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► To cite this version:

Mathilde Boussac, Christophe Arbus, Helene Klinger, Alexandre Eusebio, Elodie Hainque, et al.. Personality Related to Quality-of-Life Improvement After Deep Brain Stimulation in Parkinson's Disease (PSYCHO-STIM II). *Journal of Parkinson's disease*, 2022, 12 (2), pp.699-711. 10.3233/JPD-212883 . hal-03513907

HAL Id: hal-03513907

<https://hal.science/hal-03513907>

Submitted on 17 Jun 2022

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Research Report

Personality Related to Quality-of-Life Improvement After Deep Brain Stimulation in Parkinson's Disease (PSYCHO-STIM II)

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Accepted 17 November 2021

Abstract.

Background: Deep brain stimulation of the sub-thalamic nucleus (DBS-STN) reduces symptoms in Parkinson's disease (PD) patients with motor fluctuations. However, some patients may not feel ameliorated afterwards, despite an objective motor improvement. It is thus important to find new predictors of patients' quality of life (QoL) amelioration after DBS-STN. We hypothesized that personality dimensions might affect QoL after DBS-STN.

Objective: To evaluate associations between personality dimensions and QoL improvement one year after DBS-STN.

Methods: DBS-STN-PD patients ($n=303$) having answered the "Temperament and Character Inventory" (TCI) before surgery and the PDQ-39 before and one year after surgery were included, from the cohort study PREDI-STIM. Linear regression models were used to evaluate associations between TCI dimensions and change in PDQ-39 scores after DBS-STN.

Results: Novelty Seeking and Cooperativeness scores before surgery were positively associated with PDQ-39 scores improvement after DBS-STN (FDR-adjusted $p<0.01$). Moreover, paradoxically unimproved patients with deterioration of their PDQ-39 scores after DBS-STN despite improvement of their MDS-UPDRS-IV scores had lower Cooperativeness scores, while paradoxically improved patients with amelioration of their PDQ-39 scores despite deterioration of their MDS-UPDRS-IV scores had higher Reward Dependence scores.

Conclusion: Some presurgical personality dimensions were significantly associated with QoL amelioration and discrepancy between motor state and QoL changes after DBS-STN in PD. Educational programs before DBS-STN should take in account patient personality dimensions to better deal with their expectations.

Keywords: Cooperativeness, DBS-STN, novelty seeking, Parkinson's disease, quality of life

INTRODUCTION

Deep brain stimulation of the sub-thalamic nucleus (DBS-STN) is proposed to Parkinson's disease (PD) patients with motor fluctuations and generally leads to a great improvement of their quality of life (QoL) [1–4]. Nonetheless, some patients do not feel DBS benefits despite objective motor improvement [5, 6]. That is why it seems crucial to find some individual predictive factors of QoL improvement after DBS-STN in order to assure at best patients' amelioration after this invasive therapy.

QoL improvement is an important outcome when evaluating treatment efficiency. It depends on both

objective and subjective factors such as physical and psychological health, as well as personal feeling of well-being and happiness experienced [7, 8].

Because personality is a very individual characteristic and describes how people think, behave and manage their life [9], it seems a factor of interest to predict QoL. To assess personality, several questionnaires have been developed, based on different concepts. From them, the Temperament and Character Inventory (TCI) evaluates personality through seven dimensions [10]. It is derived from the neurobiological and psychological concept of personality made by Cloninger [9]. The TCI was already used in several studies assessing PD personality [11] and was

validated by its stability [9, 12–15]. Moreover, our preceding study on PD patients with motor fluctuations has shown the adequacy of the TCI personality questionnaire on predicting QoL in this population before DBS-STN [16].

Our first objective was thus to identify associations between presurgical personality dimensions and QoL improvement one year after DBS-STN. Our second objective was to seek for characteristics of PD patients experiencing discrepancy between motor complications and QoL changes after DBS.

MATERIALS AND METHODS

This study is an ancillary analysis using data collected from the PREDISTIM cohort which principal objective is to define the predictive factors of the therapeutic response to DBS-STN on the long-term QoL in PD. PREDISTIM is an ongoing prospective multicentric cohort (Protocol 2013-A00193-42) sponsored by the University Hospital of Lille, conducted in 17 PD expert centers from the clinical research network in France (NS-Park/F-Crin), approved from the CPP Nord Ouest-IV Ethical Committee and registered in the ClinicalTrials.gov website (NCT02360683).

Patients

Briefly, patients undergoing DBS-STN in one of the participating centers were consecutive included into the study between 11/2013 and 09/2019. Inclusion criteria are a diagnosis of PD according to the UKPDSBB, disease duration ≥ 5 years, age between 18 and 75 and indication of DBS-STN. Exclusion criteria are atypical parkinsonism, severe cognitive impairment (Montreal Cognitive Assessment (MoCA) score < 23), severe psychiatric disorders (following psychiatric evaluation by a psychiatrist), levodopa motor response $< 30\%$ and contra-indications to surgery.

Patients gave written informed consent, the study was conducted according to the good clinical practice, local regulations and data collection was compliant with GDPR rules.

Study design and clinical measures

For PREDISTIM, clinical data was collected at baseline, and then at 1-, 3-, and 5-years post-surgery. Clinical assessments at each visit included collection of demographic data, medical and treatment

history, MDS-UPDRS part I-IV [17], part-III being performed in OFF and ON state during a standardized acute levodopa challenge, neuropsychological testing, patient and caregivers' questionnaires. Along our ancillary study, only one personality questionnaire was added to evaluation at baseline: the TCI. Here, only patients evaluated before (V0) and after one year of DBS-STN (V1) were used in this study.

The MDS-UPDRS-III was evaluated for two conditions at V0: OFF and ON medication; and for four conditions at V1: ON stimulation ON medication (stimON-medON), ON stimulation OFF medication (stimON-medOFF), OFF stimulation ON medication (stimOFF-medON) and OFF stimulation OFF medication (stimOFF-medOFF).

The total Levodopa Equivalent Dose (LED) was calculated [18].

