Chapter 6

Type D, depression and anxiety in association with quality of life in patients with Parkinson’s disease and with multiple sclerosis

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(submitted)
Abstract

Background: The present study examines the role of Type D personality, anxiety and depression in quality of life (QoL) in patients of two chronic neurological diseases – Parkinson’s disease (PD) and multiple sclerosis (MS).

Methods: This cross-sectional study included 142 PD patients (73% males; mean age 67.6±9.2 years) and 198 patients with MS (32.3% males; 38.4±10.8 years). Multiple regression analyses were used to analyze the association of UDPRS (PD patients) or EDSS (MS patients), Type D personality (DS-14) and anxiety and depression (HADS) with the physical (PCS) and mental summary (MCS) of QoL, as measured by the SF-36.

Results: In PD patients, Type D was significantly associated with MCS only; in MS patients Type D was significantly associated with both dimensions - MCS and PCS. After adding anxiety and depression, the importance of Type D for the QoL model dramatically decreased. Anxiety and depression were strongly associated with lower scores in MCS and PCS in both PD and MS patients.

Conclusions: The actual mood of PD and MS patients – the level of anxiety or depression – might have a greater impact on patients’ QoL than their personality. Further longitudinal research should focus on how the pathway consisting of personality traits, anxiety and depression, and QoL might be constructed.

Introduction

The major clinical symptoms of Parkinson’s disease (PD) and multiple sclerosis (MS) significantly affect a patient’s quality of life. Symptoms associated with PD are tremor, rigidity, bradykinesia and falls, as well as non-motor symptoms like painful spasms, depression, sleep problems and fatigue [1,2]. Multiple sclerosis (MS) is a disorder of the central nervous system (brain and spinal cord) caused by demyelinations in the white matter of the central nervous system. It is marked by lack of muscle coordination, muscle weakness, speech problems, paresthesia, and visual impairments [3,4]. MS is characterized by recurrent attacks of neurological symptoms followed by a remission [4]. Other forms of MS are secondary progressive, primary progressive, progressive relapsing and the malignant course of the disease [5]. In both diseases, the symptoms lead to worse physical, mental and social well-being in comparison with people of the same age without symptoms of Parkinsonism or MS [2,6-10].

Mood disorders, especially depression, are among the clinical symptoms of both diseases. In PD patients, the prevalence of depression ranges from 20% to 40% [11,12], while depression affects 27-54% of MS patients [13,14]. Both diseases are often associated with higher scores in
anxiety [15,16]. A recent study by Goretti and colleagues clearly presented that depression had a negative impact on all QoL domains and anxiety on the mental domains in MS patients [17]. Anxiety and depression, even at moderate levels, were also positively linked with poor QoL in studies about PD [12,18].

Other psychological factors have been identified as important variables in QoL models. Personality traits, mostly high levels of neuroticism and low levels of extraversion, contributed to a worse perception of QoL in several diseases [19-26]. The construct of the Type D personality was primarily designed for measuring personality traits in coronary heart disease patients associated with an increased risk of depressive symptoms, a higher number of reinfarctions and higher mortality rates [27,28]. In further studies, its validity among non-cardiovascular diseases was also shown. Type D was associated with poor physical and mental health status among patients with melanoma, Parkinson’s disease, mild traumatic brain injury, vertigo complaints, tinnitus or sleep apnoe [29-31]. The DS-14 questionnaire, which measures Type D, was evaluated as a valid instrument for assessing and comparing Type-D personality across clinical groups as well [32].

In a previous study we concluded that Type D personality plays an important role in QoL assessment in PD patients. Having a Type D personality was, after disease severity, the second most important determinant of overall QoL and was related to the patient’s worse score in the dimensions associated with mental status, as measured by Parkinson’s Disease Questionnaire (PDQ-39) [30].

Neurologists should be aware of factors associated with a patient’s QoL in order to be able to choose the most effective interventions in the framework of treatment. For this study, Type D personality, anxiety and depression were assumed to be the variables associated with the perception of health status and thus might lead to a worse perception of QoL among patients with Parkinson’s disease and patients with multiple sclerosis. The aim of this study is to explore whether Type D was associated with the mental and physical health status of quality of life in PD and MS patients even when depression and anxiety are added to the model.

