University of Tartu
Department of Psychology

Rael-Saskia Salakka

ADAPTION OF THE PARKINSON NEUROPSYCHOMETRIC DEMENTIA ASSESSMENT (PANDA) INTO ESTONIAN

Master's thesis

Supervisor: René Randver

Subtitle: The PANDA adaption

Tartu, 2018

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Abstract

"Adaption of the Parkinson Neuropsychometric Dementia Assessment (PANDA) into Estonian"

Parkinson's disease (PD) is characterized by both motor and non-motor symptoms; the latter also include mood disorders and problems with cognitive functioning, the seriousness of which largely predicts later quality of life associated with the progression of the disease.

In Estonia, there is currently no specific screening test to measure mild cognitive impairment associated with Parkinson's disease (MCI-PD) but as the number of patients with PD increase (Kadastik-Eerme et al., 2018), there is a clear need for it. The Parkinson Neuropsychometric Dementia Assessment (abbreviated PANDA; Kalbe et al., 2008) is time-efficient, easy to administer and sensitive to MCI-PD and dementia. It has been developed to measure problems in cognitive functioning that are specific to PD and includes a short mood questionnaire.

The aim of this study was to obtain an Estonian translation of the PANDA and its normative scores. The PANDA was translated using the translation/back-translation method. The Estonian sample comprised of 47 healthy participants (12 men and 35 women, average age 61.04, SD = 9.26) who were recruited using the chain sampling method. The MMSE, the BDI and the PANDA were administered, and the results were compared against the German data.

The results show a significant correlation between the MMSE and the PANDA total score. The Estonian sample's scores were found to be significantly higher than those of the original control group. Multiple factors may partially influence this outcome. Our results, unlike the original ones, show a significant effect of education on the PANDA total score, thus a proposition is made of adding one point to the total PANDA score of those without higher education.

Future directions should entail collecting some more normative data and testing the PANDA on a clinical sample.

Keywords: Parkinson's disease, mild cognitive impairment, cognitive screening test

Kokkuvõte

“Parkinsoni neuropsühhomeetrilise hindamisskaala (PANDA) adapteerimine eesti keelde”

Parkinsoni tõvele (PD) on iseloomulikud nii motoorsed kui mitte-motoorsed sümptomid, viimaste seas muuhulgas ka depression ja kognitiivsete võimete langus, mille tõsidus ennustab paljuski edaspidist haiguse kuluga seostatud tunnetatavat elukvaliteeti.
Eestis ei ole hetkel spetsiifiliselt Parkinsoni tõvega kaasneva kerge kognitiivse häire (MCI-PD) mõõtmiseks testi, kuid PD diagnoosiga patsientide arvu tõus (Kadastik-Eerme, 2018) näitab selleks selget vajadust. Parkinsoni neuropsühhomeetriline hindamisskaala (PANDA; Kalbe jt., 2008) on aegasäästev, lihtsate juhistega ning tundlik MCI-PD ja dementsuse suhtes. See loodi spetsiifiliselt PDga kaasnevate kognitiivsete probleemide mõõtmiseks ning sisaldab ka lühikest meeleolu küsimustikku.
Käesoleva uuringu eesmärgiks oli leida PANDA eestikeelsele tõlkele normatiivsed tulemused. PANDA tõlgiti eesti keelde tõlke-tagasitõlke meetodil. Eesti kontrollgrupp koosnes 27st tervest inimesest (12 meest ja 35 naist, kelle keskmine vanus oli 61,04 aastat (SD = 9,26); osalejad leiti mugavus-lumepallvalimi meetodil. Osalejatele esitati BDI-2 küsimustik ning MMSE ja PANDA testid ning tulemusi võrreldi Saksa originaalandmete vastu.
Tulemused näitavad olulist korrelatsiooni MMSE ja PANDA lõpptulemuste vahel. Eesti kontrollgrupi tulemused olid statistiliselt olulisel määral Saksa grupi tulemustest kõrgemad. See võib olla mõjutatud mitmetest faktoritest. Eesti grupi tulemustest nähtus haridustaseme oluline mõju PANDA lõppskoorile, mida Saksa kontrollgrupil ei olnud. Seega oleks soovitatav edaspidi testi Eestis kasutades lisada ilma kõrghariduseta inimeste PANDA lõpptulemusele üks punkt.
Edasise sammuna tuleks valimi tasakaalustamiseks koguda veel normatiivseid andmeid ning testida PANDAt kliinilise grupi peal.

Märksõnad: Parkinsoni tõbi, kerge kognitiivne häire, kognitiivne sõeltest

Introduction

Parkinson's disease

Parkinson's disease (PD) is a slowly progressing chronic neurodegenerative disease, affecting 0.1-1.5% of people over 60 years of age (Riedel et al., 2016), which begins years before a definitive diagnosis can be made (Kalia and Lang, 2015). Its' prevalence worldwide is about 315 (251-571) per 100,000 people over 40 (Pringsheim et al., 2014). Prevalence in Estonia is 197-314 cases per 100,000 (Kadastik-Eerme et al., 2018). PD is characterized by both motor and non-motor symptoms, and is associated with cognitive impairment and an increased risk of developing dementia (PDD) (Galtier et al., 2015).

Pathological characteristics of PD are the presence of intraneuronal proteinacious cytoplasmic inclusions called Lewy bodies that disrupt normal neurotransmission and consequently lead to an accelerated degeneration of pigmented dopaminergic neurons in the substantia nigra pars compacta. Loss of these neurons leads to dopamine deficiency in the striatum, which is responsible for the classical motor symptoms of PD. The neurodegeneration does extend beyond just these brain structures; degeneration of hippocampal structures as well as cholinergic cortical inputs have also been found to contribute to a heightened risk of dementia related to PD.

Typical non-motor symptoms of PD include olfactory dysfunction, cognitive impairment, psychiatric symptoms (mostly depression and anxiety), autonomic dysfunction, sleep disorders, pain, and fatigue ((Dauer and Przedborski, 2003). These are frequently present before the onset of typical motor symptoms. In about 95% of cases of PD, there is no clear genetic link (Dauer and Przedborski, 2003, Kalia and Lang, 2015). Aetiology is currently unknown (Dauer and Przedborski, 2003) but some risk and protective factors have been found.