The Parkinson's Disease Questionnaire 39-items (PDQ-39) is a self-questionnaire evaluating specifically QoL of PD patients [19] and was assessed at V0 and V1. Its eight sub-scales can be divided into a Physical Component Score ("Mobility", "Activities of Daily Living" and "Bodily Discomfort" sub-scores) and a Mental Component Score ("Emotional Well-Being", "Stigma", "Social Support", "Cognition" and "Communication" sub-scores) of QoL.

The TCI was measured only at V0 in order to serve as predictive factor of QoL improvement after DBS-STN. It is a self-questionnaire of 226 binary questions used to assess patients' personality through seven dimensions [10]. It includes four temperaments (which are supposed to be genetically determined personality traits [9]): Novelty Seeking (NS), Harm Avoidance (HA), Reward Dependence (RD), and Persistence (P); and three characters (which are developmental personality traits evolving through time and life history [9]): Self-Directedness (SD), Cooperativeness (C), and Self-Transcendence (ST). Each of these seven personality dimensions are measured by an independent score: higher is the score, higher the individual will present the personality characteristic associated. NS corresponds to impulsive and curious temperament; HA to anxious and pessimist traits; RD to socially attached and sensitive individuals; P to hardworking and perseverant personality; and the three characters are associated to levels of maturity: SD to individual maturity, C to social maturity, and ST to spiritual maturity. Except the P, each of these seven dimensions is subdivided into sub-dimensions: NS and HA are formed by 4 sub-dimensions, RD and ST by 3, and SD and C by 5. Each of these twenty-four sub-dimensions represents

161 a specific aspect of the global dimension, also ranging
162 in a spectrum of scores.

163 *Statistical analyses*

164 Descriptive analyses were performed. Moreover,
165 Kruskal-Wallis tests or ANOVA (according to nor-
166 mality of our data) followed by *post-hoc* analysis
167 were done to control for homogeneity across centers
168 for several variables (age, disease duration, LED at
169 V0, percentage of PDQ-39 total score and sub-scores
170 changes at V1, and TCI dimensions).

171 *Impact of DBS-STN at V1*

172 After DBS-STN, changes between V0 and V1 in
173 LED, MDS-UPDRS, PDQ-39, Hamilton Depression
174 Rating Scale (HAMD), Hamilton Anxiety Rating
175 Scale (HAMA), Lille Apathy Rating Scale (LARS),
176 and MoCA were checked (Wilcoxon Signed Rank
177 Test for Paired Samples).

178 *Associations between TCI dimensions and* 179 *PDQ-39 scores at V0*

180 Linear regression models were performed to test
181 the association between the different PDQ-39 sub-
182 scores and total score at V0 and the seven TCI
183 dimensions. Models were univariate with only one
184 explanatory variable (each TCI dimensions) by mod-
185 els, resulting in seven models per response variable
186 (each PDQ-39 scores) which were adjusted by age,
187 sex, disease duration and LED at V0. A False Dis-
188 covery Rate (FDR) correction was applied for 31
189 comparisons with calculation of q values (corre-
190 sponding to FDR adjusted *p* values). We have chosen
191 univariate models to study if some TCI personal-
192 ity dimensions were separately associated with QoL.
193 Moreover, because studying TCI sub-dimensions as
194 well as main dimensions seemed of interest, multi-
195 variate analysis seemed inappropriate since too many
196 explanatory variables would be used (that is 31 vari-
197 ables – 7 dimensions plus 24 sub-dimensions) which
198 can be too much in view of the parsimony rule.

199 *Associations between MDS-UPDRS and* 200 *PDQ-39 scores at V1*

201 These associations were tested using linear regres-
202 sion models adjusted by age, sex, disease duration,
203 and LED at V1. The PDQ-39 scores at V1 served
204 as response variables (the total and eight PDQ-39
205 sub-scores) and the MDS-UPDRS (part-I, part-II
206 stimON-medON, part-III stimON-medON and part-
207 IV) scores at V1 as explanatory variables. Models

208 were univariate with only one explanatory variable
209 by models, resulting in four models per response
210 variable. An FDR correction was applied for 4 com-
211 parisons.

212 *Associations between TCI dimensions at V0 and* 213 *PDQ-39 changes at V1*

214 Percentages of changes from V0 to V1 were
215 calculated from the PDQ-39 total and sub-scores.
216 Linear regression models were performed. The
217 response variables corresponded to each calculated
218 percentages of PDQ-39 change. The explanatory
219 variables corresponded to each TCI dimensions and
220 sub-dimensions. As explained above, models were
221 univariate with only one explanatory variable by
222 models, resulting in thirty-one models per response
223 variable, adjusted by age, sex, disease duration and
224 LED at V0, to account for any potential center effect.
225 The same FDR correction was applied with **q values**
226 calculation for 31 comparisons.

227 PD population was also divided into two groups
228 according to the Minimal Clinically Important Dif-
229 ference (MCID) of PDQ-39 total score change [20]:
230 an “improvement” (difference of PDQ-39 total score
231 between V1 and V0 < -4.72) and a “no improvement”
232 group (difference of PDQ-39 total score between
233 V1 and V0 ≥ -4.72). TCI dimensions and sub-
234 dimensions scores were compared in these groups
235 (two-sample Mann-Whitney tests with FDR correc-
236 tion for 31 comparisons).

