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# "AQT"-A MEASURE OF COGNITIVE SPEED- IN DEMENTIA WITH LEWY BODIES

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**ABSTRACT**

**Objectives:** To investigate (a) how patients with dementia with Lewy bodies (DLB) perform on A Quick Test for Cognitive Speed (AQT) compared to patients with Alzheimer's disease (AD) and age- and sex-matched controls and (b) if this test might be helpful in distinguishing DLB from AD at comparable cognitive levels.

**Methods:** Twenty-three patients with DLB, 18 patients with AD and 24 controls were included. The time in seconds to complete the AQT were recorded for the three independent study groups according to standard directives.

**Results:** The DLB patients had significantly longer reading times than the AD patients at equivalent and relatively high Mini Mental State Examination (MMSE) levels.

**Conclusion:** We suggest that slow performance on the AQT at relatively high MMSE levels could be one way of distinguishing DLB from AD. This may have clinical implications for treatment as well as for understanding the neuropathological properties of the disease.

Keywords: AQT, dementia, Lewy bodies, cognitive speed, subcortical

## INTRODUCTION

### DEMENTIA WITH LEWY BODIES

Dementia with Lewy bodies (DLB) is claimed to be the second most prevalent neurodegenerative dementia after Alzheimer's disease (AD). A systematic review of six studies has found prevalence estimates for clinical DLB ranging up to 30.5% of all dementia cases.[1] At autopsy DLB comprises approximately 20% of cases.[2] The central feature of DLB is progressive cognitive decline accompanied by fluctuating cognition, visual hallucinations and parkinsonism. Suggestive features are REM sleep behaviour disorder, severe neuroleptic sensitivity and low dopamine transporter uptake in basal ganglia. Some of the supportive features are falls, syncope, loss of consciousness, systematised delusions, hallucinations of other modalities, depression, autonomic failure and abnormal metaiodobenzyl guanidine uptake in myocardial scintigraphy.[3-5] DLB patients often show psychomotor slowness, which is described in status evaluation but rarely measured in a standardized matter. Several studies of visuospatial function, including form and object size discrimination and figure copying, have shown much more severe debility in DLB than in AD, although episodic memory is relatively spared in patients with DLB.[2]

DLB has clinical, neuropathological and neurochemical features of both AD and Parkinson's disease (PD). The consensus guidelines for a clinical diagnosis of DLB suggests that PD patients who develop dementia more than 12 months after the initial motor symptoms should be diagnosed as PD dementia (PDD) rather than DLB.[3-5] In PD the usual focus is motor slowness and bradykinesia but cognitive impairment, such as psychomotor slowness, is also an important feature. Prominent executive, attentional, and visuospatial dysfunction, with

relatively preserved memory functions are characteristic neuropsychological findings in both DLB and PDD.[6]

AQT

A Quick Test for Cognitive Speed (AQT) is believed to measure general cognitive and perceptual speed and is performed by reading a set of colors, forms and color-form combinations, as fast as possible. An earlier study has reported preliminary evidence on the clinical utility of AQT in AD. The study compared the AQT results between AD patients, with mild or moderate disease, to age- and sex matched controls. The AD patients' mean test times were for color 39 s, for form 52 s, and for color-form 91 s while the controls' mean test times were 23 s for color, 29 s for form, and 54 s for color-form. All differences were statistically significant. The color-form naming resulted in sensitivity and specificity of 97% (with lower cut-off levels set to >70 s for color-form).[7] The test is reliable in different languages and has recently also been shown to be reliable when administered to speakers of Krio in West Africa.[8]

AQT assesses cognitive function by measuring processing speed. Tasks, consisting of familiar competing stimuli allow evaluation of cognitive functions that underlie recognition, memory, reading, and language production. The stimuli used can have a single or two dimensions (e.g. color naming or color-form naming).[9] Regional cerebral blood flow (rCBF) has shown a brain activation pattern of a parietal increase and a frontotemporal decrease during the color-form naming task.[10] This indicates that dual-dimension tests, such as the color-form test, may impose greater perceptual than executive requirements on working memory and that the test can be used to identify impairments of parietal lobe function and working memory.[10] This

differs from the Stroop test[11], which is a test of inhibition and executive function control by frontal lobe activation.

AIMS OF THE STUDY

The current study aimed to investigate: (1) How patients with DLB perform on AQT; (2) if a simple test of cognitive speed might be helpful in distinguishing DLB from AD at comparable cognitive levels as measured by Mini Mental State Examination (MMSE)[12]; (3) if there are differences in performance on AQT between DLB patients and age- and sex-matched controls. The findings will have clinical implications, since there is still a lack of diagnostic tools in the identification process of DLB. It is important to correctly diagnose DLB patients since they show good responsiveness to cholinesterase inhibitors, but extreme sensitivity to the side effects of neuroleptic drugs. It is also important, since the course and prognosis may differ from other dementias.

## METHODS

PARTICIPANTS

Twenty-three patients with DLB were included in the study together with 18 patients with mild or moderate AD in a clinical follow-up program that administered AQT at baseline. All the patients attended the Neuropsychiatric Clinic, Malmö University Hospital, Malmö, Sweden and were evaluated with a detailed clinical investigation of cognitive function. The diagnosis was given prospectively using operationalized diagnostic criteria (NINCDS-ADRDA for probable AD[13] and DLB consensus criteria for probable DLB[4]).

