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**Are non-demented patients with Parkinson's disease able to decide about their own treatment?**

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## **Abstract**

**Introduction:** Patients with Parkinson's disease (PD) are often confronted with difficult medical decisions, which might be hampered by cognitive impairment or chronic stress. Little is known, however, about the capacity to make medical decisions and the influence of cognition and stress on this ability. This study determined whether non-demented Parkinson's disease patients are able to make medical decisions and whether this capacity is influenced by cognition and stress.

**Methods:** Forty-six Parkinson's disease patients and 94 healthy controls were assessed with the MacArthur Competence Assessment Tool for Treatment during which participants were presented with deep brain stimulation as a treatment option for a fictional Parkinson's disease patient. Furthermore, all participants were examined with a stress questionnaire and a neuropsychological test battery.

**Results:** Parkinson's disease patients performed better on the total scale and 'Understanding' subscale of the MacArthur Competence Assessment Tool for Treatment than healthy controls. Lower performance on the Concept Shifting Test in the Parkinson's disease group and lower performance on Letter Digit Substitution Test in the healthy control group predicted lower medical decision-making capacity. No association was found between stress and medical decision-making.

**Conclusion:** Non-demented Parkinson's disease patients show no impairments in medical decision-making compared to healthy controls. In fact, Parkinson's disease patients have a better understanding of their disease and the benefits and risks of treatment options than healthy controls. Psychomotor speed and attention were negatively associated with medical decision-making in both groups. This implies that when these cognitive functions decline, the capacity to make medical decisions also declines.

## **Introduction**

Cognitive impairment is common in Parkinson's disease (PD) and 24% of the newly diagnosed patients already show cognitive impairment [1]. Ultimately, cognitive impairment occurs in approximately 50% of patients and are, in most cases, progressive in nature [2,3]. During the course of the disease, PD patients are often confronted with difficult medical decisions, such as whether or not to undergo deep brain stimulation (DBS) or decisions regarding medication. Decisions like these might be hampered by cognitive impairment [4,5,6].

Regarding medical decision-making, the approach of informed consent was formulated by courts of law. Informed consent requires three elements: (a) disclosure of treatment information to patients, (b) a voluntary decision by the patient, and (c) competence to make treatment decisions [7]. Disclosure requires that patients must be informed about the nature of the disorder, the nature of the proposed treatment, the benefits and risks associated with the treatment and alternative treatment options. A voluntary decision comprehends that patients can make the decision based on their own free will and without constraint or expectation of reward. Competence to consent to treatment finally includes the ability to communicate a choice, understanding relevant information, appreciation of the relevance of information for one's own circumstances and processing of information in a rational manner. The ability to give informed consent, or in other words the capacity to make medical decisions, thus requires the integrity cognition. Cognitive impairment that is present in patients with PD may therefore have a negative impact on the capacity to make medical decisions.

The capacity to make medical decisions might also be influenced by levels of experienced chronic stress. It is known that PD has a strong impact on the patients' life. Receiving the diagnosis, living with motor symptoms and cognitive impairment and dealing with different treatment options and regimes can create considerable stress. Several studies indicate that the cumulative effects of stress can have a significant negative effect on health and cognitive processes. It was for example demonstrated that the diurnal cortisol fall, which may be

altered by chronic stress, is associated with increased risk-taking [8]. Furthermore, longitudinal studies indicated that chronic stress has a negative influence on cognitive decline in patients with Mild Cognitive Impairment and dementia [9,10].

Considering the fact that PD patients are often confronted with difficult medical decisions, it is paramount to determine whether patients are able to make these decisions. Little is known, however, about the capacity to make medical decisions in patients with PD. Previous studies report that PD patients show impairments in medical decision-making, however these studies only used hypothetical medical problems that were not related to PD [4,5,6]. From a clinical perspective it is extremely relevant to determine whether PD patients can make medical decisions regarding treatments that are specific for their disease. Furthermore, the impact of cognition and chronic stress on the capacity to make medical decisions of PD patients was not explored so far. The aim of this study was therefore to determine whether PD patients are able to make medical decisions that are specific for their disease and whether cognitive impairment and levels of experienced chronic stress have a negative influence on this capacity.

