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Long-term cognitive effects after SCG-DBS in patients with treatment resistant depression: A 5-year follow-up

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ABSTRACT

Introduction: Cognitive symptoms represent a significant and persistent challenge in patients with treatment-resistant depression (TRD), substantially impacting their functional outcomes. Deep brain stimulation (DBS) targeting the subcallosal cingulate gyrus (SCG) has shown clinical efficacy. Nonetheless, its long-term effects on cognition remains insufficiently researched. This study systematically evaluates cognitive outcomes following SCG-DBS over an extended follow-up period.

Methods: This retrospective, exploratory secondary analysis used longitudinal data from 12 TRD patients treated with SCG-DBS without a control group. Cognitive and clinical assessments were conducted pre-surgery and at long-term follow-up. Potential changes were examined using the Wilcoxon signed-rank test and its corresponding effect size (r), while Reliable Change Indices (RCIs) were applied to evaluate the statistical reliability of intra-subject cognitive changes. Spearman correlations explored associations between cognitive outcomes with clinical and functional ones.

Results: After a median follow-up of 5 years following SCG-DBS, TRD patients showed statistically significant improvements in immediate and delayed verbal memory (Wilcoxon's $z = -2.28$, $p = .023$, $r = 0.66$; Wilcoxon's $z = -2.83$, $p = .005$, $r = 0.82$, respectively), both reflecting large effect sizes. RCIs indicated reliable improvement in immediate (41.7% of patients) and in delayed (75%) verbal memory. Changes in verbal memory were not significantly correlated with clinical or functional improvements.

Conclusions: These findings support the cognitive safety and benefits of SCG-DBS in individuals with TRD, particularly in verbal memory. However, further research is required to investigate the broader functional effects of SCG-DBS beyond the improvement of core clinical symptoms.

1. Introduction

Treatment-resistant depression (TRD) affects approximately one-third of individuals diagnosed with major depressive disorder (MDD), and is characterized by the persistence of depressive symptoms despite adequate trials of at least two distinct antidepressant treatments (Gaynes et al., 2020). A defining aspect of TRD is cognitive impairment, which includes difficulties in attention, processing speed, memory and executive functioning (Gregory et al., 2020). These cognitive symptoms, commonly observed in depressed patients, are often more pronounced in

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TRD (López-Solà et al., 2020; Semkovska et al., 2019; Serra-Blasco et al., 2015), potentially due to a harsher course of the disease and greater disruption of neural networks related to mood and cognitive processes (De Diego-Adeliño et al., 2014; Serra-Blasco et al., 2016).

Deep brain stimulation (DBS) has emerged as a promising neuromodulation therapy for the most refractory forms of TRD, with evidence of efficacy reported in observational studies and supported by meta-analyses of the limited available double-blind controlled trials (Berlim et al., 2014; Kisely et al., 2018). While both short-term and long-term DBS have shown effectiveness in reducing depressive symptoms (Alemany et al., 2023; Himes et al., 2025; Kisely et al., 2018), its impact on cognitive function remains less well studied. For example, Malone et al. (2009) reported no cognitive improvements following ventral striatum DBS (Malone et al., 2009). Grubert et al. (2011), however, documented significant enhancements in attention, memory, executive function, and visual perception following nucleus accumbens DBS, without evidence of cognitive side effects (Grubert et al., 2011). Further evidence suggests that stimulation of the ventral anterior limb of the internal capsule can lead to gradual improvements in delayed verbal recall, visuospatial memory, planning, and object naming over time (Bergfeld et al., 2017). Overall, the majority of studies indicate that DBS does not impair cognitive functioning, and in some cases, may yield improvements that appear independent of mood changes (Kubu et al., 2016; McNeely et al., 2008). More recently, a systematic review and meta-analysis showed no substantial cognitive changes during the first six months following DBS at different targets, but has suggested that improvements in memory, attention, and executive function can emerge after 6–18 months, raising questions about DBS's long-term cognitive impact beyond 18 months (Runia et al., 2023).

The subcallosal cingulate gyrus (SCG) has been a key DBS target for TRD (Lozano et al., 2008), as it modulates both cognitive and emotional network activity. Short-term follow-up studies of SCG-DBS (McNeely et al., 2008; Moreines et al., 2014), including our own findings (Serra-Blasco et al., 2015), consistently show no cognitive decline—and in some cases, improvements—in domains such as verbal learning, memory, processing speed, and executive function. However, evidence on cognitive outcomes beyond the first year remains extremely scarce. One study by Bogod et al. (2014) has tracked four patients for up to an average of 42 months after SCG-DBS surgery revealing cognitive stability and, at certain follow-up time points, improvements in general intellectual ability and in overall memory performance (Bogod et al., 2014). Given the scarcity of such extended follow-up analyses, further research is warranted to fully characterize the neuropsychological effects of chronic DBS.

The aim of this study is, therefore, to describe and analyse the long-term cognitive effects after SCG-DBS surgery in patients with TRD.

2. Methods

2.1. Participants

Participants were selected from a cohort of patients with severe treatment-resistant depression treated with SCG-DBS at the Treatment-Resistant Disorders Unit of the Psychiatry Service at Hospital de la Sant Creu i Sant Pau (Aibar-Durán et al., 2022; Alemany et al., 2023; Martín-Blanco et al., 2015; Puigdemont et al., 2015; Puigdemont et al., 2012). This broader cohort included patients enrolled in a clinical trial (NCT01268137, clinical. trials.gov) and others treated under a compassionate use program approved by the hospital's Medical Committee. All procedures received approval from the Hospital de la Santa Creu i Sant Pau Ethics Committee (EC/06/180/2498), and all participants provided written informed consent. It was conducted in full compliance with current data protection laws, adhered strictly to the ethical guidelines outlined in the Declaration of Helsinki, and followed the principles of Good Clinical Practice.

From this cohort, only patients who had completed a long-term cognitive follow-up, defined as at least 24 months after surgery, were included in the present secondary analysis. A total of 12 patients met this criterion: 9 had participated in the clinical trial, and three had undergone DBS under compassionate use. Five patients from the original cohort were not included in the present study because of loss to follow-up ($n = 2$), death by suicide during follow-up ($n = 1$), or discontinuation of DBS due to insufficient clinical benefit (n = 2). The implantation period ranged from January 2008 to June 2019, with follow-up assessments extending through 2023.