Methods

Participants and sample size
Patients with PD and MS in this cross-sectional study were recruited from the databases of 4 hospitals and 17 outpatient neurologists and also from MS society in the eastern part of the Slovakia between February 2004 and February 2006. Neurologists from the above mentioned institutions diagnosed all patients included in the sample as suffering from PD according to the United Kingdom Parkinson’s Disease Society
Brain Clinical Criteria [33]. MS patients were diagnosed by neurologists according to the diagnostic criteria for MS [4]. Data collection of MS patients took place between December 2003 and July 2006.

Exclusion criteria for both diseases were defined as follows: a) patients with a Mini-Mental State Examination (MMSE) score [34] below 23 points, b) co-morbidities and movement disabilities not caused by MS or PD.

Sociodemographic data were derived from questionnaires filled in by the patients themselves, and data about neurological treatment from their medical records. Disability in each patient was assessed by a neurologist. The study was conducted after informed consent was obtained from the patients prior to the interview. Participation in the research was voluntary. The local Ethics Committee of the University Hospital in Kosice approved the study in Kosice on 17 December 2002.

**Measures**

**Disease severity**

Disease severity was measured using the Unified Parkinson’s Disease Rating Scale (UPDRS) in PD patients and the Kurtzke Expanded Disability Status Scale (EDSS) in MS patients. The UPDRS and EDSS remain the most frequently used scoring systems in PD and MS neurological practice.

The UPDRS consists of four parts, pertaining to: mentation and mood (Part 1), activities of daily living (Part 2), motor function (Part 3) and complications of dopaminergic therapy (Part 4), including motor fluctuations and dyskinesias. Parts 1, 2, and 4 are interview-based; Part 3 is based on a clinical examination by a health care professional and represents the patient’s condition at the time of the examination. A neurologist can score patients from 0 to 176, where higher scores indicate increased disease severity [35].

The EDSS is based on testing functional systems: pyramidal, cerebellar, brainstem, sensory, bowel and bladder, visual, mental and “other”. Disability caused by SM is graded on a continuum from 0 (normal neurological examination) to 10 (death caused by MS) [36].

**Type D personality**

For assessing Type D personality the DS-14 was used with its constituent subscales, negative affectivity (NA) and social inhibition (SI) [28]. NA means the tendency to experience negative emotions, like anger, dysphoria, irritability, hostile feelings, depressed affect and anxiety. SI is the tendency to inhibit these emotions in social interactions [28]. Subjects rated these aspects of their personality on a 5-point Likert scale ranging from 0=false to 4=true. The NA and SI scales were scored as continuous
variables (range 0-28). A cut-off of 10 on both scales (NA ≥ 10 and SI ≥ 10) was used to classify subjects as Type D [28]. Cronbach’s alpha in the original study was 0.88 for NA and 0.86 for SI. In the current study, DS-14 had good internal consistency in both diseases: Cronbach’s alpha in PD patients was .77 for NA and .76 for SI, and for MS patients it was .84 for NA and .83 for SI.

**HADS**

The fourteen-item Hospital Anxiety and Depression Scale (HADS) was used for assessing anxiety and depression in non-psychiatric hospital departments [37]. Seven items are related to the depression and 7 to anxiety. Patients responded on a 4-point scale (from 0=absent to 3=definitely present/severe). Scores ranged from 0 to 21 for each scale, where a higher score implied more depression or anxiety. Cronbach’s alpha for depression was .79 for both MS and PD patients, and for anxiety it was .81 for MS and .69 for PD patients.

