Cued Recall and Other Cognitive Tasks to Facilitate Dementia Recognition in Primary Care

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OBJECTIVES: To compare the accuracy of commonly used tasks with that of the Visual Association Test (VAT), a conceptually different test involving cued recall of pictorial stimuli, in the recognition of dementia within primary care.

DESIGN: A cross-sectional diagnostic study of concurrent validity.

SETTING: Twenty-nine German primary care practices.

PARTICIPANTS: Four hundred twenty-three individuals in primary care participating in a longitudinal cohort study.

MEASUREMENTS: Participants underwent a comprehensive neuropsychological interview. The validated clinical dementia diagnosis was used as reference standard. Index tests comprised the VAT, Mini-Cog, clock drawing, verbal fluency, episodic memory, and subjective complaints. Validity parameters were calculated; possible confounders of test performance (age, sex, education, comorbidity, depression, language) were evaluated.

RESULTS: Twenty-one participants (5%) had dementia according to the reference standard. The VAT distinguished dementia from nondementia with a sensitivity of 95.2% (95% confidence interval (CI) = 86.1–100.0), a specificity of 96.0% (95% CI = 94.1–97.9), a positive predictive value (PPV) of 55.6% (95% CI = 39.3–71.8), and a negative predictive value (NPV) of 99.7% (95% CI = 99.2–100.0). The next-most-accurate tasks were the Mini-Cog and immediate and delayed recall. Their sensitivity and NPV are similar to those of the VAT, but their PPV and specificity were significantly lower than those of the VAT. Age and depression affected all test scores.

CONCLUSION: The VAT (cued recall of pictorial material) is superior to other tasks for the recognition of dementia in terms of higher specificity and PPV. Age-specific cutoff scores may improve the validity of all tests.
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Key words: dementia; primary care; cued recall; memory; sensitivity; specificity

Despite the severity of the effect of dementia on individuals and their families, primary care physicians (PCPs) fail to recognize a majority of cases.[1] Although there is debate as to the value of medical treatment, detecting dementia at an early stage paves the way for interventions that may address the burden of care providers, problematic behavior, psychiatric symptoms, and accidental injury. Early recognition of dementia would enable the PCP to manage the condition better and improve the decision-making process. In many cases, an accurate cognitive test might help the PCP to reduce the time lag between the onset of first symptoms and recognition of dementia.

The Mini-Mental State Examination (MMSE),[2] as the most commonly used cognitive test, has several drawbacks[3–6] and is no longer recommended in recent guidelines.[7–9]

Deficiency in cued recall is specific to Alzheimer's disease (AD),[10] and previous research has shown that cued recall tasks are effective in the detection of early AD.[11,12] Nevertheless, of the various short cognitive tests,[13–16] few include cued recall (e.g., Minimal Impairment Screen[17]), and all of these tasks use verbal material.[18] The Visual Association Test (VAT)[19] uses visual association of pictorial material as the cueing method and is intended to avoid awkward questions and bias based on language skills. The VAT has been shown to differentiate people from AD from healthy controls,[20] and VAT scores have recently been associated with cerebrospinal fluid biomarker profiles in AD.[21]

The purpose of the current study was to compare the accuracy of the VAT in recognizing dementia with the accuracy of more commonly used tasks.

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METHODS

Sample

This validation study was conducted as a subproject of the Dusseldorf study center within the prospective German Study on Ageing, Cognition and Dementia in Primary Care Patients (AgeCoDe). The basic recruitment process is outlined elsewhere.[22] Summarizing, AgeCoDe participants were selected at random from the records of 138 primary care practices in six metropolitan study centers. Inclusion criteria were aged 75 to 89 and at least one contact with a PCP within the past 12 months. Individuals were excluded in case of home visit-only consultations, residence in a nursing home, any severe illnesses being potentially fatal within 3 months, insufficient German language proficiency (although native language other than German was not an exclusion criterion), deafness or blindness, inability to provide consent, and not being a regular patient of the participating practice. The baseline sampling frame is described in Appendix S1. Two follow-up assessments (FU 1 and FU 2) were scheduled at 18 and 36 months after baseline. Individuals diagnosed with dementia at baseline were excluded from the study.