All included patients had a diagnosis of severe treatment-resistant depression (MDD, BD type I or II, based on DSM-IV-TR or DSM-5-TR criteria from 2014). Detailed clinical characteristics of the patients are described elsewhere, which include the inclusion and exclusion criteria to be eligible for DBS intervention (Puigdemont et al., 2012). Antidepressant regimens remained unchanged during the month preceding inclusion and at baseline neuropsychological evaluation, while these could be adjusted after the end of the clinical trial or after DBS intervention (for those under compassionate programme) upon clinical criterion and throughout the follow-up.

2.2. Deep Brain Stimulation procedures

The DBS surgery was performed under local anesthesia without intraoperative microrecording. All patients underwent bilateral implantation of two quadripolar leads (model 3387S-28/40 with stimloc, Medtronic, Inc.) into the SCG, which were connected to a non-rechargeable impulse generator (IPG, model Activa PC, Medtronic Inc., Minneapolis, MN, USA). The IPG was placed in the abdominal subcutaneous tissue under general anesthesia. IPG replacements were scheduled as needed when battery depletion approached.

SCG-DBS stimulation was initiated 48 h post-surgery. Voltage was gradually increased if a therapeutic response was not achieved (see below for response criteria). During the first five days after surgery, stimulation parameters (voltage, frequency, and pulse width) were adjusted before initiating chronic stimulation. The patients received continuous monopolar stimulation (3.6 V, 135 Hz, 90 ms) using the most ventral electrode contacts. Adjustments to maximize therapeutic effects followed this sequence: 1) increase voltage up to 5 V; 2) increase pulse width up to 240 ms; 3) alter active contacts while maintaining the initial voltage and pulse width; 4) switch to bipolar stimulation. In the last assessment, 9 patients ultimately received bipolar stimulation, while the last three patients were treated with monopolar stimulation, guided by preoperative tractography. Details of the methodology are described elsewhere (Aibar-Durán et al., 2022).

2.3. Study design

A comprehensive assessment was performed one week prior to DBS implantation and subsequently at regular intervals after stimulation onset, covering sociodemographic, clinical, cognitive, and functional domains. Neuropsychological assessments were conducted by neuropsychological raters who were not involved in the clinical management of the participants and were blinded to clinical response status. For the purposes of this study, only the baseline and the most long-term follow-up evaluation were considered.

2.3.1. Sociodemographic, clinical and functional assessment

Sociodemographic and clinical data were gathered on age, sex at birth, years of schooling, estimated intelligence quotient (IQ), age at illness onset, number of previous depressive episodes, length of the current depressive episode at the time of surgery, presence of melancholic features, and response to ECT prior to DBS surgery. The IQ was estimated at baseline using the Vocabulary from the Spanish version of the Wechsler Adult Intelligence Scale-IV (WAIS-IV) (Wechsler, 2008). Baseline antidepressant medication trials were quantified using the Antidepressant Treatment History Form (ATHF) (Sackeim et al., 2019).

Depressive symptomatology was assessed using the HDRS-17 (Bobes et al., 2003; Hamilton, 1960) and symptom severity was measured using the Clinical Global Impression - Severity (CGI—S) scale (Busner and Targum, 2007). Psychosocial functioning was also assessed twice via the Global Assessment of Functioning (GAF) scale that considers psychological, social and occupational functioning (Aas, 2011; Aas, 2010).

2.3.2. Neuropsychological assessment

Cognitive functioning was assessed by means of a battery of neuropsychological tests including the following standardized tests: Block design subtest (WAIS-IV) (Wechsler, 2008), Digit Span Forward and Backward (WAIS-IV) (Wechsler, 2008), Rey Auditory Verbal Learning Test (RAVLT) (Rey, 1941), Digit Symbol Substitution Test (WAIS-IV) (Wechsler, 2008), Trail Making Test Part A (TMT-A) and Trail Making Test Part B (TMT—B) (Reitan, 1992; Tombaugh, 2004), Category fluency and phonemic verbal fluency (FAS) (Casals-Coll et al., 2013; Peña-Casanova et al., 2009). To minimize practice effects at follow-up, parallel forms of cognitive tests were administered whenever available.

2.4. Statistical analysis

A descriptive analysis of sociodemographic, clinical, and functional measures was performed using mean (standard deviation) statistics for continuous variables, and absolute (frequency) measures for categorical variables. All participants' neuropsychological tests scores were converted into T-scores using age- and sex-matched normative data. Standard statistical tests were applied to calculate and interpret the potential group variables changes following DBS. Given the limited sample size, changes in cognitive, clinical, and functional variables between pre-surgery and follow-up in TRD patients were assessed using the paired samples Wilcoxon signed-rank test. Effect size of the pre-follow-up difference was also calculated to quantify the magnitude of the observed changes.

To further investigate individual cognitive changes, the reliable change index (RCI) (Jacobson and Truax, 1991) was computed for every cognitive measure for each patient, using the method proposed by Iverson (2001) in order to account for potential practice effects inherent to the neuropsychological tests (Duff, 2012). Reference values and test-retest reliability coefficients were taken from a sample of healthy controls. None had history of psychiatric disorders and fulfilled the inclusion criteria referring to lack of current medical conditions (Sala-Vila et al., 2020). A two-tailed 90% confidence interval was used to define reliable change, a change larger than that reasonability expected due to measurement error alone. Scores exceeding ±1.645 z-scores (calculated from raw subtests scores) were considered indicative of reliable improvement or decline, respectively, while scores within ±1.645 were classified as stable. Accordingly, the RCI permits the identification of statistically reliable decline, stability, or improvement in each patient's cognitive performance from pre-surgery to follow-up. In addition, among participants classified as showing reliable improvement, follow-up performance was descriptively examined to determine whether scores fell within the normative range (T-scores = 40–60). Lastly, Spearman correlation analyses were run to evaluate associations of significant cognitive changes with clinical and functional changes along time, as well as follow-up duration. Statistical analyses were performed using the Statistical Package for Social Sciences (SPSS, IL, Chicago, version 29), with statistical significance was set at $p < .05$.

Table 1
Mean scores (standard deviation) for sociodemographic, clinical, cognitive and functional baseline characteristics at pre-DBS surgery.