Risk factors include a history of anaemia and depression – although it is not certain whether depression might be an early sign of PD or whether they share common aetiological factors (Delamarre and Meissner, 2017) – advanced age, as most sufferers are over 60 years of age (Riedel et al, 2016), and male gender (Delamarre and Meissner, 2017). Exposure to the

herbicide paraquat and pesticide maneb has been linked to increased risk of developing PD (McNamara, 2011, p. 20; Vaccari, de Camargo and El Dib, 2017)

Potential protective factors include using calcium channel blockers (e.g. antihypertensive drugs), and female gender – possibly due to oestrogen being protective against PD (Delamarre and Meissner, 2017). Cigarette smoking and consumption of coffee or black tea have been found to be inversely associated with PD (Hernan et al., 2002).

UK Parkinson's Disease Society Brain Bank Clinical Diagnostic Criteria are used worldwide (including in Estonia) for diagnosing PD (Taba, 2003). Besides bradykinesia – the main inclusion symptom – at least one of the following symptoms must be present as well for establishing the diagnosis: muscular rigidity, rest tremor of 4-6 Hz, or postural instability that is not caused by primary visual, vestibular, cerebellar, or proprioceptive dysfunction. Supporting criteria include unilateral onset, progressive course, persistent asymmetry affecting side of onset most, response to levodopa treatment and clinical course of at least 10 years (Hughes et al., 1992).

Mood disorders in PD

About half of PD patients also suffer from anxiety and mood disorders, the most common of the latter being depression (Riedel et al., 2010). According to McNamara (2011), depression in PD seems to be linked with deficits in executive cognitive functions. It also increases the risk of developing dementia as the disease progresses (McNamara, 2011, pp. 162-165). If left untreated, the impact of depression extends beyond just mood symptoms – it is linked with earlier start of dopaminergic therapy, problems with activities of daily living (Ravina et al., 2007), significantly greater cognitive decline, and further advance in motor symptoms of PD (Starkstein et al., 1992; Ravina et al., 2007).

Müller et al (2013) concluded that non-motor symptoms like depression and fatigue are the most relevant symptoms in early PD and should thus be given appropriate attention in managing them. A meta-analysis of gender differences in PD by Miller and Cronin-Golomb (2010) found that although the prevalence of the disease is higher in men (Riedel, 2016), women with PD are more likely to have depression and more severe motor symptoms (Miller and Gronin-Golomb, 2010).

Mild cognitive impairment in PD

Mild cognitive impairment (MCI) stands for a degree of cognitive impairment that is not in line with normal aging but does not essentially hinder everyday activities; it is not severe enough to meet the diagnostic criteria of dementia (Pedersen et al., 2013). It is considered to be a continuum between dementia and cognitive functioning normal for one's age. Not all patients with MCI progress to dementia (Galtier et al., 2016) and some may even revert to normal cognitive functioning (Pedersen et al., 2013).

Mild cognitive impairment in Parkinson's disease (PD-MCI) may represent the earliest stage of decline in cognitive functioning in PD, and may indicate a risk of developing dementia (Galtier et al., 2016). Risk factors for developing PD-MCI are age, attention and verbal memory deficits, fewer years of education, longer disease duration (Pedersen et al., 2013), depression, early occurrence of levodopa-related psychosis or confusion, and severe motor symptoms (especially bradykinesia) (Emre, 2003). No significant difference was found in the use of levodopa, dopamine agonists, or entacapone between those who developed dementia and those who did not (Pedersen et al., 2013). Pedersen and colleagues (2013) concluded from their study that the presence of PD-MCI in the first year of PD diagnosis is highly sensitive in detecting those who will develop early PDD. They also found that patients without MCI at initial PD diagnosis are likely to not develop dementia for at least three years (Pedersen et al., 2013).

PD-MCI usually involves attentional and visuoconstructive deficits as well as problems with executive functions. The most frequently found cognitive abnormalities in PD-MCI are frontal/executive dysfunction (impaired planning ability and working memory) and amnestic deficit while cognitive problems in PD have been classified as deficits in executive, language, attentional, memory and visuospatial abilities (Pistacchi et al., 2015).

Depressive symptoms and cognitive impairment are often linked in PD. Basile and colleagues (2001) found that people with PD have a high risk of developing cognitive impairment and mood disorders and that these two conditions are often correlated. In their study, 50% of those whose means score of MMSE showed cognitive decline were also depressed according to Hamilton Rating Scale for Depression (HDRS); and 63% of patients with depression had a

cognitive decline of some degree. The mean score of MMSE was lower in patients with depression as compared to those without. The difference was found to be statistically significant. (Basile et al., 2001)

While investigating differences in cognitive functioning in early non-depressed PD patients, early PD patients with symptoms of mild depression, patients with primary depression and healthy controls, Uekermann and colleagues (2003) found that cognitive problems in early PD are likely to be worsened even by mild depressive symptoms. Early PD patients who exhibited depressive symptoms had problems with executive functions as well as alternate and phonemic verbal fluency and working memory. In their study, only early PD patients with depressive symptoms showed these deficits and not non-depressed early PD patients. Their results also suggest that early PD patients with depression suffer from more severe deficits relative to patients with primary depression. This indicates the important part of even mild depressive symptoms play in deficits of cognitive functioning in early PD and the need to take mood problems into account when first diagnosing PD (Uekemann et al., 2003). This is why it is especially important to take mood disorders into account during PD diagnosis and to continue assessing them during the progression of the disease.

Screening for problems in cognitive functioning

A task force was commissioned by the Movement Disorder Society to develop formal diagnostic criteria for PD-MCI; these were published in 2012. The guidelines provide a unified method for characterizing and diagnosing PD-MCI to provide a framework to get better understanding of the concept (Litvan et al., 2012).

