



Personality Assessment with Temperament and Character Inventory in Parkinson's Disease.

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Personality assessment with Temperament and Character Inventory in Parkinson's Disease

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Abstract

Introduction: There is a growing interest in personality evaluation in Parkinson's disease (PD), following observations of specific temperaments in PD patients. Therefore, our objective was to evaluate personality dimensions from the Temperament and Character Inventory (TCI) in a cohort of fluctuating PD patients considered for deep brain stimulation.

Methods: Fluctuating PD patients from the PREDISTIM cohort were included. Description of TCI dimensions and comparison with a French normative cohort were performed. Pearson correlations between TCI dimensions and motor, behavioral and cognitive variables were investigated. Structural and internal consistency analysis of the TCI were further assessed.

Results: The 570 PD patients presented significant higher scores in Harm Avoidance, Reward Dependence, Persistence, Self-Directedness and Cooperativeness and significant lower scores in Self-Transcendence compared to the French normative cohort; only Novelty Seeking scores were not different. Harm Avoidance and Self-directedness scores were correlated with PDQ-39 total, HAMD, HAMA scores, and anxiolytic/antidepressant treatment. Novelty Seeking scores were correlated with impulsivity. Pearson correlations between TCI dimensions, principal component analysis of TCI sub-dimensions and Cronbach's alpha coefficients showed adequate psychometric properties.

Conclusion: The TCI seems to be an adequate tool to evaluate personality dimensions in PD with good structural and internal consistencies. These fluctuating PD patients also have specific personality dimensions compared to normative French population. Moreover, Harm Avoidance and Self-Directedness scores are associated with anxio-depressive state or quality of life and, and Novelty Seeking scores with impulsivity.

Keywords:

Parkinson's Disease; Temperament and Character Inventory; Personality; Fluctuating PD patients

Introduction

In the context of personalized medicine¹, personality dimensions may represent factors to consider in Parkinson's disease (PD).

Earlier studies have often depicted PD patients as mentally rigid, introvert and cautious² with an anxious, reflective and reserved temperament³. More recently, many studies have focused on personality in PD with a more quantitative approach using validated scales to access personality dimensions⁴⁻⁷. Among them, the Temperament and Character Inventory (TCI), a personality scale developed by Cloninger, has shown particular interest in PD as summarized in a recent review⁸. This review has revealed that PD patients had lower Novelty Seeking and higher Harm Avoidance scores compared to control populations⁸. Therefore, PD patients seem to have specific personality dimensions which could be predictive to PD development⁶ and might evolve along the course of the disease⁹.

The assessment of PD personality is also interesting to understand how it could affect Quality of Life (QoL)¹⁰ and QoL improvement after different therapeutic strategies such as Deep Brain Stimulation of the Sub-Thalamic Nucleus (DBS-STN)¹¹. Moreover, it has been suggested that PD personality could be modified after DBS-STN¹² and could influence patients' indication among second line treatments for advanced PD.

Nevertheless, all these studies had been carried out on small numbers and/or at very different stages of PD patients : De Novo PD patients (never medicated)⁵, PD patients in early stages with mild symptoms⁸ and PD patients with motor fluctuations^{9,10}. While normative TCI data were already proposed on different samples (psychiatric¹³, epileptic¹⁴ patients, normative populations from France¹⁵ etc.), to our knowledge, none were ever presented on a cohort of PD patients to be used as reference.

The primary objective of this study is to describe and analyze TCI personality dimensions from a cohort of 570 PD patients at the stage of motor fluctuations compared to a French normative population¹⁵. As secondary objective, we address the psychometric qualities of this instrument in this PD population. Our working hypothesis were that PD patients present a specific personality which may change at different stages of the disease, and that these personality specificities could be correctly addressed with the TCI.

Materials and methods

This study is an ancillary analysis 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.

Standard Protocol Approvals, Registrations, and Patient Consents

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 (N° IDRCB: 2013 A0019342) and registered in the ClinicalTrials.gov website (NCT02360683).

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.

Patients

Briefly, PD patients with motor fluctuations awaiting DBS-STN were consecutively included into the study between 11/2013 and 09/2019. Inclusion criteria were a diagnosis of PD according to the UKPDSBB, disease duration ≥ 5 years, age between 18 and 75 years and indication of DBS-STN. Exclusion criteria were atypical parkinsonism, severe cognitive impairment, severe psychiatric disorders, levodopa motor response $< 30\%$ and contra-indications to surgery.

Study design and clinical measures

The whole PREDI-STIM study design is presented elsewhere in previous articles^{9,10}.

As part of our ancillary study, personality questionnaire TCI was added to evaluation at baseline (before DBS-STN).

The TCI, an auto-questionnaire developed by Cloninger according to his psycho-biosocial model of personality¹³, is formed of seven personality dimensions divided into four temperaments (Novelty Seeking (NS), Harm Avoidance (HA), Reward Dependence (RD) and

Persistence (P)) and three characters (Self-Directedness (SD), Cooperativeness (C) and Self-Transcendence (ST))¹³.

According to the original model, temperaments are supposed to be genetically homogeneous, independent and stable dimensions of personality, and rely on specific cerebral activities¹³. Novelty Seeking reflects the behavioral activation system in response to novelty stimuli. Harm Avoidance depends on the behavioral inhibition system responding to frustration and punishing signals. The two last temperaments reflect the behavioral maintenance system in absence of continuous reinforcement with a sensibility to social approbation stimuli reflected in the Reward Dependence dimension, and a dimension of perseverance despite frustration named Persistence.

Concerning characters, they reflect the degree of maturity and adaptation¹³. They are dependent of the environment and of conceptual socio-cultural learning through life. Therefore, they are less stable during time. They translate individual differences about objectives and values that would affect intentions, actions and feelings. Self-Directedness represents individual maturity (personal integrity, self-esteem, efficacy etc.), Cooperativeness social maturity (compassion, conscious of others etc.) and Self-Transcendence spiritual maturity (feelings of mysticism, religious believes etc.).

Except for the Persistence, each dimension is divided into several sub-dimensions (Novelty Seeking and Harm Avoidance, n=4; Reward Dependence and Self-Transcendence, n=3; and Self-Directedness and Cooperativeness, n=5). The TCI is so formed of 226 true/false questions to obtain a score for each of the seven dimensions of personality (NS, HA, RD, P, SD, C and ST) and their sub-dimensions.

As previously described¹⁰, we have determined an imputation method for TCI missing data, with an expert committee consisting of neurologists, biostatisticians and psychiatrists (eFigure1).