237 *Differences between groups of responding* 238 *patients*

239 As supplementary exploratory analysis, we have
240 chosen to study discrepancy between motor compli-
241 cations (MDS-UPDRS-IV) and QoL (PDQ-39 total)
242 evolution. From the two PDQ-39 groups above and
243 two similar MDS-UPDRS-IV groups (an “improve-
244 ment” group based on MCID [21] (difference of
245 MDS-UPDRS-IV score between V1 and V0 < -0.9)
246 and a “no improvement” group (difference of MDS-
247 UPDRS-IV score between V1 and V0 ≥ -0.9)), PD
248 patients were divided into three final groups of
249 responding patients: a “paradoxically unimproved”
250 group (MDS-UPDRS “improvement” group and
251 PDQ-39 “no improvement” group), a “realistic”
252 group (MDS-UPDRS and PDQ-39 “improvement”
253 groups or MDS-UPDRS and PDQ-39 “no improve-
254 ment” groups) and a “paradoxically improved”
255 group (MDS-UPDRS “no improvement” group and
256 PDQ-39 “improvement” group). Each group were
257 compared two by two in terms of TCI dimensions and

Table 1
Description of TCI dimensions and clinical characteristics at V0 and V1

	V0 (mean ± SD)	V1 (mean ± SD)	<i>p</i>	CI of the difference
Age	60.0 ± 7.4	/	/	/
Disease duration	10.1 ± 3.9	/	/	/
Novelty Seeking	16.7 ± 5.0	/	/	/
Harm Avoidance	17.4 ± 6.5	/	/	/
Reward Dependence	15.4 ± 3.5	/	/	/
Persistence	5.4 ± 1.7	/	/	/
Self-Directedness	34.4 ± 6.0	/	/	/
Cooperativeness	33.8 ± 4.7	/	/	/
Self-Transcendence	12.3 ± 5.8	/	/	/
LED	1348.6 ± 740.2	689.6 ± 480.3	$9 \times 10^{-33**}$	535.7; 674.0
HAMD	5.2 ± 4.1	4.6 ± 4.1	$4 \times 10^{-02*}$	0.0; 1.5
HAMA	5.9 ± 5.1	4.7 ± 4.2	$2 \times 10^{-03**}$	0.5; 2.0
LARS	-27.9 ± 5.7	-25.2 ± 8.3	$1 \times 10^{-06**}$	-3.0; -1.0
MoCA	27.1 ± 2.2	25.9 ± 2.8	$1 \times 10^{-11**}$	1.0; 1.5
MDS-UPDRS I	10.9 ± 5	9.3 ± 5.2	$5 \times 10^{-06**}$	1.0; 2.5
MDS-UPDRS II OFF [†]	18.7 ± 7.6	15.1 ± 8.5	$9 \times 10^{-12**}$	3.5; 5.5
MDS-UPDRS II ON [‡]	6.5 ± 5.9	8.1 ± 5.8	$8 \times 10^{-05**}$	-2.5; -1.0
MDS-UPDRS III OFF [†]	43 ± 16.2	21.8 ± 12.9	$3 \times 10^{-46**}$	19.0; 22.5
MDS-UPDRS III ON [‡]	12.5 ± 7.8	10.8 ± 7.9	$3 \times 10^{-02*}$	0.0; 2.5
MDS-UPDRS IV	8.8 ± 3.3	4.1 ± 3.7	$3 \times 10^{-33**}$	4.5; 5.5
PDQ-39 Total	31.3 ± 11.4	26.8 ± 13.5	$3 \times 10^{-11**}$	3.4; 6.0
PDQ-39 Mobility	36.7 ± 20.4	32.6 ± 22.7	$2 \times 10^{-03**}$	1.3; 6.3
PDQ-39 ADL	37.7 ± 18.1	29.2 ± 20	$5 \times 10^{-13**}$	8.3; 12.5
PDQ-39 Emotional Well-being	32 ± 17.7	31.1 ± 19.2	0.30	-0.00004; 4.2
PDQ-39 Stigma	33.2 ± 22.3	23.1 ± 20.3	$5 \times 10^{-15**}$	9.4; 15.6
PDQ-39 Social support	11.7 ± 15.9	14 ± 18	$1 \times 10^{-02*}$	-8.3; 0.0
PDQ-39 Cognition	28.3 ± 17.1	24 ± 17.2	$6 \times 10^{-05**}$	3.1; 6.3
PDQ-39 Communication	24.9 ± 17.9	28.1 ± 21	$3 \times 10^{-03**}$	-8.3; 0.0
PDQ-39 Bodily discomfort	46.3 ± 21.1	32.5 ± 21.4	$9 \times 10^{-19**}$	12.5; 20.8

Mann-Whitney tests: * $p < 0.05$; ** $p \leq 0.01$; CI, confidence interval of the difference in means at 95% confidence level; V0, baseline; V1, one year after DBS-STN; [†]MDS-UPDRS medOFF (V0) vs. stimON-medOFF (V1); [‡]MDS-UPDRS medON (V0) vs. stimON-medON (V1); ADL, Activities of Daily Living.

cognitive and behavioral (HAMD, HAMA, LARS, and MoCA) changes after DBS-STN (two-sample Mann-Whitney tests). FDR adjusted p values (q values) were calculated for 7 comparisons for the TCI dimensions analysis and for 4 comparisons for the cognitive and behavioral changes analysis.

All analyses were conducted on R Studio Software Version 1.1.456 and a threshold of bilateral statistical significance of 0.05 was used. As explained above, FDR corrections were applied and interpretations were made carefully according to strength of the results.

RESULTS

Three hundred and three PD patients were enrolled in this study (204 men (67.3%) and 99 women (32.7%)) (Table 1). Statistical testing did not show relevant significant differences across centers: only age and disease duration shown significant

differences between centers in the Kruskal-Wallis testing ($p = 0.003$ and $p = 0.03$, respectively) which no more reached significance during the *post-hoc* analysis; LED at V0, percentage of PDQ-39 changes at V1 and TCI dimensions were not different between centers ($p > 0.05$). In any case, age, disease duration, sex and LED were used as adjustment variables in the linear regression models to control for any potential center effect.

Impact of DBS-STN at V1 (Table 1)

One year after DBS-STN, PD patients had a significant decrease in their dopaminergic treatments (LED). HAMD, HAMA, and MoCA scores significantly decreased after DBS, while LARS scores slightly increased.

All parts of the MDS-UPDRS scores improved significantly after DBS-STN except the part-II-ON which worsened.

