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Visual Association Test (VAT) Recognition Trial: Difference between Older Patients with aMCI or AD and VCI or VaD Diseases

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ABSTRACT

Objectives: The main goal of this study was to differentiate patients with amnestic mild cognitive impairment (aMCI) or Alzheimer disease (AD) from patients with vascular cognitive impairment (VCI) or vascular dementia (VaD) based on the new developed Visual association test (VAT) recognition trial. Furthermore, the score difference between the VAT immediate recall trial two to the VAT delayed recall trial and the score difference between the VAT immediate recall trial two to the VAT recognition trial in comparison to the score difference of the VAT immediate recall trials (one and two). Last, we evaluated the visual VAT recognition trial in comparison to the 15 word task (15WT) recognition trial for each group.

Methods: We evaluated 55 geriatric outpatients and nursing home day care patients (19 with aMCI, 25 with AD, 6 with VCI, and 5 with VaD). Because of the low number of patients, we compared the patients with aMCI or AD (n = 44) and the patients with VCI or VaD (n = 11). We used the VAT and the 15WT. The non-parametric Mann-Whitney U-test and the Wilcoxon signed-ranks test were used to analyze data.

Results: We found that patients with aMCI or AD and patients with VCI or VaD perform equally based on the VAT recognition trial. By contrast, we found that patients with aMCI perform relatively better than patients with AD. Furthermore, we found that all patients except patients with VaD show an improvement on the VAT immediate recall trials and deterioration on the VAT delayed recall trial. All patients perform equally on the VAT recognition trial in comparison to the VAT immediate recall trial. As last, we found that patients with aMCI or AD and aMCI separately perform relatively better on the visual (VAT) recognition in comparison to the verbal (15WT) recognition trial.

Conclusion: We may conclude that, based on these data there's no differentiation possible between patients with aMCI or AD and patients with VCI or VaD based on the VAT recognition trial.

1. INTRODUCTION

Dementia is prevalent in old age, with approximately one percent affected of people aged 65 or over and approximately 25% of those aged 85 or over (Ferri et al., 2005). Cognitive impairment is the core clinical symptom of dementia. However, cognitive symptoms may differ across dementia type etiologies. Neuro-degenerative disease is an umbrella term for the progressive loss of structure or function of neurons. The most common form of neurodegenerative disease is Alzheimer's disease (AD; 50-75%; World Alzheimer report, 2009). Cerebrovascular disease (CVD) is an umbrella term for conditions caused by problems with brain vasculature. Vascular dementia (VaD) is resulting from CVD and ischemic or hemorrhagic brain injury. VaD is the second most common type of dementia (2.2%-16.3%; Leys, Pasquier & Parnetti, 1998). Mild cognitive impairment (MCI) and vascular cognitive impairment (VCI) are defined as a decline in cognition and function but that do not meet criteria for the diagnosis of dementia. Episodic memory impairment is prevalent in amnestic Mild Cognitive Impairment (aMCI) or Alzheimer disease (AD) and impaired attention, mental speed, and retrieval deficits often characterize Vascular cognitive impairment (VCI) or Vascular Dementia (VaD). A recent study of 15.367 patients with VaD reported that 16.6% were miss diagnosed with AD (Kirson et al., 2013). It's predicted that discriminating AD from VaD is possible with recognition trials, because the recognition of VaD patients is normal, whereas AD patients show impaired recognition (Lafosse et al., 1997). Neuropsychological tests such as the Visual Association Test (VAT) are useful in assessing episodic memory deficits (Lindeboom & Schmand, 2003). Recently, a VAT recognition task (Meyer, Spaan, Boelaarts, Schmand, & de Jonghe, in preparation) was constructed with the aim of expanding clinical assessment of different types of memory impairment. They developed these new parallel versions because most of the current tests (e.g. the Rey Auditory Verbal Learning Test; RAVLT or the Dutch version 15 word task; 15WT) may result in floor effects to patients with amnestic mild cognitive impairment (aMCI) or AD (Kessels, Rijken, Joosten-Weyn Banningh, Schuylenborgh-van Es & Olde Rikkert, 2009; Petersen et al., 1999; Ricci, Graef, Blundo & Miller, 2012). A floor effect refers to the diminished ability of a test to differentiate between persons at the low end of the measurement range (Cohen, Swerdlik & Sturman, 2013). Although the new VAT recognition task has been studied in normal controls, it's usefulness in clinical populations still awaits evaluation. Therefore, this study evaluated the differences between older patients with aMCI or AD in comparison to patients with VCI or VaD based on the VAT recognition trial. Furthermore, we evaluated in a exploratory manner the comparison of the VAT trials and we made a comparison of the VAT recognition trial with the 15 word

task for those group.

1.1 Memory and Brain Structures

An important neurological structure for memory is the medial temporal lobe (MTL). The MTL includes a system of anatomical related structures that are essential for declarative memory. Declarative memory can be broken down further into things that we recall about our own lives (episodic memory) and world knowledge (semantic memory). The MTL can be subdivided into the perirhinal cortex, the parahippocampal cortex, the entorhinal cortex and the hippocampus (Eichenbaum, Yonelinas & Ranganath, 2007). Regional atrophy of the MTL, particularly the hippocampus and the entorhinal cortex is present in 80-90% of AD patients, opposed to 5-10% of healthy aged-controls (Scheltens et al., 1992). The hippocampus is critical for storing new memories. The hippocampal volume of patients with AD is reduced with 16.6% and the hippocampal volume of patients with VaD is reduced with 11.6% (van de Pol, Gertz, Scheltens & Wolf, 2011). Thus, the hippocampus is also affected, but rarely does a deficit of episodic memory in these patients reach the severity presented in typical AD (Graham, Emery, & Hodges, 2004; Lafosse et al., 1997; Lamar et al., 1997). The damage to the hippocampus is correlated with performance on memory tests (Scheltens et al., 1992). The hippocampus is involved in the consolidation process, which means that memories are solidified in long-term stores over weeks, months, and years. The CA1 region of the hippocampus is the origin of connections from the hippocampus to the neocortex that are important in the consolidation process of episodic memory (Gazzaniga, 2009). Typical for AD patients is a disturbance in these connections known as antrograde amnesia (Vanderploeg, Yuspeh & Schinka, 2001). Antrograde amnesia is an inability to store new information, leading to a partial or complete inability to recall the recent past (Lezak, Howieson, Bigler & Tranel, 2012). In contrast, patients with VaD have problems with retrieving information (Vanderploeg et al., 2001). Retrieval uses the stored information to create a conscious memory to produce an action. The deficit in the retrieval process is caused by damaged connections between the hippocampus and other brain regions (Gazzaniga, 2009). Thus, patients with AD have consolidation deficits whereas patients with VaD have retrieval deficits.

