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Treatment Target Test Dementia (3TD)©

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SUMMARY

Objective So far goal-oriented therapy in dementia cannot be measured sufficiently. There are no tests that detect a profile of capacities that could describe the targets of training. Thus, it was aimed to develop a test that uncovers a profile of capacities in patients suffering from dementia.

Methods Three groups of subjects ($n = 156$), 30 patients suffering from dementia of the Alzheimer type, 28 from depressive disorder and 98 healthy age-comparable controls were included in the study. Building on already existing tests, items were developed to cover intelligence, visuo-spatial abilities, cognitive and social problem solving, emotional and executive abilities. All subjects were investigated with the Training Target Test Dementia (3TD). To calculate convergence validity, the Test for the Early Detection of Dementia from depression (TE4D) and the Beck Depression Inventory were assessed. Descriptively, profiles were calculated. Group differences were studied with the Kruskal-Wallis and the Mann–Whitney-*U*-test.

Results Characteristic neuropsychological capacity profiles were found within the three groups. Differences between the groups were significant for all subtests. Significantly, the 3TD separated patients with dementia from controls. It reached high sensitivity and acceptable specificity. The convergence validity to the TE4D was significant ($r = 0.77$).

Conclusions The capacity profiles detected may allow for specified therapeutic modules to be scheduled. Moreover, the 3TD will be suitable to discriminate between patients suffering from dementia, depression as well as healthy age-comparable controls. For therapeutic improvement, further investigation will be needed to prove its sensitivity. Copyright © 2008 John Wiley & Sons, Ltd.

KEY WORDS — Alzheimers's disease; Treatment Target Test Dementia; 3TD; sensitivity; specificity; depression; dementia

INTRODUCTION

Although degenerative dementia so far is not curable several treatment options exist. Studies on drug therapy demonstrate the usefulness of drugs such as cholinesterase inhibitors (Suh *et al*., 2004; Birks, 2006; Loy and Schneider, 2006), glutamate-modulators (Areosa *et al*., 2005; Peskind *et al*., 2006; Smith *et al*., 2006), ginkgo, a drug aimed at multiple mechanisms (Mazza *et al*., 2006; Birks *et al*., 2007; Napryeyenko *et al*., 2007) or combinations of these drugs (Geerts and Grossberg, 2006; Grossberg *et al*., 2006; Zhao *et al*., 2006). Cochrane reviews and independent evaluation groups on a methodologically high level such as the IQWIG in Germany underline the findings of the studies (Birks, 2006; McShane *et al*., 2006; IQWIG-Analyses, 2007). Some studies also demonstrate the effectiveness of some psychotherapeutic and social and environment altering therapies (Mittelmann *et al*., 1996; Spector *et al*., 2003).

First results demonstrate that single deficits can be treated as target symptoms (Spector *et al*., 2000; Dowling *et al*., 2005; Viggo Hansen *et al*., 2006).

A neverending number of psychometric tests have been published to measure different aspects of dementia. However, only a small number are sufficiently validated. Knowing that more tests are

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validated, in the following description of the areas where tests could be useful, just one example of a validated test will be named. Psychometric tests allow the detection of dementia (TE4D; Ihl *et al*., 2000; Ihl and Grass-Kapanke, 2000), describe the stages of dementia (GDS; Reisberg *et al*., 1988), behaviour problems (NPI; Cummings *et al*., 1994) and Activities of Daily Living (B-ADL; Erzigkeit *et al*., 2001) and observe the course of the disease and measure treatment effects (ADAS; Mohs *et al*., 1983, 1988). No sufficiently validated test is available to measure treatment targets in dementia.

Nevertheless, a major task in the treatment of dementia will be to detect areas in which patients can be most promisingly supported. Thus, the aim of this study was to develop an assessment that differentially detects a large part of the range of symptoms of dementia. To do this, it was necessary to identify the relevant symptom areas, to select neuropsychological tests which have already been validated for measuring this area and, if possible, combine them in a form that meets the requirements for use with older people, and to check that the resulting test corresponds to the drafted requirements. Two criteria were critical during this study of task selection. Firstly, more complex tasks should be included in order to enable the identification of slight impairments. Secondly, the tasks should be relevant to everyday life. The tasks were therefore selected from various fields in order to cover social, emotional and executive abilities. For more variables, items were extracted from already validated tests proven among younger people and combined in the '3TD' in a modular fashion. Additionally, excessive demands on the patients due to many similar tasks and questions should be avoided by the selection of very different tasks. On the other hand, the items should be formulated or combined in an age-appropriate manner.

