Treating Obsessive Compulsive Disorder: Does neurobiology help?

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What is OCD and how severe can it be?

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OCD: DSM- 5 Criteria

- **Obsessions or compulsions**
- **Cause marked distress, are time consuming (>1hr/day), or interfere with day-to-day functioning**

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DSM-5: OCD

A. Presence of obsessions, compulsions or both:

Obsessions are defined by (1) and (2)

1. Recurrent and persistent thoughts, urges or images that are experienced, at some time during the disturbance, as intrusive and unwanted, and that in most individuals causes marked anxiety or distress
2. The individual attempts to ignore or supress such thoughts, urges, or images, or to neutralize them with some other thought or action (i.e., by performing by compulsion).

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DSM-5: OCD

Compulsions are defined by (1) and (2)

1. Repetitive behaviours (e.g. hand washing, ordering, checking) or mental acts (e.g. praying, counting, repeating words silently) that the individual feels driven to perform in response to an obsession or according to rules that must be applied rigidly.
2. The behaviours or mental acts are aimed at preventing or reducing anxiety or distress, or preventing some dreaded event or situation; however these behaviours or mental acts are not connected in a realistic way with what they are designed to neutralize or prevent and are clearly excessive.

Note: Young children may not be able to articulate the aims of these behaviours or mental acts.

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DSM-5: OCD

B. The obsessions or compulsions are time-consuming (e.g. take more than 1 hour per day) or cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.

C. The obsessive-compulsive symptoms are not attributable to the physiological effects of a substance (e.g., a drug of abuse, a medication) or another medical condition.

D. The disturbance is better explained by the symptoms of another mental disorder.

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DSM-5: OCD

Specify if:

- **With good or fair insight**
- **With poor insight**
- **With absent insight/delusional beliefs**

- **Tic-related**

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OCD: Quality of Life

60 patients with moderate-severe OCD

- **impaired social functioning**
  (and related to severity of illness)
- **impaired role performance**
  (even after controlling for depression)

(Koran et al, 1996)

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OCD: Course

122 OCD patients followed for 40yrs

- **48% recovered (20% completely)**
- **most who did recover did so in early years of illness**
- **48% had symptoms for over 30yr**
- **poor outcome predicted by early onset & low baseline social functioning**

(Skoog & Skoog , 1999)

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Neurobiology of OCD

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OCD: Neurobiology

- ↑ blood flow in
  - Caudate/putamen
  - Basal ganglia
  - Orbito frontal cortex
  - Anterior cingulate cortex
- Pharmacological and psychological treatment can reverse this
- Psychosurgery and DBS "interrupt" the circuit

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OCD: Neurobiology

- Seen as a perturbation of serotonin system (SRI's work, NARI's don't)

BUT: SRIs not wildly effective and DA antagonist can augment quite effectively

- Proposed role of D_2 and also D_1
- Proposed role of other (?glutamatergic) pathways

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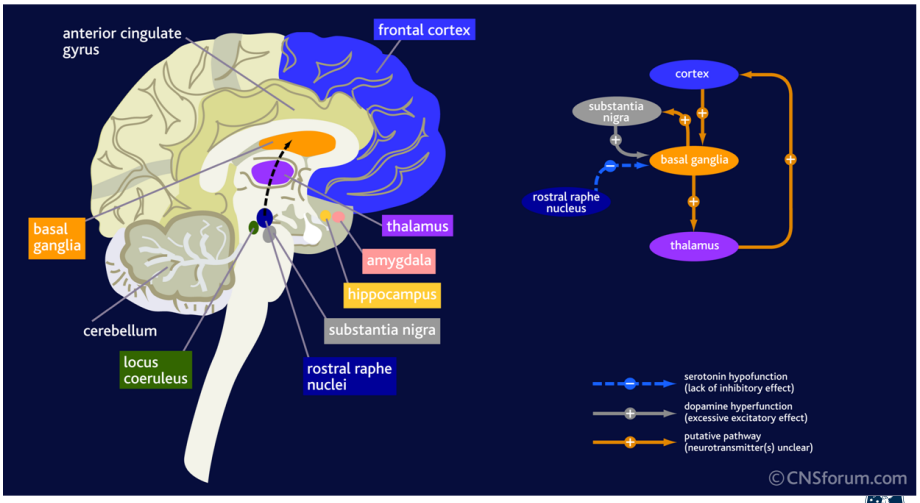

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OCD: Relationship with Other Disorders

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OCD: Co-morbidity

	CURRENT	LIFETIME
Major Depression	31%	78%
Specific Phobia	7%	28%
Social Phobia	11%	26%
Panic Disorder	6%	15%
Eating Disorder	8%	17%
Alcohol Dependence	8%	16%