Statistical analyses

Description of the TCI in a Parkinson's disease population

Descriptive analyses of PD population and TCI dimensions and sub-dimensions were done (mean, standard deviation and range) for the whole population and according to gender. Gender

differences in TCI dimensions and sub-dimensions were analyzed by regression linear models adjusted by age.

One-sample Wilcoxon tests were used for each TCI dimension for comparisons of the study population with the French normative cohort¹⁵: firstly using mean TCI scores from the full cohort ($n=602$, mean age of 46.5 ± 17.7), secondly using mean TCI scores from the elderly group of the cohort ($n=256$, aged 50-88). The 95% confidence intervals (CI95) were also calculated. A non-overlap between the CI95 was considered as a true difference between populations.

Medians and quartiles of the TCI dimensions and sub-dimensions were analyzed. Median was used as cut-off scores to classify patients into temperament types : eight temperament types being determined according to combination between low/high scores relatively to the median scores of the population in the first three temperament (Novelty Seeking, Harm Avoidance and Reward Dependence)¹³. Mature versus immature personalities were also classified: sum of Self-Directedness and Cooperativeness scores in the lowest quarter of the distribution of the whole sample, representing an immature personality. The temperament types were described first in all PD patients and then in the subgroup of patients with an immature personality. The CI95 of temperament types proportion were calculated and used for comparison to the French normative cohort.

Correlations between TCI dimensions and Parkinson's disease variables

For quantitative variables, Pearson correlations between TCI dimensions (and sub-dimensions, only if total dimension was significant) and several variables (age, disease duration, PDQ-39 total score, total LED (Levodopa Equivalent Dosage¹⁶) and LED of dopamine agonists were done on the whole population and separately by sex. Pearson correlations between TCI dimensions and motor, cognitive and behavioral variables related to PD were also tested: anxiety (HAMA : Hamilton Anxiety Rating Scale), depression (HAMD : Hamilton Rating Scale for Depression), apathy (LARS : Lille Apathy Rating Scale), parts I, II-ON, II-OFF, III-ON, III-OFF and IV of the MDS-UPDRS (Movement Disorder Society-Unified Parkinson's Disease Rating Scale, cognitive deficit (MoCA : Montreal Cognitive Assessment), and impulsivity ("positive urgency", "urgency", "lack of premeditation", "lack of perseverance" and "sensation seeking" from the UPPS-P scale (Urgency-Premeditation-Perseverance-Sensation seeking-Positive urgency)).

For qualitative variables, we used two-sample Mann-Whitney tests to compare TCI dimensions scores between groups: presence vs absence of any compulsive disorders from the QUIP scale (Questionnaire for Impulsive-Compulsive Disorders in PD), and treatment by psychotropic drugs (anxiolytics, antidepressants or clozapine) or analgesics vs absence of such treatments.

Psychometric qualities of the TCI

We analyzed psychometric proprieties of the TCI using : Pearson correlations between all seven TCI dimensions; Principal Components Analyses (PCA) separately for the four temperaments and the three characters to explore the structure of the TCI, using a varimax transformation of data^{15,17}, and selecting only components with an eigen value superior to 1. Cronbach's alpha coefficients were also calculated for each dimension and sub-dimension from responses to items, to assess internal consistency: Cronbach's alpha coefficients superior to 0.65 were considered relevant of a high internal consistency.

Because of multiple analysis, a Bonferroni correction was applied for seven comparisons (each TCI dimension): significant threshold of $p.value < 0.0071$; and only correlations with a Pearson coefficients of correlation (pcc) superior to absolute 0.3 were considered as relevant.

Analyses were proceeded on R Studio Software Version 1.1.456.

Data availability

Concerning data availability, the data used in this study is not our individual propriety. It comes from the cohort of a multicentric study. Therefore, the data can only be available upon request to Research and Innovation unit of Lille University Hospital Center (David Devos: David.DEVOS@chru-lille.fr), once all the data has been analyzed.

Results

Our PD population included 570 patients: 376 men (66%) and 194 women (34%). Patients were 60.4 ± 7.2 years old with a mean disease duration of 9.9 ± 4.0 years and a LED of 1423.6 ± 622.4 mg/day (Table 1). Age was significantly higher in women ($P < 0.001$).

Description of the TCI in a Parkinson's disease population

A description of all dimensions and sub-dimensions' scores of the TCI is presented in Table 2, with gender differences adjusted by age. Harm Avoidance, Reward Dependence and Cooperativeness scores were significantly higher in women.

Compared to the full French normative cohort ($n=602$), our PD patients presented significant higher scores in Harm Avoidance, Reward Dependence, Persistence, Self-Directedness and Cooperativeness and significant lower scores in Self-Transcendence; only Novelty Seeking scores were not different (Table 3). Compared to the elderly group of the French normative cohort ($n=256$), our PD patients presented significant higher scores in Novelty Seeking, Reward Dependence, Persistence, Self-Directedness and Cooperativeness and significantly lower scores in Self-Transcendence; only Harm Avoidance scores were not different (Table 3).

Description of median and quartiles for all TCI dimensions is presented in eTable 1. Cut-off scores for low vs high temperaments scores were assigned relatively to the median (16 for Novelty Seeking, 18 for Harm Avoidance and 16 for Reward Dependence) to classify patients into temperament types (eTable 2). In addition, immature personality was set for patients in the lowest quarter of the Self-Directedness plus Cooperativeness distribution, that is below 62. In this PD population, we found a homogeneous distribution in the eight types of temperament with a prevalence from 6.8% to 17.2%. The immature character varies from 0.4% to 6.7% in the whole population (eTable 2). In the whole PD population, prevalence of "Explosive" temperament type was superior, while prevalence of "Passive-dependent" temperament type was inferior in comparison to the French normative cohort²⁸ (Figure 1). In PD immature subgroup, only prevalence of "Passive-dependent" temperament type was inferior.

Correlations between TCI dimensions and Parkinson's disease variables

There were no correlations between TCI dimensions scores and age or disease duration or total LED or the LED of dopamine agonists.

We found significant correlations between PDQ-39 Total score and TCI dimensions (eTable 3): positive correlations for Harm Avoidance and negative correlations for Self-Directedness.

Correlations with motor, cognitive and behavioral variables are presented in eTable 4. We found only relevant correlations with behavioral parameters: HAMA and HAMD scores were positively correlated with Harm Avoidance and negatively with Self-Directedness; “Positive urgency” and “urgency” parts of the UPPS-P were negatively correlated with Self-Directedness. “Lack of premeditation” part of the UPPS-P was positively correlated with Novelty Seeking. Motor and cognitive scales (LARS, MDS-UPDRS and MoCA scales) showed no relevant correlations with any TCI dimensions.