1.2 Memory Measurement Trials

Immediate recall, delayed recall and recognition trials are the most frequently used tasks to measure consolidation and retrieval deficits. Immediate recall is recall immediately after the presentation of the stimulus, whereas delayed recall is recall after a certain period of

time. Recognition is the capacity to identify an item as one that was recently encountered. There are two different underlying processes, immediate recall and delayed recall needs active brain processes and recognition needs a passive brain process. Thus, recognition tasks are easier in comparison to immediate and delayed recall tasks. A meta-analysis of 47 studies showed delayed reproduction as the best measure for estimating the cognitive impairment of patients with AD (Bäckman, Jones, Berger, Laukka & Small, 2005). Furthermore, patients with AD had a negligible improvement in the learning curve with repeated measures (Burkart, Heun & Benkert, 1998; Bigler, Rosa, Schultz, Hall & Harris, 1989). An important characteristic of AD on memory tasks is the absence of improvement on recognition task (Dubois et al, 2007), whereas the recognition performance in VaD patients is usually normal (Jonker, Slaets & Verhey, 2009).

A few studies have evaluated memory with the uses of immediate recall, delayed recall and recognition trials. Hong et al. (2013) have evaluated these trials between patients with AD and patients with subcortical ischemic vascular dementia (SIVD) based on the Seoul Verbal Learning Test (SVLT) and the visual Rey Complex Figure Test (RCFT). Patients with AD and SIVD scored equally on the immediate recall trial based on the SVLT. They found that patients with SIVD scored significantly higher in comparison to patients with AD on the delayed recall trial and the recognition trials based on the SVLT. By contrast, there was no significant difference found on those trials based on the RCFT. Graham et al. (2004) has also studied verbal and visual immediate recall, delayed recall and recognition of patients with AD and VaD based on the Logical memory subtest of the Wechsler memory scale and the "Doors and people test". They also compared the patients with AD and VaD on these tasks. They found that patients with VaD perform significantly better on the verbal immediate recall trial and visual immediate recall trial in comparison to patients with AD based on the "Doors and people test". Furthermore, they found that patients with VaD also perform significantly better on the verbal delayed recall trial based on the logical memory subtest and on the visual delayed recall trial based on the "Doors and people test". Graham et al. (2004) used the short Recognition Memory Test (RMT; for words and faces) and the "Doors and people test" to measure visual and verbal recognition. They found that patients with VaD perform significantly better in comparison to patients with AD on verbal recognition based on the "Doors and people test". They found no significant difference in performance based on the visual recognition task. These results of the verbal recognition task are in accord with the results of Lafosse et al., (1997). They studied recognition between patients with AD and patients with VaD on a devised verbal recognition trial based on the list-learning subtest of the Memory

Assessment Scale (MAS). They found normal verbal recognition for patients with VaD, versus impaired verbal recognition for patients with AD.

The studies of Hong et al. (2014) and Graham et al. (2004) didn't evaluated the comparison of the immediate recall trial with the delayed recall trial for patients with AD and patients with VaD. They also didn't evaluate the comparison of the immediate recall trial with the recognition for those patients. Thus, the results described below are descriptive and based on mean scores. Hong et al. (2014) found that patients with AD scored approximately 10.7 words lower on the delayed recall and patients with VaD scored approximately 9.4 words lower on the delayed recall trial in comparison to the immediate recall trial based on the SVLT. Patients with AD and patients with VaD scored both better on the recognition trial in comparison to the immediate recall trial based on the SVLT. Patients with AD scored on average 51.5 more words correct on the recognition trial and patients with VaD scored on average 59.3 more words correct on the recognition trial in comparison to the immediate recall trial. By contrast, the mean of the immediate recall and the delayed recall trials for both groups were almost equally based on the RCFT. Furthermore, patients with AD scored on average 60.6 more figure parts correct on the recognition task and patients with SIVD scored on average 64.1 more figure parts correct on the recognition task in comparison to the immediate recall task. The findings of the study of Hong et al., (2014) were almost in line with the study of Graham et al. (2004), there were three differences. First, patients with AD scored almost equally on the immediate recall trial and on the recognition trial based on the visual "Doors and people test". Second, patients with VaD scored almost equally on the immediate recall trial and on the recognition trial based on the verbal "Doors and people test". Last, patients with VaD scored 4.5 photographs more correct on the immediate recall trial in comparison to the recognition trial based on the visual "Doors and people test". Thus, this suggests that patients with AD improve on the verbal recognition trial and patients with VaD didn't improve on the visual and the verbal recognition trial.

Overall, there are contradictory results based on the verbal immediate recall trial, the visual immediate recall trial and the delayed recall trial. However, as expected, all the studies concluded that patients with VaD perform relatively better in comparison to patients with AD based on the verbal delayed recall trial, the verbal recognition trial and the visual recognition trial. Furthermore, as expected, almost all studies suggest that patients with AD and VaD scored relatively better on the immediate recall trial in comparison to the delayed recall trial. By contrast, there are contradictory results between the immediate recall trial and the recognition trial. That patients with VaD improved more could be explained by the typical antrograde

amnesia in patients with AD.

1.3 Visual and Verbal Recognition Trial

The studies of Hong et al. (2013), Graham et al. (2004) and Lafosse et al., (1997) have only evaluated a difference between patients with AD and patients with VaD on a verbal and a visual recognition task separately. These studies have not evaluated a comparison of a verbal recognition task and a visual recognition task for each patient group. An example of a test with a verbal recognition trial is the 15 word task (15WT). The 15WT may result in floor effects to patients with amnestic mild cognitive impairment (aMCI) or AD. The visual VAT recognition task has not been studied in comparison with a verbal 15WT recognition task; the usefulness of this kind of visual recognition still awaits evaluation.

