The neuropsychiatry of dementia: psychometrics, clinical implications and outcome

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Neuropsychiatric symptoms of dementia: psychometric aspects of the Dutch version of the Neuropsychiatric Inventory (NPI)
ABSTRACT

Behavioural and psychological symptoms are highly prevalent in dementia. The Neuropsychiatric Inventory was constructed to measure these symptoms. Data from three studies are presented, concerning psychometric aspects of the NPI Dutch version.

The NPI was compared to the Revised Memory and Behavioral Problems Checklist (RMBPC) and the Mini Mental State Examination (MMSE) (n=24). In the three selected patient samples prevalence of behavioural or psychological symptoms was as high as 90%. Interrater agreement (n=19) was very high (kappa > .90). Factor analysis (n=199) supports NPI construct validity. The NPI correlated reasonably close (R = .42 - .63) with the relevant RMBPC subscales, but not with a cognitive measure (MMSE).

The NPI Dutch version can be scored objectively and it is a valid rating scale for measuring a wide range of behavioural and psychological symptoms of dementia.

Key words: dementia, rating scales, neuropsychiatric inventory (NPI), factor analysis
INTRODUCTION

Behavioural and psychological symptoms are highly prevalent in dementia. With Alzheimer’s disease, prevalence of anxiety, depressive symptoms, delusions, hallucinations, apathy or agitation is at an estimated 80 – 100%. Early recognition, accurate diagnostics and treatment, if possible, are important in clinical practice for several reasons. Both patients and their primary caregivers experience such symptoms as emotionally stressful. This might explain why psychiatric complications are associated with accelerated institutionalization of demented patients.

Good instruments to register changes in the severity of symptoms are needed. Several behaviour observation scales have been developed to this purpose. In the Netherlands, there is a great deal of experience with the Beoordelingsschaal voor Oudere Patiënten (BOP, or Assessment scale for Elderly patients in translation) and the Gedragsobservatieschaal voor de Intramurale Psychogeriatrische (GIP, or Behaviour observation scale for Intramural Psychogeriatrics). In addition to assessment lists to be filled out by nursing staff, scales designed for relatives of patients living at home have been developed. Examples of influential scales are, among others, the Behave-AD and the Neuropsychiatric Inventory (NPI), published relatively recently. Little is known on whether these questionnaires are usable in the Dutch situation.

Compared to many older scales, the NPI comprises a wide range of neuropsychiatric symptoms. Furthermore, the NPI uses screening- and in-depth questions, which sort of simulates a clinical interview, allowing it to be conducted relatively quick and easy. An additional advantage of this instrument is that the same interview can (optional) register emotional stress of caregivers. Next to the original version for outpatients, there is one for nursing homes, with the informant being a nurse (NPI-Nursing Home version) and a questionnaire version for relatives (NPI-Questionnaire).

Meanwhile, the NPI has been translated and validated in many countries. A Dutch version is available and is being applied in several locations. This article discusses various studies into the psychometric aspects of the Dutch translation of the NPI.

The Neuropsychiatric Inventory

The NPI was constructed to survey neuropsychiatric disorders in demented patients. By now, studies have been carried out in various patient samples, which suggest that reliability and validity of the NPI seem likely. The NPI was translated by the authors (JdJ, MK). As a check, the questionnaire was translated back into English (independently). The NPI is administered in a semi-structured interview setting with a partner or someone else highly familiar with the patient’s daily functioning. After
the purpose of the interview and questionnaire have been explained, one screening question per behaviour domain is asked, after which approximately seven in-depth questions are possible. The behaviour domains are:

1. Delusions
2. Hallucinations
3. Agitation/Agression
4. Depression/Dysphoria
5. Anxiety
6. Euphoria
7. Apathy
8. Disinhibition
9. Irritability
10. Aberrant motor behavior
11. Nighttime behavior disturbances
12. Appetite and eating abnormalities

Cummings added the latter two subscales to the NPI at a later stage. Per domain, the relatives assess the frequency of the behaviour on a 4-point scale, the severity of the symptom (3-point scale) and the emotional stress for the caregiver (6-point scale). The NPI total score is calculated by multiplying the frequency and severity rates per domain (maximum score per domain is 12) and add them up. (total NPI-score minimum is 0 and maximum 144). The English NPI seems to represent 3 underlying factors; ‘frontal behaviour’, ‘mood’ and ‘psychosis’.16 A scale for caregivers’ emotional stress was developed separately,25 the score does not count for the NPI-total score.
METHODS

Three studies into the Dutch translation successively focussed on interrater-agreement and generic- and construct validity of the NPI. In all studies, ‘informed consents’ were obtained from patients and their accompanying relatives before commencing. SPSS software (version 10) was used for the analyses.

