13 (2026) 25–32

Contents lists available at ScienceDirect

Deep Brain Stimulation

journal homepage: www.journals.elsevier.com/deep-brain-stimulation

Longitudinal outcomes and clinical predictors of VC/VS deep brain stimulation in severe obsessive–compulsive disorder: A case series

Tatyana Branco Nunes [a,*], Liesbet Goossens [a], Yasin Temel [b,e], Anne E.P. Mulders [c], David E.J. Linden [a], Ersoy Kocabiçak [e,f], Albert F.G. Leentjens [a], Sonja A. Kotz [d], Koen R.J. Schruers [a,1], Linda Ackermans [b,1]

[a] Faculty of Health, Medicine and Life Sciences, Department of Psychiatry and Neuropsychology, Maastricht University, Maastricht, the Netherlands
[b] Department of Neurosurgery, Maastricht University Medical Centre, Maastricht, the Netherlands
[c] Department of Medical Psychology, Maastricht University Medical Centre, Maastricht, the Netherlands
[d] Faculty of Psychology and Neuroscience, Department of Neuropsychology and Psychopharmacology, Maastricht University, Maastricht, the Netherlands
[e] Department of Neurosurgery, Istanbul Atlas University, Istanbul, Turkey
[f] Neuromodulation Centre, Atlas University Hospital, Istanbul, Turkey

ARTICLE INFO

Keywords:
Deep brain stimulation
Obsessive–compulsive disorder
Ventral capsule/ventral striatum

ABSTRACT

Deep brain stimulation (DBS) of the ventral capsule/ventral striatum (VC/VS) is an established treatment for severe, treatment-refractory obsessive–compulsive disorder (OCD). While efficacy is well documented, less is known about temporal response patterns, such as effects at the first follow-up after implantation, longitudinal symptom trajectories, and clinical predictors of individual responses in this cohort. Twenty patients who underwent VC/VS-DBS, were repeatedly assessed using the Yale–Brown Obsessive–Compulsive Scale (Y-BOCS) from baseline to long-term follow-ups (mean duration 22 months, range 6–99). Effects at the first follow-up were assessed by comparing baseline and first post-implantation scores. Longitudinal changes were analysed using linear mixed-effects models, including demographic, illness-related, affective, comorbidity, and symptom dimension variables as exploratory predictors in this modest sample. DBS produced significant symptom reduction at the first follow-up and sustained improvement over follow-ups, although trajectories varied across individuals. Twelve patients were full responders (≥35% reduction), two were partial responders (25–34%), and six were non-responders (<25% reduction). Age of OCD onset interacted with time, with later-onset patients showing slower improvement over time. Age at implantation also interacted with time, indicating age-related differences in symptom reduction pace. Other clinical variables were not significantly linked to symptom trajectories. Overall, VC/VS-DBS provides robust and lasting symptom relief in severe OCD, while most clinical characteristics have limited predictive value for individual treatment responses. These findings highlight the utility of longitudinal modelling, and the need to explore neurobiological markers to better understand variability in DBS outcomes.

1. Introduction

Obsessive–compulsive disorder (OCD) is a chronic psychiatric disorder affecting approximately 2% of the population [1]. It is characterized by persistent intrusive thoughts (obsessions), compulsive rituals, and severe functional impairment [2]. While first-line treatments such as selective serotonin reuptake inhibitors (SSRIs) and cognitive behavioural therapy (CBT) are effective for many, approximately 10% of patients continue to experience persistent disabling symptoms despite exhaustive treatment attempts [3]. For this subset of patients, neurosurgical interventions such as deep brain stimulation (DBS) may be considered [4].

Over the last two decades, DBS has been studied for treatment-refractory OCD (TR-OCD). DBS involves stereotactic implantation of electrodes into subcortical targets such as the anterior limb of the internal capsule (ALIC), bed nucleus of the stria terminalis (BNST) [5],

* Correspondence to: Department of Psychiatry and Neuropsychology, Maastricht University, Universiteitssingel 50, Maastricht 6229 ER, the Netherlands.
E-mail address: tatyana.branconunes@maastrichtuniversity.nl (T. Branco Nunes).
[1] These authors contributed equally to this work and share senior authorship

https://doi.org/10.1016/j.jdbs.2026.04.001
Received 6 March 2026; Received in revised form 21 April 2026; Accepted 28 April 2026
Available online 29 April 2026

ventral capsule/ventral striatum (VC/VS), nucleus accumbens (NAc), and subthalamic nucleus (STN) [6,7]. Among these, VC/VS has emerged as the most frequently targeted and consistently effective site, with several studies demonstrating robust symptom improvement compared to alternative targets such as the STN or NAc [4,8,9].

Across open-label trials and randomized controlled studies, mean reductions of 37–48% in Yale–Brown Obsessive–Compulsive Scale (Y-BOCS) scores have been reported, with response rates (defined as ≥35% in symptom reduction) of 43–60% [8–11]. Importantly, placebo effects appear minimal [12], and quality of life (QoL) improvements often accompany symptom reduction [13]. Meta-analyses further indicate that VC/VS and bilateral NAc stimulation are associated with particularly favourable outcomes, with mean Y-BOCS reductions often exceeding 40% and response rates above 50% [11]. Although efficacy is now well established, DBS for OCD remains investigational, with access limited by regulatory, financial, and clinical barriers [14].

Despite these advances, several important questions remain. First, while many studies report overall efficacy, less is known about the effects at the first follow-up of DBS following implantation and stimulation onset, including how rapidly patients respond and the extent of early symptom reduction. Second, although longitudinal follow-up studies have demonstrated sustained DBS benefits in OCD, symptom change has largely been examined within target-specific cohorts using heterogeneous analytic approaches. This makes direct comparison of symptom courses across studies difficult and leaves the longitudinal course of symptom change in VC/VS-DBS underexplored. Little is known about how symptoms change across repeated assessments in this target and how strongly patients differ in their rate of improvement over follow-up. Together, these gaps highlight the need to characterize longitudinal symptom trajectories in VC/VS-DBS and to identify clinical factors associated with individual differences in treatment response.

