in each case differed (i.e., stimulation side-effect, frustration with outcome and persistent depression, and a reaction to adjustment difficulties). Patient and caregiver beliefs about cause are important as they can dictate how they should be addressed. Discrepancies in perceived causes, and also perceived solutions, can impact interpersonal interactions. For example, Klein et al. (2016) reported that families of DBS patients would quickly point to stimulator adjustment as the solution for any residual symptoms that created relational discord. This suggestion could invalidate the patient's feelings and beliefs about what was actually causing their mood or behaviour (e.g., the family member's own difficult behaviour or interpersonal style). This example demonstrates the importance of caregiver involvement in DBS education and feedback sessions, and the need to build a shared understanding of an intervention's capabilities and limits. Much of the ethical and philosophical debate has centred on the capacity of DBS, specifically its neuromodulation effect, to alter personality, self and identity (Gilbert et al., 2018; Müller et al., 2017). Participant perspectives across all studies demonstrate that the issue of causality is highly complex and any changes not directly attributed to stimulation are both still ethically and clinically relevant (Snoek, de Haan, Schermer, & Horstkötter, 2019). This is particularly true considering the relative impact of personality changes attributed to other causes (e.g., illness, DRTs).

Impact on Individuals and Relationships

What was apparent across all interviews and participants was the substantial impact illness has upon patient personality, their experience of self and their relationships. The same applied to undesirable side-effects associated with other necessary treatments (e.g., ICDs with dopamine agonists, impaired memory with ECT). While stimulation-related hypomanic and manic episodes were unsettling and confronting, patients and caregivers had an understanding of their transience. The progressive nature of PD and enduring quality of severe depression, however, could be all-encompassing with little reprieve for patients and families. The impact of illness cannot be

downplayed and DBS needs to be considered within the wider treatment trajectory patients and caregivers have travelled along. PD clinicians suggested that because couples were often already experiencing a variety of changes related to PD, when minor personality or behavioural issues emerged after DBS they would "just roll with it", particularly if they had a stable and happy existing relationship (Nurse 5, PD). Pre-existing relationship quality appears important for determining how couples will cope with unanticipated outcomes. Of the 65% of patients in the Agid et al. (2006) sample that experienced a conjugal crisis within two years of surgery, most had pre-existing relationship issues. The clinicians working in PD made similar observations: minor personality changes and unfulfilled expectations could be the last straw for struggling relationships, but rarely was DBS the sole cause of relationship conflict or breakdown. Spousal relationships captured in the PD sample remained fairly consistent over time and relationship quality was reflected in how couples responded to and managed the challenges and stressors associated with DBS. No couples had separated at the time of the follow-up interview, but 9-months may not have been sufficient time to assess the full impact upon relationships.

How DBS impacted caregiver burden and patients' independence was also raised. Some PD clinicians believed that caregiver burden did not necessarily decrease after DBS, rather the nature of it changes (e.g., more focus on personality change, stimulation side-effects). This experience was reflected by some caregivers, with one commenting: "it's not a problem, it's just different. Our life's sort of different" (PD caregiver). Other clinicians felt patients' regained independence and outgoingness could be difficult for caregivers and couples to adapt to: "he's much better now, he doesn't need me. What's my place in the world?" (Nurse 5, PD); "everyone is a little bit lost in what their roles are" (DBS Nurse 4, PD). This dynamic, however, was not reflected in the PD dyads; regained independence was a substantial relief for caregivers and they encouraged patients to do things without them. We did, however, find evidence of TRD couples struggling to adapt to the patient's emerging independence. This appeared due to the ingrained patient-caregiver dynamic these couples had that had been established for over a decade. Caregivers considered the patients' emerging independence a positive sign, but none the less, the process of adjusting well-formed habits, routines

and patterns created tension and left caregivers uncertain of their role at times: “I guess I’m still trying to figure out where my place in all this is” (Caregiver 2).

Management of Unanticipated Outcomes

The structure of post-DBS follow-ups with PD patients, including the frequency of assessments and the clinicians involved, varied significantly. So too was the degree to which individual clinicians enquired specifically about post-DBS changes in personality and behaviour. A range of barriers were identified for why patients and caregivers might not openly disclose this information (e.g., embarrassment associated with ICDs, an assumed symptom trade-off, limited insight into the changed behaviour, or the patient enjoying the changes and not recognising them as a side-effect). This highlights the need for clinicians to actively elicit this information through direct and indirect enquiries (e.g., noting changes in bedtime). Direct enquiries from clinicians allowed patients, and to a greater extent caregivers, the opportunity to report changes. The inclusion of a DBS nurse in the team was considered valuable, as individuals may feel more comfortable raising these issues with them due to being easier to contact, having more time to talk, and more approachable than specialist doctors. Those living in remote areas who had limited contact with their specialist indicated there was insufficient time to discuss these issues in appointments and that the specialist would prioritise other problems.

Clinicians working in psychiatric DBS had very structured follow-up arrangements by virtue of rigorous research protocols, as well as ad hoc discussions and appointments to address any adverse events. In psychiatric DBS trials, caregivers probably have a greater level of involvement than most clinical trials (e.g., getting patients to appointments, assisting with physical recovery, monitoring side-effects, and providing some feedback to the clinical research team); however, some caregivers lamented not being included more in certain processes. For instance, some caregivers felt unclear on what the future plans and approaches for stimulation management were. While this information had been discussed with the patient, it was not always retained sufficiently for them to convey to the caregiver. In certain cases, caregivers were concerned the patient would not voice or would downplay uncomfortable side-effects they were experiencing to the research team. This raises an important

ethical tension between respecting patient or research participant autonomy and privacy, and inclusion of a caregiver to support and advocate in the patient's care. Confidentiality and disclosure of sensitive information is an important point to consider, as the presence of a caregiver may impact what information patients do or do not disclose (e.g., suicidal ideation, ICDs or antisocial behaviours). A combination of independent and shared appointments may address some of these issues and ensure both patient and caregiver needs are met; however, the desires and dynamics of each pair will differ, so caregiver involvement needs to be established on a case-by-case basis from participation outset.

A prominent theme across all studies was the lack of support provided to caregivers, both in terms of coping with their loved-one's illness (either PD or TRD) and assistance managing the challenges directly related to DBS. Support options for patients themselves were more widely available and accessible (e.g., PD and DBS education events and support groups run by state peak body; mental health support groups and services through local council). The sudden and abrupt changes that occur in DBS can create a variety of unique challenges for caregivers. These challenges and the existing pressures involved with providing care to a loved-one with a chronic condition highlight the urgent need for research and support to assist caregiver wellbeing. With notable exceptions (e.g., Mosley et al., 2020) there have been very few studies of interventions to support caregivers of someone undergoing DBS.

Another area of urgent need is ensuring DBS patients have on-going access to specialist care. Interviews across all three studies highlighted the limited knowledge and understanding of DBS within general medical communities and the necessity for specialist involvement to avoid undesirable outcomes (e.g., behavioural issues due to poor DBS management necessitating residential care; lowered mood in response to battery depletion or stimulation mis-management while patients undergoes ECT). This reflects the importance of patients having reasonable and ongoing access to specialist care. Telehealth may provide a method of providing ongoing specialist care, as evidenced by the rapid roll out of telemedicine following the COVID-19 pandemic. In the case of psychiatric DBS, it highlights the complex issue of post-trial responsibility for device management and patient care and the requirement for research teams to develop robust post-trial management plans that ensure patients' future access to treatment and care (Drew, 2020; Hendriks et al., 2019). As one patient

wondered: “What happens in 30 years when all these doctors are dead and who’s going to fix it then?”. The issue of post-trial responsibilities and future patient care is explored further in *Appendix D*.

Variations in DBS Experiences for Neurological and Psychiatric Patients

It was anticipated that there would be observable differences in the DBS experiences of the PD and TRD patient groups. This is due to the differing nature of these illnesses and the DBS treatment status (established versus experimental). The sample comparisons that are discussed here do not directly relate to the core narrative of the thesis; how DBS impacts personality, self and relationships. They are, however, important for recognising the vast differences that exist in the application of DBS across disorders and discourages the view of DBS as a generalisable, singular treatment. Disease-specific contextual factors influence the entire DBS procedure, including the process for seeking DBS, treatment outcomes, and patient and family needs.

In coming to the decision to pursue DBS, both patient samples where at a stage in their illness where treatment options other than DBS were diminished; however, the illness severity and disability present in the TRD sample was more advanced. This is unsurprising given DBS for TRD is an experimental intervention that is only offered as a treatment of absolute last resort (see *Appendix D* for ethical considerations in psychiatric DBS patient selection). Patients and caregivers were desperate for a treatment to provide successful antidepressant effect. This was apparent in caregiver comments that they would accept their loved-one losing valuable aspects of themselves or for their relationship to dissolve after DBS, if it meant they achieved relief from depression. Conversely, in PD, patients were still relatively early in their illness trajectory and only just beginning to experience debilitating symptoms that impacted their independence and quality of life.

The decision-making processes were also distinct. In PD, patients and caregivers had access to numerous resources to support their decision about the procedure. This included extensive online information, education from PD advocacy organisations, and DBS support groups where recipients share their experiences with prospective patients and caregivers. The patients’ treating neurologist had often flagged the option of DBS years earlier and provided them with a reasonable expectation of the

benefits they may achieve, as well as side-effects. A patient's decision to proceed was generally met with positivity and encouragement from their family and community. The process in TRD was quite different. Patients or caregivers sometimes came across DBS when conducting online research into treatments for depression or it was mentioned as a high-risk last resort by their treating psychiatrist. While these clinicians and the clinical trial research team would support patients through their decision-making process, they could not provide any reasonable expectation of an anticipated outcome because the current evidence does not allow it. One patient described the decision-making process as a "lonely place" because their family would not give an opinion on what decision they felt she should make nor could she speak with any DBS recipients about their experience. Some acknowledged the lingering stigma attached to mental illness and psychosurgery within the general community and had concerns how others might judge them (Cabrera, Courchesne, et al., 2020).

A final observation from the two samples was how DBS impacted upon freedom. Many PD patients described how restrictive their medication regime was and how it dictated their daily living. Despite variations in clinical outcome, all participants had a substantial reduction in medication dose after DBS and were no longer "tied down to a timeline". This shift from a restrictive regime is likely why no patients viewed recharging their DBS (approximately once or twice a week) as a burdensome or restrictive task. Conversely, TRD patients had less restrictive medication regimes as doses were not required so frequently. This, in addition to higher recharging needs (some multiple hours every one to two days), is likely why this process was considered burdensome, restrictive and "a real bind" for daily living. One could speculate that severe mental illness contributed to the sample's experience of recharging as highly burdensome, as compared with the PD sample's experience, but the drastic difference in recharging needs makes comparisons of this sought difficult to make.

Implications and Future Directions

The thesis findings have a number of implications and gives guidance for future developments in the areas of DBS clinical practice and research, and the ongoing ethical discussions around issues of personality, identity and self. Recommendations and key implications in each of these areas are described.

DBS Clinical Practice in PD

Perioperative education and communication of risk. Findings from PD clinicians, patients and caregivers highlighted shortcomings in the informed consent process, particularly communication and education on the risk of postoperative personality change. While some DBS centres were understood to have specific procedures and protocols (e.g., a signed advance directive) ensuring this information was communicated to patients and caregivers, this discussion was not guaranteed to translate in a meaningful way after DBS. In addition to an advance directive, what approaches could facilitate better communication? The intention is to inform patients and caregivers, and in doing so promote understanding, vigilance, preparedness and reduce distress if and when changes emerge. More interactive and experiential forms of informed consent have been recommended (Bell et al., 2010; Liddle et al., 2019). Multidisciplinary perioperative psychoeducation programs are one approach. These can involve use of DBS patient and family narrative accounts, and assessment of prospective patient and caregiver expectations followed by corrective feedback. In holding multiple education sessions, both before and after DBS, important information can be reiterated and reinforced. Periodic education in addition to the use of narrative evidence may increase the effectiveness of these messages for patients and caregivers (Mazor et al. 2007). Narrative evidence can be employed in various ways, from a clinician making reference to another patient's outcome to prospective patients and families holding extended conversations with other DBS recipients and families about their experiences. Narrative evidence is regularly used to communicate information about a procedure. Figures 1 and 2 provide brief examples of case studies and patient quotes used by Medtronic for DBS and Beyond Blue (a leading Australian non-profit mental health organisation) for ECT.