Table 2
Significant associations between TCI dimensions at V0 and percentages of PDQ-39 change at V1 (n = 303)

Percentage of PDQ-39 evolution	TCI dimensions	coefficients	P	q	R2	CI
% PDQ-39 Total	NS	-1.02	0.04*	0.46	0.07	-2.01; -0.03
	HA4	-2.41	0.03*	0.46	0.07	-4.62; -0.21
	C3	-4.48	0.03*	0.46	0.07	-8.47; -0.49
% PDQ-39 Mobility	NS1	-9.42	0.0006**	0.02 *	0.05	-14.75; -4.08
	NS4	-7.34	0.047*	0.29	0.02	-14.55; -0.13
	C	-3.11	0.01**	0.12	0.03	-5.60; -0.62
	C1	-13.17	0.004**	0.04 *	0.04	-22.15; -4.19
	C4	-9.30	0.004**	0.04 *	0.04	-15.65; -2.96
% PDQ-39 ADL	C3	-10.24	0.047*	0.978	0.02	-20.30; -0.18
% PDQ-39 Emotional Well-Being	HA	-2.30	0.02*	0.37	0.04	-4.29; -0.32
	HA4	-7.54	0.01**	0.35	0.05	-13.34; -1.74
	P	8.18	0.04*	0.40	0.04	0.46; 14.89
% PDQ-39 Stigma	RD	-2.39	0.03*	0.40	0.01	-4.53; -0.24
	RD3	-5.84	0.04*	0.40	0.01	-11.41; -0.28
	ST3	4.20	0.03*	0.40	0.01	0.40; 8.01
	ST	1.80	0.02*	0.31	0.02	0.29; 3.31
% PDQ-39 Social Support	ST3	5.30	0.02*	0.31	0.02	0.92; 9.68
	NS	-2.56	0.009**	0.262	0.03	-4.45; -0.66
	SD	1.63	0.04*	0.26	0.02	0.07; 3.19
% PDQ-39 Cognition	SD1	6.84	0.02*	0.26	0.02	0.98; 12.70
	C1	7.72	0.04*	0.26	0.02	0.30; 15.13
	C2	6.56	0.04*	0.26	0.02	0.27; 12.85
	HA4	-5.55	0.04*	0.70	0.00	-10.95; -0.15
% PDQ-39 Communication	NS	-1.90	0.01**	0.34	0.02	-3.37; -0.43
% PDQ-39 Bodily Discomfort	NS1	-3.78	0.03*	0.34	0.02	-7.20; -0.35
	C3	-6.50	0.03*	0.34	0.02	-12.45; -0.56

Adjusted linear regression models: * $p < 0.05$; ** $p \leq 0.01$; q, FDR adjusted q value; significant p value in bold; CI, confidence interval at 95% confidence level; NS, Novelty Seeking; HA4, Fatigability; C3, Helpfulness; NS1, Exploratory excitability; NS4, Disorderliness; C, Cooperativeness; C1, Social acceptance; C4, Compassion; HA, Harm Avoidance; P, Persistence; RD, Reward Dependence; RD3, Dependence; ST3, Spiritual acceptance; ST, Self-Transcendence; SD, Self-Directedness; SD1, Responsibility; C2, Empathy.

294 Total PDQ-39 scores significantly improved after
295 one year of DBS-STN as well as the “Mobility”,
296 “Activities of Daily Living”, “Stigma”, “Cogni-
297 tion”, and “Bodily Discomfort” sub-scores, whereas
298 the “Emotional Well-Being” sub-score did not sig-
299 nificantly change. The “Social Support” and “Com-
300 munication” sub-scores significantly worsened after
301 surgery.

302 Associations between TCI dimensions and 303 PDQ-39 scores at V0

304 TCI dimensions were mainly associated with
305 the Mental Component Score of the PDQ-39 at
306 V0. Indeed, the linear regression models between
307 TCI dimensions and PDQ-39 sub-scores at V0
308 showed that HA and ST scores were significantly
309 and positively associated with PDQ-39 total score
310 ($q = 1 \times 10^{-8}$, $R^2 = 0.16$; and $q = 9 \times 10^{-3}$, $R^2 = 0.07$,
311 respectively) whereas SD scores were significantly
312 and negatively associated with PDQ-39 total score
($q = 2 \times 10^{-7}$, $R^2 = 0.14$).

Associations between MDS-UPDRS and PDQ-39 scores at V1

315 At V1, the MDS-UPDRS part-I and part-II
316 stimON-medON were positively associated with
317 PDQ-39 total and 8 sub-scores ($q < 0.01$). The
318 MDS-UPDRS part-III stimON-medON and part-
319 IV were positively associated with PDQ-39 total
320 score ($q < 10^{-4}$), most of the Physical Component
321 Score (“Mobility” and “Activities of Daily Living”)
322 ($p < 10^{-3}$) and part of the Mental Component Score
323 (“Emotional Well-Being”, “Stigma”, and “Com-
324 munication”) ($q < 0.05$). The “Bodily Discomfort”
325 was associated only with the MDS-UPDRS part-IV
326 ($q < 10^{-3}$).

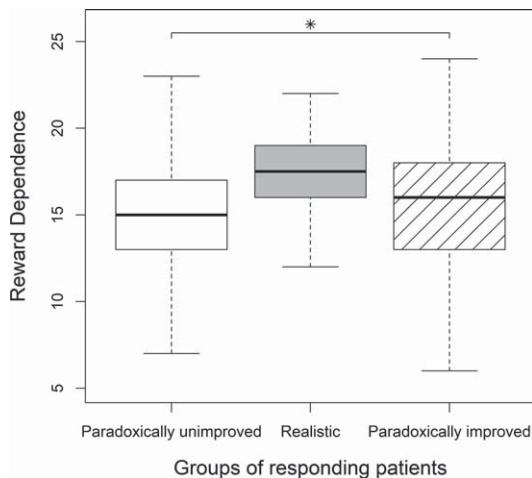
Associations between TCI dimensions at V0 and PDQ-39 changes at V1 (n = 303)

327 There were significant associations between TCI
328 dimensions and PDQ-39 sub-scores change at V1
329 (Table 2). We mainly considered TCI dimensions
330
331