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Treating OCD

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OCD: Treatment (Castle et al, 2012)

General principles:

- Psycho-education (include family)
- Reasonable expectations of treatment
- Treat comorbidities
- Least restrictive environment
- Incorporate patient's preferences
- EX/RP and SSRIs first line and best together
- Therapeutic alliance

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OCD: Treatment (Castle et al, 2012)

Psychological:

- EX/RP is mainstay
- CBT
- ACT

? Benefit of addition of D-Cycloserine

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OCD: Treatment (Castle et al, 2012)

Pharmacological agents:

- SSRI
- SNRI
- Clomipramine

Augmentation

- Atypical antipsychotics
- Bupropion
- Buspirone
- Clonidine
- Lithium
- Pregabalin
- Memantine
- Naltrexone

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OCD: Treatment (Castle et al, 2012)

Treatment resistance:

- Ensure adherence
- Augmentation strategies
- ⬆ EX/RP
- Combine pharmacological and psychological
- Inpatient treatment
- Neurosurgery (anterior cingulotomy, anterior capsulotomy, subcaudate tractotomy) rare now days
- DBS (mostly nucleus accumbens) emerging as very effective in some patients

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Evaluation of treatment response in OCD

- Symptoms: - Y-BOCS - % improved "remission": (<10?)
  - CGI –I – "improved" "much improved etc."
- Functioning - social/interpersonal
  - vocational

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First – Line Treatments

- SSRIs
  - Often require higher doses but also need time
  - ? Combinations of SSRIs
    - Mirtazapine (Pallanti et al, 2004)
    - Clomipramine – Monitor ECG and levels
- ? SNRIs – no proven advantage of venlafaxine over SSRIs
- ? Clomipramine (greater side effect burden)

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Treatment Resistance
A) General issues

- Lack of uniform definition (working suggestion is failure to achieve > 25% YBOCS improvement with 2 SRIs at max dose for 12 weeks each)
- Assess
  - Diagnosis and symptom set (e.g. hoarding)
  - Adherence
  - Comorbidities
    - Depression
    - Tics
    - ADHD
- High dosing
  - Citalopram 160mg (Bejerot et al, 1998)
  - Sertraline 400mg (Ninan et al, 2006)
  - Clomipramine 300mg (Study Group, 1991)
    - ECG, plasma levels

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Treatment Resistance
B) Intravenous Treatment

- Evidence supports benefit for ivi Clomipramine
  (Ravidran et al, 2010)
- Not practicable outside specialist centers

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Treatment Resistance
C) Switching

- Some evidence to support switching to another SSRI, but need to weigh against delayed response (Finberg et al, 2006)
- Scant evidence for switch to venlafaxine (Denys et al, 2004)

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Treatment Resistance
D) Augmenting with antipsychotics (APs)

- Putative indirect 5HT effect through DA inhibition but no evidence for efficacy for APs alone (except ? Aripiprazole)
- Atypical APs may worsen OCS
- Augmentation of SRIs with typical (haloperidol) and atypical (risperidone, quetiapine, olanzapine) effective for some patients (? especially with comorbid tics, schizotypy)

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Treatment Resistance
E) Novel pharmacological treatments

- Inositol (reverses 5HT receptor desensitisation): inconclusive
- Neuropeptides (e.g. oxytocin): little success
- Glutamatergic agents (antagonists)
  - Neurontin: benefit in uncontrolled and single-blind studies (Stewart et al, 2001)
  - Riluzole: benefit in open trials but risk of pancreatitis (Grant et al, 2010)
- NMDA receptor partial agonists (D-Cycloserine, glycine): small benefit as adjunct to CBT but poorly tolerated (Storch et al, 2007; Greenberg et al, 2009)
- Ondansteron (5HT3 antagonist): one RCT (4mg) against fluoxetine (20mg) showed some benefit (Soffami et al, 2010)
- Morphine: beneficial in double-blind cross-over vs. lorazepam and PBO; no efficacy for naloxone in two RCTs (Koran et al, 2005)
- NAC: trial underway (Sarris et al)

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Treatment Resistance
F) Other Biological Treatments

- ECT: no benefit unless depressed
- rTMS: 10 trials with 110 patients support transient efficacy for (dorsolateral prefrontal cortex, orbitofrontal cortex, supplementary motor area) in open trials but no RCTs (Blom et al, 2011)
- Neurosurgery: stereotactic neurosurgery as "last resort" – e.g. 47% response in patients (bilateral anterior cingulotomy) with no adverse effects at 24 months (Jung et al, 2006)
- DBS: promising reversible technique: target anterior limb of internal capsule, ventral striatum, or nucleus accumbens; side effects include transient hypomania (Denys et al 2012)