	TRD ($n = 12$)
Age, *years*	46.08 (8.98)
Sex, n *female (%)*	10 (83.3)
Years of schooling, *n*	13.67 (4.31)
Estimated IQ, *T-score*	54.25 (5.08)
Age at illness onset, *years*	22.0 (4.13)
Depressive episodes, *n*	5.17 (3.38)
Length current episode, *months*	53.08 (53.44)
Presence of melancholia, *n (%)*	8 (66.7%)
Response to ECT pre-DBS, *n (%)*	7 (58.3)
ATHF at pre-DBS, *n*	9.25 (2.53)
HDRS-17, *total score*	21.33 (3.53)
CGI Severity, *total score*	5.67 (0.78)
GAF, *total score*	43.08 (6.57)

TRD: Treatment-Resistant Depression, IQ: Intelligence Quotient, ECT: Electroconvulsive Therapy, ATHF: Antidepressant Treatment History Form, HDRS-17: 17-item Hamilton Depression Rating Scale, CGI: Clinical Global Impression, GAF: Global Assessment of functioning.

3. Results

3.1. Sample characteristics

The mean follow-up period was approximately five years (mean = 56.75 months, SD = 27.56; range = 29–117 months) after the initiation of chronic stimulation, with a total of 12 patients included in the analysis. Table 1 presents the baseline sociodemographic, clinical, and functional characteristics of the whole sample. TRD participants had estimated intelligence scores within the normal range. As clinically expected, patients exhibited moderate to severe symptoms on the HDRS-17 scale, and average CGI scores classifying them as markedly to severely ill. Besides, these patients showed significant severe functional impairment at pre-surgery assessment.

Table 2
Cognitive, clinical and functional characteristics at pre-DBS surgery and at follow-up.

	TRD participants (n = 12)		*Wilcoxon signed-rank test*		
	PRE-DBS	FOLLOW-UP	z-value	*p-value*	*r*
Block design subtest (WAIS-IV), *T-score*	45.17 (8.0)	43.91 (12.19)	−0.985	0.325	0.28
Category fluency, *T-score*	40.58 (6.74)	43.92 (11.19)	−1.16	0.248	0.33
Digit Span Forward (WAIS-IV), *T-score*	43.08 (7.19)	41.0 (7.63)	−1.02	0.309	0.29
Digit Span Backward (WAIS-IV), *T-score*	33.75 (11.09)	38.58 (8.43)	−1.47	0.140	0.42
RAVLT immediate recall, *T-score*	37.33 (8.23)	43.17 (9.9)	−2.28	0.023	0.66
RAVLT delayed recall, *T-score*	34.58 (11.41)	46.17 (9.2)	−2.83	0.005	0.82
Digit Symbol Substitution Test (WAIS-IV), *T-score*	47.33 (8.6)	48.42 (9.22)	−0.356	0.722	0.10
Trail Making Test Part A, *T-score*	28.08 (10.48)	32.83 (14.47)	−1.42	0.154	0.41
Trail Making Test Part B, *T-score*	37.82 (15.41)	31.67 (14.25)	−1.25	0.212	0.36
Phonemic verbal fluency (FAS), *T-score*	37.25 (8.96)	36.92 (9.95)	−0.236	0.814	0.07
HDRS-17, *total score*	21.33 (3.53)	4.0 (2.95)	−3.09	0.002	0.89
CGI Severity, *total score*	5.67 (0.78)	2.58 (0.79)	−3.13	0.002	0.90
GAF, *total score*	43.08 (6.57)	66.67 (9.13)	−3.07	0.002	0.89

TRD: Treatment-Resistant Depression, WAIS-IV: Wechsler Adult Intelligence Scale version-IV, RAVLT: Rey Auditory Verbal Learning Test, DSST: Digit Symbol Substitution Test, HDRS-17: 17-item Hamilton Depression Rating Scale, CGI: Clinical Global Impression, GAF: Global Assessment of functioning. r: effect size.

Table 3
Reliable Change Index (RCI) follow-up – pre-DBS for each participant.

	TRD participants												Change status *n (%)*		
	1	2	3	4	5	6	7	8	9	10	11	12	DECLINED (−)	STABILITY ()	IMPROVED (+)
Block design subtest (WAIS-IV), *T-score*						−							1 (8.3)	11 (91.7)	0 (0)
Category fluency, *T-score*													0 (0)	12 (100)	0 (0)
Digit Span Forward (WAIS-IV), *T-score*													0 (0)	12 (100)	0 (0)
Digit Span Backward (WAIS-IV), *T-score*									+				0 (0)	11 (91.7)	1 (8.3)
RAVLT immediate recall, *T-score*			+	+	+	+			+				0 (0)	7 (58.3)	5 (41.7)
RAVLT delayed recall, *T-score*	+		+	+		+	+	+	+	+	+		0 (0)	3 (25)	9 (75)
DSST (WAIS-IV), *T-score*	−			+					+				1 (8.3)	9 (75)	2 (16.7)
Trail Making Test - Part A, *T-score*		−					−						2 (16.7)	10 (83.3)	0 (0)
Trail Making Test - Part B, *T-score*	−			+			−	−		−			4 (33.4)	7 (58.3)	1 (8.3)
Phonemic verbal fluency (FAS), *T-score*	−			+	+			−					2 (16.7)	8 (66.6)	2 (16.7)

WAIS-IV: Wechsler Adult Intelligence Scale version-IV, RAVLT: Rey Auditory Verbal Learning Test, DSST: Digit Symbol Substitution Test. +: RCI > 1.645, improvement larger than the reasonably expected to measurement error or retest effect. −: RCI < 1.645, decline larger than the reasonably expected to measurement error or retest effect.

3.2. Cognitive changes from pre-surgery to follow-up

Table 2 presents the mean scores (standard deviations) of the neuropsychological tests at pre-surgery and at follow-up. TRD patients showed statistically significant improvements in immediate (Wilcoxon's $z = -2.28$, $p = .023$) and delayed verbal memory (Wilcoxon's $z = -2.83$, $p = .005$), with progress ranging from half to one standard deviation. Most of the other neuropsychological tests showed certain improvement at follow-up, but did not reach statistical significance. The only exception was the TMT-B test for cognitive flexibility, where scores showed a slight but not statistically significant decline. Despite these subtle changes, overall cognitive performance remained at the lower limit of normality, with persistent impairments observed in Digit Span Backward, TMT-A, TMT-B and FAS, where scores continued to fall below normative thresholds at follow-up assessment.