Table 3
Differences of TCI dimensions scores between PDQ-39 total improvement groups at V1 ($n = 303$)

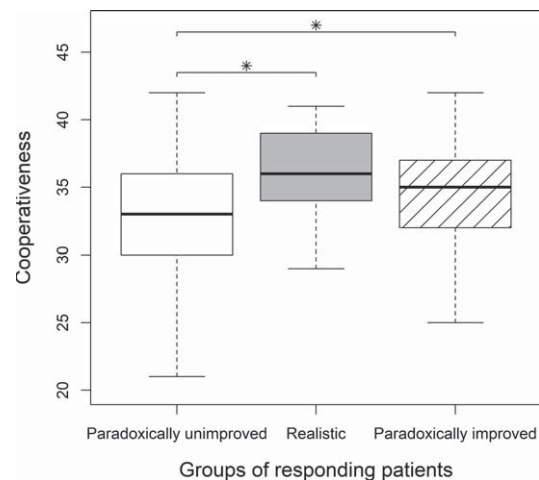
TCI dimensions	p	q	CI	Mean \pm SD	
				PDQ-39 total "improvement" group ($n = 150$)	PDQ-39 total "no improvement" group ($n = 153$)
HA4	0.03*	0.29	0; 1.0	5.4 \pm 2.0	4.7 \pm 2.4
C	0.01*	0.47	0; 2.0	34.4 \pm 4.5	33.2 \pm 4.7
C3	0.006**	0.78	0, 0.9	6.6 \pm 1.2	6.2 \pm 1.3

Mann-Whitney tests: * $p < 0.05$; ** $p \leq 0.01$; q , FDR adjusted p value; CI, confidence interval of the difference at 95% confidence level; HA4, Fatigability; C, Cooperativeness; C3, Helpfulness.



Mann-Whitney tests: * $q < 0.05$ between the "paradoxically unimproved" and "paradoxically improved" groups

Fig. 1. Differences in Reward Dependence scores between groups of responding patients.



Mann-Whitney tests: * $q < 0.05$ between the "paradoxically unimproved" and "paradoxically improved" or "realistic" groups

Fig. 2. Differences in Cooperativeness scores between groups of responding patients.

332 having the strongest association with PDQ-39 sub-
333 scores (presenting only significant FDR adjusted p
334 value that is $q \leq 0.05$) to avoid making assumption
335 about lower associations.

336 The NS1 sub-dimension and some C sub-dimens-
337 ions (C1 and C4) were significantly and negatively
338 associated with the PDQ-39 "Mobility" sub-score
339 change.

340 PD patients were separated into the PDQ-39 total
341 "improvement" ($n = 150$) and the "no improvement"
342 ($n = 153$) groups according to the MCID [20]. Among
343 the "no improvement" group, 63% of patients had
344 a no clinically relevant amelioration (that is a delta
345 PDQ-39 total score between the MCID of -4.72 and
346 0) and 37% were not ameliorated (that is a delta
347 PDQ-39 total score superior to 0). Uncorrected sig-
348 nificant differences of HA4, C and C3 scores were
349 found between the "improvement" group and the "no
350 improvement" group which did not maintain signifi-
cance with FDR correction (Table 3).

Differences between groups of responding patients ($n = 264$)

351 For this second exploratory objective, because of
352 missing data in the MDS-UPDRS-IV, only 264/303
353 PD patients were used to form the three groups of
354 responding patients according to their PDQ-39 and
355 MDS-UPDRS-IV changes: 97 patients were in the
356 "paradoxically unimproved" group, 149 in the "real-
357 istic" group, and 18 in the "paradoxically improved"
358 group.

359 Reward Dependence scores were significantly
360 higher in the "paradoxically improved" group com-
361 pared to the "paradoxically unimproved" group
362 ($q = 0.04$ and $CI = [1.0; 4.0]$) (Fig. 1). Cooperative-
363 ness scores were significantly lower in the "paradoxi-
364 cally unimproved" group compared to the "realistic"
365 and "paradoxically improved" groups ($q = 0.03$ and
366 $CI = [1.0; 3.0]$; $q = 0.04$ and $CI = [1.0; 5.0]$, respec-
367 tively) (Fig. 2).
368

Concerning the HAMA, HAMD, LARS, and MoCA changes, there were no significant differences between groups.

DISCUSSION

In this study, presurgical TCI personality dimensions such as higher Cooperativeness and Novelty Seeking sub-dimensions were associated with QoL improvement after one year of DBS-STN in PD population. This favorable outcome affected mainly the physical component of QoL (“Mobility” evolution). Secondly, patients with lower Cooperativeness scores were more paradoxically unimproved after DBS-STN: their objective motor complications improvement was not translated into QoL improvement; while patients with higher Reward Dependence scores were more paradoxically improved after DBS-STN: they had QoL improvement despite the absence of motor complications reduction.

According to the literature [1–3, 22, 23], this study reported an improvement in MDS-UPDRS and PDQ-39 scores after one year of DBS-STN and a significant reduction of dopaminergic treatments. A slight amelioration of depression and anxiety was also shown after DBS, whereas apathy and global cognition slightly deteriorated while remaining below the threshold of apathy (LARS scale) and cognitive deficit (MoCA). Thus, DBS did not affect much behavior of our PD patients which globally did not develop either anxio-depressive state or apathy or cognitive decline.

First, we confirm the results of our previous study showing that personality dimensions are associated with different QoL sub-scores before DBS-STN in PD [16].

Second, we found associations between personality dimensions and QoL improvement after one year of DBS-STN. Some Cooperativeness and Novelty Seeking sub-dimensions (C1 (Social Acceptance), C4 (Compassion), and NS1 (Exploratory Excitability)) were strongly related to the physical component of QoL (“Mobility”): PD patients with high Cooperativeness and Novelty Seeking before DBS-STN had the best QoL improvement (physical component) after DBS-STN.