The Visual Association Test (VAT; Lindeboom & Schmand, 2003) and the Dutch version of the Rey Auditory Verbal Learning Test the 15WT (Saan & Deelman, 1986) are examples of memory tests. The VAT is designed to detect visual anterograde amnesia (Lindeboom & Schmand, 2003), whereas the 15 WT (Saan & Deelman, 1986) is designed to detect verbal antrograde amnesia. The VAT has only two immediate recall trials and sometimes an informal recognition trial was used, but the informal recognition is not standardized. Whereas the 15WT includes five immediate recall trials, a delayed recall trial and a recognition trial. Meyer et al. (in preparation) have developed a new version of the VAT. This VAT includes a new parallel version, version C en D. They developed new cues and targets for the new parallel version. These new parallel versions include a delayed recall trial and recognition trial. The recognition trial of the 15WT exists of 30 nouns, and the subject was asked to say if the word occurs in the learned phase of the immediate recall trial. By contrast, in the recognition trial of the VAT, the subject learned six associations between a cue and target. In the recognition trial, the subject was shown a cue and four targets. The subject was asked to say which of the four targets belonged to the cue. It's known that patients with AD score lower on the immediate recall of the VAT than patients with VaD (Lindeboom,, Schmand, Tulner, Walstra & Jonker, 2002), but it's unknown if AD patients score lower on the recognition trials of the VAT as well. Thus, the recognition trial of the VAT and it's comparison with a verbal recognition trial for AD and VaD patients needs an evaluation.

1.4 This Study

The aim of this cross-sectional study was to determine if there is a discriminative validity possible between patients with AD on one hand and patients with VaD on the other

hand based on the VAT recognition trial. The group of patients with VaD was too small, for this reason we joined the patients with AD and the patients with aMCI. We also joined the patients with VaD and the patients with VCI. Furthermore, we have evaluated in an exploratory manner all research questions between the severities of the dementia type's and for the patients with aMCI and patients with VCI. Patients with aMCI or AD have consolidation problems, so they can't recognize what they have learned. By contrast, patients with VCI or VaD only have retrieval deficits. Therefore, it's expected that patients with aMCI or AD score relatively lower on the VAT recognition trial in comparison to the patients with VCI or VaD. In addition, it's expected that aMCI patients score relatively more items correct on the VAT recognition trial in comparison to patients with AD and patients with VCI score relatively more items correct on the VAT recognition trial in comparison to patients with VaD.

Second, we have evaluated in an exploratory manner the score difference between the VAT immediate recall trial one and the VAT immediate recall trial two in comparison to the score difference between the VAT immediate recall trial two and the VAT delayed recall trial for all groups. We also evaluated the score difference between the VAT immediate recall trial one and the VAT immediate recall trial two in comparison to the score difference between the VAT immediate recall trial two and the VAT recognition trial for all groups. Thereby, we have evaluated if there is a difference in those two scores between the groups and between the severities of dementias. Immediate recall and delayed recall are more difficult than recognition, because immediate recall and delayed recall were active processes whereas recognition is a passive process. Immediate recall is easier in comparison to delayed recall, because delayed recall calls for longer withhold of information. A characteristic of patients with AD is the absence of improvement on the recognition task (Dubois et al, 2007), whereas the recognition performance of patients with VaD is usually normal (Jonker, Slaets & Verhey, 2009). Therefore, it's expected that the score difference between the VAT immediate recall trial and the VAT delayed recall is lower in comparison to the score difference between the VAT immediate recall trial one and the VAT immediate recall trial two for all groups. It's also expected that the score difference between the VAT immediate recall trial and the VAT recognition trial is higher in comparison to the score difference between the VAT immediate recall trial one and the VAT immediate recall trial two for all groups. In addition, it's expected (1) that patients with VaD show more improvement based on the VAT recognition trial than patients with AD, (2) patients with aMCI show more improvement based on the VAT recognition trial than patients with AD and (3) patients with VCI improve more than patients with VaD based on the VAT recognition trial.

Last, we have evaluated in an exploratory manner the difference in performance on a verbal recognition task (15WT) in comparison to a visual recognition task (VAT) for patients with aMCI or AD and patients with VCI or VaD. The previous studies found only a difference on verbal recognition task in comparison to the visual recognition task between patients with AD and patients with VaD. This has never been studied using the VAT recognition trial, because the VAT recognition trial is developed recently. Furthermore, most of the current tests may result in floor effects to patients with aMCI or AD (Kessels et al., 2009; Petersen et al., 1999; Ricci, Graef et al., 2012). Thus, it is studied using the VAT recognition trial. It's expected that patients with aMCI or AD and patients with VCI or VaD score relatively more items correct on the visual recognition task of the VAT in comparison with the verbal recognition task of the 15WT.

2. METHODS

2.1 Participants

The study patients were geriatric outpatients and nursing home day care patients (N = 55). The outpatients were recruited from the Medical Center Alkmaar (MCA) geriatric memory clinic and nursing home day care facilities (MagentaZorg, SHDH, Zorgbalans, Zorgcirkel en Topaz). Patients were eligible for inclusion if they were 65 years or older, and had intact hearing and vision. Patients were also eligible for inclusion if they met the consensus diagnostic criteria for MCI, AD, VCI and VaD (Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision [DSM-IV-TR]; American Psychiatric Association, 2000; Dubois et al., 2007; Petersen et al., 2001; Román et al., 1993; Steele, Richardson & Olszewski, 1964). These diagnoses were given in a multidisciplinary consultation. Finally, patients were eligible for inclusion if they had a score of less than 10/12 on the VAT immediate recall trial one and two, because when they showed a normal immediate recall score than they can learn normally an thus recognize normally. Patients were excluded from the study if they had severe traumatic brain injury, brain tumour, epilepsy, multiple sclerosis, Parkinson's disease, psychiatric disorder, delirium, or treatment in the past for addiction to alcohol or drugs. Finally, patients were excluded if they had a mixed diagnosis with another type of dementia.

The total sample contained 41 geriatric outpatients and 14 nursing home day care patients. Thereof, were 19 patients with aMCI, 25 patients with AD, 6 patients with VCI and 5 patients with VaD. We joined the patients with aMCI and the patients with AD together and the patients with VCI and the patients with VaD together, because of the low number of pa-

tients with VCI and patient with VaD. Thus, the group with aMCI or AD consisted of 44 patients and he group with VCI or VaD consisted of 11 patients.