Finally, items were developed to cover intelligence, visuo-spatial abilities, cognitive and social problems solving, emotional and executive abilities.

Table 1. Participants

Parameter	Patients with dementia (n = 30)		Patients with depression (n = 28)		Controls (n = 98)	
	Number	%	Number	%	Number	%
Male	8	27	9	32	34	35
Female	22	73	19	68	64	65
Age (median)	79		71		72	
Years in general education (median)	9.5		11		11	

METHODS

Subjects

Three clinical groups ($n = 156$) were included in the study: 30 patients had a diagnosis of Alzheimer's disease (AD) (median age: 76.6 years, range 58–88 years, probable Alzheimer's-type dementia according to the NINCDS-ADRDA-criteria, McKhann *et al*., 1984), 28 patients had a diagnosis of a depressive disorder (median age: 71.6 years, range 59–84, ICD 10, F32, F 33), and 98 healthy elderly age-comparable controls were also included (median age: 73.3 years, range 60–91 years). As an external criterion, a second experienced psychiatrist classified patients according to the ICD-10 criteria. Table 1 shows the collected demographic information including information regarding age, gender and years in general education. Informed consent after full explanation of the procedure was a further inclusion criterion.

Test development

To filter out the most accurate neuropsychological deficit profiles, the tests listed in Table 2 were used. The selection of the test items from the neuropsychological field was based on data from existing literature and clinical findings, which can be viewed as therapeutically relevant. These subtests covering

Table 2. Tests used (3TD) and the areas covered

Test	Area covered
Standard Progressive Matrices of Raven (SPM) - (Raven *et al*., 1999) adapted version	Logical reasoning Intelligence
Standardized Link's Probe (SLP) (Metzler, 2000) adapted version	Problem solving capacity executive functions
Social Problem Solving (SPS) (Ihl, 1983) two parts, quantity (SPSQ) and quality (SPSA)	Social problem solving capacity
WST (WST) (Raven *et al*., 1998) Adapted version	Verbal communication verbal fluency
Snijders Oomen-Non-verbal Intelligence (SON-R) (Raven *et al*., 1999) Adapted version	Completing figures visuo-spatial-capacity
Pictures of expressed Emotions (EMO) (Ekman and Friesen, 1972) Adapted version	Recognizing emotions
Inventory of Complex Attention (INKA) (Heyde, 1995) Adapted version	Concentration and attention capacity

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Table 3. Mean scores for the TE4D

TE4D score	Median	Mean	SD	Minimum	Maximum
Patients with dementia	24.00	21.47	9.30	4	36
Controls	39.50	39.21	4.39	29	48
Patients with depression	38.00	37.15	7.62	15	47

different cognitive and non-cognitive domains, e.g. logical reasoning, executive functions, social problem solving capacity, verbal communication, verbal fluency, visuo-spatial-capacity, recognizing emotions, concentration and attention capacity were applied to the sample as a test battery to measure for screening neuropsychological deficits associated with dementia.

Procedure

All participants were assessed with the 3TD. It took about 45–100 minutes to administer. People with dementia and depression were recruited from the Department of Psychiatry of the University of Duesseldorf. Comparators were patients from local general practitioners or volunteers from families. To calculate convergence validity, the TE4D (Test for the Early Detection of Dementia and Discrimination from Depression, also known as the TFDD; Ihl *et al*., 2000) and the BDI Hautzinger *et al*., 1995 were assessed. We administered the TE4D as a standardised test of cognition. The TE4D is a test to differentiate early dementia from depression. It was found to have excellent specificity and sensitivity and good inter-rater and test–retest reliability. The dementia patients had TE4D scores ranging from 4–36 with a median of 24.0. The median of the TE4D score in the comparison group is 39.50. Table 3 shows the mean scores for the TE4D for all groups. Eighty percent of the depressive patients were mildly to moderately depressed, 20% had a severe depression.