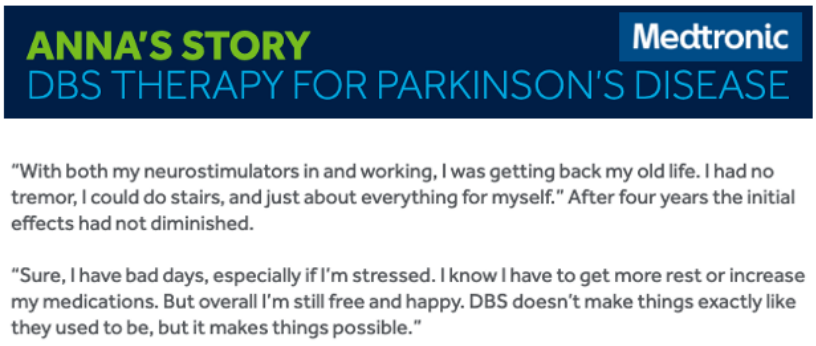

Figure 1. Example of 'Personal Stories: DBS Therapy for Parkinson's Disease' on the Medtronic website

Figure 2. Selected quotes on the Beyond Blue 'Electroconvulsive therapy (ECT)' information webpage

It is important a range of different outcomes are represented and that they include experiences relevant for the desired areas of education (e.g., personality change, speech side-effects, balance). Further research is needed to establish what forms of narrative evidence are most effective (e.g., written case studies, video case studies or in-person discussions), and provide a balanced account of risks and benefits that ensures these personal stories do not set expectations for a single, best-case scenario outcome. Caregiver involvement is vital during the education and informed consent process. Not only is this important for their own understanding and preparedness, but in order to become a source of knowledge and support for their loved-one, who due to the nature of their illness may experience cognitive difficulties that impact their comprehension and retainment of procedure information.

Monitoring and management of unanticipated outcomes. The post-DBS monitoring and management of unanticipated outcomes, such as personality and behavioural changes, are an extension of the preoperative informed consent and education process. This thesis highlights the importance of clinical teams creating time and opportunities for patients and caregivers to discuss and report these experiences. The recommendation for multidisciplinary input in the education, prevention, identification and management of unanticipated psychosocial outcomes allows for the appropriate use of specialist skills and ensures accessible and approachable clinical assistance is available (Bell et al., 2011b; Christen et al., 2014; Kubu & Ford, 2012; Mosley et al., 2019) Perioperative psychoeducation interventions are one format to provide continuity of care across the DBS journey. A 'triadic' nursing intervention, involving regular meetings between patients, spouses

and a specialist nurse was highly appreciated by participants and assisted with managing both DBS practicalities (adjusting the device) and emotional and adjustment aspects (Haahr et al., 2020). Similar 'buddy' support systems with either a nurse specialist or psychologist have been suggested to ensure discussions tailored to these psychosocial outcomes can be had (Eatough & Shaw, 2017; Mazor et al., 2007). In cases of problematic personality change where the patient may resist stimulation adjustment, such as heightened impulsivity or compulsive behaviour, a more consultative process involving multidisciplinary expert input is required. The Moral Case Deliberation protocol, which involves a consultative process between the patient, family and multidisciplinary team, is an existing example that can apply across all DBS indications (Widdershoven et al., 2014); however, more thorough and detailed protocols are required to guide this difficult process.

Clinical Research in DBS for TRD

Communication and appreciation of long-term outcomes. This thesis also demonstrates the critical need of patients and families entering experimental clinical trials of DBS having awareness and appreciation of the long-term risks and consequences of doing so. These include: the lengthy process of testing and trialling stimulator settings, stimulation-related side-effects (e.g., irritability, agitation, hypomania, sleep disturbance, suicidality), routine and lengthy device recharging, research trial commitments such as stimulation adjustments and clinical tests that can require extensive travel to and from research facilities (and can be emotionally and financially burdensome), the possibility that they will derive no benefit from the intervention, and that future surgeries (such as device explantation or periodic battery replacement) and reliance on specialist care will be required. Comprehension of long-term outcomes of DBS may also be undermined by the desperation and despair patients are often experiencing (e.g., feeling that a situation could not get worse, having no fear of risk of death or even welcoming it) when being asked to participate in an experimental clinical trial (Klein et al., 2016). Patients may also have unrealistic expectations that the procedure will provide a magic bullet or cure their condition based on overly positive and overhyped coverage of DBS in the mainstream and online media (Racine, Waldman, Palmour, Risse, & Illes, 2007). These are inherent challenges when severe, unrelenting mental illness is present; however, a thorough and considered informed consent process should still be enacted, with the long-terms

scenarios of this novel, complex and still uncertain treatment fully explored with both patient and caregiver.

Inclusion of caregiver and multidisciplinary support. In addition to inclusion in the informed consent process, our findings support a move towards involving caregivers in the research and recovery process more broadly. As noted, caregivers possess valuable knowledge of the patient and are well-positioned to provide observational feedback if behavioural or psychiatric disturbances emerge. They too can be directly affected by these changes, with repercussions for their relationship with the patient. The role of caregivers in DBS recipients' recovery is presently underexplored (Klein et al., 2016), as is the impact of the procedure on their own lives. Routine inclusion of measures of caregiver wellbeing and burden in clinical trial protocols as well as the sorts of qualitative approaches employed in this thesis are key avenues for investigating this important issue.

As is the case in PD clinical care, a multidisciplinary approach to recovery and rehabilitation is recommended for psychiatric DBS. Some clinical trials have excluded the introduction of concurrent therapies in order to examine the individual biological effect of DBS (Holtzheimer et al., 2017); however, a more holistic approach is appropriate for optimising recovery and augmenting DBS effects (Mantione et al., 2014). A multidisciplinary approach to recovery may involve ongoing psychoeducation, cognitive behavioural therapy, vocational counselling and social work engagement (Dings, 2019), aspects of which caregivers may also be involved in.

Ethical and Philosophical DBS Discourse

Acknowledging patients' existing context. The thesis findings highlight a number of features that have been overlooked or ignored in much of the conceptual and theoretical neuroethics literature. First, the neuroethics literature does not adequately recognise the impact that chronic illness has upon individuals' personality, identity and sense of self, focusing primarily on DBS in isolation. Chronic illness, however, has a substantial negative impact, both upon individuals, their loved-ones and their relationships. Second, the literature does not readily acknowledge the restorative quality that DBS can have in these regards. This is not to suggest that ethical concerns about the iatrogenic harms of DBS should be discounted, as there are clearly a subset of patients and caregivers affected by such outcomes. However, it demonstrates the need to consider them from a more nuanced, balanced and

empirically informed lens, that takes into account common patient experiences relating to both illness and DBS outcomes.

In addition to acknowledging the impact of chronic illness on personality, identity and self, the impact of therapeutic interventions other than DBS is worth noting. While the putative effects of DBS have garnered considerable interest and debate within the bioethics and neuroethics literature (Gilbert et al., 2018; Gilbert, Viaña, & Ineichen, 2020), more accessible treatment options, such as pharmaceuticals, psychotherapy and even physiotherapy, can have equally important implications for self, autonomy, control and authenticity (Browne, 2018; Dawson et al., 2019; Gardenhire et al., 2019; Jylha et al., 2012; Kramer, 1993). Similar issues are increasingly being investigated in non-invasive forms of neurostimulation (ECT, TMS and transcranial direct current stimulation) (Cabrera, Evans, & Hamilton, 2014; Cabrera, Nowak, McCright, Achtyes, & Bluhm, 2020), but further research is required. It could be argued that the direct implantation of neurotechnology in the brain with DBS creates more profound effects on self than non-invasive methods; however, the current TRD sample and others have noted the substantial impact of ECT-related memory loss on sense of self (Castillo, Bluhm, Achtyes, McCright, & Cabrera, 2020). Ablative neurosurgeries for movement and psychiatric disorders are still routinely performed, yet recent research has focused heavily on DBS rather than these irreversible methods (Cabrera, Nowak, et al., 2020). Continuing to examine both the negative and positive impact of DBS on self (e.g., compromising autonomy and authenticity; creating sustained and meaningful improvements in health status) is important, but more accessible and widely available treatments or those with permanent consequences should not be overlooked.

Developing common language and instruments for future research. There has been considerable discussion focused on the best approaches for investigating changes in patient self following implantation with DBS or other forms of neurotechnology. While efforts towards developing reliable measures to assess post-DBS changes in personality, self and identity have been made (Gilbert et al., 2018; Ineichen et al., 2016; Witt et al., 2013), some doubt the ability of these formats to fully capture these processes (Bluhm & Cabrera, 2018). For example, two patients may arrive at completely different views of the same questions; only through more in-depth discussion can their personal meaning be understood (de Haan et al., 2017; Snoek et al., 2019). Efforts have also

been made towards developing a qualitative instrument to investigate phenomenological experiences associated with implanted devices (Gilbert et al., 2019). This allows device recipients the ability to demonstrate the question's personal meaning to them and explore these complex outcomes in detail. Our results demonstrate the importance of this ability, as participants were able to reveal their personal conceptualisations of personality, which differed across participants. Furthermore, it allowed personal appraisals of observed changes to be made (e.g., two caregivers may have different appraisals of their loved-one becoming more 'expressive' depending on whether this was consistent or not with their previous behaviour).

Continuing to build the robust collection of qualitative investigations into these topics will help identify the concepts that are most relevant to patients and caregivers and refine the language that is used to assess them. The mismatch in language used within conceptual and theoretical neuroethics compared with the empirical neuroethics and clinical research literature has been noted (Gilbert et al., 2020; Snoek et al., 2019). It is important to recognise that patients' and caregivers' understanding of post-DBS changes will be informed by the language used by their clinical team (e.g., 'hypomania', 'stimulation-related side effect' rather than 'biographical disruption' or threatened 'personal identity'). I believe there is still reason to explore these philosophical concepts within empirical research, but these need to be driven by patient language and shaped by their phenomenological experiences. For example, the thesis findings, and those from DBS samples elsewhere (Klein et al., 2016; Kubu et al., 2019; Mosley et al., 2019), demonstrate that perceptions of 'control' are significant for patients, both in relation to symptoms and device management. While control is highly linked to the concepts of autonomy and agency, 'control' may be more salient to patients themselves. Interdisciplinary research teams can assist in refining relevant concepts and ensure future ethical discussions are conducted in a way that benefits rather than potentially harms patients and families (Kubu et al., 2019; Müller et al., 2017).

Original Contribution to Knowledge and Understanding in the Field

This thesis provides empirical evidence of how DBS impacts personality, self and relationships, and investigated these issues from multiple perspectives. These experiences have been

speculated upon in the conceptual neuroethics literature, but with minimal empirical evidence on the experiences of key stakeholders. This thesis attempted to bridge this gap, by evaluating these ethical issues and concerns with those directly involved. The acquisition of qualitative data from health care recipients (patient, families) also aids the bridging of a different gap – the quality chasm in clinical health care. Engagement with lived experience experts, as was done here, is recommended to promote efficient translation of research outcomes into clinical practice (Institute of Medicine, 2001). While there has been some qualitative investigation of these issues in patients with PD, there has been a notable absence in TRD. Gaining the unique perspectives of DBS recipients, particularly in emerging indications, can be used not only to address ethical challenges, but help shape the design of future trials and technological features (i.e. gathering end-user perspectives) (Klein et al., 2016). This thesis also contained the novel feature of the caregiver voice, which has been illuminated in PD to a certain degree, but has been entirely absent in TRD. After completing these interviews, a number of caregivers expressed their gratitude for being able to be involved and having the opportunity to share their experiences. These findings help lay the ground work for future investigations by continuing to build upon the language and experiences of patients and caregivers in the pursuit of optimal care and technological innovation.