Novelty Seeking was found significantly higher in PD patients with any confounded compulsive disorders (eTable 5). Concerning the use of psychotropic drugs patients treated by anxiolytics or antidepressants or analgesics had significantly higher Harm Avoidance scores than untreated patients (eTable 5). No TCI differences were found between groups of patients treated or not by clozapine.

Psychometric qualities of the TCI

Pearson correlations between each TCI dimensions are presented in eTable 6. Significant notable correlations ($p_{cc} > 0.30$) were found between Novelty Seeking and Harm Avoidance (negative), Harm Avoidance and Self-Directedness (negative), Reward Dependence and Cooperativeness (positive), and Self-Directedness and Cooperativeness (positive).

The principal component analysis of the temperaments sub-dimensions identified three factors with an eigen value superior to 1 (eTable 7) which accounted for 51% of the variance of the temperaments sub-dimensions' scores. They corresponded to the main dimensions, except for the Persistence, negatively associated with the Novelty Seeking factor.

The principal component of the characters' sub-dimensions also allowed the identification of three factors with an eigen value superior to 1 which accounted for 52% of the variance of the characters' sub-dimensions' scores (eTable 8). They corresponded to the main dimensions, except for the SD4, moderately associated with the three factors.

Analysis of Cronbach's alpha coefficients showed that all dimensions had high coefficients (>0.65) except the Persistence (0.44) (Table 2).

Discussion

This is the first study which formally describe TCI personality dimensions in a PD population of 570 patients. At this stage of the disease, PD patients had many differences in personality dimensions compared to the French normative population¹⁵ but no real differences in distribution of temperament types. Several disease-related characteristics such as duration, motor status and LED (total or dopamine agonists) were not associated with personality dimensions. Only behavioral variables (depression, anxiety and impulsivity) were correlated to some TCI dimensions. Finally, evaluation of psychometric qualities of the TCI have shown that they were relatively well preserved in this PD population, making the TCI an accurate instrument to evaluate personality dimensions in PD patients.

Description of the TCI in a Parkinson's disease population

As in mostly previous studies¹⁸, higher Harm Avoidance and Reward Dependence scores were found in women compared to men in this PD population. Cooperativeness scores were also found higher in women in our PD population as in some normative samples^{15,17}. Hence, gender differences in personality dimensions seem to be conserved in PD population. However, no significant correlation was found between age and Novelty Seeking in our PD population, unlike many studies^{13,15}, probably due to older age and lower age variability in our population.

Then, we use a French normative cohort¹⁵ to discuss the impact of PD on personality dimensions in a culturally similar population. We found personality differences between our PD population and the whole French normative cohort in most TCI dimensions. Harm avoidance, Reward Dependence, Persistence, Self-Directedness and Cooperativeness scores were higher in PD patients, while Self-Transcendence scores were lower. When compared to the elderly group of the normative cohort, there was no more difference in Harm Avoidance but Novelty Seeking scores were higher in PD patients. These results are in accordance with outcomes from our previous study on a smaller patients sample⁹. The differences in Harm Avoidance could be due to the age of the control group only. Indeed, Santangelo et al. using a younger group of healthy volunteers compared to their group of PD patients⁸, also reported higher Harm Avoidance scores in PD patients, as well as a recent study on De Novo PD patients who scored higher on Harm Avoidance compared to two French-speaking populations¹⁹. In the meta-analysis, Novelty seeking was also reported significantly different from healthy

volunteers⁸. Hence, the surprising higher Novelty Seeking scores in our PD population (as opposed to the usual lower Novelty Seeking scores from the literature^{8,19}) may be due to the advanced stage of PD in our population⁹ and to the dopaminergic treatment. We found the same results in a previous study comparing a smaller sample of fluctuating PD patients with De Novo patients without any treatment⁹. Moreover, the presence of impulsivity and gambling disorders was also associated with higher Novelty Seeking scores²⁰. In the same idea, the higher scores in Reward Dependence and Persistence in our fluctuating PD patients may be explained by the advanced stage of our population compared to De Novo PD patients¹⁹.

Therefore, this study confirms the fact that the personality of PD patients can evolve over time. In the early stage (De Novo PD patients), low Novelty Seeking scores and high Harm Avoidance scores are observed, thus patients would be more reserved and anxious^{8,19}; whereas at a more advanced stage (motor fluctuations stage), PD patients are more impulsive, anxious, sensitive and perfectionist (as observed with higher scores in Novelty Seeking, Harm Avoidance, Reward Dependence and Persistence) (Boussac et al, 2021; and present study). This highlights the importance of assessing the personality of PD patients according to the stage of disease progression.

We think that this personality change at different stages of the disease is a possible consequence of the evolution of PD (lesional damage) or the introduction of dopaminergic treatments⁹, even if we were unable to confirm our hypothesis because of the absence of correlations between TCI personality dimensions and the LED (total or dopamine agonists). Nonetheless, this could be due to the high dose of LED in all our PD patients: maybe solely the introduction of dopaminergic treatments acts on personality dimensions and it is not dose-dependent.

Regarding temperament types of personality, it is important to keep in mind that this classification is not supposed to represent personality disorders. It only reflects a tendency of personality which is a particular way of communication present in every individual. By contrast, an immature personality could be evocative of a personality disorder. In fact, immaturity character highlights the potential “pathologic” disposition of the associated temperament type²¹.

Temperament types were relatively well distributed in the whole PD population with a maximum of 17.2% of patients in the “Antisocial” type and a minimum of 6.8% of patients in the “Passive-aggressive” type (eTable 2). Only “Explosive” and “Passive-dependent” types seem to be different from the normative population with more “Explosive” and less “Passive-dependent” types in the PD population.

In the PD immature subgroup, only a tendency of less “Passive-dependent” temperament was observed that could be representative of a lower prevalence of this personality disorder in our PD population. Nonetheless, on the whole population, only 23.9% of our PD patients were considered having an immature personality (low individual and social maturities) which was similar to the French normative sample (with 23.8% of “immature” subjects). Therefore, even if personality dimensions are different in PD patients, it seems that there are not many differences in terms of temperament types and immature character between PD population and normative one suggesting the lack of personality disorder in PD.

These findings indicate that PD patients do not seem to have specific personality profiles or personality disorders compared to a normative population, despite some differences in some specific personality dimensions.