**SF-36**

The thirty-six item Short Form Health Survey (SF-36) was designed to measure health-related quality of life (HRQOL) from the patient’s point of view as part of the Medical Outcome Study (MOS). It assesses 8 health concepts: a) physical functioning; b) role limitations because of physical health problems; c) bodily pain; d) general health perception; e) vitality (energy/fatigue); f) social functioning; g) role limitations because of emotional problems; and h) general mental health [38]. These scales are further combined into 2 scales: a physical component summary score PCS (subscales a-d), which contains information about physical health status (PHS), and a mental component summary score (MCS) (subscales e-h), which informs about mental health status (MHS). All item scores are transformed into a scale from 0 (poor health) to 100 (optimal health) [39]. Cronbach’s alphas for the summary scores were .87 for PCS and .78 for MCS in PD patients, and .89 for PCS and .89 MCS for patients with MS.

**Statistical analyses**

Independent sample t-tests were conducted to assess differences between the sample of MS and PD patients in age, disease duration, anxiety, depression, PCS and MCS. Also the difference of proportions test (CIA) was used for assessing gender differences in partnership, Type D and education [40]. Next, linear regression analyses were used for assessing the contribution of the independent variables in 3 models. The first model included disease severity, gender, age, education and disease duration. In the second model Type D personality was added. The third model
Results

Descriptive statistics
Out of 512 invited patients with Parkinson’s disease, 160 patients agreed to participate and filled in the questionnaires, but 7 patients were excluded after the personal interview because of the exclusion criteria. The final sample thus consisted of 153 patients (response rate 31.3%). Non-respondents were on average older compared to the analyzed group in age (mean difference 1.69 yrs., SE=.87; t=-1.95; 95% CI .010 – -3.39) and there were significantly more women than men among non-respondents (difference -0.0110; SE=.041; 95% CI -.091 – .069).

From 412 MS patients who were asked to participate in the study, 207 patients were interviewed (52%), and 205 patients did not respond. There were no statistically significant differences between non-respondents and participants regarding gender, disease duration and clinical course of MS. However, the non-respondents were on average older than the participants (mean difference 1.69 yrs., SE=.87; t=-1.95; 95% CI .010 – -3.39).

Eleven patients with PD and nine patients with MS were removed from the sample because of missing data. The study ultimately involved 142 PD patients (73% males; mean age 67.6±9.2 years) and 198 patients with MS (32.3% males; 38.4±10.8). The majority of MS patients belonged to the relapsing-remitting clinical course (RR-MS; 70.2%).

All PD patients used antiparkinsonian therapy according international guidelines [41,42]. Fifty-six per cent of MS patients in this study were being treated with Interferon beta therapy.

Disease severity, Personality, Depression and Anxiety and Quality of Life
Three models were constructed to explore the contribution to the variance of PCS and MCS.

In Model 1, which consisted of disease severity, gender, age, education, and disease duration, worse disease severity was associated with a worse score in mental and in physical health status in PD patients, and female gender was associated with a worse PCS, as well. Older age and more serious disease severity were the main predictors of MCS and PCS in MS patients (Table 6.2).
When Type D was added (Model 2), the strength of the model increased for MCS and PCS in both diseases. In PD patients, Type D was significantly associated with MCS only. However, Type D was significantly associated with the MCS and PCS of QoL for MS patients. Except disease severity, which remained significantly associated with both domains in both diseases, age was the second most important variable in the model of PCS and MCS in MS patients only (Table 6.2).

Model 3 showed a further increase in explained variance for both diseases when the variables anxiety and depression were added (Model 3). Anxiety and depression were strongly associated with lower scores in both subscales of the SF-36 in both groups of patients. Disease severity remained significantly associated with both domains in both diseases. Type D personality, female gender and longer disease duration were associated with PCS in PD patients (p≤.05). In MS patients higher age remained significantly associated with PCS (Table 6.2).

### Table 6.1 Characteristics of the sample – means and standard deviations (SD) or N (%) on demographic and study variables