## **Methods**

### *Participants*

Patients were recruited via the outpatient clinic of the Department of Neurology of the Zuyderland Medical Center, The Netherlands and by advertisement in the magazine and on the website of the Dutch Parkinson Association. One hundred and one patients signed an informed consent. Nineteen patients dropped out before assessment for various reasons including having no transport, being too busy, having difficulties with accepting the diagnosis, etc., while eleven patients dropped out during the assessment. Seventy-one patients thus participated in this study. Patients were diagnosed with idiopathic PD according to the UK Parkinson's Disease Society Brain Bank criteria. Disease severity was assessed with the Hoehn and Yahr scale [11]. Patients were assessed in their regular on-state following medication.

One hundred and two healthy controls were recruited from the Groningen community through advertisement in local papers. All healthy controls also signed an informed consent completed the assessment.

Level of education was rated for all participants with a Dutch education scale, ranging from 1 (elementary school not finished) to 7 (university degree). Premorbid intelligence level was estimated with the National Adult Reading Test [12]. Symptoms of depression were assessed with the Beck Depression Inventory [13].

The main exclusion criterion was dementia (n=25 patients, n=8 healthy controls) based on Scales for the Outcome of Parkinson's disease COGNition (SCOPA-COG score<25) [14]. Other exclusion criteria were neurological disorders other than PD, DBS and the use of medication (other than anti-parkinsonian medication) known to influence cognition.

In table 1, demographic and clinical characteristics are displayed for PD patients and healthy controls. Groups did not differ in age ( $t=-0.17$ ;  $p=0.87$ ;  $df=138$ ) and premorbid intelligence level ( $t=0.49$ ;  $p=0.62$ ;  $df=63.69$ ). However, more males were included in the group of PD patients compared to the healthy control group (Chi-Square=10.50;  $p=0.001$ ;  $df=1$ ) and PD patients showed a lower level of education than healthy controls (Mann-Whitney U=1448.50;  $z=-3.39$ ;  $p=0.001$ ). Furthermore, PD patients reported more symptoms of depression ( $t=-4.16$ ;  $p<.001$ ;  $df=138$ ) and showed a lower score on the SCOPA-COG compared to healthy controls ( $t=2.95$ ;  $p=0.004$ ;  $df=130$ ).

### *Procedure*

All participants received a chronic stress questionnaire by post and were requested to complete this in the week before the assessment. A neuropsychological assessment, including an interview assessing medical decision-making was administered. Several assessors (n=8) were involved in the assessments. All were trained in a standardized manner and used a standardized script in order to assure equal assessments. Furthermore, all tests were scored by using standardized procedures as described in the test manuals or by using the Metrisquare DiagnoselS software which automatically scored test performance.

Since the medical decision-making test was the main outcome measure which was based on a semi-structured interview, participants' test performances were scored by two independent raters (see inter-rater-reliabilities below). After assessment all participants were debriefed. The medical ethical committee of the Zuyderland Medical Center approved this study.

## *Measures*

### Medical Decision-Making

Medical decision-making was assessed with the MacArthur Competence Assessment Tool for Treatment (MacCAT-T) [7]. The MacCAT-T is a semi-structured interview and consists of four subscales: 'Understanding', 'Appreciation', 'Reasoning' and 'Expressing a Choice' [7]. To assess inter-rater-reliability, the interviews were audiotaped and scored by two independent raters. Inter-rater-reliability was fair for 'Appreciation' (intraclass correlation (ICC)=0.74) and good to excellent for 'Understanding' (ICC=0.79), 'Reasoning' (ICC=0.75) and 'Expressing a Choice' (ICC=0.82). The MacCAT-T focuses specifically on the patient's own disorder, symptoms and treatment options. In this study participants were presented with DBS as a treatment option for a fictional PD patient.