Correlations between TCI dimensions and Parkinson’s disease variables

Factors directly related to PD (disease duration, LED (total or dopamine agonists), motor symptoms, apathy and cognition) were not associated with any TCI personality dimensions. Similarly, in the literature, personality (evaluated by several scales) was not correlated with most clinical parameters (Hoehn-Yarh stage, UPDRS, disease duration)^{4,5,22,23}. Only the severity of bradykinesia was found to be correlated with higher Harm Avoidance scores in one study⁴, and in De Novo PD patients, positive correlations between Harm Avoidance and MDS-UPDRS parts I, IB and II were found¹⁹. Significance was also found in our study for these correlations (eTable 4) but with a coefficient too low to be considered relevant. Concerning dopaminergic treatments, LED was found to be associated with lower “Extraversion” and “Openness to Experience” scores from the Big Five Model of personality²², while another study did not find any differences on the TPQ (Tridimensional Personality Questionnaire) between medicated and unmedicated PD patients⁴.

By contrast, several behavioral parameters were correlated with personality dimensions, as found in the De Novo PD population¹⁹.

As in previous studies about gambling disorders²⁴, impulsivity towards enthusiasm or contrariety (*“positive urgency” and “urgency” parts of the UPPS-P*) was correlated with lower Self-Directedness scores; whereas decision-making reflection (*“lack of premeditation” part of*

the UPPS-P scale) was correlated with lower Novelty Seeking scores. This seems coherent since Novelty Seeking investigates impulsive personality and lack of premeditation corresponds to individuals which act impulsively despite consequences. Also, since Self-Directedness reflects the ability to adapt and regulate behavior, high Self-Directedness can therefore limit impulsivity in response to emotions' experience. Conversely, low Self-Directedness is associated with deficit in emotion regulation which was associated with "negative urgency" in eating disorder symptomatology²⁵. Moreover, "urgency" and "lack of premeditation" have been shown to be associated with gambling behaviors²⁶, which we also found associated with higher Novelty Seeking scores in our PD population. Indeed, PD patients with impulsive control disorders (such as gambling, buying, eating, or addiction to medication use evaluated by the QUIP scale) had higher Novelty Seeking and lower Self-Directedness scores for buying and eating compulsion. This highlights the importance of Novelty Seeking focus on PD populations since impulsivity is part of PD and can result from dopaminergic treatments.

Depression (*HAMD*) and anxiety (*HAMA*) were positively correlated with Harm Avoidance and negatively with Self-Directedness. Depressed and anxious PD patients have therefore higher Harm Avoidance scores⁴ and lower Self-Directedness scores. On one hand, this can be explained by the close relationship between Harm Avoidance and the serotonin neurotransmitter associated with depression²⁷. On the other hand, high Self-Directedness, reflecting the ability to adapt and regulate behavior¹³, may be a character protecting against the development of depression²⁸. Similar correlations were found for anxiety. These associations are still not specific to PD patients, as they were found in other anxiety and depressive disorders as well as in general population^{27,29}.

In addition, patients treated by anxiolytics, antidepressants and analgesics had higher Harm Avoidance scores compared to patients not treated by these drugs, while neuroleptics had no impact on personality dimensions.

As expected, based on our previous study¹⁰, QoL was associated with personality dimensions in PD patients. Indeed, significant correlations were found between PDQ-39 Total score and Harm Avoidance and Self-Directedness: better QoL of PD patients with motor fluctuations is associated with higher Self-Directedness (individual maturity) and lower Harm Avoidance (less anxiety/depression²⁷).

Hence, Harm Avoidance and Self-Directedness seem closely related in opposite way³⁰. Indeed, most of variables which were found correlated to Harm Avoidance were also correlated with Self-Directedness in opposite ways: correlations with HAMA, HAMD, and PDQ-39 Total scores. Following these findings, a triangular link between QoL, anxio-depressive state, Harm Avoidance/Self-Directedness could be proposed: these two personality dimensions may modulate anxio-depressive state which in turn regulates PD patients' QoL.

Psychometric qualities of the TCI

Concerning psychometric qualities of the TCI, detailed results will not be discussed here because our aim was not to re-validate the TCI questionnaire.

Mainly, the psychometric analyses from the French normative population¹⁵ were confirmed in our PD population. This confirms that the structure of TCI seems to be as relevant for PD patients as for normative subjects. Therefore, TCI can be used in a PD population.

Limitations

The main limitation is due to the demographic characteristics of our PD population. We assessed the personality of a subgroup of PD patients: PD patients with motor fluctuations awaiting DBS-STN, an invasive surgical treatment that could temporarily disturb PD patients' affects. This specific population may not be representative of the general PD population, especially because personality dimensions might evolve through the course of the disease⁹. The second limitation results from the comparison of our data with the mean values of the normative population. Even though we used confidence interval, we cannot formally conclude that PD patients have a specific personality although strongly suggested by our results.

In conclusion, this study explores, in a large cohort of PD patients, the reliability of TCI measurements, which is needed in view of the growing interest in personality studies in PD. TCI seems to be adapted to PD populations. Indeed, results from our structural and internal consistency analyses were good and specific factors associated with PD (motor symptoms, LED, disease duration etc.) were not related with any TCI dimensions. Anxio-depressive state

and QoL were associated with Harm Avoidance and Self-Directedness scores, and behavioral symptoms (impulsivity and gambling disorders) with Novelty Seeking scores.

Thus, the influence of personality on the responses of pharmacological and surgical treatments and complementary therapy could be analysed with the TCI to move towards personalized medicine. Specifically, personality dimensions could be used as predictive factor of subjective therapeutic responses, such as QoL amelioration after different interventions¹¹.