The ethics committee of the Dusseldorf Medical Faculty approved this study. Written informed consent was obtained from all physicians and participants.

Assessment Procedures and Reference Standard

Trained physicians or psychologists conducted structured clinical interviews during visits to participants' homes at all assessments (baseline, FU 1, FU 2). The interviews at each assessment involved a neuropsychological interview including psychometric testing and clinical anamnesis, medical and family history, drug inventory, sociodemographic data, lifestyle data, and the Geriatric Depression Scale.[23] Educational level was assessed according to the Comparative Analysis of Social Mobility in Industrial Nations educational classification, which takes into account schooling and vocational training.[24] The PCP filled in a questionnaire for each participant regarding a variety of clinical diagnoses of interest. In cases of suspected cognitive impairment (the cognitive section (SICSO) of the Structured Interview for the Diagnosis of Dementia (SIDAM)[25] or activities of daily living (ADL), see below), confidants (relatives or friends) were contacted to gather additional information on cognitive status, daily living, and the duration of any problems, using scales of the SIDAM as the neuropsychological core instrument. The SISCO consists of 55 items, including the MMSE,[2] and is subdivided into one memory domain and three nonmemory domains (orientation; language, perception, praxis; reasoning and problem-solving). Memory tasks include immediate and delayed recall of verbal material (three words and a postal address), delayed reproduction of a geometric figure, digit span forward and backward, and items of long-term and biographical memory. The SISCO does not include items on cued recall, verbal fluency, or the Clock Drawing Test (CDT). Information on German age- and education-specific norms for the SISCO is available.[26]

Dementia was diagnosed according to the criteria of the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition*,[27] which features a diagnostic algorithm in the SIDAM, including cognitive impairment on the SISCO score and impairment in ADLs (score of ≥ 2 on the SIDAM ADL scale). The diagnosis of AD was established according to the National Institute of Neurological and Communicative Diseases and Stroke/Alzheimer's Disease and Related Disorders Association criteria[28] for probable AD. The diagnosis of vascular dementia was based upon the National Institute of Neurological Disorders and Stroke and Association Internationale pour la Recherché et l'Enseignement en Neurosciences criteria.[29] Mixed dementia was diagnosed in the absence of a temporal association of the cerebrovascular event with cognitive decline. The validated clinical dementia diagnosis was achieved by conferring with interviewers and study coordinators (not the participants' PCPs) and reaching a consensus. In this consensus conference, suspected cases of dementia and nondefinite cases (according to SIDAM diagnostic algorithm or interviewer impression) were reviewed using all the available information (SIDAM test results, interview data, interviewer notes, confidants' information, PCP questionnaire). As a consequence, the final diagnosis was agreed upon sometime after the interview.

VAT and Other Index Tests

In the context of the FU 2 assessments (36 months from baseline) Version A of the VAT was implemented as an additional test instrument across the Dusseldorf study cohort. All participants provided consent to undergo an additional brief test. The VAT was then administered immediately after the interview so that there was no interval between the VAT, other index tests (see below), and the SIDAM.

The VAT requires the participant to remember information linked to a cue by forming an image of two interacting objects.

Test Administration

Step 1: The individual is asked to name the objects on the six cue cards (chair, ape, balloon, saucepan, baby carriage, inkwell): "I am going to show you some pictures. Please tell me what you see." Individuals are not told at this point to remember the pictures (incidental learning).

Step 2: The six association cards are shown, and the individual is asked to name each pair of interacting subjects (a hedgehog on a chair, an ape holding an umbrella, a key hanging from a balloon, a die in a saucepan, a bird in a baby carriage, a flag standing in an inkwell). The examiner may assist in the naming process if necessary.