The 'Understanding' subscale was based on performance on three sections of the interview (Disorder, Treatment, and Benefits-Risks). A structured format was provided for disclosing the nature of the disorder, treatment and benefits and risks of the treatment options to participants. This was followed by structured inquiry (open-ended) and probing questions to assess the degree to which participants recalled and understood the various elements of the disorder and treatment options and risks.

The 'Appreciation' subscale is based on performance on the two appreciation sections (Disorder, Treatment) and was used to determine whether participants acknowledged the disorder and symptoms as disclosed. Participants were asked whether they had any reason to doubt that the fictional patient had the disorder, following an exploration of the participants' belief. Furthermore, participants were asked whether or not the proposed treatment might be of some benefit to the fictional patient, following an exploration of the reasons for this belief.

The 'Reasoning' subscale involved a discussion exploring participants' treatment choice and how they arrived at this choice. The Reasoning subscale assesses four types of reasoning: Consequential reasoning (participant mentioned at least two specific consequences when explaining the choice), Comparative reasoning (participant offered at least one statement in the form of a comparison of treatment options), Generating consequences (participant translated medical circumstances of the disorder and treatment into their practical, everyday consequences) and Logical consistency (participant's choice follows logically from the participant's own reasoning, as put forth when explaining the choice).

The 'Expressing a Choice' subscale measures participants' ability to express a choice by asking participants which of the treatment options seemed best (or that the patient most likely wants).

For all answers given during the interview participants received a score of 0, 1 or 2 based on the degree of completeness of their answer. Total scores were calculated for all subscales (maximum scores: 'Understanding'=6; 'Appreciation'=4; 'Reasoning'=8; 'Expressing a choice'=2) as well as for the complete test (maximum score=20).

Finally, at the end of the interview, a question regarding the influence of a physician's opinion on the medical decision was added. Participants were asked to score this on a three-point scale (the physician's opinion has no influence (=0), little influence (=1) or considerable influence (=2) on my treatment choice).

### Chronic stress

The level of experienced chronic stress was assessed with the Daily Problem List (Alledaagse Problemen Lijst (APL)) that measures perceived stress [15]. The APL consists of 114 items describing everyday incidents from several domains of daily life. Eight items were added to determine perceived stress that might be caused by having PD (e.g. "You experienced problems in attention and concentration"). Participants were asked to indicate whether an incident occurred during the last two months and how stressful or bothersome the incident was (0=not at all, 1=a little bothersome, 2=quite bothersome, 3=very



bothersome). The APL consists of three subscales: (1) 'Dependent', which assesses perceived stress related to the participant's functioning, (2) 'Independent', which assesses perceived stress that is not related to the participant's functioning and (3) 'Parkinson' that focuses on perceived stress due to having PD. Furthermore a Total score was calculated, which reflects perceived stress in all kinds of situations (including dependent and independent items).

### Neuropsychological tests

The total score of the Letter-Digit Substitution Test (LDST) [16], time needed for completion of the Digit Trial of the Concept Shifting Test (CST) [17] and for the Word Card of the Stroop Color-Word Test (SCWT) [18] were used as measures of attention and psychomotor speed. Three neuropsychological tests were used to examine memory: the Verbal Learning Test [19], the Rivermead Behavioral Memory Test [20] and the Digit Span Forward of the Wechsler Adult Intelligence Scale (WAIS) [21]. Executive functions were also assessed with several tests. Inhibition was assessed with the time needed for Color-Word Card divided by the time needed for the Color Card of the SCWT [18] (i.e. SCWT Interference Index). The target measure for cognitive flexibility was the time needed for the Shift Trial of the CST divided by the time needed for the Digit Trial of the CST [17]. The Digit Span Backward of the WAIS [21] was used to assess working memory. Finally, a Phonemic Verbal Fluency Test (letters D, A and T) was used to evaluate divergent thinking [22]. For an accurate timing and automatic registration of responses, some neuropsychological tests (CST, SCWT, LDST) were conducted using the Metrisquare DiagnoselS ([www.metrisquare.com](http://www.metrisquare.com)) software linked to a digital tablet monitor and stylus.