The observed changes in immediate and delayed verbal memory were associated to large effect sizes ($r = 0.66$; $r = 0.82$, respectively), suggesting gains in verbal learning and memory performance at long-term follow-up. Although no significant differences were observed in Category fluency, Digit Span Backward, Trail Making Test Part A and Part B ($p > .05$), effect sizes were moderate (range of $r = 0.33$–0.42), suggesting a trend toward improvement or decline that could be clinically meaningful.

Table 3 summarizes the RCI analysis results, indicating that no participant experienced a reliable decline on more than three of the ten cognitive measures. Nearly all patients showed reliable improvement on at least one cognitive measure. Specifically, a substantial proportion of patients demonstrated reliable improvement in verbal memory, with 41.7% improving in immediate recall and 75% in delayed recall. For cognitive flexibility, 33.4% of TRD patients showed a reliable decline. The rest of the neuropsychological measures remained largely stable over time in the vast majority of cases.

Among participants showing reliable improvement according to the RCI, the majority achieved performance within the normative range (T-scores = 40–60) at follow-up. Specifically, normative performance was observed in 1/1 (100%) participant for Digit Span Forward, 4/5 (80%) for immediate verbal memory, 7/9 (77.8%) for delayed verbal memory, 2/2 (100%) for the Digit Symbol Substitution Test, 1/1 (100%) for Trail Making Test Part B, and 2/2 (100%) for Phonemic verbal fluency.

3.3. Relation of verbal memory change with clinical and functional changes

Clinical and functional variables between pre-surgery and follow-up in TRD patients are displayed in Table 2. A paired samples Wilcoxon signed-rank test revealed a statistically significant improvement in depressive symptomatology (Wilcoxon's $z = -3.09$, $p = .002$), reflecting a large effect size ($r = 0.89$) and indicating a reduction of symptom severity from a moderate-to-severe to an almost complete absence of depressive symptoms. Severity scores on the CGI-S scale also showed a statistically significant reduction in the severity of the symptoms, reflecting a state of mildly ill or borderline mentally ill at follow-up (Wilcoxon's $z = -3.13$, $p = .002$, $r = 0.90$). A statistically significant improvement in psychosocial functioning was also observed (Wilcoxon's $z = -3.07$, $p = .002$, $r = 0.89$), progressing toward a mild-to-moderate level of impairment.

No statistically significant correlations were observed between changes in immediate and delayed verbal memory and changes in HDRS-17, CGI, and GAF were not statistically significant (immediate memory: Spearman's $\rho = 0.139$, $p = .67$; Spearman's $\rho = 0.293$, $p = .36$; Spearman's $\rho = -0.125$, $p = .70$; delayed memory: Spearman's $\rho = 0.349$, $p = .27$; Spearman's $\rho = 0.228$, $p = .48$; Spearman's $\rho = -0.458$, $p = .13$, respectively). Likewise, no significant associations were found between follow-up duration and changes in immediate (Spearman's $\rho = -0.011$, $p = .97$) or delayed verbal memory performance (Spearman's $\rho = 0.203$, $p = .53$).

4. Discussion

The present analysis provides support the long-term cognitive safety of SCG-DBS surgery in TRD. Notably, it shows statistically significant improvements and reliable individual gains in immediate and delayed verbal memory performance even after five years of chronic stimulation. Furthermore, the findings provide preliminary evidence that SCG-DBS is not associated with cognitive decline over the course of long-term stimulation. Indeed, most cognitive test scores showed a trend toward improvement, though not reaching statistical significance. Importantly, despite the lack of correlation between cognitive gains and clinical symptom changes, these improvements are accompanied by functional benefits, with daily functional difficulties diminishing to mild or moderate levels. Consequently, SCG-DBS not only alleviates depressive symptoms in TRD, as thoroughly documented in a previous systematic review and meta-analysis (Kisely et al., 2018), but is also associated with improvements in cognitive function and overall daily functioning, which underscores the long-term therapeutic benefit.

By extending the observation period, the present study substantially advances current understanding of DBS-related cognitive outcomes. Previous evidence has typically shown modest improvements over shorter follow-ups (6–18 months), mainly in verbal memory, particularly in delayed recall; visual memory, mainly in immediate recall; and executive function, especially in planning (Runia et al., 2023). As stated by these authors, the scarce evidence to date provides limited insight into the DBS effects on cognitive functioning beyond 18 months (Runia et al., 2023). Moreover, the few studies that have explored these effects

are based on very limited sample sizes; the longest follow-up reported to date included a description of four patients (Bogod et al., 2014).

Within this context, the current findings extend previous evidence by documenting outcomes over an average of five years, representing the longest follow-up reported to date. The most remarkable result was the improvement observed in verbal memory, both immediate and delayed recall. These enhancements were not only statistically significant but also associated with large effect sizes, indicating a meaningful gain that persisted after long-term continuous stimulation. Reliable change analysis confirmed that nearly all patients experienced individual-level improvement, with more than half showing reliable gains in immediate recall and three-quarters in delayed recall. These results replicate and extend previous short-term findings in a subsample of patients after one-year of DBS intervention (Serra-Blasco et al., 2015), suggesting that SCG-DBS may exert long-lasting facilitatory effects on verbal learning and consolidation processes. Beyond these domain-specific effects, most other cognitive functions remained stable or trended toward improvement, with no evidence of global cognitive decline, reinforcing the long-term cognitive safety of SCG-DBS in TRD. Nevertheless, given the exploratory nature of the study, the limited sample size, and the number of cognitive outcomes assessed, these findings should be interpreted cautiously and warrant replication in larger cohorts before definitive conclusions can be drawn.

The observed enhancement in verbal memory following SCG stimulation in TRD may involve modulation of frontolimbic circuits. SCG-DBS has been shown to normalize subgenual cingulate hyperactivity and restore functional connectivity with key cortical and subcortical regions involved in memory processing, particularly, the dorsolateral prefrontal cortex and the hippocampus (Alagapan et al., 2023; Johansen-Berg et al., 2008; Lozano et al., 2008; Riva-Posse et al., 2014). These network-level changes may support more efficient encoding and retrieval mechanisms, providing a plausible explanation for the sustained verbal memory improvements observed at long-term follow-up. Importantly, memory circuits—especially hippocampal–prefrontal networks—are highly vulnerable to chronic stress, a hallmark of TRD, which likely contributes to the frequent memory impairments seen in this population (López-Solà et al., 2020). Nonetheless, these circuits retain a considerable capacity for neuroplastic adaptation (Price and Duman, 2020). Within this framework, the observed memory improvements may be consistent with the restoration of frontolimbic network functioning and the recruitment of adaptive neuroplastic processes. However, the mechanistic underlying these cognitive changes remain speculative and warrant further investigation.