Step 3: Cued recall is tested by showing the six cue cards once more and asking the individuals to identify the missing object (e.g., "What was the ape carrying?").

Responses may be verbal, written, drawn, or mimed. If all six responses are correct in Step 3, the VAT score will automatically be 12. If not, Steps 2 and 3 are repeated, resulting in a VAT score between 0 and 11. Administration time is 4 to 6 minutes if both trials are necessary. One trial takes 2 to 3 minutes.

The validity of VAT was compared with that of other tasks commonly used in the identification of possible dementia. All of these tasks were part of the regular interview section within the AgeCoDe study. The same interviewer administered all tasks in one session. The Consortium to Establish a Registry for Alzheimer's Disease (CERAD)[30] verbal fluency (animals; administration time 1.5 minutes), CERAD word list memory (immediate recall of 10 words over three trials, score 0–30; 4–6 minutes), CERAD word list delayed recall (score 0–10; 10 minutes after immediate recall; 5–7 minutes plus 10-minute interval), CERAD word list recognition (sum of correct rejections and hits, score 0–20; 5–7 minutes plus 10-minute interval), CDT[31] (score 1–10; 1–2 minutes), Mini-Cog[32] (score 0–3; 3 minutes; this score was based on the recall of the three words in the MMSE and CDT, in line with the proposed algorithm[32]). VAT scores, CDT, and CERAD subtests were not part of the SIDAM algorithm as the core instrument of the reference standard. Because immediate and delayed recall of the three MMSE words and other verbal material are parts of the SISCO, the Mini-Cog and the CERAD word list tasks may to a certain extent be subject to incorporation bias. As a further measure, individuals were asked about subjective memory impairment (SMI): "Do you feel like your memory is getting worse?" (yes/no).[33]

Statistical Analyses

Characteristics of participants with and without dementia were compared using Mann–Whitney *U*-tests and chi-square (χ^2) tests. For continuous index test scores, nonparametric analyses were performed on the area under the receiver operating characteristic curve (AUC), with disease status as target variable (dementia, yes/no). To establish the optimal cutoff points of the index tests, Youden indices ((sensitivity + specificity) − 1) were estimated. Based on these, parameters of concurrent test validity (sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV)) were calculated, along with their 95% confidence intervals (CIs), with the target variable being the disease status. McNemar tests were performed to compare sensitivity and specificity of all tasks having a Youden index of 0.80 or greater.

To adjust for a possible cluster effect of PCP practices, the independent effects of confounders on index test scores and SMI were analyzed using generalized estimating equation (GEE) models across the whole sample. The full GEE models for each index test included age, sex, education, native language, number of diagnoses, depression score, and dementia status as influencing variables; PCP practice ID was added as a repeated-participant variable in all models. Depending on the target variable, a multinomial logistic approach with logit link was used for ordinal data (Mini-Cog), a metric approach with identity link for approximately normal distributed data (all other index tests), and a binary logistic approach with logit link for SMI. (In addition to the normal distribution models, models were alternatively calculated based on the Gamma distribution with log link for the more-skewed distributions of VAT, CDT, and CERAD-recognition. The results differed only marginally.)

Rank correlations (Kendall's tau) were calculated between the VAT and all other index tests.

RESULTS

The study cohort presented here included 423 out of 432 possible participants registered at the 29 primary care practices who took part in FU 2 at the Dusseldorf AgeCoDe study center between April 2006 and November 2007. (See STARD flow chart in Appendix S2.)

Characteristics of Participants

As shown in Table 1, participants with and without dementia were comparable in terms of age, sex, education, percentage of nonnative German speakers, and number of diagnoses. Participants with dementia had slightly higher depression scores.