### *Statistical analyses*

Statistical Package for the Social Sciences 20.0 was used. To compare patients and healthy controls with regard to medical decision-making, level of experienced stress and performance on neuropsychological tests, MANCOVAs were performed including gender and

level of education as covariates. Effect sizes were calculated, differentiating small ( $d=0.2 / \eta_p^2=0.01$ ), medium ( $d=0.5 / \eta_p^2=0.059$ ) and large effects ( $d=0.8 / \eta_p^2=0.14$ ).

Subsequently, four multiple linear regression analyses (stepwise) were conducted for both groups separately, to determine whether cognition and experienced stress predicted medical decision-making. The total score on the MacCAT-T was included as dependent variable. Independent variables were either neuropsychological test performance or reported stress (subscales of the APL). A p-value of  $\leq 0.05$  was considered significant.

## **Results**

PD patients showed significantly higher scores on the total score and 'Understanding' subscale of the MacCAT-T than healthy controls (table 2). A medium effect size was found for the 'Expressing a Choice' subscale, but the difference between groups was not significant. No significant differences were found between patients and healthy controls regarding the 'Appreciation' and 'Reasoning' subscales (table 2). Furthermore, 39% of PD patients and 23% of healthy controls answered that the physician's opinion had "no influence" on their treatment choice. Twenty-six percent of patients and 33% of healthy controls answered that it had "little influence". Thirty-five percent of patients and 44% of healthy controls answered that the physician's opinion had "a lot of influence" on their treatment choice.

Patients experienced significantly higher levels of stress in general (Total scale), in situations that were related to their own functioning (Dependent subscale) and in situations in which they were confronted with their symptoms (Parkinson subscale) as compared to controls (table 2). Regarding the Independent subscale a non-significant difference was observed between groups.

The analysis of cognitive performance revealed that PD patients performed significantly worse on the LDST and on one out of six memory variables (VLT recall) than healthy controls (table 2).

The multiple linear regression analyses showed that lower performances on the LDST predicted a poorer medical decision-making in healthy controls ( $R^2=0.08$ ,  $F=5.32$ ,  $p=0.02$ ). In PD patients, lower performance on the CST Digit predicted a poorer medical decision-making ( $R^2=0.13$ ,  $F=5.44$ ,  $p=0.03$ ). All other cognitive variables did not predict medical decision-making. None of the subscales measuring experienced stress predicted significantly the capacity to make medical decisions.

## **Discussion**

The results of the present study suggest that PD patients are able to make medical decisions about whether or not they would like to receive DBS and presumably also about other treatment options. In fact, PD patients have a better understanding of PD, treatment options and accompanying benefits and risks than healthy controls. These findings are not in accordance with previous studies demonstrating that medical decision-making is impaired in PD patients [4,5,6]. The differential findings between the current and previous studies might be due to varying sample sizes, selection criteria and the measures used to assess medical decision making. Both Dymek et al. [5] and Griffith et al. [6] included patients if they reported cognitive impairment, whereas the presence of cognitive impairment was not an inclusion criterion of the current study. Furthermore, PD patients of previous studies [5,6] were older and suffered from more severe PD than patients in the present study. The present patient sample might therefore be characterized by a better overall health and better cognitive functioning than patients of previous studies. As such, the sample included in the present study might be a better representation of the group of patients undergoing DBS, as PD patients with profound cognitive impairment and high scores on the Hoehn & Yahr scale due to gait and balance dysfunction are excluded from surgical candidacy in most centers [23]. Furthermore, previous studies [5,6] used the Capacity to Consent to Treatment Instrument (CCTI) to assess medical decision-making [6] which consists of two clinical vignettes each presenting a hypothetical medical problem (neoplasm and atherosclerotic heart disease) and two treatment options with associated benefits and risks; all of which are not relevant to

patients with PD. In the present study, however, the MacCAT-T was used, which is designed to focus specifically on the patient's own disorder, symptoms and treatment options. The present results indicate that the capacity to make medical decisions appears to be better if one is confronted with one's own disease and related treatment options than when being confronted with another, unrelated medical problem. Particularly, knowledge of one's own disease can be better due to repeated medical information provided by physicians. Also, a higher interest in and increased importance of disease information to patients can play a role. The present study thus indicates that PD patients eligible for DBS are able to decide about medical treatment options.

