A neuropsychological screening test to diagnose mild cognitive impairment and early dementia: DemTect
Przesiewowy test neuropsychologiczny do diagnozy zespołu lekkich zaburzeń poznawczych oraz otępienia typu Alzheimera.

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Keywords: DemTect, MMSE, mild cognitive impairment, dementia
Słowa kluczowe: DemTect, MMSE, łagodne zaburzenia poznawcze, otępienie

Summary

Background: We have developed a new, highly sensitive psychometric screening test (DemTect), especially designed to detect mild cognitive impairment (MCI) and dementia in early stages of Alzheimer’s dementia (DAT). DemTect covers a broad range of cognitive abilities, and consists of five tasks: a word list, a number transcoding task, a word fluency task, digit span reverse, and delayed recall of the word list. Age- and education-corrected scoring is also provided.

Material and methods: 121 patients with possible Alzheimer’s disease and mild to moderate dementia (scores of 1 or 2 on the Clinical Dementia Rating Scale), and 97 patients with Mild Cognitive Impairment according to the Peterson criteria (CDR score of 0.5), were enrolled in the study. A normative study was done on the basis of 145 healthy control subjects, classified as cognitively unimpaired by means of the CDR.

Results: Except for comparable performances of the two AD groups in the word list, the supermarket task and the delayed recall, the scores of all patient groups significantly differed from each other (all p<.001). There is no age or education effect for the transformed DemTect scores. Our study showed high correct classification rates for DemTect, with sensitivities of 80% and 100% for MCI and DAT, respectively.

Conclusions: With its high sensitivity for mild cognitive disturbances, easy administration, and non-dependence on sociodemographic factors, DemTect fulfills all essential criteria for a cognitive screening instrument to be used by a wide range of professionals working in geriatric medicine.

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Introduction

As the number of elderly people with cognitive geriatric disorders continues to grow and constitute a challenge to social and financial policy-makers, the need to develop more practical, yet valid and reliable methods to assess cognition also increases. Alzheimer's disease (AD) is the most often clinical condition of dementia [1], followed by cases with vascular and mixed dementia [2]. Recent estimates suppose that Lewy Body [3] and frontotemporal dementia [4] might be the second most frequent type of degenerative dementia. A state in between age consistent cognitive performance and dementia has been defined as "mild cognitive impairment" (MCI) [5,6]. MCI has attracted vast attention due to the high dementia-converter rate of these patients [7].

Dementia as well as MCI are often unrecognized by primary care physicians and general practitioners (GPs). As pointed out by Gifford and Cummings [8], nearly 75% of patients with moderate to severe dementia and even a higher percentage of patients with mild dementia and mild cognitive impairment remain unrecognized by primary care physicians.

Screening tests are helpful for detecting patients with cognitive impairments in clinical settings. Nevertheless, Rubin and coworkers [9] found that only 12% of primary care physicians used cognitive screening tests. Brodaty [10] reported a rate of 39% of GPs that performed regular screening for cognitive deficits in their older patients, but also found that the overwhelming majority of them would welcome a brief and economical screening test for identification of dementia. Next to the fact that most instruments are felt to be too time consuming, other reasons for not using screenings are the belief that the patients will be offended by the test and the GPs' lack of familiarity with neuropsychological tests.

According to Shulman [11] an ideal cognitive screening test should be quick to administer, easy to score, well tolerated and acceptable for patients, relatively independent of culture, language, and education, and should have good inter-rater and test-retest reliability as well as concurrent validity and predictive validity. To be effectual not only in MCI and AD but also other forms of dementia, and since dementias in general – even within categories of diagnoses - are very heterogeneous, they should also cover a broad range of cognitive domains.

However, a gold-standard is still lacking. Although the Mini Mental Status Examination (MMSE) [12] is still the benchmark for dementia it has been criticized for lack of sensitivity especially in patients with mild dementia [13] and for its education and age dependency [14]. Other cognitive screenings, like the 7 Minute Screen by Solomon and others [15], and the memory impairment screen [16], or the visual association test [17] solely refer to disturbances of memory and thus refer to only one cognitive dimension.