Twenty-one participants (5%) were diagnosed with dementia through a consensus conference (10 AD, two vascular dementia, six mixed dementia, two without identifiable etiology). This small number is most likely because of the exclusion of participants with dementia at baseline. This means that no participant had had dementia for longer than 3 years, so the sample featured only individuals in the early stages of the disease. Eleven participants had been diagnosed with dementia at FU 1, which means that manifest dementia began to develop at some point between baseline and FU 1 (between 1.5 and 3 years before administering the VAT). The remaining 10 participants were diagnosed when the VAT was administered (FU 2). In these cases, dementia began to develop at some point between FU 1 and FU 2 (at most, 18 months before

Table 1. Characteristics of the Visual Association Test Study Sample

Characteristic	No Dementia (n = 402)	Dementia (n = 21)
Age, mean ± SD	82.4 ± 3.4	82.4 ± 3.2
Female, %	68.7	61.9
Level of education, %*		
Low	62.2	61.9
Middle	28.1	28.6
High	9.7	9.5
Native language other than German, %	3.5	4.8
Number of somatic diagnoses,† mean ± SD	3.2 ± 1.9	2.9 ± 2.1
Geriatric Depression Scale score, mean ± SD[23] (range 0 (no symptoms) to 15)	2.5 ± 2.2	3.6 ± 2.4‡

* Based on the revised version of the international Comparative Analysis of Social Mobility in Industrial Nations educational classification.[24]

† Based on information from the participants' primary care physicians.

Tests of significant differences between participants with and without dementia: Mann–Whitney *U*-tests for age, number of somatic diagnoses, depression score; chi-square tests for sex, education, language (exact test).

‡ $P = .04$.

SD = standard deviation.

the VAT). The sample with dementia consisted of 10 mild cases (MMSE 18–30), 10 moderate cases (MMSE 11–17), and one severe case (MMSE ≤ 10).[34]

Validity of the Index Tests

Table 2 presents the validity parameters of all index tests. Except for CDT and recognition memory, the AUC for all scores was greater than 0.9. Using calculated cut-off points, the Youden index was greater than 0.8 for the VAT and Mini-Cog and immediate and delayed recall. The VAT's sensitivity did not differ from these three next-most-accurate tasks (exact $P > .10$ for all McNemar tests based on binomial distribution). McNemar tests for the comparison of specificities show that the VAT's specificity of 96.0 (95% CI = 94.1–97.9) was significantly higher than that of the other tasks (VAT vs Mini-Cog, χ^2 (degrees of freedom (df) = 1) = 30.95; $P < .001$; VAT vs immediate recall, $\chi^2(df = 1) = 44.33$; $P < .001$; VAT vs delayed recall, $\chi^2(df = 1) = 15.61$; $P < 0.001$). The VAT score stands out further because of its high PPV of 55.6 (95% CI = 39.3–71.8), which had only a slight overlap with the PPV of one other task (delayed recall).

Table 3 presents the 2 × 2 chart on diagnostic accuracy for the VAT (cutoff ≤ 7).

Rank correlations revealed moderate and significant associations between VAT score and all other tasks ($P < .001$ for all correlations): Kendall's tau was approximately 0.40 between the VAT and the other memory-based tasks ($\tau = 0.39$ for Mini-Cog, $\tau = 0.40$ for immediate recall, $\tau = 0.42$ for delayed recall, and $\tau = 0.39$ for recognition memory) and approximately 0.30 between the VAT and the nonmemory tasks ($\tau = 0.29$ for CDT and $\tau = 0.32$ for verbal fluency).

Influencing Factors

Scores on the Geriatric Depression Scale were significantly related to all test scores and SMI. Participants' age was also significantly related to all test scores (but not SMI). No other confounder influenced VAT, recognition memory, or SMI. At least one additional confounder affected all other tests: Mini-Cog by education; immediate and delayed recall and CDT by sex and education; verbal fluency by education, native language, and number of diagnoses (see Appendix S3 for details). Dementia status had a significant influence on all scores and SMI.