<table>
<thead>
<tr>
<th></th>
<th>Parkinson's disease</th>
<th>Multiple sclerosis</th>
<th>p / 95% CI</th>
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<tbody>
<tr>
<td><strong>Number of subjects (%)</strong></td>
<td>142 (41.8)</td>
<td>198 (58.2)</td>
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<tr>
<td><strong>Gender</strong></td>
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<td>Males (%)</td>
<td>73 (51.4)</td>
<td>64 (32.3)</td>
<td>.09; .29</td>
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<td>Females (%)</td>
<td>69 (48.6)</td>
<td>134 (67.7)</td>
<td>-.29; -.09</td>
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<td><strong>Mean age in years (SD)</strong></td>
<td>67.6 (9.2)</td>
<td>38.4 (10.8)</td>
<td>p≤0.001*</td>
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<td><strong>Married or living with a partner (%)</strong></td>
<td>96 (67.6)</td>
<td>121 (61.1)</td>
<td>-.03; .17 ns</td>
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<td>Elementary (%)</td>
<td>47 (33.1)</td>
<td>11 (5.6)</td>
<td>.19; .36</td>
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<td>Secondary (%)</td>
<td>79 (55.6)</td>
<td>152 (76.8)</td>
<td>-.31; -.11</td>
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<td>University (%)</td>
<td>16 (11.3)</td>
<td>35 (17.7)</td>
<td>-.14; .01 ns</td>
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<td><strong>Disease duration (SD)</strong></td>
<td>7.6 (5.9)</td>
<td>2.6 (0.8)</td>
<td>p≤0.001*</td>
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<tr>
<td><strong>UPDRS (SD)</strong></td>
<td>36.9 (20.2)</td>
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<td><strong>EDSS (SD)</strong></td>
<td>-</td>
<td>3.0 (1.5)</td>
<td>-</td>
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<td>Relapsing-remitting (%)</td>
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<td>139 (70.2)</td>
<td>-</td>
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<td>Secondary progressive (%)</td>
<td>-</td>
<td>27 (13.6)</td>
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<tr>
<td>Primary progressive (%)</td>
<td>-</td>
<td>29 (14.6)</td>
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<tr>
<td>Negative affectivity (SD)</td>
<td>13.2 (6.3)</td>
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<td><strong>Personality</strong></td>
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<td>Social inhibition (SD)</td>
<td>13.5 (6.2)</td>
<td>12.0 (6.3)</td>
<td>p≤0.05*</td>
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<td>Type D (%)</td>
<td>75 (52.8)</td>
<td>89 (44.5)</td>
<td>-.03; .18 ns</td>
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<td><strong>Depression (SD)</strong></td>
<td>6.6 (3.6)</td>
<td>4.4 (3.5)</td>
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<td><strong>Anxiety (SD)</strong></td>
<td>8.2 (3.9)</td>
<td>7.2 (4.2)</td>
<td>p≤0.05*</td>
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<td><strong>Physical component summary (SD)</strong></td>
<td>37.6 (22.0)</td>
<td>48.5 (20.4)</td>
<td>p≤0.001*</td>
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<tr>
<td><strong>Mental component summary (SD)</strong></td>
<td>50.9 (17.4)</td>
<td>56.5 (15.7)</td>
<td>p≤0.01*</td>
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Abbreviations: SD – standard deviation, ns - not significant. * t-tests; α difference of proportion test
Table 6.2 Multiple regression analyses of disability (UPDRS in PD patients, EDSS in MS patients), gender, age, education, disability and disease duration (Model 1), Type D personality (Model 2) and anxiety and depression (Model 3) in MCS and PCS of SF-36 in PD and MS patients

<table>
<thead>
<tr>
<th></th>
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<th>Model 2</th>
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<td>-.19*</td>
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<td>-.21**</td>
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<td>17.0***</td>
<td>23.1***</td>
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Abbreviations: UPDRS - Unified Parkinson’s Disease Rating Scale, EDSS - Expanded Disability Status Scale, PD – Parkinson’s disease, MS – multiple sclerosis
Discussion

Our findings demonstrate a significant association between Type D personality and the mental health status of both PD patients and MS patients. Type D personality was associated with both dimensions of QoL—PCS and MCS. However, this association disappeared in both dimensions in MS and in the mental dimension in PD when the variables anxiety and depression were added to the model. Higher scores in anxiety and depression were strongly associated with QoL in both diseases. We might suppose that the actual mood status influences a patient’s perception of QoL significantly more than personality traits, which over time are mostly seen as relatively stable. Actual feelings of sadness and fear are related, with MS and PD patients both reporting worse QoL. Similar results were found in inflammatory bowel disease patients, where regression analysis showed that disease activity and psychological distress were the strongest predictors of QoL impairment, and that personality traits did not play a significant role in QoL [43].