2.2 Measurement

The Visual Association Test (VAT; Lindeboom & Schmand, 2003), the two new parallel version of the Visual Association Test (VAT; Meyer et al., in preparation) and the Dutch version of the RAVLT (15WT; Saan & Deelman, 1986) were used as measurements. The VAT is designed to detect visual antrograde amnesia. Versions A, B, C and D of the VAT were used. There is a short (6 items) and a long item version (12 items). The short version is to test older adults (65+). For this study the six item version was used. The six items are pictures, exciting a cue and a target. For example a monkey (cue) holding an umbrella (target). At first, the six consecutive cues that have to be named are presented (step one). The next pictures are an interaction between the cue and the corresponding target. The subjects were asked to name the target (step two). The six cues were shown again, and the subject was asked to recall the associated target (step tree; immediate recall trial). The final step of version A en B was to repeat step two and three. The total score of the immediate recall trial is the two repeated measures together with a maximum score of 12. The internal consistency (Cronbach's alpha) is 0.86 and the test-retest reliability is 0.81. The parallel version reliability (Spearman rank correlation) is 0.84 (Lindeboom & Schmand, 2003). Meyer et al. (in preparation) has developed version C and D. The new versions have immediate recall trial as well as version A en B, but with new cues and targets. They have also added a delayed recall trial and a recognition trial. In the delayed recall trial, the six consecutive cues were shown. The subjects were asked to name the missing target (step four). In the recognition trial, four pictures were shown with the cue picture above. The four target pictures include two semantically related pictures to the cue and one semantically related picture tot the target. The subject was asked to designate the target (step 5). The recognition is impaired if 4 or less than 4/6 items were correct. The parallel versions correlated substantially (r = 0.91) with the original VAT (Lindeboom & Schmand, 2003).

The 15WT is designed to detect verbal antrograde amnesia. The subject hears a list of 15 nouns five times. After each presentation the subject was asked to recall as many words as possible (immediately recall trial; step one). The total score (maximum 75) is the sum of all the five recall trials. The immediately recall trial was followed by a delayed recall trial, where the subject was asked to recall as many words without presenting the word list (step two). Each condition consisted of 15 words. The last step is the recognition trial (step three). The

subject heard a list of 30 nouns. The subject was asked to say ‘yes’ when the word was in the learned list and say ‘no’ when the word wasn’t in the learned list. The recognition was impaired if 26 or less than 26/30 items were correct. The reliability of this test is good. The internal consistency (alpha Cronbach's) is 0.91 to 0.93 and test-retest reliability is 0.80 to 0.83 (Saan & Deelman, 1986, cited in Bouma, Mulder, Lindeboom & Schmand, 2012).

2.3 Procedure

The subjects were investigated with a screening questionnaire to determine whether patients met the inclusion and exclusion criteria. Prior to the study they were asked to read and sign the form 'informed consent patient'.

The data was collected by Meyer, Spaan, Boelaarts, Schmand & Jonghe (in preparation). The patients received the following investigations: neuropsychological assessment, clinical geriatric assessment, laboratory and imaging investigation and if necessary, a psychiatric assessment. The partners or care-givers conducted the neuropsychological tests simultaneously with the ambulatory geriatric patients. The neuropsychological assessment included the following tests: the VAT, the Groninger Intelligence Task (subtask wordlist, animals and job), Name animal plate and show animals plate task, the 15WT, the Stroop Color-Word Task (subtask card I; SKWT-Kaart I), the Amsterdamse Dementia-Screening task (subtask copying; ADS6-copying), the VAT, Cognitive Screening Task-20 (CST-20) and the Amsterdamse Dementia-Screening task (subtask Orientation; ADS6-Orientation). The 15WT wasn’t administered to the nursing home patients because of their limited mental capacity. Clinicians and neuropsychologists were blinded to the second VAT scores. Following this, the diagnosis of the patient was given in a multidisciplinary consultation. This study is a part of the neuropsychological assessment.

The main focus of this study was the VAT. The patients were randomly distributed over the four conditions (A-C, C-A, B-D, D-B) of the VAT. The conditions were counterbalanced to check for learning effect, priming, fatigue, or boredom effects. At a later moment, two new conditions were added (C-D and D-C). There was a time interval of at least 30 minutes between the first and the second test administration of the VAT (Lindeboom & Schmand, 2003). The VAT is administered two times because the old version of the VAT is used for the diagnosis of the patient and the second VAT administration was used for research purpose. By the first administration, only the VAT immediate recall was administered. By the second administration, immediate recall, delayed recall and recognition were administrated. There was a 25 minute time interval between the learned information and the VAT delayed

recall trial. Finally, the delayed recall trial was immediately followed by the recognition trial.

2.4 Statistical Analyses

Study data were analyzed, using SPSS-21 statistical software (SPSS Inc., Chicago, IL). We performed Mann-Whitney *U*-tests and the Chi-square test for inter-group comparisons of demographic and cognitive scores. The non-parametric Mann-Whitney *U*-test and the Wilcoxon signed-ranks test were used to analyze data.

Comparisons of the groups (patients with aMCI or AD – patients with VCI or VaD), subgroups (AD – VaD and aMCI – VCI) and between the severity of the dementia types (aMCI– AD and VCI – VaD) on the VAT recognition trial and the other VAT trials (immediate recall trial one, immediate recall trial two and the delayed recall trial) were made using the Mann-Whitney *U*-test. The groups were used as the independent variables and the VAT recognition trial and the other VAT trials (immediate recall trial one, immediate recall trial two and the delayed recall trial) were used as dependent variables.

Comparisons of the scores of the trials for each group (patients aMCI or AD, patients with VCI or VaD, aMCI, AD , VCI and VaD) were made using Wilcoxon Singed Ranks Test. The following comparisons were made for each group: VAT immediate recall trial one – VAT immediate recall trial two, VAT immediate recall trial two – VAT delayed recall trial and VAT immediate recall trial two – VAT recognition trial. Following this, comparison of the scores is made using the Mann-Whitney *U*-test. Before the comparison, the following new variables were calculated: ΔIm2Im1 = immediate recall trial two – immediate recall trial one; ΔDelIm2 = delayed recall trial – immediate recall trial two and ΔRecIm2 = recognition trial – immediate recall trial two. There were comparisons made between the groups, subgroups and between the severities of the dementia types as described above. The groups were used as the independent variables and the three difference variables were used as dependent variables.