Study I

This study regarded NPI reliability. The extent to which the NPI is scored objectively was examined. The data were gathered by researchers of the Psychiatries department of the VU Medisch Centrum in Amsterdam, within the framework of the so-called IMO-project (in translation, Conditions for the Implementation of the Model of Meeting Centres). The data came from nineteen primary caregivers of patients with dementia syndromes, visiting different meeting centres in Amsterdam and Amstelveen for people with dementia and their caregivers. The diagnosis of dementia syndrome was generally made by GPs, Riagg-physicians (Elderly department) or neurologists. All caregivers visiting the Amsterdam meeting centre in the period from May 2000 up to December 2000, and all caregivers first entering the support programme of the Amstelveen meeting centre were interviewed at home by trained interviewers (MK of RMD or the research-psychologist). A second, trained assessor (research assistants, psychology or medicine students), present during the interview, would also fill out an NPI. NPI-training took two (morning/afternoon) shifts, during which interviewers/assessors were trained in conducting the interview, how to score the NPI, how to handle complicated decision situations and answering frequently asked questions. Next to verbal instructions, a video in English on the backgrounds of administering the NPI was shown and there were role plays in pairs.

The average age of the caregivers interviewed was 66 years (sd 13.1), of which 73.7% were male and 26.3% were female. The majority (84.2%) were partners of the demented, the others (15.8%) were all daughters. The average age of the assessed patients was 72.9 years (sd 9.4), of which 31.6% were female. Treating physicians were asked to assess dementia severity based on the Global Deterioration Scale (GDS). This scale distinguishes six stages of dementia: uncertain, mild, moderate, moderate-severe, severe and most severe. Of the demented one showed mild, six showed moderate, nine showed moderate-severe and three showed severe dementia.

Cohen’s kappas were calculated for the separate NPI subscales scores and the Spearman rank correlation was determined for the total score.
RESULTS STUDY I
The average NPI-total score for this group was 26.9 (sd 18.4). One patient showed no abnormalities on the NPI (score 0). Interrater agreement for the separate NPI-subscales proved very high. (Kappa-coefficients: 0.91 – 1.0, p<0.01). Interrater agreement for the total score was correspondingly high (ranking correlation = 0.99, p<0.01).

STUDY II
The second study regarded NPI validity. Correlation was determined with self-rating questionnaires for caregivers and cognitive testing. A selection of Dutch data from a double blind, placebo controlled study, to be reported on elsewhere, were used to this purpose. Patients in that study were treated with an acetyl cholinesterase-inhibitor or a placebo. Readings regarded possible cognitive changes in the first place, behavioural ones in the second. Patients participating visited the geriatric outpatient clinic of the Medisch Centrum Alkmaar (n=20) or were treated elsewhere (n=4). In accordance with the research protocol they were assessed once or several times. This study used primary readings.

CLINICAL INSTRUMENTS
In addition to the NPI, the Revised Memory and Behavioural Problems Checklist (RMBPC)\(^3\) and the Mini Mental State Examination (MMSE)\(^3\) were administered. The RMBPC is a questionnaire for relatives of demented outpatients, validated for the Dutch situation.\(^3\) This self-rating questionnaire (without accessory interview) consists of 24 questions (5-points scale), allocated to three subscales based on factor analysis: Depressed behaviour, Disturbing behaviour and Memory related behavioural changes. The RMBPC also has a scale per question rating the emotional stress for caregivers (4-points scale). The MMSE is a succinct, internationally well-known test to assess the presence and severity of cognitive disorders.