The Diagnostic Criteria for Mild Cognitive Impairment in Parkinson's Disease lists several neuropsychological tests that could be used to measure deficits in attention and working memory, executive function, language, memory, and visuospatial function (Litvan et al., 2012). According to Randver, Vahter and Ennok (2015), psychologists in Estonia mostly use the Consortium to Establish a Registry for Alzheimer's disease Neuropsychology Battery (CERAD) (Pulliainen, Hokkanen, Salo, & Hänninen, 2008), the Wechsler Adult Intelligence Scale, 3rd ed. (WAIS-III) (Wechsler, 2011), the Mini-Mental State Examination (MMSE) (Folstein, Folstein, & McHugh, 1975) and Montreal Cognitive Assessment (MoCA) (Nasreddine et al., 2005) tests to assess cognitive functioning. While having variable efficacy

in describing possible impairment, none of these is designed specifically to measure cognitive deficits in PD. The MMSE, for example, has been found to have very low sensitivity to PDD (Riedel et al, 2008; Ritz et al, 2014) even though it is an established diagnostic tool for dementia in Alzheimer's disease (Larner, 2012; Stähelin et al., 1997).

As cognitive decline and dementia in PD are different from those in Alzheimer's disease – the first being of the so-called subcortical dementias characterized by deficits in attention, memory and visuospatial abilities and the latter of the cortical dementias (Cummings, 1986) – it is important to have tests that take into account the differences and are suitable for all different kinds of disorders. Currently, there is no neuropsychological test in Estonia for measuring PD-MCI specifically, although, considering the increasing number of PD patients (Kadastik-Eerme et al., 2018), there is a clear need for it.

The Parkinson Neuropsychometric Dementia Assessment

The Parkinson Neuropsychometric Dementia Assessment (PANDA) is a screening tool with five cognitive tasks and a short depression questionnaire (three items). It takes approximately 10 minutes to administer which makes it relatively short and time-efficient when compared to either WAIS-III or CERAD; it is structured, easy to administer due to clear instructions and independent of both age and education (Kalbe et al., 2008). The original German version was developed by Kalbe and colleagues in 2008 and has since been translated and adapted into French (Gasser et al., 2011) and Italian (Pignatti et al., 2014). The PANDA has turned out to be a good measuring tool for cognitive decline in both people with PD as well as people with PD-MCI (Kalbe et al., 2008).

The five cognitive tasks include a word-pair associate learning task with immediate and delayed recall, alternating verbal fluency task, visuospatial task and working memory and attention task (Kalbe et al., 2008). These have been chosen to include a diversity of domains usually affected in PD as indicated above.

When compared to three other often-used screening tests for cognitive decline – the Mini Mental State Examination (MMSE; Folstein, Folstein and McHugh, 1975), the Mini Mental Parkinson (MMP; Mahieux et al., 1995) and the clock test – in French-speaking patients, Gasser et al (2016) found that the PANDA had the highest discriminative power of the four in

detecting cognitive disorders and dementia. The PANDA had 94% specificity and 100% sensitivity for dementia, and 100% specificity and 72% sensitivity for cognitive disorders. The authors concluded that according to their results, the PANDA should be considered to be used for detecting cognitive problems in routine clinical practice (Gasser et all, 2016).

Purpose of the current study and hypotheses

The aim of this study was to collect normative data for the Estonian version of the PANDA following the examples of the original German version and the French adaption.

Based on previous literature and the French adaption of the PANDA, the following hypotheses were postulated:

1) the MMSE score and the PANDA total score are significantly positively correlated,
2) the BDI-2 score and the score of the PANDA mood questionnaire are significantly positively correlated
3) the PANDA total score and means and standard deviations of subtests' scores of the Estonian sample are not significantly different from that of the German sample
4) education does not have a significant effect on the PANDA total score.

Materials and methods

Procedure

First, the PANDA was translated by translation/back-translation method; after the translation of the test and its instructions from German to Estonian, a back-translation was made by a separate neuropsychologist fluent in both Estonian and German who was not familiar with the original German version to check if the two German versions corresponded. Mismatches were then corrected and this current study initiated to find an Estonian control group and its scores as compared with the German control group.

The study was approved by the Ethics Review Committee on Human Research of the University of Tartu. It was conducted mainly in University of Tartu Institute of Psychology but some participants wished to rather participate in their own homes or work places, and when possible, they were granted the possibility. The inclusion criteria for participation were

age of at least 50 years, and no current psychiatric or neurological diagnosis that could have an influence on the person's cognitive functioning (e.g. diagnosis of dementia, mild cognitive impairment, traumatic brain injury, etc). Exclusion criteria were current diagnosis of dementia, mild cognitive impairment or any other neurological illness that would influence memory functioning or attention; current mood disorder diagnosis, BDI-2 score higher than 10, or MMSE score lower than 26.

The procedure was described to each participant and written informed consent was obtained. They were then given the demographic data questionnaire and the Beck Depression Inventory 2nd edition to complete and if their result for BDI-2 was lower than 10 points, the MMSE and the PANDA were administered to them. The whole procedure took about 35 minutes on average from start to finish (ranging from 20 minutes to nearly 2 hours). The MMSE was used in order to be able to compare the results with the German and French studies even though it has been found to have a very low sensitivity to PDD (Riedel et al., 2008; Ritz et al., 2014). All psychological assessments were carried out under the supervision of a licensed clinical psychologist/clinical neuropsychologist.

Measures

Demographic data. For statistical purposes, we recorded each participant's gender, age, year of birth, handedness, highest level of education completed and formal education in years, occupational status (employed, unemployed, on a disability, retired, or working while on a pension), last/current or longest occupation, known current and previous neurological diagnoses, and known current and previous psychiatric diagnoses.

Beck Depression Inventory 2nd edition (BDI-2; Beck, Steer & Brown, 1996) is a widely-used 21-item self-report questionnaire with multiple choice answers. It is used to measure the severity of depression with a focus on behavioural and cognitive patterns. In order to participate in this study, participants needed to have a score lower than 10 points.