The present study aimed to address these gaps by systematically characterizing the clinical outcomes of VC/VS-DBS for OCD across multiple dimensions. First, we evaluated the effects at the first follow-up of VC/VS-DBS, defined as how symptoms improve from baseline to first post-implantation assessments. Second, we examined the longitudinal course of treatment responses, focusing on the average magnitude of improvement at final follow-up, the shape of symptom trajectories across time points, and the proportion of patients who met standard response threshold. Finally, we explored potential predictors of VC/VS-DBS efficacy, including illness duration, age at implantation, and comorbid conditions such as depression and anxiety. By addressing these questions, this study aimed to refine our understanding of the time course, durability, and heterogeneity of VC/VS-DBS outcomes in OCD, thereby informing both clinical practice and the factors that contribute to therapeutic response.

2. Methods

2.1. Sample

From 2014–2025, 23 patients underwent VC/VS-DBS for severe, treatment-resistant OCD at Maastricht University Medical Centre (MUMC+). Eligibility for surgery was determined by criteria outlined in Nuttin et al. [15], which required candidates to have an OCD diagnosis according to diagnostic DSM criteria, and a Y-BOCS total score of 30 or higher. Diagnoses were classified according to DSM-5 criteria [16]. Symptoms had to persist for at least five years despite adequate pharmacological and psychotherapeutic treatment, including two SSRIs, clomipramine, antipsychotic augmentation, and CBT. Eligible patients were at least 18 years old and capable of providing informed consent. Exclusion criteria were current or past psychotic disorders and medical or other comorbid conditions that contraindicated surgery. Candidate cases were evaluated based on two independent psychiatric assessments and subsequently reviewed by a multidisciplinary DBS panel.

This study was carried out in compliance with the Declaration of Helsinki. Institutional review board approval and informed consent were not required, as the study did not fall under the scope of the Dutch Act on Scientific Research Involving Human Subjects.

2.2. Surgical procedure

For detailed information on the surgical protocol, we refer to prior publications [17–19]. Briefly, DBS surgery was performed under general anaesthesia using remifentanil and propofol. A stereotactic frame was affixed to the skull, after which a perioperative CT scan was obtained and fused with preoperative MRI to enable precise targeting. Electrodes were implanted bilaterally in the VC/VS, using standardized stereotactic coordinates that were adjusted based on individual anatomy. A paraventricular trajectory was typically used. All patients received bilateral quadripolar electrodes (Model 3387 or Sensight, Medtronic, Fridley, USA) connected to an implanted pulse generator (Activa PC or Percept PC, Medtronic, Fridley, USA). Representative targeting and post-operative MRI images illustrating electrode placement in the VC/VS have been published previously (see Bouwens van der Vlis et al., [20]).

2.3. Clinical outcome

OCD symptom severity was measured using the Y-BOCS at baseline (pre-surgery, T0) and at multiple post-operative follow-up time points (T1–T5) according to each patient's clinical monitoring schedule. Only patients with a baseline Y-BOCS assessment and at least one post-surgery Y-BOCS measurement were included in the statistical analyses. The time between measurement was calculated in months. Statistical significance for each analysis was defined as $p < .05$. All analyses were conducted in R (v4.3.2–4.4.0).

2.3.1. DBS effects at the first follow-up

The effect at the first follow-up was defined as the change in symptom severity from baseline to the first post-implantation assessment following the establishment of stable stimulation parameters. The interval between these two time points was calculated in months. Descriptive statistics (mean, standard deviation, minimum, maximum, median) were computed for pre-DBS, post-DBS, and the difference between these scores. Paired *t*-tests were conducted to assess the significance of first follow-up changes, and Cohen's d for repeated measures was used to estimate effect sizes. Additionally, linear regression was performed to examine whether the time between surgery and post-DBS assessment predicted the magnitude of symptom change.

2.3.2. Longitudinal DBS effects

Longitudinal effects of DBS were evaluated by modelling Y-BOCS scores over time since surgery (in months). Time since surgery was included as a fixed effect in a linear mixed-effects model fitted using the lme4 and lmerTest packages in R (REML estimation). Random intercepts and slopes were specified for each participant to account for individual differences in baseline severity and rate of change. Model assumptions were assessed visually using residual and fitted-value diagnostics.

Both first follow-up and longitudinal Y-BOCS data were visualized in plots to illustrate changes over time.

2.3.3. Predictors of symptom change

To explore potential predictors of DBS efficacy, we examined whether demographic, illness-related, affective, comorbidity-related factors, and OCD symptom subtype predicted symptom improvement in individual patients, quantified as Y-BOCS scores over time. Clinical and demographic predictors included age at OCD onset, age at DBS implantation, illness duration, baseline affective symptom severity and vulnerability measured with the Montgomery–Åsberg Depression Rating Scale (MADRS) [21] and the trait subscale of the State-Trait Anxiety Inventory (STAI-TRAIT) [22], respectively, total number of psychiatric

comorbidities, and OCD symptom dimensions assessed with the Padua Inventory-Revised [23], comprising five subscales: Rumination, Washing, Impulses, Controlling/Checking, and Precision/Perfectionism.

Psychiatric comorbidities were documented by treating physicians during routine clinical care. For descriptive and analytic purposes, these diagnoses were aggregated into eight broader categories reflecting overlapping symptom domains rather than formal diagnostic classifications and were reviewed by a psychiatrist. The categories included depressive disorders, anxiety disorders, trauma- and stressor-related disorders, OCD-related disorders, neurodevelopmental disorders, feeding and eating disorders, personality disorders, and substance-related disorders. This grouping was intended to reduce fragmentation across heterogeneous clinical labels and facilitate reporting.