Statistics

Descriptively, results in subtests were calculated for every subject. For every item and subject as well as for groups, the percentage of right solutions was demonstrated. Internal consistency of the 3TD was evaluated using Cronbach's alpha. To detect inter-correlations between items, Spearman's Rho (r) was calculated. Factor analysis with Varimax Rotation was performed to investigate the test structure. Only factors with an eigenvalue of more than 1 were accepted. To detect group differences in every subtest, the Kruskal-Wallis test was calculated. To compare individual groups, the Mann–Whitney-U test was used.

RESULTS

Descriptive analysis

Descriptively, every person suffering from dementia had at least two deficits, at the most five. Every one of the demented patients had a deficit in two tests; namely SLP and INKA. All patients with depression scored in the Pictures of Expressed Emotions (EMO); 64.26% of the comparison group had no deficit. The maximal number of deficits in controls was 3.

Item analysis

Cronbach's alpha was 0.82 ($n = 156$, number of items 8, Table 4). Spearmans r showed for the most part significant correlations. The highest correlation with this was shown by SON-R ($r = 0.816$), the lowest in the quantity part, SPS ($r = 0.465$).

Factor analysis of the results of the eight subtests led to two general factors, which are responsible for 63.68% of the variance. Factor 1 included following subtests: SON-R (0.828), SPM (0.776), SLP (0.740), INKA (0.701), WST (0.656); Factor 2 included subtests SPS, respectively the quantity (0.860) and

Table 4. Internal consistency

Test	Scale mean if item deleted	Scale variance if item deleted	Corrected item-total correlation	Alpha if item deleted
EMO	271, 1253	16542, 7315	0.5644	0.8074
SLP	308, 8054	15511, 8822	0.5968	0.8000
SPSQ	300, 5209	18196, 1160	0.4386	0.8248
SPSA	287, 7370	17708, 6642	0.5465	0.8170
SONR	283, 9825	12624, 7220	0.6713	0.7926
INKA	283, 0723	11672, 3793	0.6471	0.8125
WST	277, 9629	15719, 3626	0.6793	0.7933
SPM	291, 7221	15963, 2124	0.6764	0.7954

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the quality part (0.818). The only test which cannot be clearly assigned to one of the factors is Pictures of Expressed Emotions by Ekman and Friesen (0.488). The convergence validity to TE4D was significant and resulted in a value of $r = 0.77$.

Group comparison

For all subtests, the Kruskal-Wallis-test was significant ($n = 156$, chi-square 63.48, $df = 2$, $p < 0.001$). The Mann–Whitney-*U*-test discriminated patients with AD from control persons significantly in all subtests (3TD: $n = 128$, $Z = -7.717$, $df = 1$, $p < 0.001$). Between patients suffering respectively from dementia and depression significant differences were found in five tests (SON-R, $n = 58$, $Z = -4.5$, $df = 1$, $p < 0.0018$; INKA, $n = 58$, $Z = -4.2$, $df = 1$, $p < 0.0018$; WST, $n = 58$, $Z = -3.3$, $df = 1$, $p < 0.0018$; SPM, $n = 58$, $Z = -3.2$, $df = 1$, $p < 0.0018$; 3TD, $n = 58$, $Z = -4.3$, $df = 1$, $p < 0.0018$, however, not labelled by SLP, SPS and EMO. Only in one test (SLP, $n = 128$, $Z = -4.79$ $df = 1$, $p < 0.0018$) could patients with depressive disorders and controls be significantly discriminated.

The sum score of the 3TD discriminated all groups significantly. The maximal solution rate was 40.42% for patients with dementia, 67.65% for patients with depression and 80.41% for age-matched healthy controls. At a cut-off-point of 29, the sensitivity of the 3TD to detect patients with dementia was 96.67%. Controls were correctly evaluated with a specificity of 88.78%. However, depressive patients could not be unequivocally identified, (specificity 60.71%). At a cut-off-point of 24 the test had a lower sensitivity of 83.33% and a higher specificity of 93.88%. On the other hand, there remained a good definition with regard to depressive test subjects, who were identified with a specificity of 75%.