This thesis contained one of few studies with DBS clinicians and fewer still that used qualitative interviews to explore these topics. The clinician voice is essential in these discussions. If the debate becomes too detached from the clinical context the procedure is conducted in, its real-world value is diminished and can potentially have damaging outcomes (e.g., produce unjustified fears or concerns in prospective patients and families). With clinicians' expert knowledge, exposure to a variety of patients and families, and experience detecting and managing personality change and other forms of postoperative maladjustment, this thesis ensured that these highly relevant clinical perspectives became part of the ethical discussion. The semi-structured interviews also allowed for complexity and nuance in responses, which was unable to be achieved in previous studies that employed surveys with pre-determined responses (Christen et al., 2012). The value of this method was evident when clinicians described complex issues including the multitude of factors that can

influence post-DBS outcomes, the process of establishing causal factors, and how their experiences or practices have changed across the course of their career.

Limitations and Methodological Considerations

Limits of Qualitative Research and Generalisability

As with all qualitative research, the generalisability of the research findings is limited. The recruitment of Australian participants may mean that the findings are not relevant to DBS clinicians, patients or caregivers elsewhere in the world. The intention of the qualitative approach was not to provide results wholly representative of all DBS clinicians, patients and caregivers, rather it was to explore the variance within subjective experiences of postoperative events, whether they be harmful or beneficial (Bittlinger, 2017). In this regard the thesis has achieved its aim. These qualitative findings may contribute to the development of future theories or research tools that build a body of research with greater potential for generalisability. It also provides a framework for examining the experience of patients and caregivers in other locations and contexts.

How frequently postoperative personality changes occur is an important question, but not one this qualitative thesis can resolve. Although some clinicians indicated how frequently they believed they had observed personality changes in patients, these figures should be treated with caution as they are based on retrospective recall, which is prone to distortion and bias (Schacter et al., 2003). Further, some clinicians had limited clinical experience from which to gauge prevalence on. An entirely different study design would be required to address this question robustly, such as a prospective, longitudinal mixed-methods design with a large patient sample. While a similar qualitative component of interviews with patients and caregivers could be employed, the additional collection of standard clinical research outcomes would be required, such as the Unified Parkinson's Disease Rating Scale (Fahn & Elton, 1987), Parkinson's Disease Quality of Life Scale (Jenkinson, Fitzpatrick, Peto, Greenhall, & Hyman, 1997) and Zarit Burden Interview (Bedard et al., 2001), in combination with psychometric measures of personality, impulsivity, ICDs and relationship quality. While such psychometric measures were collected from patients and caregivers in the present studies, the sample sizes did not allow meaningful statistical analyses.

Models and Definitions of Personality and Self

As discussed in Chapter 2, a range of personality models and theories have been applied to the quantitative investigation of personality change following DBS. No consensus exists on the most appropriate model or psychometric tool for this purpose and the clinical meaningfulness of any observed statistically significant findings, for patients and families in particular, is uncertain. With this, the decision was made to conduct qualitative studies that were exploratory and in which participants' own understanding and meaning of 'personality' was applied. Similarly, the concept of 'self' in relation to DBS is widely debated, particularly within philosophical literature (de Haan, 2017; Dings, 2019), yet here participants applied their own conceptualisation. This resulted in rich and informative findings regarding what is considered to constitutes personality and self (e.g., their demeanour, facial expression, bodily function). It could be argued, however, that by not providing participants with a definition or guidance, the findings lack cohesion and reflect a broad discussion of differing concepts. Additionally, while the responses from DBS clinicians provide some indication, they were not asked specifically what model or definition of personality they ascribe to. On reflection, this and how they believed it to apply (or not apply) to DBS patients would have been a valuable.

Multiple Longitudinal Assessments

A limitation of the study design was the use of a single post-DBS interview. Conducting multiple longitudinal assessments after DBS would have provided more insight into how these experiences evolve over time. While the effects of DBS in PD can be immediately observable, the process of testing and optimising stimulation in balance with medication can take months, if not years. In psychiatric DBS, with no distinctive motor symptoms, determining if and when the stimulation is having a beneficial effect can be a difficult and extremely lengthy process. The structure of the TRD clinical research trial structure meant that individualised optimisation of stimulation settings was delayed until standardised protocols had been completed. Many patients saw themselves and the DBS as a "work in progress". Seeing how this work in progress developed over time would be valuable.

Conclusions

This thesis contributes to the discussion and debate about how DBS impacts patient personality, sense of self and relationships through the much-needed voices and perspectives of key stakeholders. Through these narrative accounts important contextual factors that influence these outcomes have been recognised, including the impact of chronic illness upon individuals and loved-ones, the hopes and expectations they hold for DBS, and the existing quality and functioning of their relationship. Findings suggest DBS has the capacity to create undesirable personality changes that are either related directly to the stimulation or other indirect influences. DBS was also considered to result in positive personality changes, including a restorative process that was highly linked with good clinical outcomes. Rather than a unidirectional effect, DBS can both modulate neural activity and experiences intrinsic to one's self and capacities, including self-confidence, self-efficacy, autonomy, control and authenticity. These findings provide insight into how post-DBS experiences, whether it be a minor undesirable change in personality or restoration of a premorbid self, fit into individuals' lives and how they adjust. Rather than simply relying on fireside induction, the personal meaning and significance of these experiences for patients and families have been heard and these insights can contribute to future caring practices involving DBS.

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APPENDICES

Appendix A: Human Ethics Certificate of Approval

MONASH University

Monash University Human Research Ethics Committee (MUHREC)
Research Office

Human Ethics Certificate of Approval

This is to certify that the project below was considered by the Monash University Human Research Ethics Committee. The Committee was satisfied that the proposal meets the requirements of the *National Statement on Ethical Conduct in Human Research* and has granted approval.

Project Number:	CF16/1888 - 2016000963	
Project Title:	The Impact of Deep Brain Stimulation on Quality of Life in Neurological and Psychiatric Populations	
Chief Investigator:	Dr Adrian Carter	
Approved:	**From:** 06 July 2016	**To:** 06 July 2021

Terms of approval - ***Failure to comply with the terms below is in breach of your approval and the Australian Code for the Responsible Conduct of Research.***

1. The Chief investigator is responsible for ensuring that permission letters are obtained, if relevant, before any data collection can occur at the specified organisation.
2. Approval is only valid whilst you hold a position at Monash University.
3. It is the responsibility of the Chief Investigator to ensure that all investigators are aware of the terms of approval and to ensure the project is conducted as approved by MUHREC.
4. You should notify MUHREC immediately of any serious or unexpected adverse effects on participants or unforeseen events affecting the ethical acceptability of the project.
5. The Explanatory Statement must be on Monash University letterhead and the Monash University complaints clause must include your project number.
6. **Amendments to the approved project (including changes in personnel):** Require the submission of a Request for Amendment form to MUHREC and must not begin without written approval from MUHREC. Substantial variations may require a new application.
7. **Future correspondence:** Please quote the project number and project title above in any further correspondence.
8. **Annual reports:** Continued approval of this project is dependent on the submission of an Annual Report. This is determined by the date of your letter of approval.
9. **Final report:** A Final Report should be provided at the conclusion of the project. MUHREC should be notified if the project is discontinued before the expected date of completion.
10. **Monitoring:** Projects may be subject to an audit or any other form of monitoring by MUHREC at any time.
11. **Retention and storage of data:** The Chief Investigator is responsible for the storage and retention of original data pertaining to a project for a minimum period of five years.

[redacted]

Professor Nip Thomson
Chair, MUHREC

cc: Dr Rebecca Segrave, Ms Cassandra Thomson

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Appendix B: "I Miss You Too": More Voices Needed to Examine the Phenomenological Effects of Deep Brain Stimulation

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"I Miss You Too": More Voices Needed to Examine the Phenomenological Effects of Deep Brain Stimulation

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The potential for deep brain stiulation (DBS) to impact patients' identity and sense of self is a topic that has received substantial attention from both scientific and non-scientific communities in recent years. The theoretical and speculative approach present in much of the ethical and philosophical debates often ignores the growing neuropsychiatric, psychological, and social scientific literature in the area. Gilbert and colleagues' (2017) timely article bridges this gap by examining the experience of self-estrangement following DBS for Parkinson's disease using first-personal, subjective accounts. Despite the considerable contribution the article makes toward filling this void, there are key methodological limitations that need to be overcome if we are to develop an empirically based understanding of the effect of DBS on identity and agency.

One limitation of Gilbert and colleagues' study that the authors acknowledge is the lack of perspective from a significant other (e.g., partner or carer) to provide an informed observer's account of the patient's DBS outcomes. As noted, the inclusion of an observer would have the benefit of contributing a witness perspective to the patient's own recollections, as well as providing additional information in instances where the patient's account is impacted by lack of insight, denial, or limited recall: a common feature in cases of self-estrangement. What the authors fail to acknowledge is the importance of including significant others to specifically evaluate their own experience and the impact DBS has had upon them and their relationship with the patient. A previous study that investigated the experience of DBS patients using qualitative interviews revealed that of the participants who were partnered prior to DBS, 65% experienced a conjugal crisis in the 2 years following surgery (Agid et al. 2006). From the handful of studies that have included qualitative information from DBS caregivers, many report changes in what they feel inherently makes the patient "them" following surgery and report periods of significant psychosocial adjustment (Schüpbach et al. 2006; Haahr et al. 2013; Lewis et al. 2015). Further research that can assist in elucidating why these relationship difficulties occur—such as feelings of self-estrangement in patients that lead to extended periods of maladjustment—is required. The

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experiences of significant others are an essential component of this work. The authors discuss one patient who mentioned relationship conflict as a result of his perceived changes in self. Greater insight into this issue would have been possible with the inclusion of a partner's perspective. Certain concepts that the authors investigate, specifically embodiment, are experiences that can only truly be explored through patient first-personal perspectives. Self-estrangement, however, whether it be deteriorative or restorative, has the potential to be perceived by and impact upon others. The focus of future research should not be limited to individuals' perceptions of self-change, but should also consider outsiders' perceptions of patient change.

An additional methodological limitation that the authors acknowledge is the single post-DBS time point from which patients' experiences were collected. Extending beyond this by gathering information from multiple time points, most importantly before and in the early and later stages of response after the surgery, would illuminate the degree to which self-deception and romanticism of prior self has occurred. The authors emphasize that self-estrangement following DBS is not necessarily deteriorative. Prospective studies would help demonstrate the deteriorative and restorative potential of DBS with substantially greater clarity. The authors consider the impact of presurgery factors (i.e., patients' relationship with their Parkinson's disease), but these are not static variables and the study methodology does not allow for them to be examined prior to surgery or for their evolution over time to be taken into account.

Gilbert and colleagues focused exclusively on the experience of patients with Parkinson's disease, which is reasonable given that Parkinson's disease is the most common indication for DBS. DBS is increasingly being investigated as a treatment for a number of high-prevalence psychiatric indications, such as major depressive disorder and obsessive-compulsive disorder. While clinical research into the potential of DBS as a treatment for these conditions is ongoing (Fitzgerald and Segrave 2015), they have the potential to join the growing list of conditions commonly treated by DBS. The neuroanatomical implantation targets for psychiatric and movement disorders vary substantially, as do the treatment goals. Changes in self, including personality, identity, behavior, and relationships with others, are usually intimately linked to successful clinical outcomes when DBS is applied in chronic severe mental illness. In movement disorders, the primary aim is restoration of physical control over one's self. Given this variation, the experience and perception of self-estrangement for both the individuals and people close to them will likely vary depending on the condition, and this needs to be investigated accordingly. Comparisons between different conditions will help to ascertain to what extent post-DBS changes in identity are the result of the condition being treated and the target brain region being stimulated.