Neuropsychological assessment revealed selective cognitive impairments in PD patients who performed poorer than healthy controls in selective attention and psychomotor speed as well as aspects of memory functioning. These results confirm the findings of previous studies demonstrating that cognitive impairment (including the above mentioned functions) is common in PD [1,2,3].

The results of the present study also indicate that attention and psychomotor speed might play an important role in medical decision-making, while memory and executive functioning were not associated with this capacity. More specifically, a lower performance of PD patients on a psychomotor speed measure (CST digit) and a lower performance of healthy participants on a measure of selective attention and psychomotor speed (LDST), predict a lower medical decision-making capacity. Previous studies that investigated cognitive predictors of medical decision-making capacity in e.g. Alzheimer's disease, Mild Cognitive Impairment and Traumatic Brain Injury revealed that multiple cognitive functions are involved in medical decision-making [24,25]. Impairments in psychomotor speed or attention will particularly lead to difficulties in obtaining and processing information that is required to make adequate medical decisions. Furthermore, it has been demonstrated that these functions are often affected during the course of PD [3]. The current findings thus imply that when attention and psychomotor speed decline in PD patients, the capacity to make medical decisions

declines as well, which indicates that tests of attention and psychomotor speed should be part of eligibility screening for DBS in PD patients.

With regard to stress, PD patients reported significantly higher levels of stress than healthy controls. PD patients reported particularly higher levels of stress related to their own functioning and disease. Stress had, however, no detrimental effect on the capacity to make medical decisions. This finding was unexpected considering studies indicating a negative association between acute stress and cognitive functioning in various other diseases (e.g. testicular cancer) as well as studies showing that the diurnal cortisol fall is related to risky decision-making [8,26,27]. In this study, stress was operationalized using a questionnaire assessing daily problems within the last two months. Measuring acute stress level during a medical decision-making task could provide different results. Although medical decisions in PD are usually not taken during periods of acute stress, the decision making process might be influenced by an acute stressor.

The present study has some limitations. First, a relatively small group of patients was included. Therefore, the results should be viewed with caution and replication of the current findings seems desirable. Second, one has to be aware of the fact that the current study assessed whether PD patients were able to make decisions for a fictional PD patient, an ability that does not necessarily extrapolate to making decisions about themselves. Third, the SCOPA-COG, which was used to exclude participants with dementia, has been specifically designed for patients with PD. This test might therefore be less reliable in participants without PD. Fourth, the examiners were not blinded to the patients' diagnosis. Even though this would be impossible to realize, this bias might have had influence on the scoring of some tests. Finally, PD patients showed a lower level of education than healthy participants. Even though a statistical correction was conducted, this difference between groups might have had influence on the results.

In conclusion, non-demented PD patients are able to make medical decisions about their own treatment. Psychomotor speed and attention were negatively associated with the capacity to make medical decisions, while no association was found with levels of

experienced stress. It is therefore likely that when attention and psychomotor speed decline during the course of PD, the capacity to make medical decisions declines as well. This should, however, be confirmed in longitudinal studies.

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**Table 1. Descriptive and disease characteristics of PD patients (n=46) and healthy controls (n=94)**

	PD patients M (SD)	Healthy controls M (SD)	p
Age (years)	60.98 (8.23)	60.73 (7.83)	0.87
Education*	5.15 (1.07)	5.74 (1.02)	0.001
NART IQ	109.67 (15.27)	110.89 (9.79)	0.62
BDI	10.50 (6.90)	6.18 (5.14)	<0.001
Gender (%male)	65.22	36.17	0.001
SCOPA-COG total	30.37 (3.41)	32.33 (3.74)	0.004
H&Y	2.07 (.61)		
LEDD	564.73 (279.80)		
Disease duration (years)	5.15 (3.85)		