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Tables

Table 1. Description of Parkinson's disease population

Variables	Total (n=570) Mean \pm SD	Men (n=376) Mean \pm SD	Women (n=194) Mean \pm SD
Age (<i>in years</i>)	60.4 \pm 7.2	59.6 \pm 7.4	61.8 \pm 6.7
Disease duration (<i>in years</i>)	9.9 \pm 4	9.8 \pm 4.1	10.1 \pm 3.7
Total LED V0 (<i>in mg/day</i>)	1423.6 \pm 622.4	1478.6 \pm 656.4	1317.7 \pm 537.0
LED of dopamine agonists V0 (<i>in mg/day</i>)	284.7 \pm 318.0	263.0 \pm 308.6	326.6 \pm 332.2
MDS-UPDRS-I	11.6 \pm 5.4	11.2 \pm 5.3	12.4 \pm 5.4
MDS-UPDRS-II-ON	6.3 \pm 5.6	6.2 \pm 5.5	6.4 \pm 5.7
MDS-UPDRS-II-OFF	19 \pm 8	18.5 \pm 7.7	20.1 \pm 8.5
MDS-UPDRS-III-ON	12 \pm 8.2	12.1 \pm 8.1	11.9 \pm 8.4
MDS-UPDRS-III-OFF	42.3 \pm 16.5	41.6 \pm 16.5	43.7 \pm 16.4
MDS-UPDRS-IV	8.5 \pm 3.5	8.1 \pm 3.4	9.3 \pm 3.5
PDQ-39 Total	31.9 \pm 12.1	30.1 \pm 11.8	35.3 \pm 11.9
Hoehn & Yahr ON	1.3 \pm 0.8	1.2 \pm 0.8	1.5 \pm 0.8
Hoehn & Yahr OFF	2.7 \pm 0.9	2.6 \pm 0.9	2.8 \pm 0.9
HAMD	5.6 \pm 4.3	5.4 \pm 4.2	6.1 \pm 4.5
HAMA	6.7 \pm 5.7	6.2 \pm 5.4	7.7 \pm 6.2
LARS	-27.8 \pm 5.9	-27.2 \pm 6.1	-28.9 \pm 5.1
MoCA	26.4 \pm 2.6	26.3 \pm 2.5	26.4 \pm 2.7
UPPS-P Urgency	7.8 \pm 2.8	7.8 \pm 2.9	7.7 \pm 2.7
UPPS-P Positive urgency	9 \pm 2.8	8.9 \pm 2.8	9.1 \pm 2.8
UPPS-P Lack of premeditation	7.3 \pm 2.2	7.3 \pm 2.2	7.2 \pm 2.2
UPPS-P Lack of perseverance	6.6 \pm 2.4	6.8 \pm 2.5	6.2 \pm 2.2
UPPS-P Sensation seeking	7.5 \pm 2.8	7.9 \pm 2.8	7 \pm 2.6

LED=Levodopa Equivalent Dosage; MDS-UPDRS=Movement Disorder Society – Unified Parkinson's Disease Rating Scale; PDQ-39=Parkinson's Disease Rating Scale 39-items; HAMD=Hamilton Rating Scale for Depression; HAMA=Hamilton Rating Scale for Anxiety; LARS=Lille Apathy Rating Scale; MoCA=Montreal Cognitive Assessment; UPPS-P=Urgency-Premeditation-Perseverance-Sensation seeking-Positive urgency

Table 2. Description of TCI dimensions scores, gender differences and Cronbach's alpha coefficients

TCI dimensions	No. of items	Total (n=570)				Men (n=376)		Women (n=194)		Gender differences p.value	Cronbach's alpha coefficients
		Mean	SD	Min	Max	Mean	SD	Mean	SD		
NS	40	16.8	5.1	3	35	16.8	5.1	16.8	5.1	0.65	0.68 ¶
NS1	11	5.5	2.1	0	11	5.4	2.1	5.6	2.2	0.14	0.48
NS2	10	3.7	2.3	0	10	3.8	2.3	3.7	2.3	0.61	0.62
NS3	9	4.4	1.8	0	9	4.3	1.8	4.5	1.7	0.05	0.56
NS4	10	3.2	1.6	0	9	3.3	1.7	3.0	1.5	0.05	0.22
HA	35	17.8	6.5	2	33	17.2	6.3	19.0	6.7	0.002 *	0.84 ¶
HA1	11	4.7	2.4	0	11	4.6	2.4	4.9	2.4	0.26	0.62
HA2	7	4.3	1.7	0	7	4.0	1.8	4.8	1.6	5x10 ⁻⁶ **	0.59
HA3	8	3.7	2.2	0	8	3.5	2.2	4.0	2.2	0.03	0.71 ¶
HA4	9	5.1	2.2	0	9	5.0	2.2	5.3	2.2	0.03	0.66 ¶
RD	24	15.5	3.5	3	24	15.0	3.6	16.4	3.2	6x10 ⁻⁶ **	0.65 ¶
RD1	10	7.1	1.8	1	10	7.0	1.8	7.5	1.6	0.002 *	0.48
RD2	8	4.9	1.9	0	8	4.7	1.9	5.3	1.9	0.0004 **	0.61
RD3	6	3.5	1.4	0	6	3.4	1.5	3.6	1.4	0.007 *	0.41
P	8	5.4	1.7	1	8	5.4	1.7	5.4	1.7	0.85	0.44
SD	44	34.1	6.0	15	44	33.9	6.1	34.5	5.9	0.13	0.83 ¶
SD1	8	6.5	1.6	1	8	6.5	1.6	6.4	1.7	0.90	0.63
SD2	8	5.4	1.7	0	8	5.4	1.6	5.5	1.8	0.41	0.51
SD3	5	3.7	1.2	0	5	3.7	1.2	3.7	1.2	0.65	0.44
SD4	11	9.1	1.9	2	11	9.0	1.9	9.3	1.7	0.05	0.64
SD5	12	9.4	2.1	3	12	9.3	2.1	9.6	1.9	0.03	0.61
C	42	33.6	4.5	16	42	33.1	4.7	34.5	4.0	0.0002 **	0.74 ¶
C1	8	7.0	1.2	1	8	6.9	1.2	7.2	1.2	0.009	0.52
C2	7	4.8	1.5	0	7	4.6	1.6	5.2	1.3	5x10 ⁻⁶ **	0.41
C3	8	6.3	1.2	2	8	6.2	1.3	6.5	1.1	0.001 *	0.43
C4	10	8.5	1.8	0	10	8.4	1.9	8.7	1.6	0.08	0.72 ¶
C5	9	6.9	1.4	2	9	6.9	1.4	6.9	1.4	0.99	0.38
ST	33	12.5	5.9	1	30	12.2	5.8	13.2	5.9	0.14	0.84 ¶
ST1	11	3.9	2.9	0	13	3.7	2.9	4.3	3.0	0.02	0.77 ¶
ST2	9	4.9	2.4	0	11	4.8	2.4	4.9	2.4	0.86	0.67 ¶
ST3	13	3.8	2.0	0	9	3.7	2.1	4.0	2.0	0.29	0.63

NS=Novelty Seeking; HA=Harm Avoidance; RD=Reward Dependence; P=Persistence; SD=Self-Directedness; C=Cooperativeness; ST=Self-Transcendence; *Bonferroni corrected $p.value < 0.007$; ** $p.value < 0.001$; ¶Cronbach's alpha coefficient > 0.65