A primary methodological challenge in longitudinal cognitive research involves distinguishing genuine cognitive improvement from potential learning effects associated with repeated cognitive testing (Duff, 2012). In this study the extended follow-up helped mitigate these effects by allowing sufficient time between evaluations to minimize test-related interference. Additionally, parallel versions of cognitive assessments were employed to further reduce the likelihood of practice effects, ensuring a more accurate measurement of cognitive changes over time. Importantly, the application of the RCI provided a further step in ensuring methodological robustness, enabling the differentiation of true cognitive change from variations due to measurement error or retest effects. This approach supported the identification of reliable individual improvements, enhancing confidence in the clinical significance of the long-term cognitive effects of SCG-DBS.

One of the key considerations regarding the observed cognitive improvements is whether these changes are merely a secondary effect of improvements in depressive symptoms. In the present study, no association was observed between clinical improvement and delayed verbal memory enhancement. Although this finding should be interpreted cautiously, the results are consistent with the possibility that affective and cognitive outcomes may follow partially distinct trajectories after DBS (Bora et al., 2013; Rock et al., 2014). The neurocognitive consequences of long-standing illness burden and cumulative treatment resistance (López-Solà et al., 2020) may be more challenging to restore with DBS, even when substantial improvements occur in other dimensions of depression.

It should be noted that DBS was not originally conceived with the primary aim of cognitive enhancement, but rather to induce more general clinical and functional improvements in patients—objectives that were satisfactorily achieved in the present study. At the individual level, however, reliable decline was most frequently observed in cognitive flexibility, with one-third of participants showing deterioration over time. This finding suggests that certain aspects of executive functioning may remain vulnerable despite chronic stimulation and the overall pattern of cognitive stability observed at the group level. These observations highlight the potential value of combining DBS with adjunctive pharmacological and non-pharmacological procognitive interventions, to promote further gains in cognitive performance. Integrating clinical, cognitive, and functional targets within treatment protocols may provide a more comprehensive therapeutic approach and optimize overall patient outcomes. Further rigorous investigation is warranted to elucidate the specific cognitive contributions of these combined interventions and to determine the most effective strategies for addressing residual cognitive deficits in treatment-resistant depression.

Although the main strength of this study relies in the long-term follow-up of cognitive functioning in patients treated with DBS, the relatively small sample size imposes some limitations, particularly regarding the generalizability of the findings. Nevertheless, the continuation of this therapeutic strategy under compassionate use is expected to support the collection of additional long-term data in the near future. This is a secondary exploratory analysis of existing data. Consequently, the findings should be interpreted within the context of the study design and warrant confirmation in larger samples. However, the use of legacy data collected across both clinical trials and compassionate interventions provides a valuable opportunity to examine additional domains of interest, such as cognitive functioning. An additional limitation is the absence of intermediate neuropsychological assessments between baseline and the long-term follow-up evaluation. As a result, the temporal trajectory of the observed cognitive changes cannot be determined. Although the improvements observed at long-term follow-up are compatible with sustained cognitive benefits during chronic DBS treatment, it remains unclear whether these changes emerged gradually over time, occurred early after treatment initiation and were subsequently maintained, or reached a plateau after an initial period of improvement. Future prospective studies incorporating repeated cognitive assessments across the course of treatment will be necessary to characterize the timing, progression, and durability of cognitive outcomes associated with DBS. Although medication use and medication load at baseline and follow-up are provided, detailed longitudinal treatment exposure data were not systematically collected. Therefore, the potential influence of concomitant treatments on cognitive outcomes cannot be fully excluded, although no participant received any structured cognitive remediation during follow-up. Caution is warranted when interpreting these findings, as the requirement for long-term cognitive follow-up may have introduced a degree of survivorship bias. Patients who discontinued follow-up prematurely —whether due to complications or personal choice, or other clinical circumstances—may differ from those who continued long-term cognitive assessments. In the same venue, given the small sample size and observational design, no formal methods to control for other bias were applied such as initial selection bias (patients eligible for DBS), measurement bias (clinical rating scales), and the consequent limited generalizability. Importantly, all patients with more than two years of follow-up and available cognitive data were included, regardless of their treatment response. Despite these limitations, the scarcity of long-term cognitive outcome data in DBS, combined with the consistency of the present observations with those reported in studies with shorter follow-up periods, the present findings represent a meaningful contribution to the field.

The present outcomes raise important questions about whether specific clinical and cognitive variables can serve as reliable indicators to guide neuromodulation therapies. Emerging research emphasizes the importance of personalized neuromodulation approaches that tailor treatment parameters to individual patient profiles. Integrating clinical information, such as baseline cognitive performance, symptom severity and neural connectivity, into treatment planning could enhance the efficacy of neuromodulation therapies. Future research should explore how such variables can be systematically assessed and utilized to personalize neuromodulation interventions, thereby optimizing therapeutic outcomes for TRD patients.

In conclusion, the current findings provide evidence supporting the long-term cognitive safety of SCG-DBS in 12 patients with TRD, with particularly notable and sustained improvements in immediate and delayed verbal memory after a median follow-up of five years. These cognitive improvements, alongside sustained mood and functional benefits, underscore the broader therapeutic potential of SCG-DBS. Nevertheless, larger studies and research combining DBS with adjunctive pro-cognitive interventions are warranted to confirm these effects and further optimize functional outcomes in TRD.

CRediT authorship contribution statement

Muriel Vicent-Gil: Writing – original draft, Visualization, Project administration, Investigation, Formal analysis, Data curation. **Joan Trujols:** Writing – review & editing, Validation, Formal analysis. **Dolors Puigdemont:** Writing – review & editing, Supervision, Resources, Project administration, Methodology, Investigation, Funding acquisition, Conceptualization. **Maria J. Portella:** Writing – review & editing, Supervision, Resources, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Conceptualization. **Carlo Alemany:** Writing – review & editing, Resources, Investigation. **Victor Serrano-Gimeno:** Writing – review & editing, Resources, Investigation. **Juan Ángel Aibar-Durán:** Writing – review & editing, Resources, Investigation. **Rodrigo Rodríguez Rodríguez:** Writing – review & editing, Resources, Investigation. **Emilio Ros:** Writing – review & editing, Resources, Investigation. **Montserrat Cofán:** Writing – review & editing, Resources, Investigation. **Narcís Cardoner:** Writing – review & editing, Resources, Investigation. **Javier de Diego-Adeliño:** Writing – review & editing, Supervision, Resources, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Conceptualization.