Comparisons of the score difference between the VAT immediate recall trial one and the VAT immediate recall trial two with the score difference between the VAT immediate recall trial two and the VAT delayed recall trial were made using the Wilcoxon Singed Ranks Test. The same statistical analysis was used for the comparison of the score difference between the VAT immediate recall trial one and the VAT immediate recall trial two with the score difference between the VAT immediate recall trial two and the VAT recognition trial. The followed new variables were calculated: ΔDelIm2. Im2Im1= ΔDelIm2 – ΔIm2Im1 and ΔRecIm2.Im2Im1 = ΔRecIm2 – ΔIm2Im1. The following comparisons were made using the Wilcoxon Singed Ranks Test: ΔIm2Im1 –ΔDelIm2 and ΔIm2Im1 –ΔRecIm2. Those compari-

sons were made for all the groups. Following this, the comparison of the improvement for each group, subgroup and between the severities of the dementia types were made using the Mann-Withney *U*-test..

Comparisons of performance on the verbal recognition (15WT) trial and the visual recognition (VAT) trial for all the groups were made using the Wilcoxon Singed Ranks Test. Before the comparisons, two new variables were calculated because of an unequal number of items. The performance of the 15WT was measured as follows: (correct items/30) x 100. The performance of the VAT was measured as follows: (correct items/6) x 100.

Statistical tests were deemed significant if the two sided p value was less than 0.05.

3. RESULTS

This study sample consists of geriatric outpatients and nursing home day care patients from 65 and older. A total of 346 patients were screened for eligibility to participate in the study. Thereof, 228 patients didn't met inclusion criteria. The VAT recognition trial was not administered to a total of 56 out of the 346 patients. Of the remaining 62 patients, 7 had more than 10 out of the 12 items correct on the VAT immediate recall trial one and the VAT immediate recall trial two. The comparison for those patients with the VAT recognition trial is uninteresting because those patients already showed normal learning on the VAT immediate recall trial one and trial two. The 15WT was not administered for a total of 15 out of the 55 patients. Finally, 55 patients were included for the first and the second hypothesis and 40 patients were included for the third hypothesis in this study.

3.1 Patient Characteristics

Patient characteristics are presented in table 1. The patients with aMCI and patients with AD were taken together and patients with VCI and patients with VaD were taken together, because the patients with VCI and patients with VaD both had a low number of participants. These analyses might be biased, because patients with VCI or aMCI were low demented and patients with AD or VaD were more demented. Therefore, we also evaluated the groups separately.

We evaluated if the groups were equal on age, gender, education and MMSE. We evaluated the MMSE to check if the patients with AD or VaD were actually more demented in comparison to the patients with aMCI or VCI. Patients with aMCI or AD in comparison to the patients with VCI or VaD were both mildly demented based on the MMSE, but the pa-

tients with aMCI or AD scored significantly (on average 4.1) lower in comparison to the patients with VCI or VaD (U = 180, p < .05). Based on the subgroups, patients with VCI were higher educated in comparison to the patients with aMCI (U = 26.5, p < .05). We found also that patients with aMCI were mildly demented, whereas the patients with VCI were not demented based on the MMSE score (U = 8, p < .05). As expected, the patients with AD were more demented in comparison to the patients with aMCI. The patients with AD were moderate demented, whereas the patients with aMCI were mildly demented. (U = 131.5, p < .05). Last, the patients with VaD were mildly demented whereas the patients with VCI were not demented (U = 1, p < .05).

Table 1. Characteristics of the groups and subgroups.

	aMCI+AD (n = 44)	VCI+VaD (n = 11)	MCIa (n = 19)	VCI (n = 6)	AD (n = 25)	VaD (n = 5)
Characteristic	*M (SD)*					
Age	79.0 (5.7)	77.4 (7.4)	78.4 (6.6)	77.3 (4.4)	79.5 (5.1)	77.4 (10.7)
[1]Education	4.4 (1.6)	4.8 (1.5)	4.3(1.4)	5.5 (1.4)	4.4 (1.7)	4.0 (1.2)
MMSE	20.8 (6.0)	24.9 (5.0)	23.6 (3.4)	27.7 (.52)	18.8 (6.8)	21.6 (6.1)
Male/female	18/26	6/5	5/14	4/2	13/12	2/3

[1]Education code according to Verhage (1964): 1. less than primary school/not finished; 2. primary school finished; 3. Primary school finished + further education less than 2 years; 4. Lower than MULO/MAVO-level, b.v. LTS, LEAO, LHNO; 5. MULO/MAVO/MEAO diploma; 6. HAVO/VWO/HEAO/HBS/HBO diploma; 7. VWO/universitair diploma

3.2 Comparisons of Performance of the Groups Based on the VAT Trials

The results of the groups based on the VAT trials are presented in Table 2. The results below must be interpreted with caution, because we did multiple Mann-Whitney *u*-Tests. This means high chances to get Type-1 errors.

3.2.1 *VAT Recognition Trial*

Patients with aMCI or AD on one hand and the patients with VCI or VaD on the other hand did equally well on the VAT recognition trial (see Table 2; U = 194.00, p = .29). Nonetheless, we separated the patients with aMCI from the patients with VCI, and compared the groups. They still did equally well on the VAT recognition trial (U = 50.5, p = .58). The same was found if we took the patients with AD and the patients with VaD separately (U = 49, p = .45). All the groups, except the patients with aMCI and the patients with VCI had an impaired recognition based on the VAT recognition trial (recognition < 5/6 items correct). However, we found a possible differentiation of the severity of the dementia types based on the VAT recognition trial. Patients with aMCI scored 3.0 items more correct in comparison to the pa-

tients with AD (U = 70, p = .00). By contrast, the patients with VCI and the patients with VaD did equally well on the VAT recognition trial (U = 4.5, p = .05).

In contrast to our expectations, we found that there's no differentiation possible between the types of dementias based on the VAT recognition trial. However, we found a possible differentiation based on the VAT recognition trial between the severities of dementia types, especially between the patients with aMCI and the patients with AD.