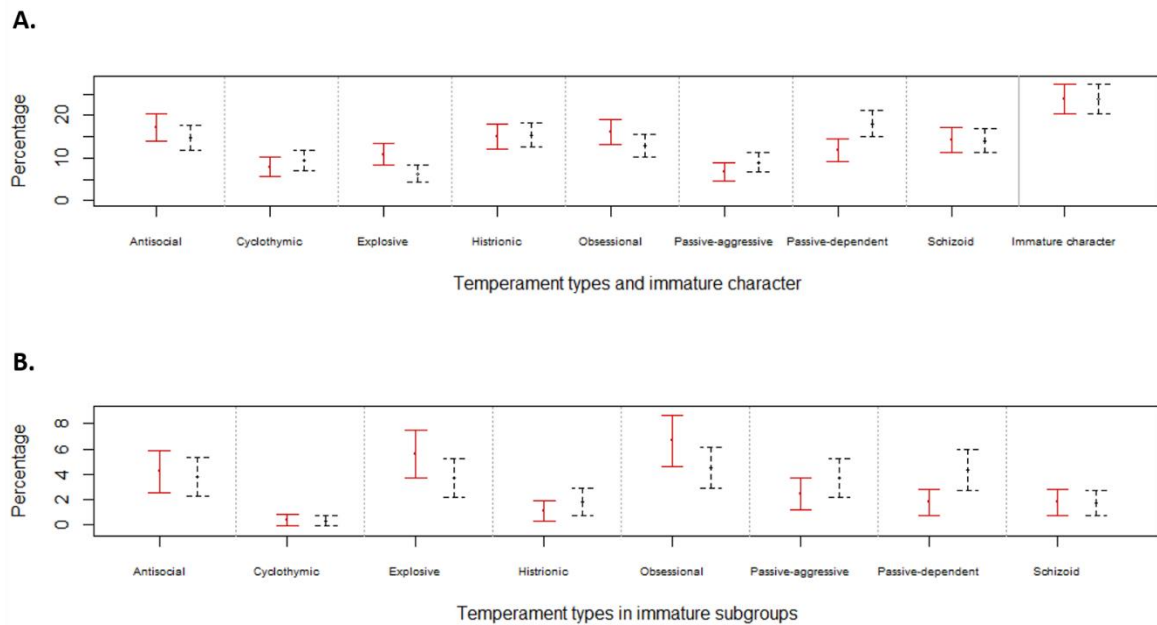
Table 3. Comparison of TCI dimensions scores between Parkinson's disease population and the French normative population

TCI dimensions	PD patients	French normative population (n=602)			Elderly group of French normative population (n=256)		
	Mean [CI]	Mean [CI]	p.value ^a		Mean [CI]	p.value ^b	
NS	16.8 [16.4 - 17.2]	16.4 [16 - 16.8]		0.04	14.5 [13.9 - 15.1]	N-O	9x10 ⁻²³ **
HA	17.8 [17.2 - 18.3]	16.1 [15.5 - 16.7]	N-O	3x10 ⁻⁷ **	16.6 [15.8 - 17.4]		5x10 ⁻⁴ **
RD	15.5 [15.2 - 15.8]	14.2 [13.9 - 14.5]	N-O	2x10 ⁻¹⁷ **	14 [13.5 - 14.5]	N-O	5x10 ⁻²² **
P	5.4 [5.2 - 5.5]	4.6 [4.4 - 4.8]	N-O	2x10 ⁻¹⁷ **	4.6 [4.4 - 4.8]	N-O	2x10 ⁻¹⁷ **
SD	34.1 [33.6 - 34.6]	31.9 [31.4 - 32.4]	N-O	4x10 ⁻²¹ **	32.7 [32 - 33.4]	N-O	1x10 ⁻¹⁰ **
C	33.6 [33.2 - 34]	31.7 [31.3 - 32.1]	N-O	2x10 ⁻²⁵ **	32.3 [31.7 - 32.9]	N-O	1x10 ⁻¹⁷ **
ST	12.5 [12.1 - 13]	13.7 [13.2 - 14.2]	N-O	7x10 ⁻⁹ **	14.6 [13.9 - 15.3]	N-O	1x10 ⁻¹⁸ **

CI=Confidence Interval; ^aone-sample Wilcoxon test between Parkinson's disease population and full French normative population; ^bone-sample Wilcoxon test between Parkinson's disease population and elderly group of the French normative population; ^{N-O}CI Non-Overlapping; ** *p.value*<0.001

Figure captions

Figure 1. Comparison of temperament types and immature character from Parkinson's disease and French normative populations.

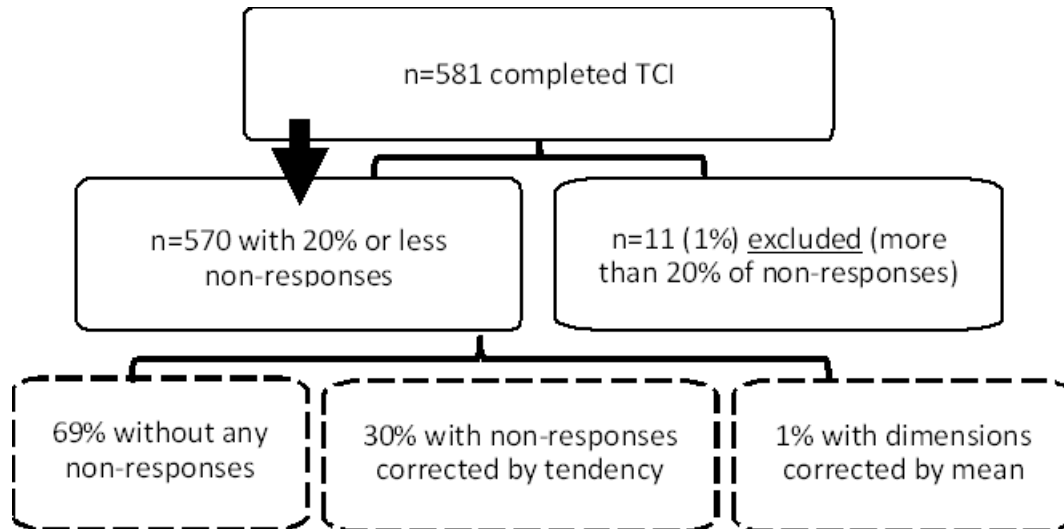


Solid lines correspond to our Parkinson's disease population with motor fluctuations Confidence Intervals; dashed lines to the French normative population from Pelissolo and collaborators (2000) Confidence Intervals - ns $\leq 16 < NS$; ha $\leq 18 < HA$; rd $\leq 16 < RD$ [Antisocial (NS, ha, rd); Cyclothymic (ns, ha, RD); Explosive (NS, HA, rd); Histrionic (NS, ha, RD); Obsessional (ns, HA, rd); Passive-aggressive (NS, HA, RD); Passive-dependent (ns, HA, RD); Schizoid (ns, ha, rd)]