Mini Mental State Examination (MMSE) was developed by Folstein, Folstein and McHugh in 1975 and is a widely used screening test for measuring cognitive impairment. It is a short 30-point interview-style questionnaire that assesses a person's orientation, ability to

follow simple commands, attention, recall, and short-term memory. In order to participate in this study, participants needed to have a score higher than 25 points.

The Parkinson Neuropsychometric Dementia Assessment (the PANDA; Kalbe et al., 2008) comprises of five subtests and a short three-item mood questionnaire. The five subtests are as follows:

1) Word pair associate learning task with immediate (subtest 1) and delayed (subtest 5) recall consists of four pairs of words that are concrete and frequently used but semantically unrelated. The word pairs are read out three times; each reading is followed by immediate recall when the first word from each pair is read out. In the 5th subtest (approximately 6-8 minutes later), all word pairs have to be completed once again. The words were translated literally from the original version without changes. The highest raw score is 12 for subtest 1, and 4 in subtest 5. These tasks were chosen for the PANDA because deficits in memory are well documented in PD and they are primarily due to ineffective strategies in encoding and retrieval (Kalbe et al., 2008).
2) Alternate verbal fluency task (subtest 2) is where the subjects have to generate as many words from two alternating semantic categories (animals and furniture) as they can in one minute. The raw score for this task is the number of correct words minus any switching errors. The categories were the same in translation as in original. Kalbe and colleagues wrote that they chose this task because PD patients frequently have a significant impairment in verbal fluency tasks, especially with semantic fluency (Kalbe et al., 2008).
3) Spatial imagery task (subtest 3) consists of three half-masked squares with different dot patterns, and the subject is expected to find the correct pattern that would emerge when the mask is removed. Highest raw score for this task is 3. According to Kalbe et al, the task was chosen due to the fact that there is considerable evidence of visuospatial dysfunction in PD patients (Kalbe et al., 2008).
4) Working memory and attention task (subtest 4) where the subjects are presented with rows of numbers in a random order (e.g. 5-8-1-3) and their task is to repeat these in a systematic order (1-3-5-8). Rows vary in length from two to six numbers; the number of items in the largest correctly repeated row is the subject's score. The highest raw score is six. Kalbe and colleagues wrote that as many studies have reported working memory dysfunction in PD patients in both the verbal and nonverbal domain, they included this task (Kalbe et al., 2008)

Participants

Participants were recruited via Tähtvere Day Centre for the Elderly in Tartu, using contacts from friends, acquaintances, and colleagues, and by the chain sampling method where previous participants recommended the study to their friends, acquaintances, or colleagues.

Five of the initial participants had a BDI-2 score that was higher than 10 and thus were excluded from further participation. They were given feedback on their score and – if necessary – were advised on where to turn to for appropriate help. None of the participants had an MMSE score lower than 25 (scores ranged from 28 to 30).

The final sample comprised of 47 people (35 women and 12 men) whose age ranged from 50 to 82 years (M = 61.04, SD = 9.26). Three of the participants had had a previous diagnosis of a mood disorder or other psychiatric illness that was not relevant at the time of the study (two had had a diagnosis on depression and one had been treated for alcoholism). Three had had a previous or current neurological diagnosis that was deemed not to have influence on their current cognitive functioning (epilepsy, previous neuritis, or meningitis in childhood). Table 1 shows the quantitative demographic characteristics of the participants.

Elke Kalbe, the corresponding author of the German study of the PANDA also agreed to send us the data of their control group (N = 108) for comparison. The group comprised of 49 men and 58 women (one participant's sex was not recorded) whose age ranged from 30 to 89 (M = 60.30, SD = 9.85). The average number of years of education the participants had received was 14.18 (SD = 2.64) ranging from 9 to 18 years. This data was used to compare the original control sample with the Estonian one.

The data was analysed using IBM SPSS Statistics Data Editor version 20.

After checking for normality with the Shapiro-Wilk test, the data was found not have a normal distribution. However, to be able to compare the results with the French adaption, we still used Independent Samples T-Test as the skewness and kurtosis of all data was between -1 and 1. The correlations were calculated using Spearman's rho.

Table 1. Demographic data of the Estonian control group (n = 47)

	n	Percent
Sex		
Male	12	25
Female	35	75
Employment		
Employed	27	57.4
Unemployed	1	2.1
Retired	11	23.4
Working while on a pension	8	17
On a disability	0	0
Education		
Basic education	1	2.1
Secondary education	4	8.5
Vocational secondary education	14	29.8
Higher education	28	59.6
Last or current employment		
Blue-collar work	9	19.1
Education (schools, kindergartens, universities)	17	36.2
Managerial position	8	17
Health care	4	8.5
Librarian	3	6.4
Engineer	2	4.3
Other	4	8.5

Results

For converting the PANDA raw scores into transformed scores, we used the conversion algorithms provided by Kalbe and colleagues (2008) which can be found in appendix 2.

Mean scores and ranges

Table 2 shows the sociodemographic and clinical characteristics as well as mean test scores with standard deviations for the German and Estonian control groups.

Correlations

The correlations were calculated using Spearman's rho.

The PANDA mood questionnaire was observed to have a significant positive correlation with the BDI-2 (ρ (47) = 0.62, p = 0.00) which was similar to the German results (ρ = 0.64, p <

0.00). The mood questionnaire did not have any other significant correlations besides a weak positive correlation with the transformed score of associate learning task with delayed recall (ρ (47) = 0.31, p = 0.03) (but not with the raw score of the same task).