Ethical statement

All procedures in this study received approval from the Hospital de la Santa Creu i Sant Pau Ethics Committee (EC/06/180/2498), and all participants provided written informed consent. It was conducted in full compliance with current data protection laws, adhered strictly to the ethical guidelines outlined in the Declaration of Helsinki, and followed the principles of Good Clinical Practice.

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Declaration of competing interest

NC: has received research grants and/or honorary fees as a consultant or speaker from various organizations, including Adamed, Angelini, Elsevier, Esteve, Exeltis, Janssen, Lundbeck, Pfizer, Recordati, Viatris, Fundació la Caixa, Carlos III Health Institute, ERA-NET Neuron, the Spanish Ministry of Science and Innovation (CIBERSAM), and Health Research and Innovation Strategic Plan (PERIS) 2016–2020, Marató TV3. **JDA:** Has participated in advisory boards and received speaker honoraria from Johnson & Johnson, Lundbeck, Pfizer, Neuraxpharm, Esteve, and Amgen. The other authors report no conflicts of interest related to the drugs, materials, or devices mentioned in this publication.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.pnpbp.2026.111882.

Data availability

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

References

Aas, I.M., 2010. Global assessment of functioning (GAF): properties and frontier of current knowledge. Ann. General Psychiatry 9, 20. https://doi.org/10.1186/1744-859X-9-20.

Aas, I.M., 2011. Guidelines for rating Global Assessment of Functioning (GAF). Ann. General Psychiatry 10, 2. https://doi.org/10.1186/1744-859X-10-2.

Aibar-Durán, J.Á., Rodríguez, R.R., De Diego Adeliño, F.J., Portella, M.J., Álvarez-Holzapfel, M.J., Blanco, A.M., Campos, D.P., Teixidó, J.M., 2022. Long-term results of deep brain stimulation for treatment-resistant depression: outcome analysis and correlation with lead position and electrical parameters. Neurosurgery 90, 72–80. https://doi.org/10.1227/NEU.0000000000001739.

Alagapan, S., Choi, K.S., Heisig, S., Riva-Posse, P., Crowell, A., Tiruvadi, V., Obatusin, M., Veerakumar, A., Waters, A.C., Gross, R.E., Quinn, S., Denison, L., O'Shaughnessy, M., Connor, M., Canal, G., Cha, J., Hershenberg, R., Nauvel, T., Isbaine, F., Afzal, M.F., Figee, M., Kopell, B.H., Butera, R., Mayberg, H.S., Rozell, C.J., 2023. Cingulate dynamics track depression recovery with deep brain stimulation. Nature 622, 130–138. https://doi.org/10.1038/s41586-023-06541-3.

Alemany, C., Puigdemont, D., Martín-Blanco, A., Rodríguez-Rodríguez, R., Aibar-Durán, J.A., Vicent-Gil, M., Álvarez, Enric, Pérez, Víctor, Portella, M.J., De Diego-Adeliño, J., 2023. Response and safety outcomes in treatment-resistant depression after subcallosal cingulate gyrus deep brain stimulation: long-term follow-up study. J. Clin. Psychiatry 84, 22m14622. https://doi.org/10.4088/JCP.22m14622.

Bergfeld, I.O., Mantione, M., Hoogendoorn, M.L.C., Ruhé, H.G., Horst, F., Notten, P., Van Laarhoven, J., Van Den Munckhof, P., Beute, G., Schuurman, P.R., Denys, D., 2017. Impact of deep brain stimulation of the ventral anterior limb of the internal capsule on cognition in depression. Psychol. Med. 47, 1647–1658. https://doi.org/10.1017/S0033291717000113.

Berlim, M.T., McGirr, A., Van Den Eynde, F., Fleck, M.P.A., Giacobbe, P., 2014. Effectiveness and acceptability of deep brain stimulation (DBS) of the subgenual cingulate cortex for treatment-resistant depression: a systematic review and exploratory meta-analysis. J. Affect. Disord. https://doi.org/10.1016/j.jad.2014.02.016.

Bobes, J., Bulbena, A., Luque, A., Dal-Ré, R., Ballesteros, J., Ibarra, N., 2003. Evaluación psicométrica comparativa de las versiones en español de 6, 17 y 21 ítems de la escala de valoración de Hamilton para la evaluación de la depresión. Med. Clin. 120, 693–700. https://doi.org/10.1157/13047695.

Bogod, N.M., Sinden, R.P.M., Woo, B.A.C., Vanessa, B.A., Defreitas, G., Ivan, M.A., Torres, J., Psych, R., Andrew, K., Howard, F.R.C.P.C., Magdalena, I., Ilcewicz-Klimek, F.R.C.P.C., Christopher, R., Honey, F.R.C.S.C., Lakshmi, N., Yatham, M.B.B.S., Lam, R.W., 2014. Long-term neuropsychological safety of subgenual cingulate gyrus deep brain stimulation for treatment-resistant depression. J. Neuropsychiatr. Clin. Neurosci. 26, 126–133.

Bora, E., Harrison, B.J., Yücel, M., Pantelis, C., 2013. Cognitive impairment in euthymic major depressive disorder: a meta-analysis. Psychol. Med. 43, 2017–2026. https://doi.org/10.1017/S0033291712002085.

Busner, J., Targum, S.D., 2007. Global impressions scale: applying a research. Psychiatry 4, 28–37.