INTERPRETATION

According to the reference standard, specificity and PPV of the VAT were better than that of the Mini-Cog,[32] CERAD[30] immediate and delayed recall and recognition of a word list, verbal fluency, CDT, and subjective memory impairment. Participant level of education, sex, morbidity, and native language, which are typical confounders of

Table 3. Cross-Tabulation of Visual Association Test (VAT) Results with Consensus Diagnosis of Dementia

	Reference Standard (Consensus Diagnosis) n (%)		
VAT Result	Dementia	No Dementia	Total
≤ 7 (dementia)	20 (4.7)	16 (3.8)	36 (8.5)
≥ 8 (no dementia)	1 (0.2)	386 (91.3)	387 (91.5)
Total	21 (5.0)	402 (95.0)	423 (100.0)

Table 2. Validity Parameters for Calculated Cutoff Points

Parameter	Area Under the Receiver Operating Characteristic Curve (95% CI)	Youden Index (Cutoff)	Sensitivity (95% CI)	Specificity (95% CI)	Positive Predictive Value (95% CI)	Negative Predictive Value (95% CI)
Visual Association Test	0.981 (0.963–0.999)	0.91 (≤ 7)	95.2 (86.1–100.0)	96.0 (94.1–97.9)	55.6 (39.3–71.8)	99.7 (99.2–100.0)
Mini-Cog	0.956 (0.931–0.982)	0.85 (≤ 1)	100.0 (82.4–100.0)	85.2 (81.4–88.4)	23.4 (15.3–34.0)	100.0 (98.9–100.0)
Immediate recall (10 words, sum of three trials)*	0.957 (0.927–0.987)	0.83 (≤ 14)	100.0 (100.0–100.0)	82.8 (79.0–86.5)	20.7 (12.2–29.2)	100.0 (100.0–100.0)
Delayed recall (10 words, 10-minute delay)*	0.951 (0.920–0.983)	0.85 (≤ 2)	94.7 (84.7–100.0)	90.3 (87.3–93.2)	31.6 (19.5–43.6)	99.7 (99.2–100.0)
Word list recognition (10/20 words; sum of correct rejections and hits)*	0.881 (0.784–0.978)	0.64 (≤ 16)	70.6 (48.9–92.2)	93.3 (90.8–95.7)	30.8 (16.3–45.3)	98.7 (97.5–99.8)
Clock Drawing Test	0.856 (0.733–0.978)	0.73 (≤ 7)	89.5 (75.7–100.0)	83.7 (80.1–87.3)	20.7 (12.0–29.5)	99.4 (98.6–100.0)
Verbal fluency (animal naming in 1 minute)*	0.918 (0.833–1.002)	0.78 (≤ 12)	89.5 (75.7–100.0)	88.3 (85.1–91.4)	26.6 (15.7–37.4)	99.4 (98.7–100.0)
Subjective memory impairment, yes/no	–	0.35	89.5 (75.7–100.0)	45.8 (40.9–50.6)	7.3 (3.9–10.6)	98.9 (97.4–100.0)

* Subtest of the neuropsychological test battery of the Consortium to Establish a Registry for Alzheimer's Disease.[30]
CI = confidence interval.

patient-based cognitive tests, did not affect VAT scores. Previous findings[20,35] showed that level of education did not affect VAT score. Age and depression score influenced all tests (including the VAT). A previous study found an optimal VAT cutoff score of 8 in the younger Amsterdam Study of the Elderly cohort (aged 65–84; mean age of healthy controls: 72.7, mean age of participants with incident AD: 78.8).[19] In the current sample of an older age group (77–93, mean 82.4) a lower cutoff score of 7 was found to be optimal. Larger studies with a wider age range (but still with a low proportion of dementia cases) can generate more-robust validity parameters and evaluate how consideration of confounders (especially age and depression) and the combination of tasks can further improve the accuracy of the VAT and other scores.