3.2.2 *VAT Immediate and Delayed Recall Trials*

Patients with VCI or VaD scored 1.6 correct items more on the VAT immediate recall trial two (U = 144.5, p = .03) and they scored 1.8 correct items more on the delayed recall trial (U = 129.0, p = .01) in comparison to the patients with aMCI or AD (see Table 2). There was no significant difference found between patients with VCI or VaD and patients with aMCI or AD based on the VAT immediate recall trial one (U = 193, p = .29). When we separated the patients with aMCI from the AD patients and the patients with VCI from the patients with VaD, we found that patients with VCI scored 1.8 correct items more on the VAT delayed recall trial in comparison to the patients with aMCI (U = 24.5, p = .03). There was no significant difference found between patients with VCI and patients with aMCI based on the VAT immediate recall trial one (U = 56.5, p = .98) and the VAT immediate recall trial two (U = 28.5, p = .06). There was also no significant difference found between patients with VaD and patients with AD based on the VAT immediate recall trial one (U = 48, p = .38), VAT immediate recall trial two (U = 42.5, p = .24) and the VAT delayed recall trial (U = 38, p = .14). However, we found a possible differentiation of the severities of the dementia types based on the VAT trials. We found that patients with aMCI scored on average 1.7 correct items more on the VAT immediate recall trial two (U = 134.5, p = .01) in comparison to patients with AD. Furthermore, they scored on average 1.5 correct items more on the delayed recall trial (U = 138, p = .01). There was no significant difference found between those patients based on the VAT immediate recall trial one (U = 159, p = .05). In contrast, we found no significant difference between the patients with VCI and the patients with VaD based on the VAT immediate recall trial one (U = 15, p = 1.00), VAT immediate recall trial two (U = 7.5, p = .16) and the VAT delayed recall trial (U = 7, p = .14).

Thus, as expected, we found a possible differentiation for the patients with aMCI or AD on one hand and patients VCI or VaD on the other hand based on the VAT immediate recall trial two and the VAT delayed recall trial. Last, the same is found for the patients with

aMCI and the patients with AD.

Table 2. Performances on the VAT trials

	aMCI+AD	VCI+VaD	*p*	aMCI	VCI	*p*	AD	VaD	*p*
Im1	1.8 (1.8)	2.4 (1.5)	.286	2.4 (1.8)	2.5 (1.0)	.974	1.3 (1.6)	2.2 (2.0)	.384
Im2	2.5 (2.2)	4.1 (2.1)	.037*	3.5 (1.8)	5.0 (1.1)	.063	1.8 (2.2)	3.0 (2.5)	.244
Del	2.1 (2.1)	3.9 (1.9)	.014*	3.0 (1.9)	4.8 (.98)	.033*	1.5 (2.1)	2.8 (2.3)	.138
Rec	3.9 (2.3)	4.8 (2.0)	.287	5.6 (.84)	5.8 (.41)	.580	2.6 (2.3)	3.6 (2.5)	.445

Values are mean (SD). Im 1 = Immediate recall trial one; Im 2 = Immediate recall trial two; Del = delayed recall; Rec = Recognition

* $p < .05$

3.3 Comparison of the VAT Trials

The results of the differences between the VAT trials for each groups and between the groups are presented in Table 3 and the comparison of Δom2Om1 with ΔDelOm2 and ΔRecOm2 for each group and between the groups are presented in Table 4. The results below must also be interpreted with caution, because we did multiple Mann-Whitney *u*-Tests. This means high chances to get Type-1 errors.

3.3.1 *Comparison of the VAT Trials with the VAT Immediate Recall Trial Two*

Patients with aMCI or AD (Z = -3.71, p =.00), patients with VCI or VaD (Z = -2.57, p = .01), patients with aMCI (Z = -2.76, p =.01), patients with AD (Z = -2.65, p = .01) and patients with VCI (Z = -2.23, p = .03) except the patients with VaD (Z = -1.13, p = .26) improved significantly from VAT immediate recall trial one to the VAT immediate recall trial two (see Table 3).

After this improvement, we expected deterioration from the VAT immediate recall trial two to the VAT delayed recall trial. But this was only the case for patients with aMCI or AD (Z = -2.80, p = .01) and for patients with aMCI (Z = -4.78, p = .00).

Conversely, patients with aMCI or AD (Z = -4.78, p = .00), patients with VCI or VaD (Z = -2.07, p = .04), patients with aMCI (Z = -3.65, p = .00), patients with AD (Z = -3.09, p = .00) except the patients with VCI (Z = -1.63, p = .10) and the patients with VaD (Z = -1.34, p = .18) significantly improved from the VAT immediate recall trial two to the VAT recognition trial.

However, we found significant improvement difference between the groups based on the severity of the dementias. Patients with aMCI improved significantly with .68 items more correct from the VAT immediate recall trial one to the VAT immediate recall trial two in comparison to patients with AD (U = 158, p = .048). By contrast, we found no significant

deterioration group difference from the VAT immediate recall trial two to the delayed recall trial for patient with aMCI in comparison to patients with AD (U = 202.5, p = .33). Furthermore, we found also that aMCI patients with 1.34 correct items more improved from the VAT immediate recall trial two to the VAT recognition trial (U = 110, p = .00). By contrast, patients with VCI and patients with VaD perform equally from the VAT immediate recall trial one to the VAT immediate recall trial two (U = 5.5, p = .08), from the VAT immediate recall trial two to the VAT delayed recall trial (U = 14.5, p = .89) and from the VAT immediate recall trial two to the VAT recognition trial (U = 13, p = .69).

As expected, all patients except the patients with VAD significantly improved from the VAT immediate recall trial one to the VAT immediate recall trial two. We only found that patients with aMCI or AD and patients with aMCI deteriorate from the VAT immediate recall trial two to the VAT delayed recall trial. We found group differences based on the severity of the dementia types. Patients with aMCI improve significantly more from the VAT immediate recall trial one to the VAT immediate recall trial two and from the VAT immediate recall trial two to the VAT recognition trial in comparison to patients with AD.