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DBS for treatment-refractory OCD Study at SVHM

6 participants, 18-65 years,5 year history of OCD, Y-BOCS ≥ 24, GAF < 45, CBT ≥ 16 sessions, medication (SSRI x2, clomipramine, antipsychotic augmentation) and CBT refractory

Prescribed psychotropic medications will continue to be taken without change for two months prior to implantation and during the first two phases of the study (that is for 9 months after implantation)

Pre-op Phase 2 months	DBS Surgery	Open Phase 8 months	Controlled Phase 1 month	Maintenance Phase 12 months
		• Stimulator on	• 2 weeks with stimulator on and 2 weeks with stimulator off	• Stimulator on
• Cognitive Testing I (3 hours over 1-2 sessions) • MEG Session I • MRI • PET Session I	• Bilateral implantation using Medtronic 3389 lead • Electrical measurements	• Evaluate every 2 weeks • Once see reduction in Y-BOCS by ≥ 6 points, a CBT program is added	• Evaluate at start • Evaluate after 2 weeks • Evaluate after 4 weeks • CBT program ongoing • Stimulator on	• Evaluate periodically

- Cognitive Testing II (3 hours over 1-2 sessions)
- MEG Session II
- PET Session II (Performed at end of Open Phase once Y-BOCS score reduced by ≥ 6 points)

Black – St Vincent's Hospital Melbourne
Green – Swinburne University
Orange – Austin Health

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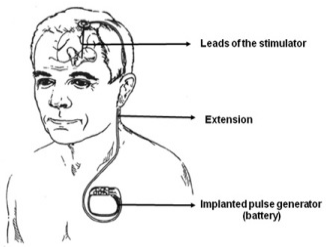
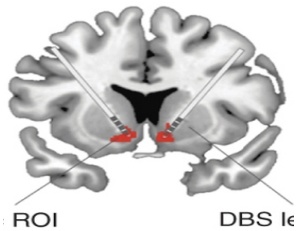
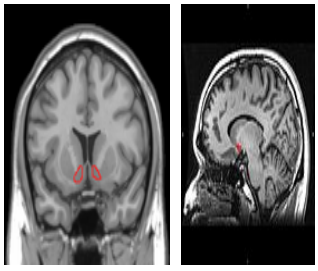
DBS- nucleus accumbens







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DBS in treatment-refractory OCD
YBOCS
6 participants

YBOCS	1	2	3	4	5	6
	32	29	29	35	33	29
	27	27	21	35	33	27
	24	24	21	35	33	27
	23	19	17	35	17	27
	20	20	13	24	17	27
	19	28	13	21	23	27
	17	21	14	21	20	27
	13	26	14	21	20	27
	13	23	16	21	24	27
	13	22	12	21	18	27
	12	18	11	21	18	27
	12	18	11	20	20	27
	6	13	11	20	20	27
	0	13	14	20	20	27
9 months	0	15	17	22	20	27
	9	24	19	22	23	27
	2	21	17	22	18	27
	5	23		22		27
	5	21		22		27
	8	26		22		27
	5	15		24		27
	7	16		24		
	7			24		
	7			24		
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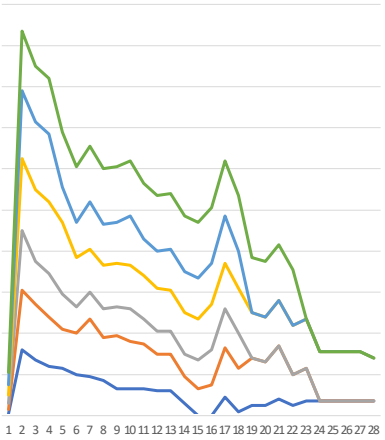
	63 months	30 months	46 months	26 months	9 months	10 months



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DBS in treatment-refractory OCD at SVMH

Deep brain stimulation in obsessive-compulsive disorder

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To the Editor

We commend Farrand et al. (2017) on their report of the outcome of deep brain stimulation (DBS) in seven patients with treatment-resistant obsessive-compulsive disorder (OCD). The authors acknowledge the need for structured assessment of quality of life and qualitative assessments in future studies, and the centrality of multidisciplinary input throughout all phases of care.