DISCUSSION

The study aimed to develop a test to measure capabilities in a broad spectrum of symptoms in early to moderate dementia. The results presented as profiles should allow for a more specified therapy in dementia.

Before discussing the results methodological limitations should be discussed. The study did not attempt to cover the whole range of symptoms in dementia. The selection of areas was based on clinical experience and there might be a reason to favour other areas. However, to our knowledge there are no studies demonstrating that there are other relevant areas not correlating with the ones used in this study. Moreover, subtests could be seen as being too easy or too hard to solve. Observing the results of the control group it can be seen that the mean solution rate varied in between subtests, however, none of the means hit the ceiling. Thus, the tasks should not have been too easy. Concerning the bottom, equivalent observations were made. The usefulness of the test in therapy was not investigated. Further studies will be needed to uncover the range of improvements that will be possible in the areas measured.

Specific profiles of capacities were found for patients suffering from dementia or depression as well as healthy controls. A tool was developed that not only detects treatment targets in dementia but will also allow to prove specific effects of drug treatment.

Although the quantity and quality part of SPS were separate from that of the other tests, they were still found in the same region, and a connection between the subtests can be assumed.

The 3TD thus represents various abilities. This test structure confirms studies in accordance with Heidrich and Denney (1994), which showed that there is no connection between cognitive variables and social problem solving.

The differences between the groups proved to be significant in the comparison of patients with AD to controls and patients with depressive disorders. As there are often deficits only in specific areas, these can be indicative for the therapeutic process. In this way, targeted therapy and prophylactic measures are made possible for the afflicted. The profiles not only evaluate the relevant deficits, but can also be used to discover which connection neurotransmitters have with the various respective functions. A lack of the neurotransmitter acetylcholine, for example, leads to impairment of short-term memory function. By detecting the relevant unsatisfactorily completed tasks in the social problem solving area, in the emotional area and/or in the executive function area, the specific problem of the patient can be adequately approached pharmacologically, so that the effects of corresponding medication can be targeted to improve the impaired function. The high internal consistency shows that the test is homogeneous and meaningful in its current configuration.

CONCLUSION

The clarification of the causes and risk factors of AD as a basis for early diagnosis and/or care has become indispensable in the face of the rapidly changing age

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KEY POINTS

- In the early stages of dementia neuropsychological testing is important for differential diagnosis. Specific neuropsychological deficit profiles can be helpful and point at defined disease entities. There is a need to develop a test that allows finding targets for therapy in milder states of dementia.
- This screening test differentially detects a large part of the range of symptoms of dementia. The tasks selected cover social problem solving, emotional and executive abilities.
- The 3TD has high sensitivity with an acceptable specificity and significant convergence validity. Characteristic neuropsychological deficit profiles exist within the three clinical groups.
- The 3TD is well-suited for screening of dementia and for the various cognitive and non-cognitive domains. It is a suitable instrument for discovering specific deficits within the scope of dementia.

of the population and the present rising medical costs (Jellinger, 2005).

Early detection is also of prominent importance because there is a 'lead time' of 10–30 years with such disease before great functional impairment ensues (Schecker, 2003). Therefore, dementia is often first discovered in its advanced stages.

Psychometric screening tests, which evaluate performance impairment objectively and economically, are helpful in improving the still unsatisfactory early diagnosis of dementia (Grass-Kapanke *et al*., 2005).

Basis for the realisation of the 3TD procedure consists of already validated, classical tests, which cover different cognitive, social and emotional abilities. In statistical analysis the developed test discriminates all patients suffering from dementia or depression from healthy aged controls.

The results show that we have succeeded in constructing a test that is well-suited for the various cognitive and non-cognitive domains in screening of dementia. In summary, the 3TD proved itself to be a suitable instrument for discovering certain deficits within the scope of dementia.

CONFLICT OF INTEREST

None known.

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