In this study we introduce a neuropsychometric screening instrument (DemTect) that was designed to be sensitive enough to detect mild dementia as well as MCI. This test is already well introduced in the German speaking area [18]. In this paper, its development, the normation of the English version, and a study proving its effectiveness in patients with MCI and mild AD in comparison with the MMSE is presented.

Patients and Methods

Subtest selection for the DemTect

We selected five tasks that cover a broad range of cognitive abilities, and have proved to be highly sensitive in the psychometric diagnosis of dementia: a word list, a number transcoding task, a semantic verbal fluency task ("supermarket"), digit span reverse, and delayed recall of the word list.

1 and 5) Learning and retrieval (Word List and Word List Delayed Recall)

Memory impairments are the core symptom of MCI and the most prominent feature of dementia in general [19] and specifically AD [20]. Thus, this function has to be documented in any neuropsychological screening instrument (DemTect) that was designed to be sensitive enough to detect mild dementia as well as MCI. This test is already well introduced in the German speaking area [18]. In this paper, its development, the normation of the English version, and a study proving its effectiveness in patients with MCI and mild AD in comparison with the MMSE is presented.
logical test for geriatric cognitive disorders. Word lists with immediate and delayed recall are well established paradigms for the assessment of verbal short and long term memory. There are different variants with either written or orally presented items, different lengths of word lists and numbers of trials, selective or full repetition of words after the first trial, and tasks with or without announcement of the delayed recall. For dementia patients, word lists have to be long enough to be sensitive for impairment but short enough to avoid bottom effects. A previous pilot study showed that a ten-item word list given twice to be adequate to assess verbal memory. Thus, we selected ten items which are easy to imagine, comparable in syllable length and phonologically different. They are read to the subject slowly and have to be recalled in two trials independent of the presented order. The subjects are not informed of a delayed recall.

2) Number transcoding task
Numbers can be represented by different code systems such as Arabic numbers, number words, Roman numbers etc.. Switching from one code into the other is called “number transcoding”, and is performed e.g. when writing down a telephone number (transcoding number words to Arabic numbers) or when writing a check (Arabic numbers to number words). Number transcoding is impaired in patients with dementia in early stages of the disease [21]. Demented patients produce specific errors that have not been observed in other brain damaged patients. In these so-called “shift errors” or “intrusion errors” which not only occur in AD patients but also in patients with other dementias, the wrong number code is used in total, or elements of one code are intruded into the other so that, for example, the number “209” becomes 2hundred9, or “nine thousand four hundred and eleven” becomes 90004hundred11. Shift errors have mainly been attributed to impaired executive functioning (in special, attention and control of behavior), and a tendency to persevere the stimulus [21]. Thus, number transcoding involves various cognitive domains, such as language processing including writing and reading, number processing, and executive functions (in particular code shifting), and is therefore liable for different cognitive impairments. For the DemTect, four items for written numeral transcoding (two Arabic numbers that have to be converted into number words, and two number words to do the opposite) that in a previous study [22] have been proved to cause a large number of errors in demented patients have been selected.

3) Semantic word fluency task: “Supermarket”
In verbal fluency or “word generation” tasks subjects have to generate words in a restricted time (usually 1 minute) and with restrictive search conditions with either words beginning with a specific letter (e.g. F or A, so-called “letter fluency tasks”), or words from a given semantic category (e.g. animals, tools, or things that can be bought in a supermarket, “semantic or category fluency tasks”). Their high sensitivity for cognitive impairment is most probably caused by the diversity of cognitive domains that are involved, such as attention and working memory (to not repeat words within that minute), cognitive flexibility and problem solving (for generating search strategies), imagery (as one possible search strategy), semantic memory (concerning lexical access), language (word production), and speed of processing (since time is limited) (Kessler et al., 1997). Many studies show that verbal fluency is impaired in early stages of dementia [23] with both quantitative (i.e. in the number of words mentioned) and qualitative output changes (in the type of output). Due to their reduced lexical access and their lack of use of strategies, dementia patients frequently only use general concepts or form very short word clusters.