Our own experience of DBS in treatment-refractory OCD comprises four implanted patients; we have also targeted the nucleus accumbens. The outcomes thus far have been encouraging, albeit heterogeneous: one patient had a dramatic, almost total resolution of OCD symptoms, while the others have had a slower improvement trajectory. Clinical heterogeneity, psychiatric comorbidity and lack of clear treatment response predictors bedevil the work-up and prognostication. We have focussed on the severity and impact on daily life of the obsessive-compulsive symptoms as our primary target, aligned with the RDoC approach; this raises the possibility of using DBS in OCD-related disorders. Related to this is our use of magnetoencephalographic and positron emission tomographic imaging along with neuropsychological assessments to try better to understand the underlying neurobiology. Of interest is that patients seem to show, along with improved core symptoms, enhanced episodic (declarative) memory for situational awareness using the Autobiographical Memory Interview. Our patients (and their families) have described how difficult it can be to come to terms with a 'life after OCD': this has been described as the 'burden of normality' and requires careful attention in the planning and follow-up phases (Gilbert, 2012). We concur with Farrand et al. (2017) about the importance of a multidisciplinary team approach. We have found in particular that the inclusion of an expert mental health occupational therapist in the work-up and follow-up, within in-reach into the patients' own living environments, to be a seminal component of recovery. We have also found that patients are able to re-engage in Exposure and Response Prevention exercises when they are less overwhelmed by their symptoms, post implantation.

Although the use of DBS in OCD can have excellent outcomes in individual patients, more consistent clinical staging for treatment-refractoriness, prognosis and response along with more personalized DBS treatment algorithms are required. Also, psychological and life skill multidisciplinary interventions, in context of the subjectivity of quality of life beyond obsessive-compulsive symptomatology, are imperative. We call for an Australia-wide network of all those involved in this work, to pool knowledge and help refine this work.

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Farrand S, Evans AH, Mangelsdorf S, et al. (2017) Deep brain stimulation for severe treatment-resistant obsessive-compulsive disorder: An open-label case series. *Australian and New Zealand Journal of Psychiatry*. Epub ahead of print 1 September. DOI: 10.1177/0004867417731819.

Gilbert F (2012) The burden of normality: From 'chronically ill' to 'symptom free'. New ethical challenges for deep brain stimulation postoperative treatment. *Journal of Medical Ethics* 38: 408–412.

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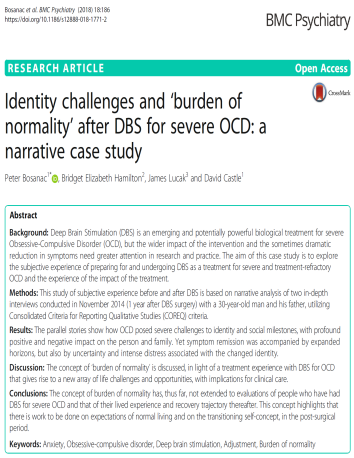
Burden of normality



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BMC Psychiatry

RESEARCH ARTICLE Open Access

Identity challenges and 'burden of normality' after DBS for severe OCD: a narrative case study

Peter Bosanac*, Bridget Elizabeth Hamilton2, James Lucak3 and David Castle1

Abstract

Background: Deep Brain Stimulation (DBS) is an emerging and potentially powerful biological treatment for severe Obsessive-Compulsive Disorder (OCD), but the wider impact of the intervention and the sometimes dramatic reduction in symptoms need greater attention in research and practice. The aim of this case study is to explore the subjective experience of preparing for and undergoing DBS as a treatment for severe and treatment-refractory OCD and the experience of the impact of the treatment.

Methods: This study of subjective experience before and after DBS is based on narrative analysis of two in-depth interviews conducted in November 2014 (1 year after DBS surgery) with a 30-year-old man and his father, utilizing Consolidated Criteria for Reporting Qualitative Studies (COREQ) criteria.

Results: The parallel stories show how OCD posed severe challenges to identity and social milestones, with profound positive and negative impact on the person and family. Yet symptom remission was accompanied by expanded horizons, but also by uncertainty and intense distress associated with the changed identity.

Discussion: The concept of 'burden of normality' is discussed, in light of a treatment experience with DBS for OCD that gives rise to a new array of life challenges and opportunities, with implications for clinical care.

Conclusions: The concept of burden of normality has, thus far, not extended to evaluations of people who have had DBS for severe OCD and that of their lived experience and recovery trajectory thereafter. This concept highlights that there is work to be done on expectations of normal living and on the transitioning self-concept, in the post-surgical period.

Keywords: Anxiety, Obsessive-compulsive disorder, Deep brain stimulation, Adjustment, Burden of normality

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Future directions

- Personalised medicine- informing benefit (likelihood response to DBS/neurotherapeutics OCD [RDoC and qualitative data rather than rating scales alone] vs risk)
- Mechanistic (assessment, functional neuroimaging, qualitative feedback) understanding of consumer journey
- Timelier adjustments to stimulation parameters based on MEG or closed loop data
- Other

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