For all predictors, descriptive statistics were first inspected, and normality was assessed using Shapiro–Wilk tests [24]. Linear mixed-effects models (LMEs) were fitted using the lmer function in R to quantify the relationship between each predictor and repeated Y-BOCS scores. For all continuous predictors (age at OCD onset, age at DBS implantation, illness duration, months since surgery, MADRS, STAI-TRAIT, as well as number of comorbidities), variables were grand-mean centred to facilitate interpretation of model intercepts and interactions. Predictors were either examined jointly (e.g., age-related variables in the same model) or separately, depending on conceptual grouping and multicollinearity considerations. Each model included months since surgery and its interaction with the predictor(s) as fixed effects. Random intercepts and slopes were included to account for individual differences in baseline Y-BOCS severity, as well as individual variability in symptom trajectories over time, respectively. If models exhibited singular fit, indicating overparameterization relative to the available data, the random-effects structure was simplified to include random intercepts only. All LMEs were fitted using restricted maximum likelihood estimation, with *t*-tests for fixed effects computed via Satterthwaite's approximation. Model fit was assessed using Akaike's and Bayesian Information Criteria, and variance explained by fixed effects (marginal R^2) and the full model (conditional R^2) was calculated following Nakagawa and Schielzeth [25]. Model assumptions were evaluated visually using residual diagnostics to confirm approximate normality and homoscedasticity, and effect sizes were primarily interpreted from the fixed-effect slopes, representing the influence of each predictor on Y-BOCS trajectories.

All predictor analyses were exploratory and hypothesis-generating in nature. Therefore, formal corrections for multiple comparisons (e.g., Bonferroni) were not applied, as such corrections substantially reduce statistical power in small samples and increase the risk of overlooking potentially meaningful associations.

3. Results

3.1. Patient characteristics and clinical outcomes

Data were available for 23 patients who had undergone DBS for treatment-refractory OCD, though repeated Y-BOCS scores were available for only 20 patients. Clinical outcomes of a subset of these patients (n = 8) were previously reported [20]. Demographic and clinical characteristics are summarized in Table 1. The sample included 14 females and 9 males, with a mean age at DBS implantation of 44.2 years (SD = 12.3, range 26.5–66.4) and a mean age of OCD onset of 16.0 years (SD = 6.7, range 6–29), corresponding to an average illness duration of 27.8 years (SD = 12.1, range 8.5–51.4). The mean baseline MADRS score was 21.4 (SD = 8.6, range 4–39), and baseline trait anxiety (STAI-TRAIT) averaged 68.4 (SD = 7.2, range 54–80), reflecting elevated depression and trait anxiety levels. OCD symptom dimensions were assessed using the subscales of the Padua Inventory–Revised. Padua subscale scores showed considerable variability. Rumination had the highest mean with 32.3 (SD = 8.9). Washing showed wide variability (SD = 13.2, range 0–39), indicating large inter-individual differences. Impulses and Precision were relatively lower and more homogeneous. At baseline, 14 patients were receiving pharmacotherapy, most commonly clomipramine (n = 7) and quetiapine (n = 5). At the last available follow-up for each participant, pharmacotherapy remained common (n = 14), while 3 participants were receiving psychotherapy, primarily Exposure and Response Prevention (see Table A.1 in the Appendix).

Additionally, patients had an average of 1.96 comorbid psychiatric conditions (SD = 1.4, range = 0–5), most frequently depressive disorders (n = 16) and personality disorders (n = 10). Almost all patients presented at least one comorbidity.

Baseline Y-BOCS scores (T0) averaged 34.5 (range 28–38) and decreased over follow-up (T1-T5), with marked reductions among responders (Table 2). Twenty patients had a baseline and at least one available post-operative Y-BOCS measurement, yielding 61 observations in total and an average of 3 assessments per patient including baseline. Follow-up availability varied according to individual post-surgery monitoring timelines, with the number of follow-up assessments per patient ranging from 1 to 5 (T1-T5). The mean follow-up duration ranged from 6 to 39 months, while the mean time from baseline to the

Table 1
Demographic and clinical sample characteristics.

	N	Mean	Std	Min	Max
Sex					
Female	14				
Male	9				
Age at Implantation	23	44.24	12.31	26.49	66.43
Age of OCD onset	23	15.95	6.67	6	29
≤ 18	17				
> 18	6				
Illness Duration (years)	23	27.81	12.10	8.49	51.37
MADRS	23	21.38	8.55	4	39
STAI-TRAIT	23	68.38	7.19	54	80
Number of comorbidities		1.96	1.43	0	5
Depressive disorders	16				
Anxiety disorders	3				
Trauma-related disorders	3				
OCD-related disorders	7				
Neurodevelopmental disorders	6				
Eating disorders	3				
Personality disorders	10				
Substance-related disorders	2				
OCD symptom dimensions (Padua)					
Rumination	23	32.3	8.87	8	44
Washing	23	16.1	13.2	0	39
Impulses	23	10.1	6.84	2	23
Controlling	23	19.4	8.62	0	28
Precision	23	15.6	4.95	9	24

Table 2
Clinical outcome per timepoint.

	N	Mean	Min	Max
Y-BOCS				
T0	23	34.52	28	38
T1	20	24.6	7	37
T2	12	19.25	0	33
T3	7	13.57	4	27
T4	2	20	15	25
T5	2	14.5	6	23
Response rates				
Responders (≥ 35%)	12	−22.83 (-64.91%)	-14 (-37.84%)	-38 (-100%)
Partial responders (25–34%)	2	−11 (-31.45%)	-11 (-30.56%)	-11 (-32.35%)
Non-responders	6	−2.5 (-7.36%)	2 (5.71%)	-6 (-16.67%)

Note. T0 represents the pre-surgery assessment, and T1–T5 correspond to successive postoperative follow-up time points. For response rates, values indicate the absolute change in Y-BOCS scores from baseline. Negative values represent a decrease in score, and positive values represent an increase. Percent changes are shown in parentheses.

last available measurement was 45.99 months (range 6–99 months; Table A.2), indicating substantial variability in both the number and timing of observations across patients.