More than 100,00 DBS surgeries for Parkinson's disease have been performed to date. As the use of DBS in Parkinson's grows, along with interest in its application in psychiatric conditions, empirical and conceptual understanding of patients' experiences, including specific phenomena such as self-estrangement, needs to be extended upon. Future research that builds on the approach of Gilbert and colleagues by including multiple perspectives, numerous time points, and a range of clinical indications, will vastly improve understanding of the impact of DBS upon the self and self-estrangement and the consequences of such changes. Such research will be necessary if clinical guidelines for its use are to be developed. ■

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Appendix C: Patients' Weighing of the Long-Term Risks and Consequences Associated with Deep Brain Stimulation in Treatment-Resistant Depression

treatment, then it is worthwhile to ensure that these framing effects are minimized through an alternative, yet accurate, description. ■

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Patients' Weighing of the Long-Term Risks and Consequences Associated With Deep Brain Stimulation in Treatment-Resistant Depression

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The capacity of individuals with treatment-resistant depression (TRD) to understand and judge information related to deep brain stimulation (DBS) as a novel treatment for depression is often debated. Lawrence and colleagues (2019) conducted interviews with non-DBS-seeking individuals with TRD to gauge their views on DBS and willingness to participate in a clinical trial. This study provides important insights about TRD patients' understanding of the risks and benefits. However, half of the participants in this study had not previously heard of DBS; among those that had, the extent of prior knowledge was unclear; and all received only a very brief information sheet about DBS for TRD. Individuals seriously considering undergoing DBS for TRD are provided with far more detailed information about the intervention, as well as engaging in in-depth and ongoing discussions with their treating clinician, the trial team, and with their family and loved ones. This limitation could undermine the ecological validity of the findings. However, our study of the experiences, knowledge, and concerns of individuals who have agreed to participate in a clinical trial of DBS for TRD (unpublished data) support Lawrence and colleagues' observations of a relatively DBS-naive TRD sample. In discussing these similarities we (1) highlight the capacity of patients with TRD to consent to novel treatments and the stigma that surrounds this issue, (2) highlight the tendency for patients with TRD to focus primarily on the short-term rather than long-term risks associated with DBS, and (3) provide suggestions for future research specifically investigating the decision-making process for individuals with TRD seeking DBS.

Lawrence and colleagues (2019) conclude that the members of their sample were thoughtful and cautious in their evaluation of DBS. This is consistent with the outlook reflected in our sample and with that described in previous studies evaluating prospective DBS patients (Fisher et al. 2012; Leykin et al. 2011). Fisher and

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colleagues noted that none of their sample demonstrated impaired capacity to consent, and while some participants demonstrated misconceptions about the primary purpose of the clinical trial (known as therapeutic misconception), this was not in excess of that demonstrated in other clinical as well as nonclinical samples. Fisher and colleagues suggest that the persistent concern regarding the capacity of TRD individuals to make informed decisions about novel treatments is disproportionate and reflects a general stigma and prejudice against those with psychiatric conditions. We too question the influence of stigma and whether a bias exists in how psychiatric participants' capacity to make informed decisions about novel treatments is evaluated compared with, say, a movement disorder population. We conducted interviews with patients with Parkinson's disease (PD) preparing to undergo DBS that indicate they have difficulty comprehending and retaining DBS risk and benefit information provided at consent. Patients with PD tended to demonstrate elevated hopes, greater impatience for surgery, and appeared less informed of the potential risks and likely benefits, as compared with TRD participants. A number of factors could contribute to this, including that (1) DBS for PD is known to have better clinical outcomes compared with TRD; (2) the influence of depressive realism (the hypothesis that depressed individuals make more accurate inferences than nondepressed individuals) in the TRD sample; (3) PD-related impulsivity (as either a result of disease progression or a medication-induced side effect); (4) PD-related cognitive impairment; and (5) a less stringent informed consent process for general surgical procedures (as in PD) than for an experimental clinical research trial (as in TRD). In some Australian states, individuals seeking DBS for a psychiatric condition must seek approval to undergo DBS from legislative review panels (Loo et al. 2010). Patients are not able to make this application themselves and must instead engage with a psychiatrist to apply on their behalf, a process that inevitably takes many months. Not only does this undermine the individual's autonomy, it also places a prolonged and potentially harmful emotional burden on the individual. Of note, this process is not required for patients seeking DBS for neurological indications.

Similarly, our sample also focus primarily on the risks associated with the surgical procedure itself (e.g., hemorrhage, seizure, infection, death) and aesthetic concerns (e.g., shaving hair, stitches) (unpublished data). They appear to be less concerned with the potential long-term stimulation-induced side effects, such as agitation (Lozano et al. 2012), hypomania (Malone et al. 2009), sleep disturbance (Holtzheimer et al. 2017), and suicide (Mosley, Marsh, and Carter 2015). For some psychiatric patients, battery recharging can be required as often as every 1 to 2 days, which can be burdensome and restrictive. Ongoing adjustment to stimulation parameters can require extensive travel to and from research facilities and can involve a significant emotional and financial burden for patients and families. There are a limited number of medical professionals with speciality knowledge and understanding of deep brain stimulation for psychiatric conditions. Future access to clinical care is another long-term consideration—one that can influence patients' decisions about living location. If patients do receive some benefit from DBS and choose to retain their device, future surgeries to periodically replace the battery are required. These long-term implications tend not to be the focus of presurgery discussions.

Prospective patients also rarely focus on the potential challenges that could accompany a reduction or remission from their chronic mental illness—rather, they consider this as what Lawrence and colleagues (2019) describe as an "unmitigated good" (223). The authors provide examples of previous studies in which patients experienced feelings of self-estrangement with DBS and concerns that their emotions and behaviors were being generated by the device, rather than themselves. In our discussions with DBS patients, caregivers, and clinicians, a more prevalent psychosocial concern associated with clinical improvement is the challenges involved in reintegrating into relationship, familial, and societal roles. Couples that have often developed a well-ingrained patient/caregiver dynamic must navigate a more balanced and reciprocal spousal relationship. Similarly, individuals who have been primarily housebound may experience a desire and motivation to spend more time in the community. However, this requires them to now consider their physical appearance, as well as their ability to manage the nuances of social interaction. With DBS, their increased capacity to engage with life undoubtedly brings more opportunities for positive experiences and interactions, but it also brings about new stressors. For this reason, clinical trials of DBS for psychiatric conditions worldwide emphasize the importance of concurrent psychological support (Denys et al. 2010; Park et al. 2018).

More research is still needed about the factors that may influence patients' ability to provide fully informed consent. Lawrence and colleagues (2019) and others have noted the potential influence of the media on patient views on DBS, but few studies have directly explored the role of media, including online and social media, in prospective DBS patients' decision making. For example, did patients or family members view media stories or online videos prior to making their decision about undergoing DBS? Did these stories provide a balanced view of the treatment or rely on overly optimistic "silver bullet" portrayals? If so, how did these stories influence their decision? Exploration of what information or whose opinion was most influential in prospective DBS patients' decision making is needed (e.g., opinion from specialist medical researcher, feedback from someone who has already undergone the procedure, or online YouTube videos). Although researchers attempt to ensure that participants are fully informed about the long-term risks and consequences associated with the procedure, methods for

communicating this information need to be improved to ensure participants give them full consideration.

Future research also needs to explore family and caregivers' understanding of DBS and their beliefs about the potential outcomes for their loved one. Although it is the individual undergoing DBS who must provide informed consent, it is vital that spouses or caregivers are closely involved in the process as much as possible. Not only is it appropriate for family to have an awareness of what their loved one is signing up for, but (1) the individual considering DBS will likely draw upon family feedback in their process of making a decision; (2) the decision will heavily impact families' lives; and (3) spouses and close family members are likely to first notice any behavioral or psychiatric disturbances that can emerge after surgery and are key to treating them. ■

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Appendix D: Ethical Issues in Experimental Treatments for Psychiatric Disorders: Lessons from Deep Brain Stimulation

Thomson, C., & Carter, A. (2020). Ethical issues in experimental treatments for psychiatric disorders: Lessons from deep brain stimulation. *Translational Issues in Psychological Science*, *6*(3), 240-246. doi:10.1037/tps0000267

Abstract

Experimental trials of deep brain stimulation (DBS) are occurring worldwide for a variety of psychiatric disorders, including depression and obsessive-compulsive disorder, and to a lesser extent substance use disorders and anorexia nervosa. DBS is a neurosurgical procedure that comes with serious risks and the relative benefits for psychiatric indications are still being determined. The application of DBS in psychiatric populations raises a number of ethical challenges that research teams need to consider and manage. Here we highlight a number of pertinent issues and recommendations, many of which were relevant in our interviews with DBS patients, caregivers and clinicians on their perspectives and experiences. Given psychiatric DBS trials are both experimental and resource-heavy, careful patient selection is required. Independent oversight is recommended in the recruitment process. Disorder-related cognitive and emotional factors need to be considered during informed consent, with a process structured to promote and assess comprehension. Patients, families and clinical teams need to have an awareness and understanding of surgical and stimulation-related risks, which can have both short and long-term implications. Patients and families are often desperate for a cure and may be persuaded to undergo DBS by media portrayals of 'miracle cures'. Research teams therefore need to be mindful of unrealistic expectations and take steps to ensure the media is balanced in their reporting of trial results. As a potentially life-long treatment, DBS raises important questions regarding medical, financial and legal responsibility. For this reason, ethically rigorous post-trial management plans between patients and research teams are recommended.

Keywords: deep brain stimulation, experimental trials, consent, decision-making, coercion

Public Significance Statement

This review highlights a number of pertinent ethical issues associated with the application of deep brain stimulation in psychiatric disorders. DBS is far from a straightforward technological fix for psychiatric disorders and patients and families entering trials need to be appropriately selected, informed and supported through this challenging experimental process. The subjective experiences of key stakeholders (patients, caregivers and clinicians) are important when assessing these issues and are discussed within.

Introduction

Clinical trials of experimental and invasive neurosurgical treatments for psychiatric disorders raise a number of significant ethical issues, such as potential risk, patient selection, informed consent and posttrial responsibility (Hendriks et al., 2019). The intervention often involves surgical insertion of technology into the brain that can carry serious surgery and technology-related risk of harm. The benefit of the procedure is also uncertain. This review focuses on ethical issues raised by conducting clinical research into deep brain stimulation (DBS) for psychiatric disorders, as it is an intervention for which we have considerable experience. However, similar issues are raised by experimental and first-in-human trials of other invasive neurotechnologies, such as implanting of cortical brain computer interfaces or neural stem cells, in desperate and vulnerable patients (Viaña, Carter, & Gilbert, 2018).

DBS is a neurosurgical procedure that involves implanting electrodes deep within target nuclei that receive electrical impulses via a pulse generator located in the patient's chest. It differs from other neuromodulation techniques (e.g., transcranial magnetic stimulation (TMS), electroconvulsive therapy (ECT), deep TMS and transcranial focused ultrasound), which are non-invasive and do not require neurosurgical device implantation. DBS has received approval from the Food and Drug Administration (FDA) as an established treatment for various movement disorders, including Parkinson's disease, essential tremor and dystonia. DBS is being trialled in an increasing number of psychiatric disorders. In 2009, DBS received FDA approval for treatment-resistant obsessive-compulsive disorder (OCD) under a humanitarian device exemption, but is not yet considered an established treatment (Hendriks et al., 2019). Mean reductions in the Yale Brown Obsessive Compulsive Scale have varied from 21%-72% and the best neuroanatomical target is still debated (Naesström, Blomstedt, & Bodlund, 2016). Similarly, numerous targets have been proposed for treatment-resistant depression (TRD) without consensus. Study outcomes in depression vary somewhat according to trial protocols, but responder rates are typically around 50% (responder defined as >50% reduction in primary outcome measure) (Dandekar, Fenoy, Carvalho, Soares, & Quevedo, 2018). DBS has also been investigated in Tourette's syndrome, anorexia nervosa and

substance use disorders. While some promising effects have been reported, these come from small open-label or individual case studies (Naesström et al., 2016).

Psychosurgery has a troubled and ethically dubious history, in particular the 1950s to 1970s that were marked by the widespread use of frontal lobotomies and archaic research programs using electrical brain stimulation for treatment of schizophrenia, depression and homosexuality (Baumeister, 2000; Valenstein, 1986). Renewed interest in psychosurgery has focused on stimulatory over ablative techniques, but researchers remain wary of repeating the ethical mistakes of the past (Fins, Rezai, & Greenberg, 2006). Consensus guidelines and neuroethical frameworks have been developed in tandem with experimental trials to address the safety and ethical issues related to DBS for specific disorders (anorexia nervosa) (Park, Singh, Pike, & Tan, 2017) and psychiatric disorders more broadly (Nuttin et al., 2014). This review highlights a selection of pertinent issues and recommendations, many of which were relevant in our interviews with patients, caregivers and clinicians exploring their perspectives and DBS experiences (in both movement and psychiatric disorders) (Thomson, Segrave, & Carter, 2019; Thomson et al., 2020, under review).