Compared to letter fluency tasks, semantic word generation is impaired earlier and more severe in demented patients [23]. Among these tasks, the supermarket variant seems to be the most valuable for detecting dementia, and, in some studies, this single task that only takes 1 minute could separate Alzheimer patients from controls with high sensitivity and specificity [24]. We therefore selected a supermarket variant for the DemTect.

4) Working memory task: “Digit span backward”
Working memory is the ability to keep information online to perform different mental operations simultaneously. This capacity is involved in many cognitive processes such as language production and comprehension (to produce and understand complex sentences), calculation (for storing inter-
mediate results), or any kind of multitasking (to not lose track of the processes that are worked on). Deficits in working memory belong to the very early signs of dementia [25]. Among different tests to assess working memory, the digit span reverse in which subjects have to repeat digits in reverse order is a classical and sensitive task, and, in contrast to dual tasks, is easy to understand and short. It was thus selected for the DemTect.

Subjects

For the normation of the English DemTect version, a total of 145 control subjects (control group, CG, mean age 64.4 years, SD=10.6, range 45-89) who were classified as cognitively unimpaired by means of the Clinical Dementia Rating Scale (CDR) (Hughes et al., 1982), (CDR score = 0) were included in the study. Furthermore, 121 patients with possible Alzheimer´s disease (NINCDS-ADRDA criteria, [20]), AD, mean age 73.2 years, SD=9.1, range 45-92) and mild to moderate dementia with CDR scores of 1 or 2, and 97 patients with mild cognitive impairment according to the Peterson criteria [26], (MCI, mean age 72.1, SD=9.0, range 45-89) with a CDR score of 0.5, were enrolled in the study. All patients underwent detailed neurological and psychiatric examinations including standard laboratory tests as well as magnetic resonance tomography or computer tomography.

To control for age effects of the neuropsychological tests, and to have a population of healthy subjects that is comparable to the patient groups concerning age, the CG was split in two groups, one aged below 60 years, the other aged 60 years or older. Also, since the DemTect was designed to particularly detect mild forms of dementia, the AD patients were divided into two groups with MMSE scores of 21 or higher and MMSE scores below 21, respectively. An description of the groups is given in table 1. In all groups, there are more female than male subjects. All patient groups have comparable age but significantly less years of education than the older CG (p<.01). For the DemTect, this possible influence on cognitive performance is adjusted by an education correction (see below).

Table 1: Description of Study groups

<table>
<thead>
<tr>
<th></th>
<th>Control group</th>
<th>Control group</th>
<th>AD Patients</th>
<th>AD Patients</th>
<th>MCI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt; 60 years</td>
<td>≥60 years</td>
<td>≥21</td>
<td>&lt; 21</td>
<td></td>
</tr>
<tr>
<td>n</td>
<td>48</td>
<td>97</td>
<td>88</td>
<td>33</td>
<td>97</td>
</tr>
<tr>
<td>Age in years</td>
<td>mean (SD)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>52.4 (4.3)</td>
<td>70.2 (7.5)</td>
<td>73.3 (8.6)</td>
<td>71.5 (8.3)</td>
<td>72.1 (9.0)</td>
</tr>
<tr>
<td>Sex</td>
<td>male - female</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>15 - 33</td>
<td>27 - 70</td>
<td>35 - 53</td>
<td>8 - 25</td>
<td>46 - 51</td>
</tr>
<tr>
<td>Education in years</td>
<td>mean (SD)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>11.2 (1.5)</td>
<td>11.4 (2.3)</td>
<td>9.8 (1.2)</td>
<td>10.0 (1.3)</td>
<td>10.0 (1.2)</td>
</tr>
<tr>
<td>MMSE</td>
<td>mean (SD)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>29.4 (0.8)</td>
<td>28.5 (1.6)</td>
<td>24.1 (1.7)</td>
<td>17.8 (2.2)</td>
<td>26.9 (1.5)</td>
</tr>
</tbody>
</table>

Neuropsychological Testing

The cognitive state of the subjects was evaluated with the CDR. All subjects were tested with the DemTect and the MMSE [12]. All tests were administered by neurologists or neuropsychologists of the Memory Assessment Centre, Bradford, Department of Geriatric Medicine, Queen’s University Belfast, and Kingshill Research Centre, Swindon.