Based on baseline and last available post-operative Y-BOCS scores, 12 patients were full responders (≥35% Y-BOCS reduction), two were partial responders (25–34% Y-BOCS reduction), and six were non-responders (Table 2).

3.1.1. Adverse events

All surgeries in this cohort (N = 20) were reported as uncomplicated, and most adverse events occurred acutely, either shortly after the procedure or following stimulation adjustments. Device- and post-operative complications primarily consisted of wound infections and cases requiring DBS system revision or repositioning, with occasional device-related discomfort. Psychiatric adverse effects were relatively infrequent and generally mild. The most common adverse events overall were somatic, particularly fatigue or tiredness, followed by nausea or dizziness and sleep disturbances. Cognitive, behavioural, and sensory effects were rare. Notably, long-term adverse effects were mainly limited to fatigue and device-related discomfort. A detailed overview of all reported adverse events is provided in Table 3. For a more extensive discussion of side effects in a subset of this sample, see Baldi et al. [26].

3.2. First follow-up and longitudinal effects of DBS on OCD severity

First follow-up DBS effects were assessed in 20 patients (Table 4). Mean Y-BOCS scores decreased from 34.5 pre-DBS to 24.6 at the first post-DBS assessment, corresponding to an average absolute reduction of 8.8 points (25.6%). This first follow-up reduction is illustrated in Fig. 1A. A paired *t*-test confirmed a significant reduction in Y-BOCS scores from pre- to post-DBS ($t(19) = 5.84$, $p < 0.000$, Cohen's $d = 1.31$). A linear regression revealed that the time from DBS surgery to the first post-DBS assessment did not predict symptom improvement ($\beta = 0.007$, $SE = 0.087$, $t = 0.08$, $p = 0.939$).

For longitudinal analyses, data were available from 20 patients with a baseline Y-BOCS assessment and at least one post-surgery follow-up. Mixed-effects modelling revealed a significant main effect of time on Y-BOCS scores ($\beta = -0.34$, $SE = 0.07$, $t(10.76) = -4.95$, $p = 0.0005$), indicating an average decrease of approximately 0.34 points per month. Longitudinal trajectories of total, obsession, and compulsion Y-BOCS scores for each patient are shown in Fig. 1B–D. Analysis of random effects indicated limited between-subject variability in baseline severity ($SD = 0.84$), relative to substantial within-subject residual variability ($SD = 5.43$).

Note. Panels show changes in Y-BOCS scores from baseline to the first available post-operative assessment (A), as well as trajectories of total Y-BOCS scores (B), Obsessive scores (C), and Compulsive scores (D) over time for each patient. Each line represents an individual patient.

Table 3
Adverse events following VC/VS-DBS.

Domain	Adverse event	N (= 20)
Device / post-op complications	Wound infection	5
	DBS system revision/removal/repositioning	3
	Device discomfort/mechanical burden (pressure, seating, positioning)	3
	Post-op seizure	1
Psychiatric effects	Low mood	1
	Agitation/irritability	2
	Emotional instability	2
	Restlessness	1
Somatic / physical effects	Fatigue/tiredness	6
	Nausea/dizziness	4
	Sleep disturbance	3
	Muscle pain	2
	Headache	1
	Reduced appetite	1
	Vivid dreams	1
	Breathing/airway complaints	1
Cognitive / behavioural effects	Memory complaints	1
	Difficulty initiating/finishing activities	1
Sensory effects	Head tightness/pressure sensation	2
	Taste reduction	1

Table 4
First follow-up DBS effects on Y-BOCS scores.

	N	Mean	Std	Min	Max	Median
Pre-DBS	20	34.52	2.68	28	38	35
Post-DBS	20	24.58	8.81	7	37	25
Percent Change (%)	20	25.6	24.4	−10	80	20.5
Time to First Post (months)	20	22.20	21.77	5.75	99.59	20.78

Note. First follow-up DBS effects are shown as pre- and post-surgery Y-BOCS scores, along with the percent change in symptom severity, calculated as the reduction from pre- to post-DBS. Post-DBS refers to the first available Y-BOCS measurement following DBS surgery. The time between pre-DBS and the first post-DBS assessment is also provided.

3.3. Predictors

A summary of all predictor results is shown in Table 5.

3.3.1. Age of disease onset and age at implant

Linear mixed-effects models were used to examine the association of age of OCD onset, age at DBS implantation, and illness duration with longitudinal changes in Y-BOCS scores. Across all models, months since surgery showed a significant main effect, indicating reductions in Y-BOCS scores over time following DBS.

For age of OCD onset, a significant interaction with months since surgery ($\beta = 0.013$, $SE = 0.01$, $t = 2.71$, $p = 0.01$) indicated that patients with later onset showed a slower rate of symptom improvement compared to those with earlier onset. Similarly, age at implantation interacted significantly with months since surgery ($\beta = 0.012$, $SE = 0.01$, $t = 2.64$, $p = 0.011$), with younger patients showing faster symptom improvement over time. Overall, the model explained 66.7% of the variance through fixed effects alone (marginal R^2) and 70.6% when accounting for both fixed and random effects (conditional R^2).

3.3.2. Other predictors

No significant main or interaction effects were observed for illness duration, MADRS, STAI-TRAIT, number of comorbidities, or OCD symptom dimensions. Trend-level effects were observed for STAI-Trait as a main effect ($\beta = 0.38$, $p = .064$), suggesting a possible association with higher overall Y-BOCS scores, and for the rumination subscale as an interaction with time ($\beta = -0.01$, $p = .066$), suggesting a potential association with greater symptom improvement over time. However, neither effect reached statistical significance. Model fit across these analyses ranged from moderate to high (marginal $R^2 = 0.45–0.57$, conditional $R^2 = 0.55–0.84$).