Patient Selection and Recruitment

DBS for psychiatric disorders remains an intrusive experimental intervention with uncertain benefit that poses substantial risks (e.g., related to surgery, device hardware and stimulation). It is therefore only pursued as a treatment of last resort. The disorder needs to be associated with a high probability of significant harm (e.g., life threatening, irreversible morbidity) to justify experimental investigation (Carter, Bell, Racine, & Hall, 2010). This condition is often met in severe psychiatric cases, such as self-harm and suicide in depression and life-threatening health complications in anorexia nervosa. Individuals seeking DBS for psychiatric disorders should present with a severe, chronic and refractory course of illness and demonstrate that all available evidence-based treatments have been fully exhausted. This invasive and experimental procedure should not be pursued while less intrusive evidence-based options that may provide benefit remain untrialled.

Prospective patients should also demonstrate a capacity to meet trial commitments. DBS clinical trials are often restricted to a limited number of metropolitan centres. Patients need to attend scheduled assessments and unscheduled reviews (e.g., adverse events) over months to years. Good

psychosocial support (typically family member/s) is often vital for meeting the logistical challenges of participation (e.g., getting to appointments, managing the device) and is associated with better outcomes post-DBS (Okun et al., 2008). Our research has found caregivers provide critical observations about how the patient is responding to treatment (e.g., more active, engaged; irritable, manic) (Thomson, Segrave, & Carter, 2019; Thomson et al., 2020, under review). In medical research, it is generally unethical to exclude participants due to their location or an absence of support. But for early trials of a risky procedure of uncertain benefit where researchers aim to maximise chances of positive outcomes, it may be an acceptable trade-off. If the trial is deemed effective, subsequent studies can be extended to a broader sample.

Informed Consent and Coercion

To consent to DBS trials, patients must have capacity to understand and appreciate the risks and benefits of the procedure. Surgical risks include intracerebral haemorrhage (3-4%), seizures (1-2%), infection (1-2%), plus standard surgical and anaesthetic complications (Kleiner-Fisman et al., 2006). For the implanted device, there is risk of hardware malfunction, lead breakage and skin erosion/exposed leads. Patients themselves often describe the brain surgery, where they are awake for substantial periods, as traumatic. DBS can also affect patients' safety to undergo other treatments in the future (e.g., TMS, ECT) (Vila-Rodriguez, McGirr, Tham, Hadjipavlou, & Honey, 2014). Stimulation-related side-effects depend on the target nuclei and disorder being treated, but include: emotional changes (anxiety, panic, fear, agitation, irritability, euphoria), psychiatric symptoms (psychosis, hypomania, mania, depression, suicide attempts/completed), impulse-control disorders (hypersexuality, gambling), cognitive changes (planning difficulties, reduced verbal fluency) and bodily disruptions (weight loss/gain, vertigo, nausea, sleep disturbance) (Fraint & Pal, 2015; Kleiner-Fisman et al., 2006). Stimulation-induced side-effects typically remit following adjustment of the stimulation parameters, but in some cases the patient's actions and behaviours while they were present can have on-going ramifications (e.g., financially, legally and relationally) (Thomson, Segrave, & Carter, 2019). Suicide occurring after DBS is a complex issue, both in terms of establishing contributing factors and its management. An overview of these challenges when applying DBS in high suicide risk populations are explored in Mosley, Marsh, & Carter, 2015.

In severe psychiatric disorders, cognitive function can be impaired and may impact an individual's capacity to absorb and retain information (Nuttin et al., 2014). For this reason, the informed consent process should not be rushed, but involve repeated sessions of increasing depth of information from multiple sources across a multi-disciplinary team. In our interviews with patients with TRD before and after DBS, many acknowledged the impact of depression on their ability to retain and recall information. These interviews also showed that patients and caregivers were more inclined to focus on short-term risks (i.e., surgical) rather than long-term (i.e., stimulation-related side-effects, battery recharging) (Thomson, Segrave, Gardner, & Carter, 2019). As an implanted and possibly life-long intervention, research teams must thoroughly explore both the short and long-term consequences of DBS with patients.

A patient's decision to undergo DBS must also be free from external coercion. Certain regions (e.g., China and Russia) hold highly punitive policies towards substance dependence, with compulsory detoxification, imprisonment and forced labour the first line of 'treatment'. The option to participate in a DBS trial and undergo a risky and invasive procedure should not be offered as an alternative to these punitive rehabilitation measures. Such incentives and soft coercion impact an individual's capacity to provide free and informed consent (Carter et al., 2010). Stigma and discrimination associated with many psychiatric disorders can also affect access to currently available effective treatments. For instance, opioid substitution treatments (the gold standard in the treatment of opioid dependence) are not available in some jurisdictions or may be provided in a sub-optimal manner (e.g., insufficient substitution medication doses and punitive responses to positive urine tests) (Carter & Hall, 2007). DBS should not be used as a solution for the failure to provide currently effective treatments to patients (Carter et al., 2010). Similarly, given its experimental status, DBS is not suitable as an involuntary intervention, like other involuntary administered treatments in psychiatric cases (e.g., ECT, antipsychotic medication). Finally, caregivers of those with severe and refractory psychiatric conditions can face significant burden and naturally hope for a treatment to relieve their loved one's suffering. While support from a caregiver to participate is desirable, it is important they do not exert undue influence on a patient's decision to participate in the trial.

Desperation and Managing Patient Expectations

DBS is considered a treatment of last resort and patients and families are often desperate for a cure. To be eligible for trials of DBS for psychiatric conditions, individuals must have lived with severe psychiatric symptoms for decades and have a history of repeated failures with evidence-based therapies (including pharmacological, psychotherapeutic and non-pharmacological (e.g., TMS/ECT)). Our interviews with patients with TRD revealed many had also trialled other experimental (e.g., transcranial direct current stimulation, ketamine) and alternative treatments (e.g., neurofeedback) without benefit. Patients state that their situation "couldn't get any worse" or they have "nothing to lose" (quotes from patients with TRD) (unpublished data). Researchers need to confront this thinking by exploring with patients the possibility that their situation could decline or become more difficult by entering an experimental trial of DBS. Surgery-related complications or stimulation-related side-effects are possible and the necessity to recharge (sometimes for multiple hours every 1-2 days) can be substantial (Thomson, Segrave, Gardner, et al., 2019). These may be acceptable trade-offs for symptom relief (e.g., in mood, cravings, compulsions), but if that is not achieved, provide an additional layer of burden. Studies have shown some patients who do not experience an immediate benefit can develop improvements over months and years (Greenberg et al., 2010; Holtzheimer et al., 2017; Liu et al., 2020). An uncertain and distant chance of improvement can be a difficult prospect for individuals experiencing acute mental ill health. The failure of DBS to provide any benefit can have serious psychiatric outcomes in patients undergoing a treatment of last resort, including suicidal ideation. Researchers need to explore these scenarios with patients and their families.

Unrealistic or inflated expectations of DBS can be a challenge during assessment. Occasionally patients are alerted to DBS clinical trials through their treating clinician, but often seek it out after seeing favourable media reports. There have been numerous examples of optimistic media reports for DBS in psychiatric disorders that have been premature and misleading (Gilbert & Ovadia, 2011; Racine, Waldman, Palmour, Risse, & Illes, 2007). Similarly, the internet and YouTube are dominated by positive and uncritical media stories and personal testimonials that portray best-case-scenarios that few will experience. Research teams need to identify and correct inaccurate beliefs and place such reports into an appropriate context. Optimism and hope alone are not problematic, but

when it reflects a misunderstanding of the purpose of research or the prospect of benefit, it can be harmful (Horng & Grady, 2003). Routine inclusion of a clinical ethicist during patient recruitment would help to identify these therapeutic misconceptions and misestimations and to manage unrealistic expectations (Fins et al., 2006; Park et al., 2017). Researchers also have a responsibility to ensure media provide a balanced portrayal of their trial outcomes that avoids overly selective or optimistic depictions.

Autonomy and Responsibility

DBS can be associated with significant changes in a person's behaviour, personality and cognition that have substantial personal, financial and legal implications (Carter et al., 2010; Thomson, Segrave, & Carter, 2019). These behaviours include impulse control disorders (hypersexuality, compulsive gambling, shopping and eating), mania, aggression, self-harm and suicide (Kleiner-Fisman et al., 2006; Mosley et al., 2019). The incidence of DBS-induced behaviours raises questions about whether the individual is morally or legally responsible for those behaviours. Court cases of post-DBS suicide in Parkinson's have also considered the extent to which DBS contributed to the suicide and whether the medical team may be responsible for the behaviour.

Who is responsible for making decisions regarding the management of stimulation parameters when the patient enjoys the stimulation side-effects (e.g., mania, impulsivity) and opposes adjusting settings, despite them being problematic or challenging for the family? A pre-operative approach that has been discussed are advanced directives that allow patients to request a future course of action (e.g., adjustment of stimulation) should their decision-making capacity be compromised (e.g., during a stimulation-induced manic episode) (Müller, Bittlinger, & Walter, 2017). A post-operative approach is the Moral Case Deliberation protocol (Widdershoven, Meynen, Hartman, & Denys, 2014), which involves a consultative process between the patient, family and multidisciplinary team. This approach seeks to resolve discrepant perspectives on the stimulation side-effects while promoting the patient's autonomy and authenticity.

Who is responsible for the long-term management of a DBS device that can become a life-long component of patients' on-going care? Ethically rigorous post-trial management plans are essential and need to be discussed openly with patients and families during consent. During a trial,

researchers and sponsors are responsible for a patient's device from an ethical, medical, financial and legal perspective; however, this becomes less clear after the trial concludes. If a patient receives benefit from DBS, they should have the option to retain the device with clear knowledge of who holds responsibility for future costs (e.g., hardware issues, replacement batteries, future surgeries). Similarly, if the patient wishes to have the device removed, either during or after the trial phase, they need to be aware if this will come at a personal cost (approximate device explantation cost = $11,500USD) (Chen et al., 2017). Legally, research teams are not always required to cover post-trial costs (such as device explantation), but ethically it has been argued to be part of the researchers' duty of care (Sierra-Mercado et al., 2019). In adherence with the ethical principle *fidelity and responsibility* and ethical obligation to *non-abandonment*, investigative teams are responsible for patients' on-going clinical care and remain accountable until such time that care can be transferred to a suitably qualified clinician (Fins, 2009; Nuttin et al., 2014). Given the limited number of clinicians specialising in psychiatric neuromodulation and restriction of speciality clinics to metropolitan areas, research teams should anticipate and prepare to remain DBS patients' clinical point-of-contact for future years and decades. This is a critically unresolved ethical issue in invasive, experimental neurosurgical trials that warrants urgent attention.

Conclusions

The pursuit of DBS for psychiatric disorders is understandable given its demonstrated success alleviating debilitating movement disorders and the failure of existing therapies to successfully treat subsets of psychiatric patients. However, it is critical that studies are designed to optimise the likelihood of patients experiencing positive outcomes, including that patients and families are fully informed of the potential risks and benefits of participating in a trial. Multidisciplinary teams are also needed to provide patients and families with necessary psychosocial support. Researchers should avoid selective reporting and are encouraged to publish negative results (e.g., no improvement and/or adverse events). This information is essential for establishing efficacy, developing the field and avoiding undue duplication of research (Schlaepfer & Fins, 2010). Based on our interview experiences, we recommend regular collection of qualitative feedback, as it shows the significance and meaning of changes patients experience and provides context for primary outcome measure

scores. Research teams also need to consider the long-term management of clinical trials and their posttrial responsibilities. Despite the urgency for new treatments such as DBS, it is essential that these ethical issues are considered while taking a cautious approach to examine its efficacy and safety. DBS is far from a straightforward technological fix for psychiatric disorders and patients and families entering trials need to be appropriately selected, informed and supported through this challenging experimental process.

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Appendix E: Supplementary Materials from Paper One

SUPPLEMENTARY MATERIAL - INTERVIEW SCHEDULE

To begin, can you briefly tell me about your role and what your involvement is with a typical patient that's undergoing DBS?