Statistical Analysis

All statistical analyses were carried out with the Statistical Package for the Social Sciences (SPSS) version 10.0 for Windows (Release 10.0.7 [1. June 2000] Chicago: SPSS Inc.). After checking for normal distribution of the data with the Kolmogorov-Smirnov-Test we used parametric methods.
(t-Tests, univariate and multivariate analyses of variance, and Pearson correlations). Discrimination analyses were performed to define sensitivities and specificities of test scores.

Results

**MMSE**

The MMSE scores of all study groups are indicated in table 1. A univariate analysis of variance in the control group (young and old together) elicited a highly significant effect of age (p<.001) but not of gender or education. Both AD groups and the MCI patients scored significantly below the older CG (p<.001). In a discriminant analysis with the older CG and all patients, the MMSE had a total classification rate of 73% with a sensitivity of 67% and a specificity of 86%. When the older CG and AD patients with MMSE scores of 21 or higher were compared, the MMSE correctly classified 89% of the subjects with a sensitivity of 92% and a specificity of 86%. For the older CG group and MCI patients, the MMSE classified 73% of all subjects with a sensitivity of 69% and a specificity of 77%.

**DemTect raw scores**

The DemTect raw scores for the study groups are shown in table 2. In a multivariate analysis of variance in the control group (young and old together), there was a significant age effect for the word list and delayed recall (both p<.001) and the supermarket task (p<.01). Furthermore, a significant education effect was observed for the transcoding task, supermarket task, and digit span backward (p<.01). There was no effect of gender. An ANOVA with post-hoc-Scheffé tests showed that both AD groups and the MCI group scored significantly lower than the older CG in all subtests (all p<.001 except transcoding and digit span in MCI with p<.05 and p<.01). Except for comparable performances of the two AD groups in the word list, the supermarket task and the delayed recall, the scores of all patient groups significantly differed from each other (all p<.001).

<table>
<thead>
<tr>
<th></th>
<th>Control group &lt;60 years</th>
<th>Control group ≥60 years</th>
<th>AD Patients MMSE ≥21</th>
<th>AD Patients MMSE &lt;21</th>
<th>MCI</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Word List</strong></td>
<td>13.10 (2.16)</td>
<td>12.03 (2.24)</td>
<td>6.26 (1.99)</td>
<td>5.36 (2.07)</td>
<td>8.83 (2.31)</td>
</tr>
<tr>
<td><strong>Transcoding</strong></td>
<td>3.77 (0.55)</td>
<td>3.79 (0.51)</td>
<td>2.19 (1.41)</td>
<td>0.81 (0.98)</td>
<td>3.28 (1.00)</td>
</tr>
<tr>
<td><strong>Supermarket</strong></td>
<td>23.52 (5.09)</td>
<td>21.88 (5.61)</td>
<td>10.50 (4.21)</td>
<td>7.90 (4.24)</td>
<td>15.15 (5.06)</td>
</tr>
<tr>
<td><strong>Digit Span</strong></td>
<td>4.87 (1.00)</td>
<td>4.79 (0.88)</td>
<td>3.64 (0.84)</td>
<td>2.72 (1.09)</td>
<td>4.27 (0.81)</td>
</tr>
<tr>
<td><strong>Delayed Recall</strong></td>
<td>5.60 (1.94)</td>
<td>4.07 (1.84)</td>
<td>0.36 (0.96)</td>
<td>0.06 (.24)</td>
<td>1.64 (1.66)</td>
</tr>
</tbody>
</table>

In the number transcoding task various errors were observed including “shift errors” that show the patients’ disability to use the right number code.