RESULTS STUDY II
The average age of the 16 women and 8 men was 74.3 years (sd 10.4). Twenty patients lived at home and four stayed in a (nursing) home. The informants interviewed were mostly partners,\(^\text{18}\) in five cases it was a daughter or a son and in one case there was another relative. Regarding clinical diagnostics: there was one case of amnestic disorder, one case of fronto-temporal dementia and one case of mixed dementia, there were two cases of cerebro-vascular accidents and nineteen patients were diagnosed with (senile) dementia of the Alzheimer type.

The severity of the cognitive disorders in this group was relatively mild; the average
MMSE score was 21.5 (sd 4.6, range 12-29). The average NPI-total score was 12.9 (sd 9.9), which is lower than in experiment I (Mann-Whitney U 122.5, Z 2.58, p=0.01). One patient showed no abnormalities on the NPI (score 0). The average RMBPC total score was 24.3 (sd 11.1) and the average scores on the cognition, depression and disturbing behaviour parts were 15.2 (sd 7.1), 6.8 (sd 5.6) and 2.3 (sd 2.7) respectively. NPI-assessments were not associated with patients’ age or sex. Table 1 shows the correlations between NPI, RMBPC and MMSE.

Table 1. Rank correlations NPI, RMBPC en MMSE (n=24).
‘Spearman rank correlations NPI, RMBPC and MMSE (n=24).’

<table>
<thead>
<tr>
<th>NPI subscales</th>
<th>RMBPC Total</th>
<th>RMBPC Cognitive dis.</th>
<th>RMBPC Depression</th>
<th>RMBPC Disinhibition</th>
<th>MMSE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Delusions</td>
<td>.51**</td>
<td>.53**</td>
<td>-</td>
<td>.47**</td>
<td>-.61**</td>
</tr>
<tr>
<td>Hallucinations</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Agitation/agression</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>.36*</td>
<td>-</td>
</tr>
<tr>
<td>Depression/dysphoria</td>
<td>-</td>
<td>-</td>
<td>.60**</td>
<td>-.35*</td>
<td>-</td>
</tr>
<tr>
<td>Anxiety</td>
<td>.39*</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Euphoria</td>
<td>-.38*</td>
<td>-</td>
<td>.35*</td>
<td>.36*</td>
<td>-</td>
</tr>
<tr>
<td>Apathy</td>
<td>.52**</td>
<td>-</td>
<td>.57**</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Disinhibition</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Irritability</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>.42*</td>
<td>-</td>
</tr>
<tr>
<td>Aberrant motor behavior</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-.48**</td>
</tr>
<tr>
<td>Nighttime behavior disturbances</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>.47*</td>
<td>-</td>
</tr>
<tr>
<td>Appetite and eating abnormalities</td>
<td>-</td>
<td>.33*</td>
<td>-</td>
<td>(.32)</td>
<td>-</td>
</tr>
<tr>
<td>NPI total score</td>
<td>.57**</td>
<td>.35*</td>
<td>.49**</td>
<td>.45**</td>
<td>-</td>
</tr>
</tbody>
</table>

*: p < 0.05, **: p < 0.01 (unilateral check). Non-significant findings are not included in the table, nearly significant results are displayed between brackets.

The NPI total score correlated with the RMBPC’s. ‘Depression’ and ‘Disinhibition’ on the RMBPC showed relatively close correlation with the NPI-total score. Furthermore ‘Delusions’, ‘Purposeless repetitive behaviour’ and, to a lesser degree, ‘Changed Appetite-/eating behaviour’ on the NPI were positively associated with observed or tested
cognitive disorders. There was a (moderately) strong correlation between the NPI-and RMBPC depression subscales. Several NPI-subscales correlated with ‘Disinhibition’ on the RMBPC. Four of the twelve NPI-behavioural domains (Hallucinations, Anxiety, Disinhibited behaviour and purposeless, repetitive behaviour) proved not to be associated with the RMBPC depression- and disinhibition subscales.