Table 2. Sociodemographic and clinical characteristics and mean scores of the German and Estonian control groups

	German (N = 108)	**Estonian (N = 47)**	***p***
Age (mean and SD)	60.30 (9.85)	61.04 (9.26)	0.66
Gender (percent of M to F)	46 to 54	25 to 75	0.01**
Years of education (mean and SD)	14.18 (2.63)	14.98 (3.00)	0.13
BDI-2 (mean and SD)	6.7 (5.7)	4.89 (3.16)	<0.01**
MMSE (mean and SD)	28.8 (1.3)	29.09 (0.78)	<0.01**
PANDA total (mean and SD)	23.92 (4.89)	25.85 (3.26)	<0.01**
Associate learning immediate raw score (mean and SD)	7.62 (2.78)	8.09 (2.01)	<0.01**
Fluency raw score (mean and SD)	16.81 (5.16)	16.83 (3.29)	0.98
Spatial imagery raw score (mean and SD)	2.29 (0.74)	2.19 (0.88)	0.49
Working memory raw score (mean and SD)	5.46 (0.75)	5.68 (0.51)	0.04*
Associate learning delayed raw score (mean and SD)	2.57 (1.37)	3.21 (0.93)	<0.01**
Associate learning immediate transformed score (mean and SD)	4.08 (1.38)	4.45 (0.97)	0.06
Fluency transformed score (mean and SD)	6.05 (1.36)	6.17 (0.96)	0.57
Spatial imagery transformed score (mean and SD)	3.93 (1.26)	3.79 (1.43)	0.55
Working memory transformed score (mean and SD)	5.32 (1.06)	5.66 (0.60)	0.01**
Associate learning delayed transformed score (mean and SD)	4.59 (2.37)	5.83 (1.51)	<0.01**

*. significant at the 0.05 level (2-tailed).
**. significant at the 0.01 level (2-tailed).
Note: 50 subjects of the German control group were tested with the MMSE and the BDI but their data exept for the mean score and standard deviation was unavailable for this study. This analysis was done with the One-Sample T-Test

The PANDA total score had a significant correlation with the MMSE score (ρ (47) = 0.33, p = 0.02). The MMSE was negatively correlated with age at a significant level (ρ (47) = -0.33, p =

0.02) but the PANDA total score was not. Gasser and colleagues (2011) had similar results in the French adaption.

The total score for PANDA was found to have a statistically significant positive correlation with all subtasks. Correlations were strongest with word pair associate learning task with immediate recall (ρ (47) = 0.73, $p < 0.001$) and delayed recall (ρ (47) = 0.72, $p < 0.001$). Correlations between the total score and other subtests were found to be of medium strength: alternating verbal fluency task (ρ (47) = 0.46, $p < 0.001$), visuospatial task (ρ (47) = 0.44, $p < 0.001$), working memory task (ρ (47) = 0.41, $p < 0.001$). Years of education had a statistically significant positive medium-strength correlation with the PANDA total score (ρ (47) = 0.49, $p < 0.001$). All correlations can be found in Table 3.

Table 3. Spearman correlation coefficients of the Estonian control group

	Sex	Age	Educ	Yrs of educ	BDI-2	MMSE	Ass.learn.imm	Fluency	Sp.im	Wm	Ass.learn.del	Total	Mood
Sex	_	0.065	0.124	0.027	0.114	-0.05	-0.067	0.035	0.101	-0.28	0.075	0.089	0.03
Age	0.065	_	-0.18	-,331*	0.137	-,332*	0.01	-0.098	-,325*	-,311*	-0.045	-0.183	0.222
Educ	0.124	-0.177	_	,867**	-0.07	0.209	0.217	0.255	0.237	0.044	0.268	,336*	0.061
Yrs of educ	0.027	-,331*	,867**	_	-0.04	0.274	0.269	0.269	,368*	0.244	,320*	,486**	0.054
BDI-2	0.114	0.137	-0.07	-0.036	_	0.043	0.201	0.086	-0.13	-0.04	0.287	0.214	,623**
MMSE	-0.05	-,332*	0.209	0.274	0.043	_	0.137	0.078	0.233	,374**	0.24	,329*	-0.084
Ass.learn.imm	-0.07	0.01	0.217	0.269	0.201	0.137	_	,438**	-0.049	0.226	,698**	,726**	0.282
Fluency	0.035	-0.098	0.255	0.269	0.086	0.078	,438**	_	-0.194	0.14	0.23	,461**	0.005
Sp.im	0.101	-,325*	0.237	,368*	-0.13	0.233	-0.049	-0.194	_	,298*	-0.036	,441**	-0.052
Wm	-0.28	-,311*	0.044	0.244	-0.04	,374**	0.226	0.14	,298*	_	0.051	,407**	-0.035
Ass.learn.del	0.075	-0.045	0.268	,320*	0.287	0.24	,698**	0.23	-0.036	0.051	_	,720**	,315*
Total	0.089	-0.183	,336*	,486**	0.214	,329*	,726**	,461**	,441**	,407**	,720**	_	0.274
Mood	0.03	0.222	0.061	0.054	,623**	-0.084	0.282	0.005	-0.052	-0.04	,315*	0.274	_

* Correlation is significant at the 0.05 level (2-tailed).

** Correlation is significant at the 0.01 level (2-tailed).

Note: Educ – highest formal education; Yrs of educ – years of education; BDI-2 – Beck Depression Inventory 2nd edition; MMSE – Mini Mental State Inventory; Ass.learn.imm – the PANDA subtest 1, associate learning with immediate recall (transformed score); Fluency – the PANDA subtest 2, verbal fluency (transformed score); Sp.im – the PANDA subtest 3, spatial imagery (transformed score); Wm – the PANDA subtest 4, working memory (transformed score); Ass.learn.del . the PANDA subtest 5, associate learning with delayed recall ((transformed score); Total – the PANDA total score, Mood – the PANDA mood questionnaire.

Comparisons of control groups

Comparison of the German and Estonian control groups with independent samples T-test shows that the groups did not have a significant difference in regards of age ($M_{Estonian}$ = 61.04; M_{German} = 60.30; $t(153) = 0.44$, $p = 0.66$) or years of education ($M_{Estonian}$ = 14.98; M

$_{German}$ = 14.18; $t(132) = 1.53$, $p = 0.13$). However, the Estonian control group had significantly higher transformed scores in working memory subtest ($M_{Estonian} = 5.66$; $M_{German} = 5.32$; $t(142.50) = 2.50$, $p = 0.01$, $d = 0.42$), associate learning delayed subtest ($M_{Estonian} = 5.83$; $M_{German} = 4.59$; $t(132.39) = 3.90$, $p = 0.0001$, $d = 0.68$), and total score ($M_{Estonian} = 25.85$; $M_{German} = 23.92$; $t(127.68) = 2.89$, $p = 0.0001$, $d = 0.51$).