Cooperativeness is a character reflecting social maturity and described as a tendency to consider and accept others [24, 25]. PD patients with higher Cooperativeness probably better listen to their relatives and believe them, which can help them to

remember their past difficulties and to realize the strong motor improvement they benefit from DBS-STN. Indeed, it is usual that PD patients forget their past difficulties after DBS and need a reminder from their relatives or caregivers to become aware of their improvements [26]. In literature, low Cooperativeness was associated with treatment-resistance in depressive patients [27], and high Cooperativeness was also linked with good QoL or life satisfaction in different populations [28–30]. Also, this hypothesis makes sense because Cooperativeness mostly impact physical QoL improvement after DBS, only part of QoL that can be assessed by patients’ relatives. Therefore, relatives probably have a more objective feeling on these improvements which may contrast with patients’ subjective one. Moreover, it is interesting to compare personality-QoL associations before and after DBS. Before, Self-Directedness (representing the individual maturity) was associated with better QoL [16]; whereas, after, Cooperativeness (social maturity) becomes associated with better QoL. This may reflect that, before surgery, PD patients were used to their disease and to their relatives’ comments because of adaptive process through chronic disease; whereas, after DBS, PD patients are confronted to abrupt changes [31] and motor improvement are often obvious. Thus, their relatives can appreciate these improvements and inform the patients, helping them to become more aware of these changes. Hence, before surgery, in case of a slowly evolving chronic disease, PD patients may rely more on their personal resources (individual maturity) to adapt and have a better QoL [16]; whereas, after DBS, they focus more on the external comments (social maturity) to adapt to the abrupt changes. It would thus be interesting to see the impact of Cooperativeness on QoL after long-time of DBS, when PD patients would have become used to these changes, with the PREDISTIM 5-year QoL evaluation.

Novelty Seeking is a temperament representing a tendency to respond positively and with excitation to new stimuli [24, 25]. It reflects good adaptability to new situations and motivation facing change. PD patients with higher Novelty Seeking may thus better adapt to the abrupt changes caused by DBS-STN and so really feel the strong motor improvement they benefit from the stimulation. In literature, higher Novelty Seeking was also associated with better global QoL and physical health in patients with schizophrenia [32].

Interestingly, Novelty Seeking and/or Cooperativeness are two personality dimensions potentially

470 implicated in placebo responses [33–35]. Therefore,
471 these two personality dimensions may enhance the
472 part of placebo effect induced by DBS-STN [36].
473 For example, the sub-dimension C3 (Helpfulness)
474 reflects solidarity and good level of team work which
475 may enhance placebo effect [37].

476 Moreover, our study has shown good associa-
477 tions between the more objective evaluation of PD
478 symptoms (MDS-UPDRS) and the subjective eval-
479 uation of PD QoL (PDQ-39). Mainly, the objective
480 motor examination, MDS-UPDRS-III, as well as the
481 motor complications assessed by the MDS-UPDRS-
482 IV, were mostly associated with physical components
483 of the PDQ-39 evaluation, assuring that both scales
484 are reliable and evaluate PD patients in the same
485 way [38]. Nonetheless, some PD patients (43.6%)
486 had a feeling of evolution after DBS-STN that differs
487 from the objective motor complications examina-
488 tion (MDS-UPDRS-IV). Indeed, eighteen patients
489 (6.8%) felt “paradoxically improved” after DBS: they
490 felt improvement of their QoL, whereas the MDS-
491 UPDRS-IV showed no improvement of their motor
492 complications. Also, ninety-seven patients (36.7%)
493 felt “paradoxically unimproved” after DBS: they did
494 not feel any improvement of their QoL, whereas the
495 MDS-UPDRS-IV showed an improvement of their
496 motor complications. This dissociation between real-
497 ity of PD symptoms improvement after DBS and PD
498 patients’ feelings has already been shown in several
499 studies [5, 6] and can be explained by differences
500 between patients’ expectations and reality, difficul-
501 ties of psychosocial adjustment, mood and behavioral
502 changes [26, 31, 39, 40], etc. Moreover, we have
503 decided to focus our analysis on discrepancy between
504 QoL evolution and MDS-UPDRS-IV change since
505 DBS preferentially improves motor complications.

506 Here, paradoxically unimproved PD patients had
507 lower Cooperativeness scores than realistic and para-
508 doxically improved ones. This result seems to be
509 congruent with our previous observation that lower
510 Cooperativeness scores before surgery lead to less
511 improvement of QoL after DBS-STN. Moreover,
512 paradoxically improved PD patients had higher
513 Reward Dependence scores than the paradoxically
514 unimproved ones. Reward Dependence temperament
515 is associated with sensitive, dependent and social
516 individuals [41]. It is a system facilitating condi-
517 tioning to reward stimuli [25] and therefore may
518 be associated with placebo effect. Indeed, some
519 studies have found associations between higher
520 Reward Dependence scores and better outcomes
521 after interpersonal therapy [42] or antidepressants

522 [43]. Moreover, treatment adherence was shown to
523 be related to higher Reward Dependence tempera-
524 ment in a weight-loss therapy, probably thanks to
525 better collaborative relationship with the clinicians
526 [44]. Nonetheless, these differences between realis-
527 tic, paradoxically improved or unimproved patients
528 could not be explained by differences in cognitive or
529 behavioral changes after DBS-STN.