As depression is a clinical symptom for both diseases MS and PD, we included all patients into the analyses although the HADS-score could be multifactorially determined, e.g. by other organic changes in the brain or by psychological reasons associated with factors of non-parkinsonian character. To better understand this effect of the origin of the HADS, we repeated the analysis after exclusion of clinically depressed and anxious patients from the sample and in those patients only. We found that in the non-A/non-D sample not only the association between personality traits, anxiety, depression and MCS and PCS disappeared except for depression and MCS in MS, but also in both diseases the association between UDPRS/EDSS and MCS disappeared in the full model. In the clinically depressed and anxious sample the association between UDPRS/EDSS and MCS and PCS is only statistically significant in PD and not in MS. A statistically significant association between anxiety and MCS is found in PD, not in MS, but with PCS only in MS and not in PD. Depression is significantly associated with MCS in both diseases, not with PCS. These findings need further exploration. Nevertheless, having a chronic disease combined with depression is a severe disabling combination [44].

The predictive value of Type D disappeared in Model 3, although there is no doubt that its importance on QoL exists. In a previous study, the association between Type D, its subscales and QoL was explored in patients with PD [30] and other studies have reported similar results [29,31]. Thus, an important question is how personality fits into the final model consisting, besides personality, also of mood variables determining QoL in chronically ill patients. A possible answer might be that personality traits are associated indirectly with QoL via another variable. Mood variables mediating the relationship from personality to QoL was recently
suggested by Bartels et al. (2010) in the field of tinnitus. The authors in that study presented a model in which Type D personality on QoL is mediated by anxiety and depression in patients with tinnitus [31]. A similar model could be assumed for other diseases, as PD or MS.

Also coping style has been proposed as an important mediating factor with regard to adaptation to illness [17, 45-47]. Patients who more frequently used the emotional coping style reported being more disabled by their disease and suffering from poorer mental health and quality of life [48-50]. A higher level of neuroticism and a low level of extroversion were found to be related to the emotion-focused coping strategy of MS patients [51]. Also, in a sample of young adults suffering from headache, those reporting lower levels of active pain-coping showed the highest level of depressive symptoms [47]. Wahl et al. emphasized that being informed about coping strategies and their relationship to aspects of quality of life in patients with chronic diseases is important in order to establish health care interventions aimed to enhance coping skills [48].

Strengths and limitations

The study’s main strength is its comparison of both chronic neurological diseases from, to our knowledge, a new point of view. The results of this study could be helpful for understanding the complexity of QoL and its factors in patients with chronic progressive neurological diseases. One of the limitations of the study is its cross-sectional design, which does not provide us with information about changes to the patient over time, and thus does not enable us to compare pathways. The low response rate might also have an impact on generalization of the results to the total population of PD and MS patients. Regrettably, we have no information about the disease duration and disease severity of non-respondents. However, it might be supposed that they refused to participate in the study because of serious motor complications found in the higher stages of PD and MS and due to the need for help from their social surroundings.

Implications

Identification of the mechanisms and consequences of functioning health perception in chronically ill patients is still a big challenge for further research. Research on QoL in patients with MS and PD should in further studies incorporate personality as an integral part of the explanatory models of quality of life; next, the relationship between mood status or psychological distress, personality traits and QoL should be explored, as well as other psychological factors which could contribute to clarify the pathways of the variables predicting quality of life of patients with chronic diseases [52]. For neurological practice the study outcomes suggest that good treatment of mood disorders could substantially contribute to a better quality of life.
Conclusion

Our findings show that actual mood status of MS and PD patients could be more important than their personality traits in assessment of QoL. To complete the model and to clarify the pathway predicting QoL, which could explain most of the variance of QoL in chronically ill patients, is a great challenge for further research. A similar model could have great meaning for clinicians, enabling them to modify their treatment style such that each patient can benefit optimally from it.

Acknowledgements

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References