4. Discussion

In this study, we examined clinical outcomes following VC/VS-DBS in patients with treatment-refractory OCD. Across 20 patients with repeated Y-BOCS measurements, we observed a significant first follow-up reduction in OCD severity, with mean Y-BOCS scores decreasing by approximately 25% from baseline to the first post-DBS assessment, which occurred between 6 and 99 months after surgery. Importantly, the magnitude of this first follow-up improvement was not related to the length of the interval between surgery and the first assessment. Additionally, there was considerable variability in baseline severity between patients, underscoring the heterogeneity of treatment-refractory OCD even within a highly selected DBS cohort.

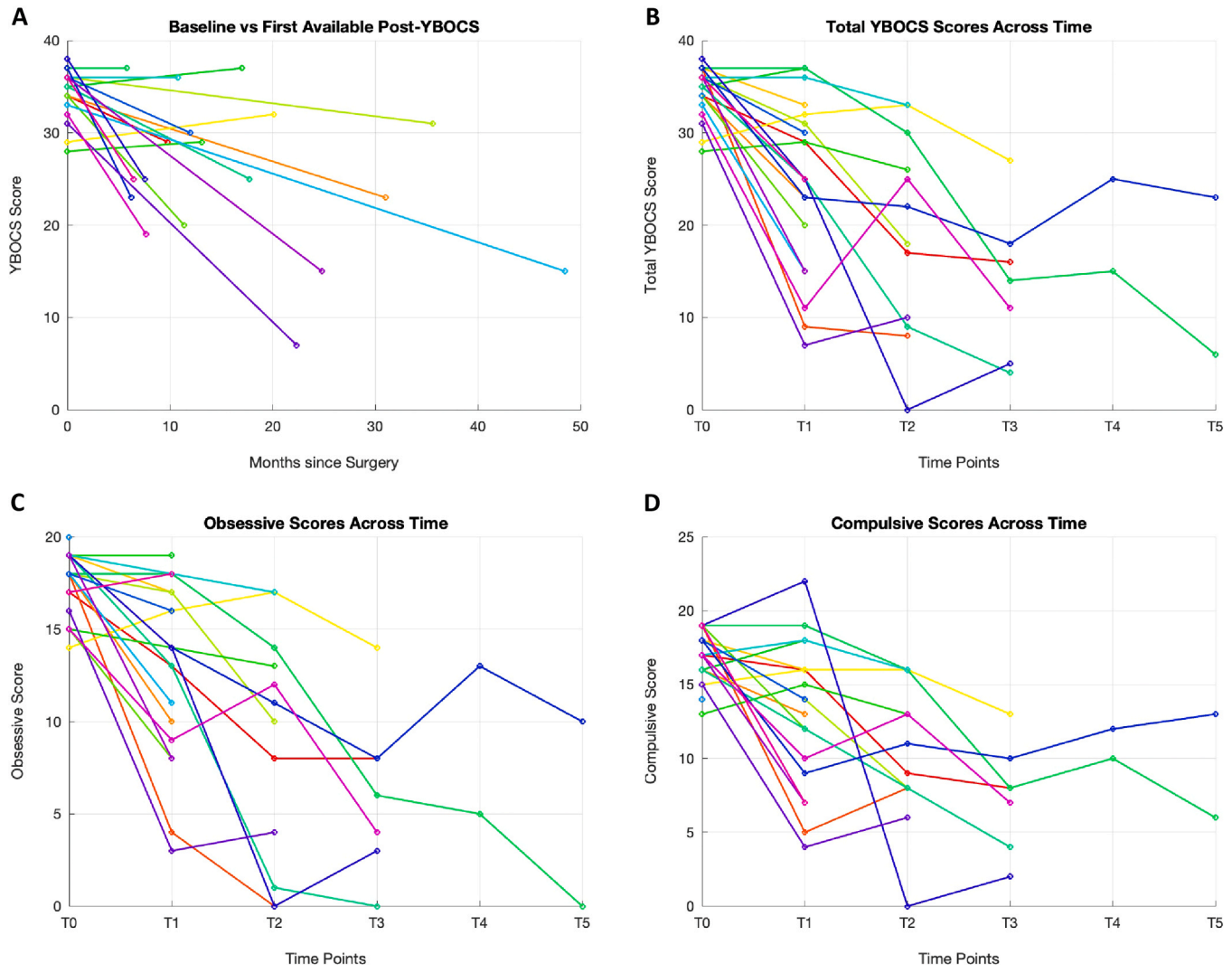

Fig. 1. First follow-up and longitudinal DBS effects on OCD severity.

Longitudinally, patients continued to experience gradual symptom improvement after the first follow-up postoperative reduction. Notably, 60% of patients met the criteria for full response, defined as at least a 35% reduction in Y-BOCS scores following DBS. This suggests that the therapeutic effects of VC/VS-DBS are not limited to the immediate period after surgery but are sustained and may continue to increase over the following months.

Regarding predictors, age-related factors emerged as the most consistent clinical factors of DBS outcome. Age of OCD onset showed a significant interaction with time since surgery. Patients with a later age of OCD onset exhibited a slower rate of symptom reduction over time compared with patients whose OCD began earlier. This finding contrasts with several reports in which later age of onset was associated with greater symptom reduction or responder status following DBS [27,28], and with work showing lower long-term symptom severity in earlier-onset patients treated with STN stimulation [9]. Other studies, particularly in ALIC/BNST cohorts, have reported no significant influence of age of onset on longitudinal Y-BOCS trajectories [29]. Taken together, these mixed findings suggest that age of OCD onset may influence the pace of subsequent improvement following DBS, with effects that vary by DBS target, cohort characteristics, and statistical modelling rather than reflecting a uniform predictor of response.