530 This study has some limits. Being the first study on
531 this subject, only analyses of associations between
532 QoL outcomes and personality dimensions were
533 done. Thus, our results are not predictive but rather
534 suggestive. Hence, they should be used in order to
535 prevent disappointment of PD patients after DBS-
536 STN (not to select PD patients for DBS) acting in two
537 ways: 1) by supporting them upstream and explain-
538 ing them at best what they should expect of DBS, and
539 2) by preparing and encouraging their relatives to be
540 really present with the patients after the operation to
541 enhance their cooperation (which seems to facilitate
542 their positive outcomes). Additionally, our models
543 explaining less than ten percent of the variance (R^2)
544 of QoL improvement after DBS-STN, we are aware
545 that personality dimensions are not enough to guar-
546 anty PD patients’ QoL improvement after stimulation
547 and that other variable are needed to explain at best
548 QoL outcome after surgery. However, our focus being
549 concentrated on personality dimensions’ evaluation,
550 we did not look for other potential predictive variables
551 as it will be the aim of the main PREDI-STIM study.
552 Finally, only personality dimensions before DBS
553 were evaluated (there was no re-evaluation of person-
554 ality after stimulation), and it remains possible that
555 some personality dimensions evolve after DBS. Even
556 if temperaments are not supposed to change with
557 time [9], personality in PD patients seems to evolve
558 with the disease course particularly with the intro-
559 duction of dopaminergic treatments [45]. DBS could
560 also impact personality as shown by some studies
561 [46–50]. In any case, our aim was to find “predic-
562 tive” factors of QoL improvement after DBS. Thus,
563 even if personality changes after stimulation, it is not
564 supposed to affect our results. Lastly, our three groups
565 of responding PD patients (“paradoxically unim-
566 proved”, “realistic” and “paradoxically improved”) were
567 done according to their motor complications
568 improvement (reflected by MDS-UPDRS part-IV)
569 since it is the main purpose of DBS-STN action.
570 Nonetheless, improvements of non-motor symptoms
571 (pain, fatigue etc.) were not accounted in these anal-
572 yses, although non-motor symptoms can benefit of
573 DBS-STN [51] and are best predictors of QoL in PD

[52], because we were interested in more objective assessments than MDS-UPDRS parts I and II. Moreover, we are aware that using MCIDs to classify into groups of “improvement” or “no improvement” may not precisely reflect the evolution of patients after DBS, mainly since at this stage of motor fluctuations a change of 0.9 points in the MDS-UPDRS part-IV may not be sufficient to be clinically significant. Nonetheless, the choice of this MCID was done accordingly with literature. Ultimately, we are aware that there are other models of personality that could have been explored in this study to depict a more complete exploration of personality associated with QoL. Nonetheless, the TCI being a long questionnaire, we thought that using a multilayer approach (through different personality investigations) would have been too complex in clinical practice and too tiring for the PD patients.

In conclusion, PD patients with higher Cooperativeness and Novelty Seeking scores at baseline seem to have the best QoL outcome after one year of DBS-STN in the physical component of QoL. A tendency of being more trustful towards relatives and more motivated by changes could explain the ability of these PD patients to feel a better QoL improvement following the abrupt changes after surgery. Moreover, PD patients with low Cooperativeness were more paradoxically unimproved after DBS, whereas PD patients with high Reward Dependence were more paradoxically improved after DBS. Therefore, systematic TCI examination could be proposed as standard evaluation before DBS. Subsequently, according to PD patients’ scores at the Novelty Seeking and Cooperativeness dimensions, specific educational programs should be proposed to patients with higher risk of QoL unimprovement after DBS to prepare them at best for the stimulation. For this, we are now looking for cut-off scores for these dimensions.

ACKNOWLEDGMENTS

The study was funded by the France Parkinson charity and French Ministry of Health (PHRC national 2012). This is an ancillary study to Protocol ID: 2013-A00193-42; ClinicalTrials.gov: NCT02360683.

We thank all participants for their cooperation, and Déborah Meline from ToNIC (Toulouse NeuroImaging Center–INSERM, University of Toulouse III) for her reflection. The authors are also grateful

for support from the French clinical research network NS-Park/F-Crin and the Fédération de la Recherche Clinique du CHU de Lille (with Anne-Sophie Rolland, Alain Duhamel, Maeva Kheng, Julien Labreuch, Dominique Deplanque, Edouard Millois, Nolwen Dautrevaux, Victor Laugeais, Maxime Cailier, Aymen Aouni, Pauline Guyon, Francine Niset, Valérie Santraine, Marie Pleuvret, Julie Moutarde and Laetitia Thibault).

We also thank all the members of the PREDI-STIM study group: Dr Caroline Moreau, Pr Luc Defebvre, Dr Nicolas Carriere, Dr Guillaume Grolez, Dr Guillaume Baille, Dr Kreisler, Pr Jean-Pierre Pruvo, Pr Leclerc, Dr Renaud Lopes, Dr Romain Viard, Dr Gregory Kuchcinski, Mr Julien Dumont, Pr Kathy Dujardin, Mme M Delliaux, Mrs M Brion, Dr Gustavo Touzet, Pr Nicolas Reyns, Pr Arnaud Delval, Mrs Valerie Santraine, Mrs Marie Pleuvret, Mrs Nolwen Dautrevaux, Mr Victor Laugeais, Thavarak Ouk, Camille Potey, Celine Leclercq and Elise Gers (for Lille University Hospital); Jean-Christophe Corvol, Marie-Vidailhet, Elodie Hainque, Marie-Laure Welter, Lucette Lacomblez, David Grabli, Emmanuel Roze, Yulia Worbe, Cécile Delorme, Hana You, Jonas Ihle, Raquel Guimeraes-Costa, Florence Cormier-Dequaire, Aurélie Méneret, Andréas Hartmann, Louise-Laure Mariani, Stéphane Lehericy, Virginie Czernecki, Fanny Pineau, Frédérique Bozon, Camille Huiban, Eve Benchetrit, Carine Karachi, Soledad Navarro, Philippe Cornu, Arlette Welaratne, Carole Dongmo-Kenfack, Lise Mantsi, Nathalie Jarry, Sophie Aix and Carine Lefort (for the AP-HP, Paris); Dr Tiphaine Rouaud, Pr Philippe Damier, Pr Pascal Derkinderen, Dr Anne-Gaelle Corbille, Dr Elisabeth Calvier-Auffray, Mrs Laetitia Rocher, Mrs Anne-Laure Deruet, Dr Raoul Sylvie, Dr Roualdes Vincent and Mrs Le Dily Séverine (for Nantes University Hospital); Dr Ana Marques, Dr Berangere Debilly, Pr Franck Durif, Dr Philippe Derost, Dr Charlotte Beal, Carine Chassain, Laure Delaby, Tiphaine Vidal, Pr Jean Jacques Lemaire, Isabelle Rieu and Elodie Durand (for Clermont-Ferrand University Hospital); Pr Alexandre Eusebio, Pr Jean-Philippe Azulay, Dr Tatiana Witjas, Dr Frédérique Fluchère, Dr Stephan Grimaldi, Pr Nadine Girard, Eve Benchetrit, Marie Delfini, Dr Romain Carron, Pr Jean Regis, Dr Giorgio Spatola and Camille Magnaudet (for the AP-HM, Marseille); Dr Ansquer Solène, Dr Benatru Isabelle, Dr Colin Olivier, Pr Houeto JL, Pr Guillevin Remy, Mrs Fradet Anne, Mrs Anziza Manssouri, Mrs Blondeau Sophie, Dr Richard Philippe, Dr Cam Philippe, Dr Page Philippe, Pr