The most sensitive tasks were the delayed recall with a total classification rate of 84.3% for the older CG versus AD patients with MMSE scores 21 or higher (sensitivity: 93.4%, specificity: 76.3%), and of 72.2% for the older CG and MCI patients (sensitivity: 68%, specificity: 76.3%), and the supermarket task with a total classification rate of 86.5% for the older CG and AD patients with MMSE scores 21 or higher (sensitivity: 92%, specificity: 81.4%) and of 70.2% in the older CG and MCI patients (sensitivity: 71.1%, specificity: 69.1%).

**Transformation of raw scores, determination of the test score and clinical interpretation of the DemTect**

In analogy to the German version of the DemTect which has a maximum transformed score of 18, transformation tables of the raw scores were defined to increase discrimination rates for the test and
to account for effects of sociodemographic variables (age and education). The first step was to weight subtests according to their sensitivities. As in the German version, the delayed recall best classified control subjects and patients, followed by the supermarket task (see above). The distribution of transformed scores was thus taken from the German version with maximum scores of 5 for the delayed recall, 4 for the supermarket, and 3 for the other tasks. The second and third step included age and education corrections of the scores. The age correction was performed on the basis of the data of the two CGs. While the mean raw score of the corresponding CG was usually given the highest transformed score, scores of at least two standard deviations below the mean score was given the lowest transformed score (i.e. 0 points). The values in between were distributed accordingly. Some exceptions were made depending on the distribution of the scores.

After age correction, the mean total scores of the two CGs are comparable (15.3, SD=2.5 and 15.2, SD=2.2 for the young and older CG, respectively) but still depend on education (univariate analysis of variance, p<.001). A subdivision of all controls into a group of subjects with 11 or less years of (i.e. basic) education and a group of subjects with 12 or more years of education shows a significant difference (p<.01) of approximately 1 point in the total score (14.7, SD=2.2 versus 15.8, SD=2.2). It was thus defined that 1 point is added to the transformed total score of the subjects with only basic education.

With these corrections, there is no age or education effect for the transformed DemTect scores. All patient groups performances were significantly below that of the older CG (p < .001) and different from each other (p<.001). There was a slight but not significant increase of the transformed DemTect score from 15.8, SD=2.4 up to 16.2, SD=2.4. The intrarater reliability tested in a subpopulation of 80 AD patients is .993.

**Discrimination Analyses**

A discrimination analyses showed a total classification rate of 89% for the older CG versus all patients with a sensitivity of 85.1% and a specificity of 97%. After determining the sensitivities and specificities of the transformed DemTect scores for the CG in comparison with all patients with MCI and AD (MMSE >=21) at various cut-offs, a score of 13 was determined as the cut-off point between age-consistent and below-average performance. For the older CG versus AD patients MMSE >=21, the overall classification rate of the DemTect at that cut-off is 96% with a sensitivity of 100% and a specificity of 92%. For the older CG versus MCI patients, it was 86% with a sensitivity of 80% and a specificity of 92%. The range below that cut-off was further split into a range of 9-12 points in which mild cognitive impairment can be assumed and a range of 0 to 8 points in which a dementia can be suspected (see table xy). With those cut-offs, the DemTect correctly classifies 81% of the MCI and 85% of the AD patients (total classification rate of 85.4). In any case of suspected cognitive impairment, further testing is recommended. The administration time for the DemTect including transformation of the raw scores and interpretation is 8-10 minutes.

**Table 3: Interpretation of DemTect scores**

<table>
<thead>
<tr>
<th>Total Points</th>
<th>Diagnosis</th>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-8</td>
<td>Suspected dementia</td>
<td>Further diagnostic clarification, start treatment</td>
</tr>
<tr>
<td>9-12</td>
<td>Mild cognitive impairment</td>
<td>Retest after 6 months - observe course</td>
</tr>
<tr>
<td>13-18</td>
<td>Cognitive powers appropriate for the subject´s age</td>
<td>Retest after 12 months or if problems develop</td>
</tr>
</tbody>
</table>
The DemTect total transformed score highly correlates with the MMSE (p<.001 in the CG with r=.43 and AD group with r=.55, p<.01 in the MCI group with r=.31). A regression analysis shows that DemTect scores can be transformed into MMSE scores with the formula MMSE = 0.567 x DemTect score + 19.997, but as evident in table 4, DemTect scores only correspond to MMSE scores higher than 20.