The Estonian control group had higher transformed scores, but the difference was not significant in associate learning immediate subtest ($M_{Estonian} = 8.09$; $M_{German} = 7.62$; $t(121.74) = 1.17$, $p = 0.244$) and fluency subtest ($M_{Estonian} = 16.83$; $M_{German} = 16.81$; $t(153) = 0.02$, $p = 0.98$). The German control group had higher scores in spatial imagery subtest ($M_{Estonian} = 2.19$; $M_{German} = 2.29$; $t(153) = -0.70$, $p = 0.49$) but that did not reach statistical significance, either. The raw scores had a similar pattern.

In the French adaption of the PANDA, the comparisons showed that the German and French control groups did not differ regarding age or MMSE score whereas there was a significant difference in years of education in favour of the German sample. The German participants had higher scores in all the PANDA subtests except for the working memory subtest (Gasser et al., 2011)

The PANDA total score and education

In the French adaption process, Gasser and colleagues (2011) divided their sample into two groups based on their years of education: those with up to 11 years of education and those with 12 years of education or more. These showed a significant difference in the mean PANDA total score of approximately 1 point [M = 21.72 (SD = 4.7) versus M = 22.79 (SD = 4.6)]. Thus they decided that one point should be added to the total transformed score of subjects without higher education. This procedure is used in some other cognitive screening tests like MoCA (Gasser et al., 2011).

As the total years of education had a statistically significant positive medium-strength correlation with the PANDA total score (ρ (47) = 0.49, $p < 0.001$), we wanted to know whether we needed to do the same. Following the example of Gasser and colleagues, we subdivided the control group into two: those without higher education (group 1, n = 19; up to 14 years of education) and those with higher education (group 2, n = 28; 15 years of education

or more). The mean age of group 1 (M = 62.79; SD = 10.32) was a bit higher than that of group 2 (M = 59.86; SD = 8.45) but it was not statistically significant (t(33.51) = 1.03; p = 0.31). However, the mean PANDA total score of group 1 (M = 24.37; SD = 3.69) was statistically significantly lower than the PANDA total mean of group 2 (M = 26.86; SD = 2.55): t(29.51) = -2.56; p = 0.02, d = -0.94. These results mirror the findings by Gasser and colleagues and therefore we would also suggest adding 1 point to the PANDA total score to those without higher education.

Discussion

Of the four hypotheses postulated in the beginning, the first two were found to be correct and the last two not: the MMSE score and the PANDA total score were found to be significantly positively correlated, and the BDI-2 score and the score of the PANDA mood questionnaire were also found to be significantly positively correlated, just as the German results showed. Unlike the German results, education was found to have a significant effect on the PANDA total score in the Estonian control group.

The analysis of demographic data shows that the German and the Estonian control groups were similar in terms of age and years of education but differed in terms of sex. The Estonian sample had significantly higher scores in MMSE, the PANDA total score, the working memory subtest, and associate learning delayed recall subtest. The Estonian control group had higher mean scores in associate learning immediate recall subtest and verbal fluency subtest but these scores did not reach statistical significance. The German sample had higher scores in spatial imagery subtest but this difference was not statistically significant. The German control group also had significantly higher mean scores in BDI-2 and the PANDA mood questionnaire, which could also somewhat influence their scores.

During testing, some problems with the translation appeared. The discussion about this topic as well as possible solutions to be taken into account in revising the translation can be found in Appendix 3.

Cut-off scores

To obtain cut-off scores for cognitive impairment and dementia, Kalbe and colleagues (2008) used the standard procedure of determining cognitive dysfunctions on the basis of the results of the control group. All scores within one standard deviation below the mean of the total score were regarded as "age adequate" (30-18 points in total), and scores below 1.5 standard deviations of the control group results were viewed as indicating dementia (14 points and fewer). Scores between 1 and 1.5 standard deviations were taken to indicate mild cognitive impairment (15-17 points) (Kalbe et al., 2008).

We used independent samples T-test to compare the means of the Estonian and the German control groups' PANDA total scores. As can be seen from Table 1, the mean PANDA total score for the Estonian control group was almost 2 points higher than the German one ($p < 0.01$). Thus, using the same procedure, the Estonian scores would be 30-23 points for "age adequate", 22 points for mild cognitive impairment and 21 points and fewer for dementia. These cut-offs would suggest 6 people from the control group have dementia which would be highly unlikely given their average MMSE score of 28.5 points. Using this method of finding cut-off scores does not seem adequate with this particular control group.

There are three possible reasons for the higher PANDA total scores of the Estonian control group: the differences could stem from the populations, the assessment tool, or the sample(s). According to the PIAAC Survey of Adult Skills (OECD, 2013), the Germans scored higher than the Estonians in proficiency in problem solving in technology-rich environments, were approximately on the same level regarding numeracy proficiency level, and scored lower in literacy proficiency among adults. Thus it is unlikely that the difference is based on the characteristics of the nationalities.

It is possible that the differences arise from the test, specifically from subtle variances of the translation and the original as every nuance in the way words are used in different languages can never be taken into account.

It is also possible that the differences in scores were due to differences of control groups. The Estonian group is fairly small with only 48 participants and most of them (75%) are female. It must also be taken into account that in the Estonian control group, 59.6% of participants (N = 28) had higher education but in the German group, the percentage was 24.1 (N = 26). As the

Estonian control group is heavily biased towards women and people with higher education, it is very likely that the differences might stem from this. For having a more balanced control group, more data needs to be gathered.

Conclusion

As a result of this study, the PANDA test has the initial normative scores for the Estonian population. Collection of norms is a cumulative process and further language revisions of this tool would serve to collect data from a larger sample. The original cut-off scores may initially be used but in the future, one point should be added to the total score to those patients who have not received higher education. The total score is independent of other sociodemographic variables.

The PANDA will be a useful tool for neurologists, psychologists, psychiatrists, and other specialists working with PD patients. This is the first assessment tool in Estonian to specifically measure problems with cognitive functioning in Parkinson's disease.