(A) Comparison of the eight temperament types and immature character between Parkinson's disease population (n=570) and French normative population (n=602); **(B)** Comparison of the eight temperament types between immature subgroups of the Parkinson's disease population (n=136) and the French normative population (n=143)

Supplementary material

eFigure 1. Flow chart from all gathered TCI to conserved ones accordingly to our imputation method.



eTable 1. Description of TCI dimensions medians and quartiles

Total (n=570)					
TCI dimensions	Median	Quartiles			
		1st	2nd	3rd	4th
NS	16	0-13	13-16	16-20	20-35
HA	18	0-13	13-18	18-22	22-33
RD	16	0-13	13-16	16-18	18-24
P	5	0-4	4-5	5-7	7-8
SD	35	0-30	30-35	35-39	39-44
C	34	0-31	31-34	34-37	37-42
ST	11	0-8	8-11	11-16	16-30

NS=Novelty Seeking; HA=Harm Avoidance; RD=Reward Dependence; P=Persistence;

SD=Self-Directedness; C=Cooperativeness; ST=Self-Transcendence

eTable 2. Temperament types and immaturity

Temperament types*							Temperament types plus immature character**			
				n	%	CI	n	% ^a	% ^b	CI ^b
Antisocial	NS	ha	rd	98	17.2	14.1 - 20.3	24	4.2	17.6	11.2 - 24.1
Cyclothymic	ns	ha	RD	45	7.9	5.7 - 10.1	2	0.4	1.5	-0.6 - 3.5
Explosive	NS	HA	rd	62	10.9	8.3 - 13.4	32	5.6	23.5	16.4 - 30.7
Histrionic	NS	ha	RD	86	15.1	12.1 - 18	6	1.1	4.4	1 - 7.9
Obsessional	ns	HA	rd	92	16.1	13.1 - 19.2	38	6.7	27.9	20.4 - 35.5
Passive-aggressive	NS	HA	RD	39	6.8	4.8 - 8.9	14	2.5	10.3	5.2 - 15.4
Passive-dependent	ns	HA	RD	67	11.8	9.1 - 14.4	10	1.8	7.4	3 - 11.7
Schizoid	ns	ha	rd	81	14.2	11.3 - 17.1	10	1.8	7.4	3 - 11.7

NS=Novelty Seeking; HA=Harm Avoidance; RD=Reward Dependence; * ns $\leq 16 < NS$; ha $\leq 18 < HA$; rd $\leq 16 < RD$; CI = Confidence Interval for population proportion; ** immature character: SD + C < 62; ^apercentage of temperament types plus immaturity from total population (n=570); ^bpercentage of each temperament type from immature subgroup (n=136)

eTable 3. Pearson correlations between TCI dimensions and PDQ-39 Total score (n=532)

TCI dimensions	Total (n=532)			Men (n=350)			Women (n=182)		
	coefficient		95% CI	coefficient		95% CI	coefficient		95% CI
NS	0.01		-0.08 - 0.09	0.00		-0.11 - 0.1	0.02		-0.13 - 0.16
HA	0.35	**	0.27 - 0.42	0.30	**	0.2 - 0.39	0.37	**	0.24 - 0.49
HA1	0.29	**	0.21 - 0.37	0.26	**	0.16 - 0.36	0.32	**	0.19 - 0.45
HA2	0.22	**	0.14 - 0.3	0.14		0.04 - 0.24	0.30	**	0.16 - 0.42
HA3	0.26	**	0.18 - 0.34	0.23	**	0.13 - 0.33	0.28	**	0.14 - 0.41
HA4	0.27	**	0.19 - 0.35	0.24	**	0.14 - 0.34	0.29	**	0.15 - 0.42
RD	-0.01		-0.09 - 0.08	-0.08		-0.18 - 0.02	0.02		-0.13 - 0.16
P	0.00		-0.08 - 0.09	0.00		-0.11 - 0.1	0.00		-0.14 - 0.15
SD	-0.31	**	-0.39 - -0.23	-0.31	**	-0.4 - -0.21	-0.36	**	-0.48 - -0.22
SD1	-0.31	**	-0.38 - -0.23	-0.29	**	-0.38 - -0.19	-0.35	**	-0.47 - -0.22
SD2	-0.28	**	-0.36 - -0.2	-0.26	**	-0.35 - -0.16	-0.35	**	-0.47 - -0.22
SD3	-0.18	**	-0.26 - -0.1	-0.20	**	-0.3 - -0.1	-0.12		-0.26 - 0.03
SD4	-0.12	*	-0.2 - -0.03	-0.15	*	-0.25 - -0.04	-0.12		-0.26 - 0.02
SD5	-0.23	**	-0.31 - -0.15	-0.23	**	-0.33 - -0.13	-0.28	**	-0.41 - -0.14
C	-0.09		-0.17 - 0	-0.11		-0.21 - 0	-0.15		-0.29 - -0.01
ST	0.17	**	0.09 - 0.25	0.17	*	0.06 - 0.27	0.13		-0.02 - 0.27

NS=Novelty Seeking; HA=Harm Avoidance; RD=Reward Dependence; P=Persistence;

SD=Self-Directedness; C=Cooperativeness; ST=Self-Transcendence; *Bonferroni corrected

p.value < 0.0071; **p.value < 0.001; notable coefficients (superior to absolute 0.30) in bold

eTable 4. Pearson correlations between TCI dimensions and quantitative variables

TCI	HAMA (n=530)	HAMD (n=533)	LARS (n=546)	MoCA (n=528)	MDS-UPDRS					
					part I (n=532)	part II ON (n=538)	part II OFF (n=508)	part III ON (n=402)	part III OFF (n=556)	part IV (n=533)
NS	-0.02	0.02	-0.06	-0.01	0.11	0.06	-0.05	0.03	-0.05	0.03
HA	0.36 **	0.36 **	0.17 **	0.01	0.24 **	0.12 *	0.15 **	0.07	0.10	0.18 **
RD	0.00	-0.03	-0.27 **	0.05	-0.03	-0.04	0.03	0.03	0.06	-0.02
P	-0.02	-0.05	-0.25 **	0.06	0.01	-0.06	-0.02	-0.06	-0.07	-0.04
SD	-0.32 **	-0.35 **	-0.28 **	0.10	-0.19 **	-0.07	-0.07	0.01	0.08	-0.01
C	-0.15 **	-0.18 **	-0.27 **	0.12 *	-0.11	-0.01	0.06	0.07	0.15 **	0.05
ST	0.15 **	0.14 *	-0.05	-0.06	0.07	0.01	0.05	-0.09	-0.07	-0.05