Strengths and Limitations

In terms of disease severity, only half of the participants in the sample were considered to have mild dementia. Because the identification of mild cases is the principal task of any screening test, the VAT should be subject to further investigation using samples with a higher proportion of mild dementia. With regard to the duration of the disease, the participants were all at a relatively early stage of dementia (no more than 3 years since the occurrence of dementia).

The participants' language skills were not assessed in depth, and participants with insufficient German language proficiency were excluded at baseline. As a result, it was necessary to use the native language as a surrogate parameter, so no concrete conclusions can be made about the effectiveness of the VAT in settings in which highly diverse language skills prevail.

Table 1 shows that participants with dementia were comparable with those without in terms of the number of diagnoses. It must be assumed that these individuals with dementia represent a relatively healthy group. One reason for this, as well as for the low number of individuals with dementia in the sample, may be a significant dropout rate among (frail) participants with dementia over the 3-year course of the study from baseline to FU 2.

Although the VAT and the other index tests were not explicitly part of the reference standard, the same interviewers administered them. It is possible that the results of these tests, and not exclusively by the reference instruments (especially SIDAM) influenced an interviewer's decision to pass a case over to the consensus conference to some degree (consciously or not), although this verification bias is more likely in the CERAD subtests or CDT because interviewers were more familiar with the way these tests are interpreted than they were with the relatively new VAT. Therefore, if verification bias carries any weight at all, an overestimation of test accuracy is more likely for CERAD and CDT than for the VAT.

The small proportion of participants with dementia (5%) resembles the low-prevalence setting of primary care. Validating a test using such a sample indicates a methodologically rigorous approach and paves the way for the calculation of realistic predictive values that are critical for any test application in a primary care setting. Most studies on dementia tests have employed smaller samples with artificially high numbers of participants with dementia, so realistic predictive values could not have been estimated.[14,16] In the majority of studies relating to short dementia tests, PPVs are low.[15] In contrast, the VAT reveals a satisfactory PPV, considering the low proportion of participants with dementia in the present study.

CONCLUSION

The VAT is an accurate test that seems not to be affected by typical confounders such as language or educational level. In settings in which the risk of false-positive findings should be kept as low as possible, the VAT may offer a good alternative to other tests because of its higher specificity and PPV. The lower risk of false-positive results can allay the PCP's fear of unnecessarily disconcerting patients. The pleasant way that the VAT is administered may reduce any potential for embarrassment between patient and doctor resulting from awkward questions or a focus on any deficiencies in other tests,[36,37] although this thesis was not explored in the current study. The VAT was not superior to other tests with regard to its sensitivity. In settings with a focus on recognizing as much dementia cases as possible, the VAT may not be the best instrument.

A combination of verbal cued recall (extended Dutch version of the Minimal Impairment Screen[17]) and nonverbal cued recall (VAT) has been found to be useful for differentiating individuals with AD from those with depression and healthy controls.[38] In individuals with lower language proficiency or aphasia, the VAT may be one of the few helpful instruments. The results of the current study further underline the importance of age-adjusted cut-off scores and taking depression into account. In conclusion, this study points to the possible usefulness of the VAT. Further investigations in larger primary care samples are needed to confirm this.

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Author Contributions: AF, AW, and MP contributed to study conception and design, recruitment of PCPs and participants, and data acquisition. BW organized data management and assured data quality. AF, BW, and MP contributed to data analysis and performed the statistical analyses based on the discussions of all authors. All authors contributed to interpretation of data. AF and MP drafted the article. BW, AA, and AW critically discussed all versions of the manuscript. All authors revised and approved the final version to be published. AF, BW, and MP had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. AF is guarantor.

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SUPPORTING INFORMATION

Additional Supporting Information may be found in the online version of this article:

Appendix S1. Baseline sampling of the whole AgeCoDe study (6 study centers).

Appendix S2. STARD flowchart for VAT with a cutoff score of 7/8.

Appendix S3. Multivariable analyses (Generalized Estimating Equations, GEE) of confounder effects on test scores and SMI.

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