1. Patient selection, information and consent

- How do you determine whether a patient is a suitable candidate for DBS surgery?
- What information do you provide to prospective patients and caregivers and how is their comprehension of this information assessed?
- Can you discuss the decision-making process for patients and to what extent caregivers/family are involved?
- What kinds of post-surgical changes in quality of life are discussed?

3. Patient expectations

- Do you see many patients and caregivers who hold unrealistic expectations for the surgery? If so, how are these expectations managed?
- What are some of the typical complaints or concerns patients or caregivers have raised following surgery? How are these managed?

5. Personhood, narrative, and identity

- How often do you see changes in patient personality following surgery? Can you describe the type of changes you see?
- What kind of impact do these changes have on the patient and caregiver that you've seen?
- In your experience what impact does DBS have on patients' identity or how they see themselves? Or on patients' agency or sense of control?
- Have you had any patients that appear to have had difficulty adjusting to being a 'well' or having new capabilities after being 'ill' for so long?
- Are these types of changes or adjustment difficulties discussed prior? How are they described?
- If patients and/or caregivers experience adjustment difficulties following surgery, what advice or options are made available?

6. Relationships

- In what ways have you seen DBS positively and negatively impact upon patient/caregiver relationships?

4. Future assistance

- How are patients followed up after DBS and what treatment outcomes are assessed?
- What options are discussed for patients' future care with the stimulator (e.g., adjusting settings, managing battery recharging, keeping stimulator on/off).
- Are there specific plans in place should the patient have any difficulty or concerns with their device or managing it?

Last questions:

Is there anything in particular you think is important for the general public and those considering DBS to know about? Anything to add?

Appendix F: Supplementary Materials from Paper Two

Table 1. Participant Demographic Information

Variable	**Patients (*n* = 11)**		**Caregivers (*n* = 11)**	
Gender	Male = 7	Female = 4	Male = 2	Female = 9
	Mean (*SD*)	**Range**	**Mean (*SD*)**	**Range**
Age (years)	62.5 (8.5)	45-73	60.5 (7.6)	51-69
Time since diagnosis	6.5 (2.6)	3-12		
Education	13.5 (3.4)	10-20	14.0 (1.8)	12-17
Relationship length			41.0 (8.3)	29-51
Interview length (mins)				
Before	40.3 (11.4)	24-62	36.8 (9.8)	24-53
After	42.4 (15.1)	28-70	45.6 (28.6)	23-121
	Before (*n* =11)	**After (*n* = 9)**	**Before (*n* =11)**	**After (*n* = 9)**
Work status				
Full time	2	1	5	4
Part time/casual	4	4	2	2
Volunteer	1	0	0	0
Retired	4	4	4	3
Psychiatric history	4		0	
Medical condition/comorbidity	7	6	5	2

Table 2. Anticipation Themes and Example Quotes

Theme: Impact of illness on personality and self

Ideas expressed during interviews:

Disease sits incongruently with patient's self and inhibits expression of their true personality

- *[She] has always been very independent. Independent in thought, in mind…that's one of her strong traits, I think. This dependency on us is not favoring her and the inability to do things she would normally do is curbing her personality too.* (Caregiver [C])
- *You can't say 'no' to [spouse], he doesn't accept no…so, to have something like Parkinson's, which is a big 'no' in some ways…is so against his personality.* (C)
- *The way I have sort of finished up with the Parkinson's is the antithesis of how I've lived the bulk of my life.* (Patient [P])

Disease negatively impacts patient self-confidence through reduced sense of control

- *Sometimes I think she's unaware or afraid of what these symptoms would cause her to do or she's not in control of it. So then, she wants someone else to be near her or around her. So, maybe after this operation she won't have those fears…she'll have more confidence back in her. I think she's lost a bit of confidence in herself, you know, being this very fiercely independent human being.* (C)

Onset of disease and medication-related changes (e.g., amotivation, apathy, compulsive shopping), some of which are problematic and distressing

- *He will buy packets of biscuits and lollies and eat them secretly…sexually – oh my God, Jesus Christ!…it's all about him. I'm just the woman at the end…No one talks to you about that. That's revolting…He was secretly gambling there for a little while.* (C)
- *I have never been one to spend. I spend a little more freely than I used to, that's for sure. Yeah, but it's not a problem. I've always been one to go like a dog with a bone at a project. That's the way I get involved with things, very keenly. I suspect that that's partly the medication.* (P)

Theme: Awareness and beliefs about potential personality change

Ideas expressed during interviews:

Limited awareness of association between DBS and personality change

- *No, we haven't discussed anything like that at all.* (C)

Is that something that you've heard of before? (Interviewer)

No, we haven't – I haven't anyway. (C)

Belief that the procedure could result in changes, as it involves interfering with the brain

- *I guess we're dealing with the brain and its regions, aren't we? So, it's quite possible that the procedure may affect another area of the brain.* (P)

Likelihood of personality change considered low due to no psychiatric history, being cognitively intact

- *Do you think that the surgery could change who you are in any way?* (Interviewer)

No, I don't think so, not overall. There's reason for that…I'm not fortunately involved with any depression or things like that. I've got a very, I think, a positive outlook on life and fairly good mental skills in the sort of areas I need to do things I want to do…Look, if I lose a little bit that's okay [laughs]. (P)

Changes would be temporary if addressed medically, but may also involve permanent change

- *If they weren't addressed, they could be long-term issues or changes…we could maybe bring that to the awareness of our specialists and say let's see if we can get this working a bit better because [I'm]…whatever [laughs]. Acting differently, doing uncharacteristic things, yeah…the length of time that would last for is only until we can nip it in the bud.* (P)

Theme: Hopes and fears

Ideas expressed during interviews:

Concerns DBS will result in undesirable personality changes

- *I think I've got more of a concern from comments people have made that he might – his personality might change because he's been a very placid sort of person. So, you know, I'm just hoping that that won't change too much.* (C)

Fears DBS will impact most-valued aspects of patient or involve dramatic changes

- *I wouldn't like him to be fearful of things. He's not a fearful person. I wouldn't like him to be someone who…was not willing to take life in both hands just because he gets a bit more mobility, that wouldn't be good…because that's in essence, that's who he is.* (C)
- *I think my attitude…everyone says I have a very positive attitude to life, and I would hate to be one of those grumpy old people [laughs] that complains about everything and sees the negative in everything. So, if that changed, that would be a concern to me.* (P)

Hope for a restoration of patient's pre-morbid personality

- *I'm hoping they [family/friends] see the [patient name] back that they all know as well…they've gone through this with both of us, but they've all noticed changes in him.* (C)

- *I'm hoping I suppose it will give him back the personality he used to have a bit more so he's a bit more positive and a bit more energy…just a bit more fun loving I suppose, that's been zapped a bit…I think his whole demeanor hopefully…He gets really easily frustrated…so, probably just going back to getting a bit more easy-going with it.* (C)
- *Hopefully more engaged with other people, yes, hopefully. As I said before, I'm a bit of a loner. That's what I want to try and get myself out of.* (P)

Table 3. Adjustment Themes and Example Quotes

Theme: Restoration of the 'old self'
Ideas expressed during interviews:
Pre-morbid sense of self restored, ability to express true self
- *I think what it has done is probably allowed me to be a bit more sort of back to my old self…There's nothing, no real change in personality other than I said, probably more positive, getting back to more like the person I was before.* (P)
- *A lot more energy, more stable, he was clearer, he was like his old self…he just wanted to, as he normally does, grab life with both hands and get on with it…There was no tremors and there was no shuffling…He was standing up straight, his facial movements, he was smiling, he didn't have his deadpan face anymore…it was like a switch – to normal.* (C)

External observations of a physically restored self
- *The difference probably externally we most noticed when he had the surgery done was he had a lot of life back in his face again.* (C)
- *That's the most remarkable thing [video footage]…because I didn't see that, you know? I mean I saw it, but I didn't really see it. Like outside of myself, I didn't see that I was this guy who's got no control of his body…the brain tricks the body. The body tricks the brain…everyone is saying 'you look so good'. I guess what they're meaning is you're not twisting and writhing, and perhaps you're standing up a bit taller.* (P)
- *People at work say that I seem to be – happier. I think – actually, one of the girls at work said to me that I smile a lot more than I used to [laughs], so that's a good thing. I do feel like people respond to me differently, so maybe there is something there.* (P)

Restorative and deteriorative impact on self-confidence and control
- *He's more willing to socialize. Because he had tremors in his hands, he didn't like to go out to restaurants because he had a problem with cutlery. He hasn't got that anymore. For his birthday last week, we went out for dinner in a restaurant, so that was good.* (C)
- *You just get far more involved…As I was telling you about that fog being lifted because you're feeling more alert, you're more confident and you feel like you obviously want to be more involved. It's all with your kids and close friends and giving advice and etcetera and that's certainly happened, which is great.* (P)
- *Would you say that you feel like a different person at all or in any way*? (Interviewer)

Not a totally different person. More confident about going out and doing things on my own, which I wasn't so much beforehand. (P)
- *Yeah, my speech has got worse…it comes out in blurs and slurs…I try not to talk anymore because it's not clear. That's Parkinson's I suppose.* (P)
- *He's probably lost some confidence in terms of in particular around speech and in decision-making. But I don't know whether that's down to the [DBS]…speech, I'm sure is. I think there was something that was triggered there. We've had some speech therapy and stuff, but it hasn't really made a lot of difference.* (C)
- *After DBS my voice was soft all the time, it gradually got worse and worse…all affecting my confidence and things like that. In fact, didn't do much work in that first six months…I've got no problems now, but I did miss four- or five-months' work, which is a bummer because I was doing quite well before the operation…What happened was, with one of the adjustments…lots of side effects, but one of them was my speech came back!* (P)

Theme: Lived experiences of personality change
Ideas expressed during interviews:
Types of changes experienced and perceived causes
- *[Spouse] tells me that when I'm fixated on something – and fixation is another thing – then I have to go now; I have to do it now… I think it's the procedure [DBS]. I think so. But also, I think the brain*

– if it was the procedure and the brain's not functioning to some degree somewhere, it will fix itself. Won't it? It'll…it's the plasticity - maybe it could settle down still? But then I have no idea. I'm just guessing. (P)

- *I do think he's cognitively got slower and a little bit more confused about things…the slowness of mind, bit of forgetfulness, a few of those sort of – forgetfulness and reassuring perhaps from me more what we're doing…Whether they [cognitive changes] were just marred by the movement prior to and you concentrate just on one thing and forget about the others…because we concentrated so much on the movement and trying to help with that.* (C)
- *Luckily, I was going to the appointments initially and I mentioned that he was driving me insane with this sort of behaviour… He [neurologist] just did a few tweaks with the machine and it disappeared. So, it was really quite strange.* (C)

Transient and sustained changes

- *[He] experienced quite a lot of…anxieties and hearing things and not sure where he was or where I was, quite mixed up and confused for the first few days, which we didn't expect…Yes, and then the lack of sleep when he wasn't sleeping was starting to compound his sort of teariness and anxiety of where I was and when I was coming back. He's never been overly reliant on me being there; he's quite good like that. So, that was a little bit different…but it did go on for a good week.* (C)
- *He was fairly – quite unwell obviously for a week afterwards and a bit disoriented…it probably took six to eight weeks before I felt that he was back…he was pretty needy, you know, for quite a while afterwards.* (C)
- *I thought in rehab it was super! I felt normal sort of thing, but then it all crashed.* (P)
- *[He] had a fit of giggles and he wouldn't stop laughing, it was so funny…I'm thinking, 'I've got to get him back to hospital!' [laughs] So, it just goes to show what can happen.* (C)

Patient awareness and insight into changes

- *Yeah so there's a little bit of that compulsiveness with ideas; he just doesn't go and buy anything, so he still talks things over, but he'll want to suggest something and I'll think 'I don't think we need that' and it might – and then the next day he's forgotten really about it or he'll say 'yeah, no I don't think we do need that'. I'll go 'no, I don't think so'.* (C)

Response to changes and relational impact

- *That was probably the main thing and the most worrying, and just wondering when it [postoperative confusion] would settle.* (C)
- *So, if I want to go to the shop and buy ice cream, then it can easily be construed that I've said 'let's go; come on, let's go and do it now'. [Spouse] has employed a great tactic – because she's always been on time and always ready to go, so she says 'I'll go start the car'. She sits patiently in the car, waiting for me. It's just beautiful. No tooting, just waiting.* (P)
- *It must be like a tiny kind of inflection on the words that I use, that [spouse] picks up on as being demanding…Yeah, it's almost a demand. I say 'I need to do this'. It's funny. I mean it's not funny…it just must be so subtle to everyone else, but [she] notices.* (P)
- *[He's] a little bit more ready to jump to his own defense, which is like 'oh, okay', which I don't mind, I think 'good'! Whereas I think he was so tired before and just sick of the movement and I think he just couldn't be bothered a lot of the time.* (C)

Theme: Clinical management of personality changes

Ideas expressed during interviews:

Clinician enquiry into postoperative personality change

- *He [neurologist] briefly made reference to it and as far as I know I said 'no, nothing, no change at all'.* (P)
- *No. Nobody's asked I don't think…we might have just told [neurologist] when we've seen him. But it's nothing major really.* (C)

Caregiver involvement for detecting and reporting changes

- *I know what to look for more I suppose too, because any unusual behaviors I will be reporting straight away, not putting up with them [laughs].* (C)

Social support for managing negative change and outcomes

- *When they heard of my outcome, they rang me up and they couldn't believe it. Their operations were so successful. They rang up and said 'What happened? What happened?' It's a really strange symbiosis – connecting with patients with vastly different experiences in outcome.* (P)

SUPPLEMENTARY MATERIAL

PATIENT INTERVIEW SCHEDULE - PRE-SURGERY

1. Background on DBS, PD

We are going to start with a brief discussion about your Parkinson's and how the option of DBS came about:

- Can you tell me about your condition and the treatments you have tried for PD?
- What has changed for you in the way you live your life since being diagnosed?
- Do you remember when you first learnt about DBS? Can you tell me about it?
- Who proposed DBS surgery to you?