In addition, age at implantation significantly interacted with time since surgery, indicating that age influenced the rate of symptom change following DBS. Specifically, patients implanted at a younger age exhibited a steeper decline in Y-BOCS scores over time than those implanted later in adulthood. Importantly, while this interaction highlights differences in how quickly patients respond to stimulation, it does not necessarily imply that younger patients achieved lower absolute Y-BOCS scores at the end of follow-up. Prior meta-analytic work has not consistently identified age at surgery as a robust predictor of overall DBS response across targets [27], suggesting that age may shape the temporal dynamics of improvement without uniformly determining the ultimate clinical benefit.

In contrast, other clinical variables, including baseline depressive symptoms, trait anxiety, illness duration, psychiatric comorbidity burden, and OCD symptom dimensions did not show meaningful associations with symptom trajectories. Rather than implying these factors are unimportant, these null findings suggest that VC/VS-DBS exerts a broadly consistent effect across diverse patient profiles. This aligns with prior research reporting limited predictive value of depression severity, comorbidities, or symptom subtypes for DBS outcomes, although some target-specific effects have been observed in other cohorts [27,29]. Collectively, the minimal influence of most clinical predictors underscores the importance of avoiding overly restrictive selection criteria and highlights the potential of neurobiological or mechanistic markers to better account for individual differences in treatment response. These findings reinforce the view that VC/VS-DBS can produce both rapid and

Table 5
Linear mixed-effects model results for predictors of longitudinal Y-BOCS scores.

Predictor	Effect	β	SE	t-value	p-value	Direction
Age of OCD onset	Main effect	0.35	0.19	1.83	.087	n.s
	Interaction with time*	0.013	0.01	2.71	**.01**	Later onset associated with slower symptom improvement
Age at implantation	Main effect	0.08	0.08	0.97	.338	n.s.
	Interaction with time*	0.01	0.01	2.64	**.011**	Younger age associated with faster improvement
Illness duration	Main effect	−0.11	0.12	−0.97	.345	n.s.
	Interaction with time	0.003	0.004	0.87	.388	n.s.
MADRS	Main effect	0.24	0.17	1.45	.164	n.s.
	Interaction with time	0.004	0.004	0.98	.332	n.s.
STAI-Trait	Main effect	0.38	0.19	1.99	.064	n.s
	Interaction with time	0.005	0.01	0.72	.478	n.s.
Number of comorbidities	Main effect	−0.29	0.99	−0.29	.772	n.s.
	Interaction with time	−0.013	0.04	−0.41	.685	n.s.
Padua: Rumination	Main effect	-0.01	0.14	-0.07	.939	n.s.
	Interaction with time	−0.01	0.01	−1.88	.066	n.s.
Padua: Washing	Main effect	−0.11	0.11	−1.02	.332	n.s.
	Interaction with time	−0.004	0.003	−1.40	.167	n.s.
Padua: Impulses	Main effect	−0.28	0.21	−1.33	.200	n.s.
	Interaction with time	−0.01	0.01	−1.29	.202	n.s.
Padua: Controlling	Main effect	-0.03	0.18	-0.14	.890	n.s.
	Interaction with time	−0.004	0.01	−0.55	.585	n.s.
Padua: Precision	Main effect	−0.18	0.29	−0.63	.537	n.s.
	Interaction with time	−0.01	0.01	−0.64	.525	n.s.

Note. Fixed-effect estimates (β), standard errors (SE), t-values, and p-values from linear mixed-effects models predicting longitudinal Yale–Brown Obsessive–Compulsive Scale (Y-BOCS) scores. For each predictor, main effects and interactions with time (months since surgery) are shown. Significant results are highlighted by an asterisk (*).

sustained symptom relief in severe OCD, largely independent of comorbid psychiatric complexity or specific symptom phenotypes.

Several limitations should be acknowledged. The modest sample size limits statistical power to detect small effects, particularly for interaction terms and secondary predictors, and necessitates cautious interpretation of individual associations. Follow-up intervals varied across patients, introducing heterogeneity in symptom trajectories. In addition, the study was explicitly exploratory in nature, and multiple potential predictors were examined without formal correction for multiple comparisons. While this approach increases sensitivity to detect potentially meaningful associations in a small and rare clinical sample, it also increases the risk of false-positive findings, and results should therefore be considered hypothesis generating rather than definitive. Furthermore, this study did not explicitly model stimulation parameters, volume of activated tissue, or concurrent psychosocial interventions, all of which may contribute to outcome variability. Finally, because this study followed patients longitudinally without experimental manipulation or random assignment, the observed relationships reflect associations rather than causal effects. Future studies with larger samples, more frequent and standardized follow-up assessments, and explicit modelling of stimulation parameters and psychosocial factors will be essential to confirm these findings and clarify the mechanisms underlying individual differences in DBS response.

5. Conclusions

This study demonstrates that VC/VS-DBS is associated with both substantial first follow-up and sustained longitudinal reductions in OCD symptom severity in patients with severe, treatment-refractory illness. Among the clinical variables examined, age-related factors emerged as the most consistent correlates of outcome. Earlier age of OCD onset and younger age at implantation were associated with a faster rate of symptom improvement following DBS. In contrast, most other clinical characteristics did not show robust associations with treatment response. These results are particularly relevant because they indicate that meaningful and durable symptom improvement can be achieved across a clinically heterogeneous population. They further suggest that age-related illness characteristics may help inform expectations about the trajectory of response to DBS rather than defining strict eligibility criteria for treatment. Given the exploratory nature of the predictor analyses and the single-centre observational design with modest sample size, these findings should be interpreted with caution and replication in larger samples is warranted.