**Table 4:** and corresponding MMSE scores, transformed with the regression formula
MMSE=0.567x DemTect transformed score+19.997

<table>
<thead>
<tr>
<th>DemTect</th>
<th>18</th>
<th>17</th>
<th>16</th>
<th>15</th>
<th>14</th>
<th>13</th>
<th>12</th>
<th>11</th>
<th>10</th>
<th>9</th>
<th>8</th>
<th>7</th>
<th>6</th>
<th>5</th>
<th>4</th>
<th>3</th>
<th>2</th>
<th>1</th>
</tr>
</thead>
<tbody>
<tr>
<td>MMSE</td>
<td>30</td>
<td>30</td>
<td>29</td>
<td>28.5</td>
<td>28</td>
<td>27</td>
<td>27</td>
<td>26</td>
<td>26</td>
<td>25</td>
<td>25</td>
<td>24</td>
<td>23</td>
<td>23</td>
<td>22</td>
<td>22</td>
<td>21</td>
<td>21</td>
</tr>
</tbody>
</table>

**Discussion**

The DemTect has shown to be a highly sensitive screening instrument which is short (administration time including scoring is 8-10 minutes), well accepted by the patients, easy to handle, and – after score transformation - independent of age and education. Its five subtests cover a broad range of cognitive abilities including short, long term and working memory, language and number processing, and executive functioning. With these subtests which are well established in testing for dementia the DemTect has high construct validity, and it also has high test-retest and interrater reliability.

Our data suggest that the DemTect is not only powerful in detecting mild AD patients (sensitivity of 100%), but is also effective in detecting MCI (sensitivity of 80%). While, unlike other studies, we found that also the MMSE is rather satisfying in discriminating control subjects from mild AD patients (sensitivity: 92%), our data confirms previous findings [27] that it is not useful for MCI patients (sensitivity: 69%). Still, a regression analysis showed that to some extent DemTect scores can be transformed into MMSE scores. Importantly, they only correspond to MMSE scores of 21 and above, and in several cases, one MMSE score corresponds to several DemTect scores (e.g. DemTect scores of 8 and 9 would both be comparable to an MMSE score of 25). Although the transformation has to be treated with care, it further illustrates that, while the MMSE is useful for staging of dementia up to moderate and severe stages, the DemTect is much more powerful to differentiate cognitive performance in the upper levels both in healthy controls and mild forms of cognitive decline (i.e. MCI and early stages of dementia).

An essential feature of the DemTect is its independency of sociodemographic variables. Due to an education and age effect in several subtests, corrections for both parameters are defined in the transformation algorithms. Although like other studies [28] we found age dependency for the MMSE, no age correction is provided for this screening. As a further advantage compared to the MMSE, the DemTect does not humiliate subjects with basic questions such as “Which year do we have?” or “Which city are we in?”.

Further studies will have to proof if the DemTect is also powerful in detecting other forms of cognitive decline such as frontotemporal Dementia or Lewy body variants of Alzheimer’s Dementia. The fact that it covers such a broad range of cognitive abilities suggests that it might also be useful for vascular dementia.

Finally, it has to be emphasized that cognitive screenings in general can only serve as instruments to detect candidate patients that suffer from cognitive decline. They represent a first step in a diagnostic makeup that, if a suspicion of diagnosis has been verified by the screening, includes elaborate neuropsychological testing as well as extensive neurological and psychiatric examination. Screenings are thus of crucial help to find patients that are in need of social and medical care at the earliest
possible point of time. Our test helps to decide if the cognitive performance of a subject is age-consistent or if mild cognitive impairment or dementia may be suspected. With its high sensitivity for mild cognitive disturbances, its easy administration, and its independency of sociodemographic factors, DemTect fulfills all essential criteria for a cognitive screening instrument to be used by a wide range of professionals such as neuropsychologists, neurologists or other specialists working in geriatric medicine.

References


Otrzymano / Received 23.08.2004
Zatwierdzono do druku / Accepted 31.08.2004