This study was the first phase in adapting the PANDA into Estonian. The next step is to find groups of PD-MCI and PDD patients and test the PANDA on them. It would be advisable to find more participants for the control group sample and see whether the differences between the Estonian and the German samples remain.

Limitations

The main limitation of this study was the modest sample size. The control group could have been more evenly distributed in terms of gender, age, and education. The results may be skewed in favour of women with higher education. Some changes in the current translation should also be made (see Appendix 3).

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Acknowledgements

This study was partially financed by the Academica Stipend of the German Nordrhein-Westfalen Regional Employers' Union. The author would like to thank Kadi Epler for translating the PANDA, Tiina Kalda for back translation, and Mari Meidla for editing. Many thanks for all participants, my friends and family for support, and my supervisor René Randver for the opportunity to be a part of this interesting study.

Appendix 1. The PANDA in Estonian with instructions

PANDA – Parkinsoni tõve neuropsühhomeetriline hindamisskaala

Vajalikud materjalid: protokollileht, stopper või sekundiosutiga kell.

Nimi: Kuupäev:

---

1. **Sõnapaariseoste õppimine**

„*Ma loen teile nüüd ette neli sõnapaari. Palun jätke need meelde. Seejärel ütlen ma teile ainult esimese sõna paarist ning teie peate ütlema sellega kokku kuuluva teise sõna. Näiteks kui ma loen teile ette sõnapaari „tool/laps" ja annan teile seejärel ette sõna „tool", peate ütlema „laps". Kokku teeme seda ülesannet kolm korda*."

Läbiviimine: sõnapaaride nimekiri loetakse korduste vahel veel korra ette. Paariliste küsimisel ei anta tagasisidet, kas vastus oli õige, või kui patsient vastust ei tea, ei öelda, mis oli õige vastus.

	1. kordus	2. kordus	3. kordus
leht – konn	banaan – (ülikond)	sulg – (sall)	torm – (pall)
banaan – ülikond	leht – (konn)	banaan – (ülikond)	sulg – (sall)
torm – pall	sulg – (sall)	torm – (pall)	banaan –(ülikond)
sulg – sall	torm – (pall)	leht – (konn)	leht – (konn)
	Punkte:	*Punkte:*	*Punkte:*

Kokku:

---

2. Sõnaline voolavus

„*Järgmiseks ütlen ma teile kaks üldmõistet, mille kohta peaksite vaheldumisi nimetama võimalikult palju näiteid. Näiteks kui ma annan teile mõisted „köögivili" ja „rõivad", peate te esmalt nimetama ühe köögivilja ja seejärel ühe rõivaeseme, siis jälle köögivilja ja samamoodi edasi. Niisiis „kartul" – „püksid" – „sibul" – „särk" ja nii edasi. Palun nimetage nüüd ühe minuti jooksul võimalikult palju sõnu, mis vaheldumisi sobivad järgmistesse kategooriatesse: „loomad" ja „mööbel"."*

Läbiviimine: kõik nimetatud sõnad pannakse kirja.

Loomad ja mööbel Korrektseid sõnu: Vaheldumisvead:

.....
.....
.....
.....
.....
.....

---

3. Ruumiline kujutlusvõime: mentaalne peegeldamine

„*Selle ülesande puhul palun teil ette kujutada, et see joonistus siin vasakul kujutab nelinurkset paberilehte, mis on diagonaalselt kokku volditud ja millesse on augurauaga löödud kaks või kolm auku (kõige parem on demonstreerida seda pabernäidisel). Mustad punktid tähistavad neid auke. Teie ülesanne on nendest neljast joonisest, mida te paremas tulbas näete, välja valida see, mis kujutaks vasakul olevat lehte lahtivoldituna. Palun tehke õige variandi kõrvale ristike. Näide: siin (palun näidake näidisreal) näete te kaht punkti, mis kujutavad kaht auku. Kui see paber lahti voltida, paistab välja selline muster (näidake äramärgitud näidispildil).*"

(eraldi lehel)

Õigeid vastuseid:

---

4. Töömälu

„*Ma loen teile nüüd ette rea arve. Palun sorteerige need peas suuruse järgi ja korrake järele, alustades kõige väiksemast. Kui ma ütlen nt „5-2", oleks õige vastus „2-5". Näite „6-1- 9" korral oleks õige vastus „1-6- 9"."*

Läbiviimine: vajadusel korrake instruktsiooni. Vea korral on patsiendil võimalik veel korra proovida (järgmiselt realt). Kui ka seda rida ei korrata õigesti, lõpetatakse ülesanne.

6 - 3 ☐	9 - 4 - 6 ☐	7 - 2 - 8 - 6 ☐	4 - 1 - 8 - 5 - 2 ☐	9 - 2 - 6 - 4 - 7 - 1 ☐
3 - 6	4 - 6 - 9	2 - 6 - 7 - 8	1 - 2 - 4 - 5 - 8	1 - 2 - 4 - 6 - 7 - 9
8 - 4 ☐	1 - 7 - 3 ☐	3 - 1 - 9 - 4 ☐	7 - 9 - 6 - 3 - 5 ☐	7 - 3 - 8 - 5 - 4 - 2 ☐
4 - 8	1 - 3 - 7	1 - 3 - 4 - 9	3 - 5 - 6 - 7 - 9	2 - 3 - 4 - 5 - 7 - 8

Pikim õigesti korratud rida:

---

5. Viivisega kordamine

„Ma lugesin teile enne ette sõnapaare. Nüüd ütlen ma teile veel ühe korra ühe sõna igast paarist ja Teie nimetate selle juurde kuuluva teise sõna."

banaan – (ülikond) leht – (konn) torm – (pall) sulg – (sall)

Punkte:

„*Ma esitan nüüd kolm väidet teie meeleolu kohta. Palun märkige valik ristikesega vastavalt sellele, kas see väide kehtib teie kohta „täielikult", „enamasti", „vähesel määral" või „ei kehti üldse"."*