Casals-Coll, M., Sánchez-Benavides, G., Quintana, M., Manero, R.M., Rognoni, T., Calvo, L., Palomo, R., Aranciva, F., Tamayo, F., Peña-Casanova, J., 2013. Estudios normativos españoles en población adulta joven (proyecto NEURONORMA jóvenes):

normas para los test de fluencia verbal. Neurologia 28, 33–40. https://doi.org/10.1016/j.nrl.2012.02.010.
De Diego-Adeliño, J., Pires, P., Gómez-Ansón, B., Serra-Blasco, M., Vives-Gilabert, Y., Puigdemont, D., Martín-Blanco, A., Álvarez, E., Pérez, V., Portella, M.J., 2014. Microstructural white-matter abnormalities associated with treatment resistance, severity and duration of illness in major depression. Psychol. Med. 44, 1171–1182. https://doi.org/10.1017/S003329171300158X.
Duff, K., 2012. Current topics in science and practice evidence-based indicators of neuropsychological change in the individual patient: relevant concepts and methods. Arch. Clin. Neuropsychol. 27, 248–261. https://doi.org/10.1093/arclin/acr120.
Gaynes, B.N., Lux, L., Gartlehner, G., Asher, G., Forman-Hoffman, V., Green, J., Boland, E., Weber, R.P., Randolph, C., Bann, C., Coker-Schwimmer, E., Viswanathan, M., Lohr, K.N., 2020. Defining treatment-resistant depression. Depress. Anxiety. https://doi.org/10.1002/da.22968.
Gregory, E., Torres, I.J., Ge, R., Blumberger, D.M., Downar, J.H., Daskalakis, Z.J., Lam, R.W., Vila-Rodriguez, F., 2020. Predictors of cognitive impairment in treatment-resistant depression. J. Affect. Disord. 274, 593–601. https://doi.org/10.1016/j.jad.2020.05.101.
Grubert, C., Hurlemann, R., Bewernick, B.H., Kayser, S., Hadrysiewicz, B., Axmacher, N., Sturm, V., Schlaepfer, T.E., 2011. Neuropsychological safety of nucleus accumbens deep brain stimulation for major depression: effects of 12-month stimulation. World J. Biol. Psychiatry 12, 516–527. https://doi.org/10.3109/15622975.2011.583940.
Hamilton, M., 1960. A rating scale for depression. J. Neurol. Neurosurg. Psychiatry 23, 56–62. https://doi.org/10.1136/jnnp.23.1.56.
Himes, L.M., Mayberg, H.S., Husain, M.M., Holtzheimer, P.E., Lozano, A.M., Kennedy, S. H., Gross, R.E., Kopell, B.H., Figee, M., Slavin, K.V., Pilitsis, J.G., Neimat, J.S., Hamani, C., Pouratian, N., Giacobbe, P., Mogilner, A.Y., Nanduri, D., Cheeran, B.J., Pathak, Y.J., Riva-Posse, P., 2025. Revisiting subcallosal cingulate deep brain stimulation for depression: long-term safety and effectiveness outcomes from a pooled analysis of 172 implanted patients. Brain Stimul. 18, 1632–1640. https://doi.org/10.1016/j.brs.2025.08.017.
Jacobson, N.S., Truax, P., 1991. Clinical significance: a statistical approach to defining meaningful change in psychotherapy research. J. Consult. Clin. Psychol. 59 (1), 12–19. https://doi.org/10.1037/0022-006X.59.1.12.
Johansen-Berg, H., Gutman, D.A., Behrens, T.E.J., Matthews, P.M., Rushworth, M.F.S., Katz, E., Lozano, A.M., Mayberg, H.S., 2008. Anatomical connectivity of the subgenual cingulate region targeted with deep brain stimulation for treatment-resistant depression. Cereb. Cortex 18, 1374–1383. https://doi.org/10.1093/cercor/bhm167.
Kisely, S., Li, A., Warren, N., Siskind, D., 2018. A systematic review and meta-analysis of deep brain stimulation for depression. Depress. Anxiety. https://doi.org/10.1002/da.22746.
Kubu, C.S., Brelje, T., Butters, M.A., Deckersbach, T., Malloy, P., Moberg, P., Tröster, A.I., Williamson, E., Baltuch, G.H., Bhati, M.T., Carpenter, L.L., Dougherty, D.D., Howland, R.H., Rezai, A.R., Malone, D.A., 2016. Cognitive outcome after ventral capsule/ventral striatum stimulation for treatment-resistant major depression. J. Neurol. Neurosurg. Psychiatry 0, 1–4. https://doi.org/10.1136/jnnp.
López-Solà, C., Subirà, M., Serra-Blasco, M., Vicent-Gil, M., Navarra-Ventura, G., Aguilar, E., Acebillo, S., Palao, D.J., Cardoner, N., 2020. Is cognitive dysfunction involved in difficult-to-treat depression? Characterizing resistance from a cognitive perspective. Eur. Psychiatry 63. https://doi.org/10.1192/j.eurpsy.2020.65.
Lozano, A.M., Mayberg, H.S., Giacobbe, P., Hamani, C., Craddock, R.C., Kennedy, S.H., 2008. Subcallosal cingulate gyrus deep brain stimulation for treatment-resistant depression. Biol. Psychiatry 64, 461–467. https://doi.org/10.1016/j.biopsych.2008.05.034.
Malone, D.A., Dougherty, D.D., Rezai, A.R., Carpenter, L.L., Friehs, G.M., Eskandar, E.N., Rauch, S.L., Rasmussen, S.A., Machado, A.G., Kubu, C.S., Tyrka, A.R., Price, L.H., Stypulkowski, P.H., Giftakis, J.E., Rise, M.T., Malloy, P.F., Salloway, S.P., Greenberg, B.D., 2009. Deep brain stimulation of the ventral capsule/ventral striatum for treatment-resistant depression. Biol. Psychiatry 65, 267–275. https://doi.org/10.1016/j.biopsych.2008.08.029.
Martín-Blanco, A., Serra-Blasco, M., Pérez-Egea, R., De Diego-Adeliño, J., Carceller-Sindreu, M., Puigdemont, D., Molet, J., Álvarez, E., Pérez, V., Portella, M.J., 2015. Immediate cerebral metabolic changes induced by discontinuation of deep brain stimulation of subcallosal cingulate gyrus in treatment-resistant depression. J. Affect. Disord. 173, 159–162. https://doi.org/10.1016/j.jad.2014.10.035.
McNeely, H.E., Mayberg, H.S., Lozano, A.M., Kennedy, S.H., 2008. Neuropsychological impact of Cg25 deep brain stimulation for treatment-resistant depression: preliminary results over 12 months. J. Nerv. Ment. Dis. 196, 405–410. https://doi.org/10.1097/NMD.0b013e3181710927.