TCI	Total LED (n=541)	LED of dopamine agonists (n=541)	UPPS-P				
			Urgency (n=530)	Positive urgency (n=531)	Lack of premeditation (n=535)	Lack of perseverance (n=530)	Sensation seeking (n=534)
NS	0.03	-0.04	0.08	0.23 **	0.46 **	0.17 **	0.18 **
HA	0.01	-0.03	0.23 **	0.13 *	0.00	0.16 **	-0.24 **
RD	0.03	-0.02	-0.03	0.01	-0.02	-0.09	-0.09
P	-0.04	0.00	-0.11	-0.06	-0.20 **	-0.29 **	0.13 *
SD	-0.04	0.04	-0.36 **	-0.33 **	-0.24 **	-0.27 **	-0.06
C	-0.02	0.07	-0.24 **	-0.22 **	-0.09	-0.12 *	-0.13 *
ST	0.00	-0.03	0.17 **	0.23 **	-0.01	-0.05	0.18 **

NS=Novelty Seeking; HA=Harm Avoidance; RD=Reward Dependence; P=Persistence; SD=Self-Directedness; C=Cooperativeness; ST=Self-Transcendence; HAMA=Hamilton Rating Scale for Anxiety; HAMD=Hamilton Rating Scale for Depression; LARS=Lille Apathy Rating Scale; MoCA=Montreal Cognitive Assessment; MDS-UPDRS=Movement Disorder Society – Unified Parkinson’s Disease Rating Scale; PDQ-39=Parkinson’s Disease Rating Scale 39-items; LED=Levodopa Equivalent Dosage; UPPS-P=Urgency-Premeditation-Perseverance-Sensation seeking-Positive urgency; *Bonferroni corrected *p.value* < 0.0071; ***p.value* < 0.001; notable coefficients (superior to absolute 0.30) in bold

eTable 5. Two-sample Mann-Whitney tests between TCI dimensions and QUIP or treatments (psychotropic drugs or analgesics)

TCI	QUIP any compulsion (n=538) 95% CI	Anxiolytics (presence n=82) 95% CI	Antidepressants (presence n=100) 95% CI	Clozapine (presence n=14) 95% CI	Analgesics (presence n=71) 95% CI
NS	-2 - -1 **	-2 - 1	-2 - 1	-1 - 4	-1 - 2
HA	-1 - 1	-4 - -1 **	-4 - -1 **	-5 - 1	-5 - -1 *
RD	0 - 1	-1 - 1	-2 - 0	-3 - 1	0 - 1
P	0 - 1	0 - 0	0 - 1	-1 - 1	0 - 0
SD	0 - 2	0 - 3	0 - 2	-1 - 5	-1 - 2
C	0 - 1	-1 - 1	-1 - 1	-2 - 2	-1 - 1
ST	-1 - 1	-3 - 0	-2 - 1	-5 - 2	-2 - 1

NS=Novelty Seeking; HA=Harm Avoidance; RD=Reward Dependence; P=Persistence; SD=Self-Directedness; C=Cooperativeness; ST=Self-Transcendence; QUIP=Questionnaire for Impulsive-Compulsive Disorders in Parkinson's Disease; *Bonferroni corrected *p.value* < 0.0071; ***p.value* < 0.001; significant differences in bold

eTable 6. Pearson correlations between TCI dimensions

	NS	HA	RD	P	SD	C	ST
NS							
HA	-0.32 **						
RD	0.08	0.01					
P	-0.10	-0.24 **	0.11				
SD	-0.02	-0.46 **	0.16 **	0.17 **			
C	0.03	-0.22 **	0.46 **	0.13 *	0.43 **		
ST	0.09	-0.04	0.20 **	0.14 **	-0.24 **	0.05	

NS=Novelty Seeking; HA=Harm Avoidance; RD=Reward Dependence; P=Persistence; SD=Self-Directedness; C=Cooperativeness; ST=Self-Transcendence; *Bonferroni corrected $p.value < 0.0071$; ** $p.value < 0.001$; notable coefficients (superior to absolute 0.30) in bold

eTable 7. Principal Component Analysis on temperaments sub-dimensions

	RC1	RC2	RC3
Eigen Values > 1	2.91	1.66	1.58
NS1	-0.54	0.28	0.39
NS2	0.00	0.72	-0.14
NS3	-0.23	0.59	0.25
NS4	-0.12	0.66	-0.09
HA1	0.76	-0.08	0.00
HA2	0.77	-0.03	0.14
HA3	0.70	-0.18	-0.11
HA4	0.74	0.11	0.13
RD1	0.10	-0.18	0.51
RD2	-0.15	0.12	0.78
RD3	0.08	-0.07	0.68
P	-0.40	-0.50	0.12
Proportion of explained variance	0.23	0.14	0.14
Cumulative % of explained variance	0.23	0.38	0.51

NS=Novelty Seeking; HA=Harm Avoidance; RD=Reward Dependence; P=Persistence; RC = Regression Coefficient for each component; relevant RC between sub-dimension and component in bold

eTable 8. Principal Component Analysis on characters' sub-dimensions

	RC1	RC2	RC3
Eigen Values > 1	3.53	2.04	1.22
SD1	0.69	0.25	-0.24
SD2	0.76	0.19	0.09
SD3	0.78	0.06	-0.08
SD4	0.25	0.47	-0.31
SD5	0.75	0.19	-0.13
C1	0.10	0.73	-0.11
C2	0.32	0.56	0.16
C3	0.21	0.58	-0.01
C4	-0.07	0.69	0.11
C5	0.13	0.40	0.05
ST1	-0.03	0.06	0.78
ST2	-0.26	-0.10	0.78
ST3	0.03	0.12	0.77
Proportion of explained variance	0.19	0.17	0.16
Cumulative % of explained variance	0.19	0.36	0.52

SD=Self-Directedness; C=Cooperativeness; ST=Self-Transcendence; RC = Regression

Coefficient for each component; relevant RC between sub-dimension and component in bold