Table 3. Difference between the VAT trials for each groups and between the groups

	aMCI+AD	VCI+VaD	*p**	aMCI	VCI	*p**	AD	VaD	*p**
Om2-Om1	.80 (1.2)*	1.7 (1.6)*	.052	1.2 (1.4)*	2.5 (1.4)*	.080	.52 (.87)*	.80 (1.5)	.706
Del-Om2	-.41 (1.1)*	-.18 (.41)	.321	-.53 (1.5)	-.17 (.41)	.400	-.32 (.56)*	-.20 (.45)	.787
Rec-Om2	1.3 (1.3)*	.73 (.91)*	.179	2.1 (1.4)*	.83 (.98)	.069	.76 (.97)*	.60 (.89)	.746

Values are mean (SD). Im 1 = Immediate recall trial one; Im 2 = Immediate recall trial two; Del = delayed recall; Rec = Recognition

* $p < .05$

3.3.2 *Comparison of the VAT Immediate Recall Trials with the VAT Delayed Recall and Recognition Trial*

We have also evaluated the score difference between the VAT immediate recall trial one and the VAT immediate recall trial two in comparison to the score difference between the VAT immediate recall trial two and the VAT delayed recall trial for all groups. Patients with aMCI or AD (Z = -3.73, p =.00), patients with VCI or VaD (Z = -2.57, p = .01), patients with aMCI (Z = -2.51, p =.01), patients with AD (Z = -2.86, p = .01) and patients with VCI (Z = -2.23, p = .03) except the patients with VaD (Z = -1.13, p = .26) significantly deteriorated from the VAT immediate recall trial two to the VAT delayed recall trial in comparison to the VAT immediate recall one to the VAT immediate recall trial two (see Table 4). There was no

significant deterioration found between the patients with aMCI or AD and patients with VCI or VaD, between the patients with aMCI and VCI and between the patients with AD and VaD.

Therefore, we have evaluated the score difference between the VAT immediate recall trial one and the VAT immediate recall trial two in comparison to the score difference between the VAT immediate recall trial two and the VAT recognition trial for all groups. Patients with aMCI or AD (Z = -1.62, p =.11), patients with VCI or VaD (Z = -1.41, p = .16), patients with aMCI (Z = -1.64, p =.10), patients with AD (Z = -.74, p = .46), patients with VCI (Z = -1.63, p = .10) and patients with VaD (Z = -1.13, p = .26) improve equally from the VAT immediate recall trial two to the VAT recognition trial in comparison to the VAT immediate recall one to the VAT immediate recall trial two. Patients with aMCI or AD improved more from the VAT immediate recall trial two to the VAT recognition trial in comparison to the improvement from the VAT immediate recall trial one to the VAT immediate recall trial two in comparison to patients with VCI or VaD (U = 146.5, p = .04). The same was found for patients with aMCI and patients with VCI, only patients with aMCI improve from the VAT immediate recall two to the VAT recognition (U = 24.5, p = .04).

Overall, as expected, all patient groups except patients with VaD deteriorate from the VAT immediate recall trial two to the VAT delayed recall trial in comparison to the VAT immediate recall trials (trial one and two). Furthermore, in contrast to our expectations, all the patient groups improve equally from the VAT immediate recall trial two to the VAT recognition trial in comparison to the VAT immediate recall trials (trial one and two). We found also that patients with aMCI or AD and patients with aMCI improved more from the VAT immediate recall trial two to the VAT recognition trial in comparison to the VAT immediate recall trials (trial one and two).

Table 4. Comparison of Δom2Om1 with ΔDelOm2 and ΔRecOm2 for each group and between the groups.

	aMCI+AD	VCI+VaD	p*	aMCI	VCI	p*	AD	VaD	p*
ΔDelOm2	-1.2 (2.1)*	-1.9 (1.8)*	.231	-1.7 (2.8)*	-2.7 (1.5)*	.366	-.84 (1.2)*	-1.0 (1.9)	.914
ΔRecOm2	.52 (1.9)	-1.0 (2.2)	.042*	.90 (2.4)	-1.7 (2.2)	.036*	.24 (1.5)	-.20 (2.2)	.516

Values are mean (SD). Im1 = Immediate recall trial one; Im 2 = Immediate recall trial two; Del = delayed recall; Rec = Recognition

* $p < .05$

3.4 Comparison of the Visual (VAT) and the Verbal (15WT) Recognition Trial

The results on the visual (VAT) and the verbal (15WT) recognition trial of each group are presented in Table 5. Patients with aMCI or AD performed 10.8% better on the visual

VAT recognition trial in comparison to the verbal 15WT recognition trial (Z = -2.15, p = .03) By contrast, patients with VCI or VaD showed no significant difference on the visual VAT recognition trial in comparison to the verbal 15WT recognition trial (Z = -.71, p = .48). Patients with aMCI or AD and patients with VCI or VaD both showed impaired recognition only on the 15WT recognition trial.

When we took the groups separately, aMCI patients performed 22.6% better on the visual VAT recognition trial in comparison to the verbal 15WT recognition trial (Z = -3.29, p = .00). By contrast, there were no significant difference found for patients with VCI (Z = -1.37, p = .17), patients with AD (Z = -.83, p = .41) and patients with VaD (Z = -.54, p = .59). Patients with AD and patients with VaD showed an impaired recognition on the visual VAT recognition trial and the verbal 15WT recognition trial. It's remarkable that patients with aMCI and patients with VCI showed impaired recognition only on the verbal 15WT recognition trial.

In the end, as expected, we may conclude that only patients with aMCI or AD and patients with aMCI scored relatively higher on the visual VAT recognition trial in comparison to the verbal 15WT recognition trial.

Table 5. Performance of the recognition of the VAT and the recognition of the 15WT

		Recognition VAT		Recognition 15WT			
	N	*M (SD)*	% correct[1]	*M (SD)*	% correct[2]	% correct difference	*p* value*
aMCI + AD	31	4.9 (1.7)	81.2%	21.1 (3.1)	70.4%	10.8%	.032*
VCI + VaD	9	5.3 (1.3)	88.9%	25.8 (3.6)	85.9%	3%	.476
aMCI	19	5.6 (.84)	93.0%	21.1 (2.8)	70.4%	22.6%	.001*
VCI	6	5.8 (.41)	97.2%	26.0 (4.3)	86.7%	10.5%	.172
AD	12	3.8 (2.1)	62.5%	21.2 (3.6)	70.6%	8.1%	.410
VaD	3	4.3 (2.1)	72.2%	25.3 (2.1)	84.4%	12.2%	.593

[1] ((*M* correct VAT recognition / 6) x 100%); [2]((*M* correct 15WT recognition / 30) x 100%)