Moreines, J.L., McClintock, S.M., Kelley, M.E., Holtzheimer, P.E., Mayberg, H.S., 2014. Neuropsychological function before and after subcallosal cingulate deep brain stimulation in patients with treatment-resistant depression. Depress. Anxiety 31, 690–698. https://doi.org/10.1002/da.22263.
Peña-Casanova, J., Quiñones-Úbeda, S., Gramunt-Fombuena, N., Quintana-Aparicio, M., Aguilar, M., Badenes, D., Cerulla, N., Molinueva, J.L., Ruiz, E., Robles, A., Braquero, M.S., Antúnez, C., Martínez-Parra, C., Frank-García, A., Fernández, M., Alfonso, V., Sol, J.M., Blesa, R., 2009. Spanish multicenter normative studies (NEURONORMA project): norms for verbal fluency tests. Arch. Clin. Neuropsychol. 24, 395–411. https://doi.org/10.1093/arclin/acp042.
Price, R.B., Duman, R., 2020. Neuroplasticity in cognitive and psychological mechanisms of depression: an integrative model. Mol. Psychiatry 25, 530–543. https://doi.org/10.1038/s41380-019-0615-x.
Puigdemont, D., Pérez-Egea, R., Portella, M.J., Molet, J., De Diego-Adeliño, J., Gironell, A., Radua, J., Gómez-Anson, B., Rodríguez, R., Serra, M., De Quintana, C., Artigas, F., Álvarez, E., Pérez, V., 2012. Deep brain stimulation of the subcallosal cingulate gyrus: further evidence in treatment-resistant major depression. Int. J. Neuropsychopharmacol. 15, 121–133. https://doi.org/10.1017/S1461145711001088.
Puigdemont, D., Portella, M.J., Pérez-Egea, R., Molet, J., Gironell, A., de Diego-Adeliño, J., Martín, A., Rodríguez, R., Álvarez, E., Artigas, F., Pérez, V., 2015. A randomized double-blind crossover trial of deep brain stimulation of the subcallosal cingulate gyrus in patients with treatment-resistant depression: a pilot study of relapse prevention. J. Psychiatry Neurosci. 40, 224–231. https://doi.org/10.1503/jpn.130295.
Reitan, R.M., 1992. Trail Making Test: Manual for Administration and Scoring. Reitan Neuropsychology Laboratory.
Rey, A., 1941. L'examen clinique en psychologie. Presses Universitaires de France, Paris.
Riva-Posse, P., Choi, K.S., Holtzheimer, P.E., McIntyre, C.C., Gross, R.E., Chaturvedi, A., Crowell, A.L., Garlow, S.J., Rajendra, J.K., Mayberg, H.S., 2014. Defining critical white matter pathways mediating successful subcallosal cingulate deep brain stimulation for treatment-resistant depression. Biol. Psychiatry 76, 963–969. https://doi.org/10.1016/j.biopsych.2014.03.029.
Rock, P.L., Roiser, J.P., Riedel, W.J., Blackwell, A.D., 2014. Cognitive impairment in depression: a systematic review and meta-analysis. Psychol. Med. 44, 2029–2040. https://doi.org/10.1017/S0033291713002535.
Runia, N., Mol, G.J.J., Hillenius, T., Hassanzadeh, Z., Denys, D.A.J.P., Bergfeld, I.O., 2023. Effects of deep brain stimulation on cognitive functioning in treatment-resistant depression: a systematic review and meta-analysis. Mol. Psychiatry. https://doi.org/10.1038/s41380-023-02262-1.
Sackeim, H.A., Aaronson, S.T., Bunker, M.T., Conway, C.R., Demitrack, M.A., George, M. S., Prudic, J., Thase, M.E., Rushi, A.J., 2019. The assessment of resistance to antidepressant treatment: rationale for the antidepressant treatment history form: short form (ATHF-SF). J. Psychiatr. Res. 113, 125–136. https://doi.org/10.1016/j.jpsychires.2019.03.021.
Sala-Vila, A., Valls-Pedret, C., Rajaram, S., Coll-Padrós, N., Cofán, M., Serra-Mir, M., Pérez-Heras, A.M., Roth, I., Freitas-Simoes, T.M., Doménech, M., Calvo, C., López-Illamola, A., Bitok, E., Buxton, N.K., Huey, L., Arechiga, A., Oda, K., Lee, G.J., Corella, D., Vaqué-Alcázar, L., Sala-Llonch, R., Bartrés-Faz, D., Sabaté, J., Ros, E., 2020. Effect of a 2-year diet intervention with walnuts on cognitive decline. The walnuts and healthy aging (WAHA) study: a randomized controlled trial. Am. J. Clin. Nutr. 111, 590–600. https://doi.org/10.1093/ajcn/nqz328.
Semkovska, M., Quinlivan, L., O'Grady, T., Johnson, R., Collins, A., O'Connor, J., Knittle, H., Ahern, E., Gload, T., 2019. Cognitive function following a major depressive episode: a systematic review and meta-analysis. Lancet Psychiatry 6, 851–861. https://doi.org/10.1016/S2215-0366(19)30291-3.
Serra-Blasco, M., de Vita, S., Rodríguez, M.R., de Diego-Adeliño, J., Puigdemont, D., Martín-Blanco, A., Pérez-Egea, R., Molet, J., Álvarez, E., Pérez, V., Portella, M.J., 2015. Cognitive functioning after deep brain stimulation in subcallosal cingulate gyrus for treatment-resistant depression: an exploratory study. Psychiatry Res. 225, 341–346. https://doi.org/10.1016/j.psychres.2014.11.076.
Serra-Blasco, M., de Diego-Adeliño, J., Vives-Gilabert, Y., Trujols, J., Puigdemont, D., Carceller-Sindreu, M., Pérez, V., Álvarez, E., Portella, M.J., 2016. Naturalistic course of major depressive disorder predicted by clinical and structural neuroimaging data: a 5-year follow-up. Depress. Anxiety 33, 1055–1064. https://doi.org/10.1002/da.22522.
Tombaugh, T.N., 2004. Trail making test a and B: normative data stratified by age and education. Arch. Clin. Neuropsychol. 19, 203–214. https://doi.org/10.1016/S0887-6177(03)00039-8.
Wechsler, D., 2008. Wechsler Adult Intelligence Scale (WAIS-IV), 4th ed. Pearson, San Antonio, Texas.