Läbiviimine: näidake seletuse juurde ka vastavaid veerge paberil (eraldi leht)

	Sõnapaariseosed	**Sõnaline voolavus**	**Ruumiline kujutlusvõime**	**Töömälu**	**Viivisega kordamine**
Toorpunktid	(max 12)	(summa)	(max 3)	(max 6)	(max 4)
Koondskoor	(max 5)	(max 7)	(max 5)	(max 6)	(max 7)

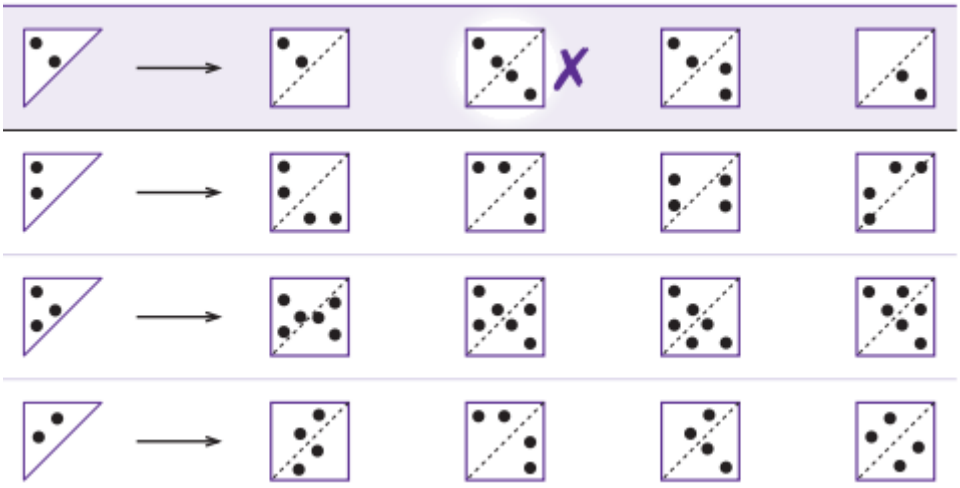
Lisada lõppskoorile üks punkt, kui testitaval ei ole kõrgharidust.

Punkte kokku (max 30):
Vaheldusvead:
Lõppskoor (max 30)**:**

18-... punkti – kognitiivsed võimed normtasemel
15-17 punkti – mõningane kognitiivsete võimete langus
...-14 punkti – võimalik dementsus

Nimi: Kuupäev:

Ruumiline kujutlusvõime: mentaalne peegeldamine
Märkige õige vastuse taha ristike



Meeleoluküsimused

	A) Nõustun täiesti (3)	B) Pigem nõustun (2)	C) Pigem ei nõustu (1)	D) Ei nõustu üldse (0)
1. Ma olen viimasel ajal rusutud meeleolus.				
2. Ma pean ennast kõigeks sundima.				
3. Asjad, mis mind varem rõõmustasid, ei huvita mind enam				

Punkte:

Appendix 2. Conversion table for the PANDA total score

Table 2. Conversion table for the PANDA

Up to 59 years of age		**From 60 years of age**	
Associate learning immediate		Associate learning immediate	
Raw score	Transformed score	Raw score	Transformed score
8-12	5	7-12	5
7	4	6	4
6	3	4-5	3
5	2	3	2
4	1	2	1
0-3	0	0-1	0
Fluency		Fluency	
Raw score	Transformed score	Raw score	Transformed score
≥19	7	≥15	7
17-18	6	13-14	6
14-16	5	11-12	5
12-13	4	8-10	4
9-11	3	6-7	3
7-8	2	4-5	2
4-6	1	2-3	1
0-3	0	0	0
Spatial imagery		Spatial imagery	
Raw score	Transformed score	Raw score	Transformed score
3	5	3	5
2	3	2	4
1	1	1	2
0	0	0	0
Working memory		Working memory	
Raw score	Transformed score	Raw score	Transformed score
6	6	6	6
5	5	5	5
4	3	4	3
3	2	3	2
2	1	2	1
0	0	0	0
Associate learning delayed		Associate learning delayed	
Raw score	Transformed score	Raw score	Transformed score
4	7	4	7
3	4	3	6
2	3	2	5
1	2	1	3
0	0	0	0

Appendix 3. Suggestions for a revised translation of the PANDA

The authors of the original, German version of the PANDA chose the word pairs for the first task so that they would have words that are concrete, frequent, but semantically unrelated (Kalbe et al, 2008). The first word pair (paper – frog) has been translated as *leht – konn* (sheet/leaf – frog) and this sounds quite a bit like a type of frog in Estonian (*lehekonn*). For this semantic relation I would argue for changing the word *leht* for *paber*.

Also two words from two other pairs – in English ball and scarf – sound very similar in Estonian (*pall* and *sall* respectively). In German, the words sound also a bit more similar than those in English (*Ball* and *Schal*) but not as much as in Estonian – the phoneme for "a" is pronounced with different lengths. I would, therefore, suggest changing *sall* for another concrete, frequent word like *saal* that would preserve both the degree of similarity and the degree of difference as in the original German version of the PANDA.

Many participants said after (and during) the second (alternating verbal fluency) task that in Estonian, it is fairly difficult to find enough different words for furniture. They did not say that about finding different words for animals. It may seem that maybe there is not a varied enough furniture-related vocabulary in the Estonian everyday language because – as a participant said – nearly everything is either a table (*laud*), a chair (*tool*) or a cupboard (*kapp*). When contacting Mr. Elke Kalbe, the author of the original German version of PANDA, he confirmed that this choice of having two categories with different degrees of difficulty was intentional.

During this study we used BDI-2 to measure depression but for many participants aged over 60-65 it proved often to be rather difficult to choose the appropriate response. Olin and colleagues (1992) have also found that older adults may have more difficulties choosing only one response per item on the BDI than on the GDS, and depressed subjects were even more likely to do so. This may reflect the difficulties depressed older adults have with decision-making (Olin et al, 1992).Thus the GDS may be more appropriate to use with older populations and might be considered for later steps on adapting the PANDA for use in Estonian population.

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