The emotional stress experienced by primary caregivers increases with severer behavioural problems (correlation NPI total score and emotional stress score: \( R = 0.69, \ p < 0.01 \)). The correlation with the RMBPC emotional stress scale supports the validity of the NPI emotional stress scale for primary caregivers (\( R = 0.51, \ p < 0.01 \)).

**Study III**

The third study regards the factor structure of the NPI (construct-validity). Data were gathered from the MAAstricht Study of BEhaviour in Dementia (MAASBED), to be reported on elsewhere.\(^3^4\) MAASBED focuses on course and risk factors of behavioural problems with dementia. The study consists of two parts: Firstly, the course of the behavioural problems and the patient’s characteristics that influence it are assessed. Secondly, the characteristics of caregivers that influence the onset and course of the patients’ behavioural problems are examined. It is a multidisciplinary study, resulting from a co-operation between the Hersenen en Gedrag (Brains and Behaviour) institute of the Universiteit Maastricht, the Geheugenpoli (Memory policlinic) of the Academisch Ziekenhuis Maastricht and the Ouderenzorg (Elderly care) department of the RIAGG Maastricht.\(^3^5\)

Participating patients (n=199) met the DSM-IV criteria for the diagnosis of dementia: 146 patient with a dementia syndrome of the Alzheimer type, 32 vascular dementias, 3 frontal dementias, 5 Parkinson dementias, 2 Dementias with Lewy Bodies, 4 primary progressive aphasias, 1 alcohol dementia and 6 patients with both Alzheimer and vascular aetiology. Their average age was 76.4 years (sd 8.0) and 43 % were male patients. 71.4 % of the patients showed moderately severe dementia (Global Deterioration Scale, stages 3 and 4). Comparable to earlier research into the English version, a Principal-components analysis (Varimax) of the NPI subscales scores was conducted for the construct validity study.

**Results study III**

One or more symptoms were shown on the NPI by 181 (91%) of the 199 patients. Apathy and depression were reported most frequently, euphoria, disinhibition and hallucinations least (table 2).
Table 2. Average NPI scores (frequency times severity; range 0-12) and percentage patients with symptoms (n=199).

<table>
<thead>
<tr>
<th>NPI items</th>
<th>Average and SD</th>
<th>% patients with symptoms (score ≥ 1)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Factor Psychosis</strong></td>
<td></td>
<td>36.7</td>
</tr>
<tr>
<td>Delusions</td>
<td>1.95 ± 3.41</td>
<td>34.7</td>
</tr>
<tr>
<td>Hallucinations</td>
<td>0.83 ± 2.52</td>
<td>13.1</td>
</tr>
<tr>
<td><strong>Factor Hyperactivity</strong></td>
<td></td>
<td>59.8</td>
</tr>
<tr>
<td>Agitation</td>
<td>1.50 ± 2.94</td>
<td>28.6</td>
</tr>
<tr>
<td>Euphoria</td>
<td>0.34 ± 1.54</td>
<td>7.0</td>
</tr>
<tr>
<td>Disinhibition</td>
<td>0.61 ± 2.12</td>
<td>12.6</td>
</tr>
<tr>
<td>Irritability</td>
<td>2.37 ± 3.83</td>
<td>39.7</td>
</tr>
<tr>
<td>Aberrant motor behavior</td>
<td>2.23 ± 3.73</td>
<td>34.7</td>
</tr>
<tr>
<td><strong>Factor Mood /Apathy</strong></td>
<td></td>
<td>80.4</td>
</tr>
<tr>
<td>Depression/Dysphoria</td>
<td>3.48 ± 4.22</td>
<td>57.3</td>
</tr>
<tr>
<td>Apathy</td>
<td>3.27 ± 3.72</td>
<td>59.3</td>
</tr>
<tr>
<td>Nighttime behavior dist.</td>
<td>1.22 ± 2.98</td>
<td>18.1</td>
</tr>
<tr>
<td>Appetite and eating abn.</td>
<td>1.73 ± 3.46</td>
<td>24.6</td>
</tr>
<tr>
<td>Anxiety</td>
<td>1.99 ± 3.53</td>
<td>39.2</td>
</tr>
</tbody>
</table>