2. Expectations and perspectives

- In your discussions with your medical team/neurologist, did they discuss what they hope to achieve with DBS? Do you remember what that was?
- What are your expectations regarding surgery outcomes?
- In which areas do you expect improvements?
    - *Prompt:* life activities, specific symptoms (motor, non-motor), quality of life
- In which areas do you not expect improvements?
    - *Prompt:* life activities, specific symptoms (motor, non-motor), quality of life
- How would you like to see yourself a year after surgery?
    - *Prompt:* life activities, specific symptoms (motor, non-motor), quality of life

3. Informed consent and decision-making

We are now going to discuss the decision to undergo DBS:

- Can you describe the process of making this decision?
    - Did you seek advice from anyone?
    - Have you had an opportunity to talk to anyone who has had the procedure?
- What level of choice do you feel you have?
    - To what extent do you feel like you are participating in the decision?
- What risks or side effects *related to the surgery* are you aware of?
- What are your greatest concerns about the surgery?
- After surgery, what risks or side effects *related to the stimulation* are you aware of?
- Do you feel you are well-informed of the DBS risks and side effects?

4. Stimulator management

After the surgery, managing and controlling the stimulator becomes an important issue:

- Has your medical team/neurologist talked to you about what to expect regarding adjusting your stimulation settings?
    - Did they discuss how long it might take to find optimal stimulation settings?
    - How long do expect it to take?
    - What changes do you anticipate if your stimulation is set too low or too high?
- What difficulties or challenges managing your stimulator do you anticipate?
    - *Prompt:* stimulation settings, usability, recharging, travelling with stimulator
- What might you do if you have a problem with the stimulator?
    - Who can help you? Who can you contact?

5. Stimulator control

- How much control do you expect will you will have over your stimulator after surgery?
    - *Prompt:* switching ON vs OFF, adjusting voltage (with or without a range), recharging option
- How do feel about having that level of control?

6. Personality, identity and relationships

We are going to shift focus now to discuss changes following surgery that are non-motor related:

- Has anyone in your medical team talked to you about the potential for there to be non-motor changes following surgery? What did they say?
    - *Prompt:* sensory, mood or behavioral changes?
- How long do you expect these changes to last?
- Do you think DBS could change who you are or your personality at all? If *yes*, how?

- Is there anything about who you are that you wouldn't be willing to lose/change in exchange for improvement in your motor symptoms?
- Do you think your relationship with (caregiver) will change after DBS? If *yes*, how?
- Do you have any concerns about how your relationship may change after DBS?
- Do you think your relationships with other family and friends will change after DBS? If *yes*, how?

We're going to wrap up soon, I just have one final questions:

- Since your diagnosis, are there any activities that you do less or have stopped that you hope to do again after surgery?
    - *Prompt:* socializing, leisure activities/hobbies, work/volunteering/study

Is there anything that we haven't talked about that you would like to add?

PATIENT INTERVIEW SCHEDULE – POST-SURGERY

1. Background on DBS, PD

We met several months ago before you underwent DBS. We'd like to understand your experience since receiving DBS.

- Briefly describe your experience of the surgery.
- Can you explain what has happened since then? Has anything changed in your life?

2. Expectations and perspectives

- Can you describe your experience living with DBS?
- What were your expectations regarding DBS? Were they met?
    - *Prompt:* life activities, specific symptoms (motor, non-motor), quality of life
- Can you describe any improvements in motor symptoms you have experienced?
- Can you describe any improvements in non-motor symptoms you have experienced?
- Are there any areas that you expected to see improvements that you haven't?

3. Informed consent and decision-making

- Knowing what you know about your outcome today, would you undergo DBS again?
- Looking back, are there things you would have liked to have known beforehand?
- Do you feel like you had an appreciation of the risks and benefits of surgery?

4. Stimulator management and control

We're now going to discuss your experience with the stimulator

- Can you tell me a bit about your experience using the stimulator, such as recharging the battery and adjusting stimulation settings? Has it brought about any challenges?
- Are you satisfied with your current stimulation parameters/settings and the process for making adjustments?
- How long did it take to reach optimal settings?
- Who controls your stimulator being on/off or changes the parameters? If *them*, are you confident doing this? How do you feel about controlling these settings?
- Has your neurologist given you clear instructions for appropriate stimulation settings? Do you follow these instructions? If *no*, why?

5. Personhood, identity and relationships

- Do you think the surgery has changed who you are/your personality at all? If *yes*, how so? When did these changes start to occur?
- Would you say you feel like you are a different person now? Do you see yourself differently since the surgery? If *yes*, in what ways?
- What do you think brought on these changes, e.g., stimulation, feeling better, other?

- How did you adjust to these changes and to having the stimulator?
- Did your relatives and/or close friends notice changes in you? If *yes*, what kind of comments/observations have they made?
- Do you think people see you differently now? If *yes*, in what way?

- Have any medical professionals enquired about any changes in mood, personality or behaviour?

- How did (caregiver) react to the DBS?
- How has your relationship changed since the DBS?
- Are there tensions or conflicts between you now that are related to the DBS outcomes?
- Are there tensions or conflicts that have been resolved since having DBS?

- How did other family and friends react to the DBS?
- How have your relationships with family and friends changed since DBS?
- Are there tensions or conflicts between you now that are related to your DBS outcomes?
- Are there tensions or conflicts that have resolved since DBS?

- (*If tension/conflicts have been raised*) Is there someone who you can seek advice from or discuss these issues with?
- Do you ever discuss these sorts of issues with your medical team at follow up appointments?

- When we last spoke you said that after DBS you would like to do more/restart (insert previously stated activity). Has this happened? If *no*, why so?

6. Public understanding and knowledge transfer
We're coming to the end now, just a couple of final questions about the public's understanding of DBS:
- Are there things you feel that the general public should know about DBS?
- Have you or would you recommend DBS to other patients/caregivers?

Is there anything that we haven't talked about that you would like to add?

CAREGIVER INTERVIEW SCHEDULE – PRE-SURGERY

1. Background on DBS, PD
We are going to start with a brief discussion about _____ 's Parkinson's and how the option of DBS came about:
- Can you tell me about your relationship to _____ (spouse, father, mother…) and the treatments they have tried for PD thus far?
- What has changed for you in the way you live since _____ developed PD?
- Can you please describe to me how you first learnt about DBS?
- How was DBS proposed to _____?

2. Expectations and perspectives
- What are your expectations regarding surgery outcomes?
- In which areas do you expect _____ to experience improvements?
    - *Prompt:* life activities, specific symptoms (motor, non-motor), quality of life
- In which areas do you not expect _____ to experience improvements?
    - *Prompt:* life activities, specific symptoms (motor, non-motor), quality of life
- We know that some people can hold high expectations for DBS, what about _____'s expectations?
- How would you like to see_____ a year after surgery?
- How would you like to see yourself a year after surgery?

3. Informed consent and decision-making
We are now going to discuss the decision for _____ to undergo DBS:
- Can you describe the process of making this decision?
    - Did you or _____ seek advice from anyone?
    - Have you or _____ had an opportunity to talk to anyone who has had the procedure?
- What level of choice do you feel there is?
    - Do you feel like_____ is participating in the decision?
    - Do you feel like you are participating in the decision?
- What risks or side effects *related to the surgery* are you aware of?
- What are your greatest concerns about the surgery?

- After surgery, what risks or side effects *related to the stimulation* are you aware of?
- Do you feel well-informed of the DBS risks and side effects?

4. Stimulator management
After the surgery, managing and controlling the stimulator becomes an important issue:
- Has _____'s medical team/neurologist talked to you about what to expect regarding adjusting their stimulation settings?
    - Did they discuss how long it might take to find optimal stimulation settings?
    - How long do expect it to take?
    - What changes do you anticipate if the stimulation is set too low or too high?
- What difficulties or challenges managing the stimulator do you anticipate?
    - *Prompt:* stimulation settings, usability, recharging, travelling with stimulator
- What might you do if there is a problem with the stimulator?
    - Who can help you? Who can you contact?

5. Stimulator control
- How much control do you expect you will have over the stimulator after surgery?
    - *Prompt:* switching ON vs OFF, adjusting voltage (with or without a range), recharging option
- How do feel about having that level of control?

6. Personality, identity and relationships
We are going to shift focus now to discuss changes following surgery that are non-motor related:
- Has anyone in _____'s medical team talked to you about the potential for there to be non-motor changes following surgery? What did they say?
    - *Prompt:* sensory, mood or behavioral changes?
- How long do you expect these changes to last?
- Do you think DBS will change who _____ is or their personality at all? If *yes*, how?
- Is there anything about who _____ is that you wouldn't be willing to lose/change in exchange for improvement in their motor symptoms?

- Do you think your relationship with _____ will change after DBS? If *yes*, how?
- Do you have any concerns about how your relationship may change after surgery?

- Do you think _____'s relationships with other family and friends will change after DBS? If *yes*, how?

We're going to wrap up soon, I just have one final questions:
- Since _____'s diagnosis, are there any activities that you do less or have stopped that you hope to be able to do again after surgery?
    - *Prompt:* Socializing, leisure activities/hobbies, work/volunteering/study

Is there anything that we haven't talked about that you would like to add?

CAREGIVER INTERVIEW SCHEDULE – POST-SURGERY

1. Background on DBS, PD
We met several months ago before _____ underwent DBS. We'd like to understand your experience since _____ received DBS.
- Can you explain what has happened since then? Has anything changed in your life?

2. Expectations and perspectives
- Can you describe your experience living with a (spouse, partner, father etc.) with DBS?
- What were your expectations regarding DBS? Were they met?
    - *Prompt:* life activities, specific symptoms (motor, non-motor), quality of life
- In which areas has _____ seen improvements?
- In which areas has _____ not seen any improvements?
- Are there any areas that you expected to see improvements that you haven't?

3. Informed consent and decision-making

- Knowing what you know about the outcome today, would you recommend _____ undergo DBS again?
- Looking back, are there things you would have liked to have known beforehand?
- Do you feel like you and _____ had an appreciation of the risks and benefits?

4. Stimulator management and control

We're now going to discuss your experience with the stimulator

- Can you tell me a bit about yours and _____ experience using the stimulator, such as recharging the battery and adjusting stimulation settings? Has it brought about any challenges?
- Are you satisfied with _____'s current stimulation parameters/settings and the process for making adjustments?
- How long did it take to reach optimal settings?
- Who controls your stimulator being on/off or changes the parameters? If *them*, are you confident doing this? How do you feel about controlling these settings?
- Has your neurologist given _____ clear instructions for appropriate stimulation settings? Does _____ follow these instructions? If *no*, why?