\*Dutch education scale ranging from 1 (elementary school not finished) to 7 (university degree); NART = National Adult Reading Test; BDI = Beck Depression Inventory; SCOPA-COG = Scales for the Outcome of Parkinson's disease COGnition; H&Y = Hoehn and Yahr scale; LEDD = Levodopa Equivalent Daily Dose (i.e. regular levodopa dose x 1 + slow release levodopa x 0,75 + bromocriptine x 10 + apomorphine x 10+ ropinirole x 20 + pergolide x 100 + pramipexole x 100 + rotigotine x 40 + [regular levodopa dose + (slow release levodopa x 0,75)] x 0,2 if taking entacapone).

**Table 2. Performances of PD patients (n=46) and healthy controls (n=94) on tests of medical decision making and stress as well as on tests of attention / psychomotor speed, memory and executive functions**

	PD patients	Healthy controls	F	p	ES
	M (SD)	M (SD)	(df)		
<u>Medical Decision Making</u>			5.68 (5)	<0.001	0.19
Total	12.21 (2.84)	11.30 (2.99)	6.05 (1)	0.02	0.31
Understanding	4.34 (0.99)	3.84 (1.02)	16.06 (1)	0.001	0.50
Appreciation	3.41 (0.92)	3.39 (0.92)	0.17 (1)	0.68	0.01
Reasoning	2.64 (1.49)	2.46 (1.61)	1.31 (1)	0.25	0.12
Expressing a choice	1.80 (0.50)	1.56 (0.77)	3.03 (1)	0.08	0.35
<u>Stress</u>			14.75 (4)	<0.001	0.31
Total	33.84 (28.29)	26.60 (18.24)	4.31 (1)	0.04	0.33
Dependent	9.91 (9.86)	6.47 (5.42)	10.69 (1)	0.001	0.48
Independent	6.02 (5.06)	5.18 (3.70)	0.82 (1)	0.366	0.20
Parkinson	6.70 (5.68)	1.04 (2.00)	55.44 (1)	≤0.001	1.57
<u>Attention/ Psychomotor speed</u>			4.63 (3)	0.004	0.10
CST Digit	23.52 (5.59)	21.15 (5.53)	1.24 (1)	0.27	0.43
SCWT Word Card	49.65 (10.63)	47.59 (8.54)	0.00 (1)	1.00	0.22
LDST	40.09 (8.15)	48.32 (8.36)	13.35 (1)	≤0.001	0.99

<u>Memory</u>			1.30 (6)	0.27	0.07
VLT learning score	39.09 (7.81)	44.83 (10.16)	3.62 (1)	0.06	0.61
VLT recall	7.35 (2.56)	9.34 (3.37)	5.37 (1)	0.02	0.64
VLT recognition	27.63 (4.30)	28.90 (1.68)	2.61 (1)	0.11	0.44
RBMT immediate recall	17.64 (5.28)	18.98 (6.34)	0.12 (1)	0.73	0.22
RBMT delayed recall	14.09 (4.79)	14.96 (6.18)	0.01 (1)	0.92	0.15
Digit Span Forward	8.80 (1.91)	9.00 (2.01)	0.06 (1)	0.81	0.10
<u>Executive functions</u>			0.74 (4)	0.57	0.02
SCWT Interference Index	1.67 (0.35)	1.58 (0.27)	0.57 (1)	0.45	0.30
CST Shift / Digit	1.48 (0.36)	1.49 (0.38)	1.56 (1)	0.21	0.03
Digit Span Backward	6.58 (1.83)	7.03 (2.22)	0.04 (1)	0.84	0.21
Phonemic Fluency total	41.74 (13.55)	43.70 (10.02)	0.39 (1)	0.53	0.17

ES = effect size; CST = Concept Shifting Test; LDST = Letter Digit Substitution Test; VLT = Verbal Learning Test; RBMT = Rivermead Behavioural Memory Test; SCWT = Stroop Color-Word Test