* $p < .05$

4. DISCUSSION

The main goal of this study was to attempt to find a discriminative validity between patients with aMCI or AD and patients with VCI or VaD based on the VAT recognition trial. The new parallel versions of the VAT were developed because most of the current tests may result in floor effects to patients with amnestic mild cognitive impairment (aMCI) or AD (Kessels et al., 2009; Petersen et al., 1999; Ricci et al., 2012). Thus, there has no study been done to compare patients with aMCI or AD with patients with VCI or VaD. Furthermore, we

have evaluated in an exploratory manner the score difference of the VAT immediate recall trial one to the VAT immediate recall trial two in comparison to the score difference of the VAT immediate recall trial two to the VAT delayed recall trial and the score difference of the VAT immediate recall trial to the VAT recognition trial for each group and between the groups. Last, we have also evaluated in an exploratory manner the visual (VAT) recognition trial in comparison with a verbal (15WT) recognition trial. The VAT recognition trial is new developed. Thus, there's no study done with the visual VAT recognition trial in comparison to the verbal 15WT recognition trial. The results of this study both negate and support some of the hypotheses.

4.1 Findings

It was predicted that patients with VCI or VaD scored more items correct on the VAT recognition trial in comparison to the patients with aMCI or AD, but this turned out not to be the case, they performed equally well. The same is found if we separate the groups. This result could be due to the low number of patients with VCI or VaD, and thus the unequal groups. By contrast, our results suggested there only is a discriminative validity of the severity of the dementias based on the VAT recognition trial, especially between patients with aMCI and patients with AD. But, this result is obvious because patients with AD are more demented and therefore they show more impaired recognition. The result of our study is the same as the result of the study of Hong et al. (2013) and Graham et al., (2004). Conversely, our study is not supported by the theory. The theory suggests that patients with AD have consolidation deficits and patients with VaD have retrieval deficits. Thus, it seems to be that patients with AD score relatively lower on a recognition trial in comparison to patients with VaD (Lafosse et al., 1997).

It was expected that the score difference between the VAT immediate recall trial and the VAT delayed recall is lower in comparison to the score difference between the VAT immediate recall trial one and the VAT immediate recall trial two for all groups. It's also expected that the score difference between the VAT immediate recall trial and the VAT recognition trial is higher in comparison to the difference score between the VAT immediate recall trial one and the VAT immediate recall trial two for all groups. In addition, it's expected that patients with VaD show more improvement on the VAT recognition trial than patients with AD. And patients with aMCI show more improvement on the VAT recognition trial than patients with AD and patients with VCI improve more than patients with VaD on the VAT recognition trial. The study of Hong et al. (2013) based on the visual RCFT did support our

findings with regard to the lower score of the VAT delayed recall trial in comparison to the VAT immediate recall for patients with AD and for patients with VaD. But, the results based on the better score on the RCFT recognition trial in comparison to the RCFT immediate recall trial for patients with AD and patients with VaD are not in line with our results. We found the same score difference between the VAT immediate recall trial two and the VAT recognition trial in comparison to the VAT immediate recall trial one to the VAT immediate recall trial two. By contrast, our results are in accord with the results of the study of Graham et al. (2004) with regard to patients with AD that they deteriorate from the immediate recall trial to the delayed recall trial. But these results are interpreted mean scores of the trials. There were no studies found were they did a statistical analysis based on the comparison of the immediate recall trials with the delayed recall trial and with the recognition trial.

Last, it was predicted that patients with aMCI or AD and patients with VCI or VaD scored relatively better on the visual VAT recognition trial in comparison to the verbal 15WT recognition trial. This is only the case for patients with aMCI or AD and for aMCI patients separately. The previous studies focus only on the trials between a verbal or a visual task for patients with AD and patients with VaD. We found no study that compares a visual task with a verbal task for patients with AD and patients with VaD. But it is well known that a verbal task is more difficult in comparison to a visual task.

4.2 Limitations and Strengths

The current study had several limitations. First, in this study there was a low number of patients with VCI and patients with VaD. This may be explained by the prevalence of each diagnosis. The prevalence for patients withVaD is 2.2-16.3%, whereas the prevalence for patients with AD 50-75% is (Leys, Pasquier & Parnetti, 1998). By contrast, the study of Hong et al. (2013) used a lot more patients (*n* AD = 148; *n* VaD = 60). This could explain the contradictory result. The consequence of the low number of patients was that we had to use multiple Mann-Withney *u*-Tests. Thus, our results must be interpreted with caution because of high chances of Type-1 errors. We attempt to reduce this problem by comparing patients with aMCI and patients with AD and by comparing patients with VCI and patients with VaD, which brings us to the second limitation. A distorted view is presented if low demented patients were compared with high demented patients. Third, the diagnosis was based on clinical findings and structural brain imaging rather than on confirmative pathological data. It is possible that patients with AD had concomitant VaD pathology and vice versa. This is confirmed by the study of Kirson et al., (2013). They found that 16.6% patients with VaD were misdiag-

nosed with AD. Fourth, these results were not generalizable to patients with severe dementia, because we used patients with AD with moderate dementia (MMSE = 18.8) and patients with VaD with moderate dementia (MMSE = 21.6). Patients with AD in the other studies were mild demented (Hong et al., MMSE= 20.1; Graham et al., MMSE = 24.2). By contrast, the VaD patients in the study of Hong et al., (2013) were also moderate demented (MMSE=20.8) but in de study of Graham et al., (2004) were the VaD patients not demented (MMSE =25.3). Thus, the results of the studies were applicable to patients with different kind of dementia severities.

Despite these limitations, there are also a few strengths to this study. First, this is believed to be the first study to find a discriminative validity between patients with aMCI or AD and patients with VCI or VaD based on the VAT recognition trial. Furthermore, this study is also the first study which evaluated the score difference of the VAT trials for the patients with AD and the patients with VaD. Last, this is also the first study which compares the verbal 15WT recognition trial with the visual VAT recognition trial.

4.3 Recommendations

With our results, we still cannot provide scientific input, but only suggestions for further research in this area. Further studies should include more patients and especially patients with VCI and patients with VaD, this ensures a more powerful result. If there were more patients included, parametric test could be used instead of non-parametric tests. Another suggestion for further research is using more patients with severe dementia, because none of the previous studies used severe demented patients. These suggestions hopefully allow for differentiation of the AD patients from the VaD patients and greater generalizability.

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