5. Personhood, identity and relationships

- Do you think DBS has changed who _____ is or their personality at all? If *yes*, how so? When did these changes start to occur?
- Do you feel like _____ is themselves since having DBS?

- What do you think brought on these changes, e.g., stimulation, feeling better, other?
- How have you adjusted to these changes?
- Did relatives and/or close friends notice changes in _____? What kind of comments/observations have they made?
- Have any medical professionals enquired about any changes in mood, personality or behaviour?

- Do you see yourself differently since _____ underwent DBS? How so? When did these changes start to occur?
- How has your relationship with _____ changed since the DBS?
- Are there tensions or conflicts between you and _____ now related to the DBS outcomes?
- Are there tensions or conflicts that have resolved since DBS?

- How did other family and friends react to the DBS?
- How has _____'s relationships with family and friends changed since DBS?
- Are there tensions or conflicts between _____ and others now that are related to the DBS outcomes?
- Are there tensions or conflicts between _____ and others that have resolved since DBS?

- (*If tension/conflicts have been raised*) Is there someone who you can seek advice from or discuss these issues with? Have you been able to discuss these sorts of issues with _____'s medical team at follow up appointments?

- When we last spoke you said that after surgery you would like to do more/restart (*insert previously stated activity*). Has this happened? If *no*, Why so?

6. Public understanding and knowledge transfer

We're coming to the end now, just a couple of final questions about the public's understanding of DBS:

- Are there things that the general public should know about DBS?
- Have you or would you recommend this DBS to other patients/caregivers?

Is there anything that we haven't talked about that you would like to add?

Appendix G: Supplementary Materials from Paper Three

SUPPLEMENTARY MATERIAL

PATIENT INTERVIEW SCHEDULE – PRE-SURGERY

1. Background on DBS
We are going to start with a brief discussion about deep brain stimulation:

- Do you remember when you first learnt about DBS? Can you tell me about it?
- Have you done any personal research?
    - *Prompt:* e.g., newspapers, online, websites, blogs, spoken to others

2. Expectations and perspectives

- What changes would you like to see as a result of DBS? What do they want from the procedure?
- How do you picture yourself a year after surgery?
- In which areas do you hope to experience changes?
- In which areas do you **not** expect changes?
- What are your thoughts on the extent of the benefits DBS could provide?
- After DBS, how much work do you anticipate you will have to contribute towards your recovery?
    - *Prompt:* Amount of psychological/therapeutic work, other medical interventions, support services?

3. Personality and identity
We are now going ask some questions about the impact DBS might have upon you as a person:

- Do you think DBS could change who you are? Or change your personality? If *yes*, how? If *no*, is it something you've thought about?
    - *Prompt:* be like the person you were before you were ill? / be a new and different person? / be more or less the same?
    - How long do you expect these changes to last?
- How do you feel about the prospect of having the stimulator as a part of you and your body?
    - Do you anticipate it will change how you see yourself? How?

4. Inter-personal relationships
I now want to ask you about the impact DBS might have upon your relationships with others:

- Do you think your relationship with (caregiver's name) will change after DBS? If yes, how might it look like?
- In what ways would you like your relationship to change?
- Do you have any concerns about how your relationship may change after DBS?
- Do you have any concerns about how your relationship may **not** change?
- Do you think your relationships with other family and friends will change after DBS? If yes, how?

5. Informed consent and decision-making
We are now going to discuss the decision to undergo DBS:

- Can you describe the process of making this decision? For instance, did you go through stages of changing your mind?
- When you were making the decision to undergo DBS, whose opinion or what information was most influential or important to you?
- What risks or side effects *related to the surgery* are you aware of?
- What concerns do you have about the surgery?
- After surgery, what risks or side effects *related to the stimulation* are you aware of? What worries do you have about the stimulation?
- How informed do you feel you about the risks and side effects of DBS? In the short term (i.e. in undergoing surgery)? In the long-term?

6. Stimulator management
After the surgery, managing and controlling the stimulator becomes an important issue. Your stimulator settings are going to be adjusted throughout the trial.

- What changes do you expect could occur when these adjustments happen?

- How long do you think it will take for the changes to happen?
- Do you have any concerns about the stimulation adjustments and what changes might occur?
- Do you feel prepare to manage it?
- In terms of managing the stimulator yourself, have you thought about any issues you might face?
    - *Prompt:* recharging, travelling with stimulator

We're going to wrap up soon, I just have one final questions:

- Are there things that you would like to do or are looking forward to doing after DBS?
    - *Prompt:* socialising, leisure activities/hobbies, work/volunteering/study

I'm just going to take a moment to look through my questions and make sure there are no points we've missed, while I'm doing this do you want to take a moment and think whether there are any issues important to you that we haven't discussed?

PATIENT INTERVIEW SCHEDULE – POST-SURGERY

1. Background on DBS

We met several months ago. We would like to better understand your experience since receiving DBS.

- Can you explain what has happened since then? Has anything changed in your life? If so, please describe?
- Can you briefly comment on the experience of having the DBS surgery itself?

2. Experiences and perspectives

- Do you recall what your original expectations regarding DBS? Were they met? (e.g., in terms of life activities and specific symptoms)?
- Have you seen any improvements?
- Are there areas you have not seen improvements that you expected to?

3. Personality and identity

- If at all, how has DBS changed who you are or your personality?
- Do you feel like you are a different person in anyway now?
- Do you see yourself differently since DBS? In what way? When did these changes start to occur?
- Have your relatives and/or close friends noticed changes in you? What kind of comments or observations have they made?
- What do you think brought on these changes (the device or feeling better)?
- How have you adjusted to having the device as part of you and your body?

- Inter-personal relationships
- How has (caregiver) reacted to the DBS?
- Do others see you differently since the DBS?
- How would you describe your relationships with others since DBS?
    - *Prompt:* better, easier, strained, more complex?
- Are there tensions or conflicts between you and others that have arisen since DBS? Or that have resolved?
- Who do you seek advice from regarding any issues like these? Do you ever discuss these sorts of issues with your team at follow-up appointments?

4. Informed consent and decision-making

- Knowing what you know now, if you have your time again would you undergo DBS?
- How informed about the risks and side effects of surgery do you think you were? Do you think you fully appreciated these?
- Are there things that have come as a surprise to you?
- Looking back, are there things you would have liked to have known?

5. Device control issues

- Who controls your stimulator being on/off or change the parameters? Has it brought about any challenges?

- Who do you contact if you have concerns about your stimulator?

6. Public understanding and knowledge transfer
- Are there things that the general public should know about DBS for depression?
- Have you or would you recommend this procedure to other patients/caregivers?

Is there anything that we haven't talked about that you would like to?

CAREGIVER INTERVIEW SCHEDULE – PRE-SURGERY

1. Background on MDD, DBS
We are going to start with a brief discussion about _____'s depression and how the option of DBS came about:
- Can you briefly tell me about your relationship with _____ and the treatments they have tried for depression thus far?
- What has changed for you in the way you live since _____ developed depression?
- Do you remember when you first learnt about DBS? Can you tell me about it?
- How was the option of DBS proposed to _____?
- Can you describe the process of making this decision? For instance, did you and/or _____ go through stages of changing your minds?
- When you were making the decision to undergo DBS, whose opinion or what information was most influential or important to you?
- Have you done any personal research?
    - *Prompt:* e.g., newspapers, online, websites, blogs, spoken to others

2. Expectations and perspectives
- What changes would you like to see as a result of DBS? What do you want the procedure to do for _____?
- How do you picture_____ a year after surgery?
- How do picture yourself a year after surgery?
- In which areas do you hope _____ will experience changes?
- In which areas do you **not** expect _____ to experience changes?
- What are your thoughts on the extent of the benefits DBS could provide?
- After DBS, how much work do you anticipate _____ will have to contribute towards their recovery?
    - *Prompt:* Amount of psychological/therapeutic work, other medical interventions, support services?
- We know that some people can hold high expectations for DBS, what about _____'s expectations?

3. Personality and identity
I want to shift focus now and ask some questions about the impact DBS might have upon _____ as a person:
- Do you think DBS could change who _____ is? Or change their personality in some way?
    - If *yes*, how? If *no*, is it something you've thought about?
    - *Prompt:* become like the person they were before they were ill? / be a new and different person? / be more or less the same?
    - How long do you expect these changes to last?
- Is there anything about who _____ is that you wouldn't be willing to lose/change in exchange for an improvement in their depression symptoms?

4. Inter-personal relationships
I now want to ask you about the impact DBS might have upon _____'s relationships with others, including yourself:
- Do you think your relationship with _____ will change after DBS?
    - If *yes*, how might it look like?
- In what ways would you like your relationship to change?
- Do you have any worries about how your relationship might change after DBS?
- Do you think _____'s relationships with other family and friends will change after DBS? If yes, how?

5. Informed consent
Like any surgical procedure, there are a number of risks and side effects associated with DBS:

- What risks or side effects *related to the surgery* are you aware of?
    - What concerns do you have about the surgery?
- After surgery, what risks or side effects *related to the stimulation* are you aware of?
    - What worries do you have about the stimulation?
- How informed do you feel you about the risks and side effects of DBS? In the short term (i.e. in undergoing surgery)? In the long-term?

6. Stimulator management
After the surgery, managing and controlling the stimulator becomes an important issue. _____'s stimulator settings are going to be adjusted throughout the trial.

- What changes do you expect could occur when these adjustments happen?
- How long do you think it will take for the changes to happen?
- Do you have any concerns about the stimulation adjustments and what changes might occur?
- Do you feel prepared to assist managing this?
- In terms of managing the stimulator yourself, have you thought about any issues you might face?
    - *Prompt:* recharging, travelling with stimulator

We're going to wrap up soon, I just have one final questions:

- Are there things that you would like to do or are looking forward to doing after DBS?
    - *Prompt:* socialising, leisure activities/hobbies, work/volunteering/study

I'm just going to take a moment to look through my questions and make sure there are no points we've missed, while I'm doing this do you want to take a moment and think whether there are any issues important to you that we haven't discussed?

CAREGIVER INTERVIEW SCHEDULE – POST-SURGERY

1. Background on DBS
We met several months ago. We would like to better understand your experience since _____ received DBS.

- Can you explain what has happened since then? Has anything changed in your life? If so, please describe?
- Can you briefly comment on the experience of _____ having the DBS surgery itself?

2. Experiences and perspectives

- Do you recall what your original expectations regarding DBS? Were they met? (e.g., in terms of life activities and specific symptoms)?
- Have you seen any improvements in _____?
- Are there areas you have not seen improvements that you expected to?

3. Personality and identity

- Do you think having DBS has changed _____'s personality in anyway? If so, how?
- Do you feel like _____ is themselves since the surgery?
- Have your relatives and/or close friends noticed changes in _____? What kind of comments or observations have they made?
- What do you think brought on these changes (the device or feeling better)?
- Do you think _____ see themselves differently in anyway now?
- How have they adjusted to having the device as part of them and their body?

4. Inter-personal relationships

- Do you see yourself differently since _____ underwent DBS? When did these changes start to occur?
- Do you feel like you and _____ are different people now? How do you feel about the change?
- How would you describe your relationship since DBS?
    - *Prompt:* better, easier, strained more complex?
- Are there tensions between you and _____ now related to the outcome of DBS?

- Are there tensions or conflicts that have resolved since DBS?
- Who do you seek advice from regarding any issues like these? Do you ever discuss these sorts of issues with your team at follow up appointments?
- How has _____'s relationships with others changed since having DBS?

5. Informed consent and decision-making

- Knowing what you know now, if you have your time again would you support _____ to undergo DBS?
- How informed about the risks and side effects of surgery do you think you were? Do you think you fully appreciated these?
- Are there things that have come as a surprise to you?
- Looking back, are there things you would have liked to have known?

6. Device control issues

- Who controls the stimulator being on/off, change the parameters, recharging? Has it brought about any challenges?
- Who do you contact if you have concerns about the stimulator?

7. Public understanding and knowledge transfer

- Are there things that the general public should know about DBS for depression?
- Have you or would you recommend this procedure to other patients/caregivers?

Is there anything that we haven't talked about that you would like to?