CRediT authorship contribution statement

Tatyana Branco Nunes: Writing – original draft, Writing – review & editing, Formal analysis, Data curation, Methodology, Investigation. **Liesbet Goossens:** Writing – review & editing, Supervision, Methodology. **Yasin Temel:** Resources, Investigation, Writing – review & editing. **Anne E.P. Mulders:** Investigation, Data curation, Writing – review & editing. **David E. J. Linden:** Conceptualization, Methodology, Writing – review & editing. **Ersoy Kocabiçak:** Resources, Investigation, Writing – review & editing. **Albert F.G. Leentjens:** Investigation, Writing – review & editing. **Sonja A. Kotz:** Supervision, Methodology, Writing – review & editing. **Koen R.J. Schruers:** Conceptualization, Supervision, Methodology, Writing – review & editing. **Linda Ackermans:** Conceptualization, Supervision, Methodology, Investigation, Writing – review & editing.

Ethical standards

This study analysed clinical data from patients receiving deep brain stimulation as part of routine care at Maastricht University Medical Centre+ (MUMC+). The study was observational and did not influence patient treatment or clinical decision-making. According to Dutch legislation (the Medical Research Involving Human Subjects Act, WMO), this study did not fall within the scope of the WMO and therefore did not require formal medical ethical committee approval or additional informed consent. All procedures were conducted in accordance with the principles of the Declaration of Helsinki.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors. Tatyana Branco Nunes receives partial funding through a PhD grant from the Centre for Integrative Neuroscience, Maastricht University.

Declaration of Competing Interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Given his role as Editor-in-Chief of Deep Brain Stimulation, Yasin Temel had no involvement in the peer review of this article and had no access to information regarding its peer review. Full responsibility for the editorial process for this article was delegated to another journal editor.

Given his role as Associate Editor of Deep Brain Stimulation, Ersoy Kocabiçak had no involvement in the peer review of this article and had no access to information regarding its peer review. Full responsibility for the editorial process for this article was delegated to another journal editor.

Given her role as Editorial Board Member of Deep Brain Stimulation, Linda Ackermans had no involvement in the peer review of this article and had no access to information regarding its peer review. Full responsibility for the editorial process for this article was delegated to another journal editor.

Given his role as Editorial Board Member of Deep Brain Stimulation, Albert F.G. Leentjens had no involvement in the peer review of this article and had no access to information regarding its peer review. Full responsibility for the editorial process for this article was delegated to another journal editor. If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements

The authors thank A. Bonekamp-Tilmans, S. Verkaart and N. Bongaerts for their essential support with data acquisition and organization. We are grateful to W. Viechtbauer for his advice and assistance with the statistical analyses.

Appendix A

Table A.1
Number of patients on medication and psychotherapy at baseline and last follow-up

	At baseline	At last follow-up
Treatment	**N**	**N**
On medication	14	14
On psychotherapy	0	3
Not on treatment	2	3
Not reported	7	1
Type of medication		
Clomipramine	7	7
Quetiapine	5	5
Fluoxetine / Fluvoxamine / Escitalopram	4	4
Venlafaxine	2	1
Aripiprazole	1	0
Type of psychotherapy		
Exposure and Response Prevention	0	3
Acceptance and commitment therapy	0	1
Schematherapy	0	1

Table A.2
Time in months between measurements

Comparison	Mean	Std	Min	Max
T0-T1	22.20	21.77	5.75	99.59
T1-T2	19.15	17.64	2.73	51.33
T2-T3	38.65	15.40	14.37	54.76
T3-T4	5.97	8.44	0	11.93
T4-T5	11.13	1.13	10.33	11.93
First-Last	45.99	31.42	6.49	99.59

Note. First-Last row represents the time difference in months between the baseline and last available measurement.

References

[1] National Institute of Mental Health, Obsessive–compulsive disorder. ⟨https://www.nimh.nih.gov/health/topics/obsessive-compulsive-disorder-ocd⟩, 2022 (accessed 10 January 2026).
[2] Ruscio AM, Stein DJ, Chiu WT, Kessler RC. The epidemiology of obsessive–compulsive disorder in the national comorbidity survey replication. Mol Psychiatry 2010;15:53–63. https://doi.org/10.1038/mp.2008.94.
[3] Hirschtritt ME, Bloch MH, Mathews CA. Obsessive–compulsive disorder: advances in diagnosis and treatment. JAMA 2017;317:1358–67. https://doi.org/10.1001/jama.2017.2200.
[4] Greenberg BD, Gabriels LA, Malone Jr DA, Rezai AR, Friehs GM, Okun MS, et al. Deep brain stimulation of the ventral internal capsule/ventral striatum for obsessive–compulsive disorder: worldwide experience. Mol Psychiatry 2010;15:64–79. https://doi.org/10.1038/mp.2008.55.
[5] Goulas A, Mavridis I. Bed nucleus of the stria terminalis deep brain stimulation in treatment-refractory obsessive–compulsive disorder: a systematic review. Eur Arch Psychiatry Clin Neurosci 2025:1–12. https://doi.org/10.1007/s00406-025-02156-z.
[6] Raviv N, Staudt MD, Rock AK, MacDonell J, Slyer J, Pilitsis JG. A systematic review of deep brain stimulation targets for obsessive compulsive disorder. Neurosurgery 2020;87:1098–110. https://doi.org/10.1093/neuros/nyaa249.
[7] Chabardès S, Polosan M, Krack P, Bastin J, Krainik A, David O, et al. Deep brain stimulation for obsessive-compulsive disorder: subthalamic nucleus target. World Neurosurg 2013;80:S31.e1–8. https://doi.org/10.1016/j.wneu.2012.03.010.
[8] Denys D, Mantione M, Figee M, van den Munckhof P, Koerselman F, Westenberg HG, et al. Deep brain stimulation of the nucleus accumbens for