- 675 Bataille Benoit, Mrs Rabois Emilie and Mrs Guille-
676 main Annie (for Poitiers University Hospital); Dr
677 Drapier Sophie, Dr Frédérique Leh, Dr Alexandre
678 Bonnet, Pr Marc Vérin, Dr Jean-Christophe Ferré,
679 Mr Jean François Houvenaghel, Pr Claire Haegen-
680 len, Mrs Françoise Kestens and Mrs Solenn Ory
681 (for Rennes University Hospital); Pr Pierre Burbaud,
682 Dr Nathalie Damon-Perriere, Pr Wassilios Meiss-
683 ner, Pr Francois Tison, Dr Stéphanie Bannier, Dr
684 Elsa Krim, Pr Dominique Guehl, Sandrine Molinier-
685 Blossier, Morgan Ollivier, Marion Lacoste, Nicolas
686 Auzou, Marie Bonnet, Pr Emmanuel Cuny, Dr Julien
687 Engelhardt, Olivier Branchard, Clotilde Huet and
688 Julie Blanchard (for Bordeaux University Hospital);
689 Pr Rascol Olivier, Dr Christine Brefel Courbon, Dr
690 Fabienne Ory Magne, Dr Marion Simonetta Moreau,
691 Pr Christophe Arbus, Pr Fabrice Bonneville, Dr Jean
692 Albert Lotterie, Marion Sarrail, Charlotte Scotto
693 d'Apollonia, Pr Patrick Chaynes, Pr François Caire
694 and Estelle Harroch (for Toulouse University Hos-
695 pital); Pr David Maltete, Dr Romain Lefaucheur,
696 Dr Damien Fetter, Dr Nicolas Magne, Mrs San-
697 drine Bioux, Mrs Maud Loubeyre, Mrs Evangéline
698 Bliiaux, Mrs Dorothée Pouliquen, Pr Stéphane Der-
699 rey, Mrs Linda Vernon and Dr Frédéric Ziegler
700 (for Rouen University Hospital); Mathieu Anheim,
701 Ouhaïd Lagha-Boukbiza, Christine Tranchant, Odile
702 Gebus, Solveig Montaut, S Kremer, Nadine Long-
703 gato, Clélie Phillips, Jimmy Voirin, Marie des Neiges
704 Santin, Dominique Chaussemy and Dr Amaury
705 Mengin (for Strasbourg University Hospital); Dr Car-
706 oline Giordana, Dr Claire Marsé, Lydiane Mondot,
707 Bruno Giordana, Robin Kardous, Bernadette Bailet,
708 Héloïse Joly, Denys Fontaine, Dr Aurélie Lepus,
709 Amélie Faustini and Vanessa Ferrier (for Nice Uni-
710 versity Hospital); Pr Pierre Krystkowiak, Dr Mélissa
711 Tir, Pr Jean-Marc Constans, Sandrine Wannepain,
712 Audrey Seling, Dr Michel Lefranc, Stéphanie Blin
713 and Béatrice Schuler (for Amiens University Hos-
714 pital); Pr Stephane Thobois, Dr Teodor Danaïla, Dr
715 Chloe Laurencin, Pr Yves Berthezene, Dr Roxana
716 Ameli, Helene Klinger, Dr Gustavo Polo, Patrick
717 Mertens, A Nunes and Elise Metereau (for Lyon
718 University Hospital); Dr Lucie Hopes, Dr Solène
719 Frismand, Dr Emmanuelle Schmitt, Mrs Mylène
720 Meyer, Mrs Céline Dillier, Pr Sophie Colnat and
721 Mrs Anne Chatelain (for Nancy University Hospi-
722 tal); Dr Jean- Philippe Brandel, Dr Cécile Hubsch,
723 Dr Patte Karsenti, Dr Marie Lebouteux, Dr Marc
724 Ziegler, Dr Christine Delmaire, Dr Julien Savatowky,
725 Mrs Juliette Vrillac, Mrs Claire Nakache, Dr Vin-
726 cent D'Hardemare and Mr Lhaouas Belamri (for the
Rotschild fondation of Paris); Dr Philippe Gravelau,
Dr Camille Decroq, Dr Frédéric Bourdain, Dr Vadim
Afanassiev, Dr Anne Boulin, Mrs Elodie Dupuy, Dr
Bérénice Gardel, Pr Béchir Jarraya, Mrs Delphine
Lopez and Mr Christophe Fruit (for the Foch Hos-
pital of Paris-Saclay University); David Gay, Robin
Bonichel, Fouzia El Mountassir, Clara Fischer, Jean-
François Mangin, Marie Chupin and Yann Cointepas
(for CATI (MRI acquisition management, prepro-
cessing and data management)); Bertrand Accart,
Patrick Gelé, Florine Fievet, Matthieu Chabel, Vir-
ginie Derenaucourt, Loïc Facon, Yanick Tchanchou
Njosse and Dominique Deplanque (for CRB of
Lille (Center of Biological Resources)); and Alain
Duhamel, Lynda Djemmane and Florence Duflot (for
Data management of Lille).
- CONFLICT OF INTEREST**
- The authors have no conflict of interest to report.
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