Analysis shows three factors (55.1% explained variance). The first factor is a ‘hyperactive’ (or agitated) one, consisting of the symptoms agitation, euphoria, sensitiveness, disinhibition and motor agitation. The second one is a ‘mood/apathy’ factor, consisting of depression, apathy, sleeping and eating disorders. The third one is a psychosis factor, consisting of the symptoms delusions and hallucinations. Anxiety is considered a symptom on its own, which can occur separately or in combination with the three factors.
DISCUSSION

This study focuses on some psychometric aspects of the Dutch version of the NPI, an assessment scale increasingly used in international research into behavioural and psychological symptoms of dementia. The data of three selected patient samples confirm these symptoms occur in approximately 90% of the patients. The NPI-interview yields reliable, particularly objective results in that respect. The factor structure found, the correlations with other clinical instruments and even the lack of correlations with scales with other rating claims support NPI validity.

During the NPI-interview, two raters score almost exactly the same. The method is reliable in that respect and the results concur with the original American study. This does not mean that two interviews, shortly after each other and by different raters, will produce the same. One might go on longer asking questions (or better) than the other. Such differences might lead to varying symptom assessments. However, the caregivers considered two interviews shortly after each other too big a burden. Such a reliability study needs to be done in the future. The preliminary conclusion is that the NPI produces reliable, objective results.

What makes the NPI a relatively unique, clinical instrument is what it strives to assess. Not many other scales pay as much and such specific attention to neuropsychiatric symptoms of dementia as the NPI. From a validation point of view, the question is with which scale the NPI is best to be compared. The longer existing RMBPC has been translated and validated for the Dutch situation. With a relatively small number of patients in this study, some NPI symptoms showed correlation with the behavioural domains of the RMBPC. For a number of NPI-items, however, this is not the case. Small wonder, considering the items the RMBPC consists of; for instance, the scale has no items on hallucinations or euphoria. An additional explanation might be that a patient with relatively mild dementias (only 4 out of 24 scored under 18 points on the MMSE), shows behavioural and psychological symptoms in a milder form or less frequently, relatively speaking (the comparison between studies I and II supports this supposition). Subsequently, the restricted score range may have kept down the maximum correlation between both clinical instruments. Anyway, the comparison with the RMBPC does support NPI validity. The advantage of the RMBPC over the NPI is that it also rates the core, cognitive aspect of dementia, the advantage of the NPI is that it focuses more closely on behavioural-/psychological disorders. For accurate assessments the NPI is perhaps preferably to be used in combination with a cognitive measure like the MMSE.

On the NPI validity, it should furthermore be noted that – although the studied
samples were not exactly comparable – the results indicate that neuropsychiatric disorders occur more frequently in patients with more advanced dementia. Meanwhile, correlation with cognitive tests and cognitive decline assessments is very modest. Similar associations have repeatedly been demonstrated by others too.\textsuperscript{10} In other words, the NPI does not merely assess the extent of cognitive decline with dementia, which supports the divergent validity of the clinical instrument.

Finally, the NPI-factor structure is virtually the same as found elsewhere.\textsuperscript{25} This finding advocates construct validity of the instrument. Frisoni et al. also pointed out three factors in an earlier analysis: ‘frontal behavior’ (disinhibition and euphoria), ‘mood’ (depression and anxiety) and ‘psychosis’ (delusions, hallucinations, agitation and sensitiveness).\textsuperscript{25} These highly concur with the factors found in MAASBED. The Frisoni study, however, could not link the NPI symptoms apathy and motor agitation to any of the factors. An earlier, 10-item version of the NPI, used in the Frisoni et al. study, might explain the differences found. This 10-item version – without the symptoms eating- and sleeping disorders- is hardly ever used anymore. Factor analysis of the 10-item version of the MAASBED-data resulted in the same factors as for the 12-item version.

The NPI is a relatively new, clinical instrument for assessing various, neuropsychiatric symptoms in dementia. Moreover, it allows for emotional stress to caregivers to be quantified. Considering the number of patients with behavioural and psychological symptoms, assessing these symptoms as a standard procedure in routine, dementia diagnostics and treatment evaluations deserves recommendation.
CHAPTER 2

Reference List