treatment-refractory obsessive–compulsive disorder. Arch Gen Psychiatry 2010;67:1061–8. https://doi.org/10.1001/archgenpsychiatry.2010.122.
[9] Mallet L, Polosan M, Jaafari N, Baup N, Welter ML, Fontaine D, et al. STOC study group, subthalamic nucleus stimulation in severe obsessive–compulsive disorder. N Engl J Med 2008;359:2121–34. https://doi.org/10.1016/j.brs.2019.04.004.
[10] Goodman WK, Foote KD, Greenberg BD, Ricciuti N, Bauer R, Ward H, et al. Deep brain stimulation for intractable obsessive–compulsive disorder: pilot study using a blinded, staggered-onset design. Biol Psychiatry 2010;67:535–42. https://doi.org/10.1016/j.biopsych.2009.11.028.
[11] van Westen M, Rietveld E, Figee M, Denys D. Deep brain stimulation for obsessive–compulsive disorder: a systematic review and meta-analysis. Curr Behav Neurosci Rep 2015;2:146–61. https://doi.org/10.1007/s40473-015-0036-3.
[12] Schruers K, Baldi S, van den Heuvel T, Goossens L, Luyten L, Leentjens AF, et al. The effects of deep-brain non-stimulation in severe obsessive–compulsive disorder: an individual patient data meta-analysis. Transl Psychiatry 2019;9:183. https://doi.org/10.1038/s41398-019-0522-6.
[13] Ooms P, Mantione M, Figee M, Schuurman PR, van den Munckhof P, Denys D. Deep brain stimulation for obsessive–compulsive disorder: effects on quality of life. J Neurol Neurosurg Psychiatry 2014;85:1200–5. https://doi.org/10.1136/jnnp-2012-302550.
[14] Visser-Vandewalle V, Andrade P, Mosley PE, Greenberg BD, Schuurman R, McLaughlin NC, et al. Deep brain stimulation for obsessive–compulsive disorder: a crisis of access. Nat Med 2022;28:1529–32. https://doi.org/10.1038/s41591-022-01879-z.
[15] Nuttin BJ, Gabriëls LA, Cosyns PR, Meyerson BA, Andréewitch S, Sunaert SG, et al. Long-term electrical capsular stimulation in patients with obsessive–compulsive disorder. Neurosurgery 2008;62:SHC966–77. https://doi.org/10.1227/01.NEU.0000333764.20575.D6.
[16] American Psychiatric Association. Diagnostic and statistical manual of mental disorders. Fifth ed. Washington, DC: American Psychiatric Publishing; 2013. https://doi.org/10.1176/appi.books.9780890425596.
[17] Ackermans L, Kuhn J, Neuner I, Temel Y, Visser-Vandewalle V. Surgery for Tourette syndrome. World Neurosurg 2013;80:S29.e15–20. https://doi.org/10.1016/j.wneu.2012.06.017.
[18] Kocabicak E, Temel Y. Deep brain stimulation of the subthalamic nucleus in Parkinson's disease: Surgical technique, tips, tricks and complications. Clin Neurol Neurosurg 2013;115:2318–23. https://doi.org/10.1016/j.clineuro.2013.08.020.
[19] F.L.W.V.J. Schaper Y, Zhao MLF, Janssen GL, Wagner AJ, Colon DMW, Hilkman E, et al. Single-cell recordings to target the anterior nucleus of the thalamus in deep brain stimulation for patients with refractory epilepsy. Int J Neural Syst 2019;29:1850012. https://doi.org/10.1142/S0129065718500120.
[20] van der Vlis TAMBouwens, Ackermans L, Mulders AEP, Vrij CA, Schruers K, Temel Y, et al. Ventral capsule/ventral striatum stimulation in obsessive-compulsive disorder: toward a unified connectomic target for deep brain stimulation? Neuromodulation 2021;24:316–23. https://doi.org/10.1111/ner.13339.
[21] Montgomery SA, Åsberg M. A new depression scale designed to be sensitive to change. Br J Psychiatry 1979;134:382–9. https://doi.org/10.1192/bjp.134.4.382.
[22] Spielberger CD, Gorsuch RL, Lushene R, Vagg PR, Jacobs GA. Manual for the State-Trait Anxiety Inventory. Palo Alto, CA: Consulting Psychologists Press; 1983.
[23] Van Oppen P. Obsessions and compulsions: dimensional structure, reliability, convergent and divergent validity of the Padua Inventory. Behav Res Ther 1992;30:631–7. https://doi.org/10.1016/0005-7967(92)90008-5.
[24] Shapiro SS, Wilk MB. An analysis of variance test for normality (complete samples). Biometrika 1965;52:591–611. https://doi.org/10.1093/biomet/52.3-4.591.
[25] Nakagawa S, Schielzeth H. A general and simple method for obtaining R^2 from generalized linear mixed-effects models. Methods Ecol Evol 2013;4:133–42. https://doi.org/10.1111/j.2041-210x.2012.00261.x.
[26] Baldi S, Vandenberk E, Bors J, Goossens L, de Cort K, Ackermans L, et al. Deep brain stimulation-related experiences for obsessive–compulsive disorder: In-depth interviews with operated patients and relatives. Deep Brain Stimul 2024;4:1–8.
[27] Alonso P, Cuadras D, Gabriëls L, Denys D, Goodman W, Greenberg BD, et al. Deep brain stimulation for obsessive–compulsive disorder: a meta-analysis of treatment outcome and predictors of response. PLoS One 2015;10:e0133591. https://doi.org/10.1371/journal.pone.0133591.
[28] Graat I, Mocking RJT, de Koning P, Vulink N, Figee M, van den Munckhof P, et al. Predicting response to vALIC deep brain stimulation for refractory obsessive–compulsive disorder. J Clin Psychiatry 2021;82:37759.
[29] Raymaekers S, Vansteelandt K, Luyten L, Bervoets C, Demyttenaere K, Gabriëls L, et al. Long-term electrical stimulation of the bed nucleus of the stria terminalis for obsessive–compulsive disorder. Mol Psychiatry 2017;22:931–4. https://doi.org/10.1038/mp.2016.124.