Twenty-four age- and sex-matched controls were included. The controls were recruited through advertisements. Volunteers went through physical examination and cognitive testing. Inclusion criteria were: (a) absence of memory complaints or any other cognitive symptoms, (b) preservation of general cognitive functioning and (c) no active neurological or psychiatric disease. Individuals with other medical conditions that did not affect cognition were not excluded.

Color blindness was routinely screened for, but is not a factor that considerately influences the result of the test. All subjects were monolingual. No information was collected about years of education. The study was approved by the ethics committee of Lund University.

AQT

The AQT color-form naming task consists of three tests, each with 40 visual stimuli. The first test plate shows eight lines of colored squares (black, blue, red, yellow). These colors are used to avoid problems with the most common type of color blindness (distinguishing red from green). The second test plate shows eight lines of black colored shapes (circle, line, square, triangle), randomly repeated. The third test plate features eight lines with combinations of the colors and forms on the first two plates. According to test instructions the patient is allowed to use other names to describe the colors and forms as long as the naming is consistent throughout the test. The time in seconds to complete the color, the form and the combined color-form tests were recorded for the three independent study groups according to standard directives. Each task was preceded by a short practice task (one line of colored squares, one line of black colored shapes, two lines of color-form combinations). The reading times were measured using a digital stopwatch. The test plates were always presented in the same order.

STATISTICAL ANALYSIS

Statistical analysis was performed with use of The Statistical Package for Social Sciences (SPSS) software (version 12.0.1 for Windows, SPSS Inc., Chicago, Ill., USA). To avoid bias with non-normally distributed variables non-parametric statistics (Mann-Whitney U test) were used to detect significant group differences. Binary variables were compared using Chi-Square Tests. A power analysis for 80% power and a significance level of 0.05 was performed.

**RESULTS**

In this study, AQT was performed by 23 clinically diagnosed DLB patients, 18 clinically diagnosed AD patients and 24 age- and sex-matched controls. The power analysis showed that the study was underpowered to detect differences in the form test between AD and DLB. Otherwise, there was enough power to detect the differences between AD and DLB as well as between DLB and the normal controls.

There were no significant differences in age, sex or mean MMSE score between the DLB and the AD patients. The controls had a significantly higher MMSE score than the dementia patients. (Table 1)

[Insert Table 1 about here]

The time in seconds to complete the color, form and color-form tests were recorded for the three independent study groups. There was a significant difference in cognitive speed between the DLB and the AD patients. The differences in reading time for color ($p<0.001$, $Z$ –3.719 DLB vs. AD, $Z$ –4.300 AD vs. controls, $Z$ –5.727 DLB vs. controls) and color-form ($p<0.001$

Z-5.662 DLB vs. controls and Z –3.639 AD vs. controls, p=0.003 Z –3.022 DLB vs. AD) were more significant than the difference in reading time for form alone ($p<0.001$ Z-5.409 DLB vs. controls and Z –4.032 AD vs. controls, p=0.043 Z –2.023 DLB vs. AD). To read the colors the DLB patients needed 76 seconds compared to 39 seconds for the AD patients and to read the combined color-forms the DLB patients needed 151 seconds compared to 103 seconds for the AD patients. (Table 1) The controls had significantly faster reading times with a narrower range than the AD and control groups. (Figure 1,2)

[Insert Figure 1 and 2 about here]

With cut-off set at >100 sec reading time for the combined color-form test the sensitivity and specificity for separating the DLB patients from the AD patients and the controls were calculated as 0.78 and 0.86 respectively. (Figure 3)

[Insert Figure 3 about here]

**DISCUSSION**

This is the first study to report how patients with DLB perform on AQT. The study shows that DLB patients have longer reading times than AD patients at equivalent and relatively high MMSE levels, suggesting that slow performance on the AQT at relatively high MMSE levels could be one way to distinguish DLB from AD. The power analysis showed that the study was underpowered to detect differences in the form test between AD and DLB. With larger study groups we might have found that the difference in this test also had a strong significance level.

The tests were performed in a standardized manner with the sections always presented in the same order (color, form, color-form). Fatigue is not likely to alone explain the results since the DLB patients had a slower performance in test one and three, and not just the last test. The AQT is an objective (based on total naming time) test of cognitive speed, highly reliable and there is no evidence of habituation, learning, or fatigue in repeated trials over 10 minutes. Test-retest reliability coefficients (r) are high for each test (color 0.91, form 0.92 and color-form 0.95).[14 15] A possible limitation of the study is that all cases were diagnosed clinically. Furthermore, a core feature of DLB is fluctuating cognition, even on a second-to-second basis, which might explain the relatively large standard deviations for reading time in this group.[16]

Cognitive testing based on processing speed, rather than memory content (as the MMSE), may allow for earlier detection of cognitive impairment.[9] A previous study, designed to explore the influence of age and sex on rapid naming tasks showed a significant naming time difference for age but not for sex, with older age groups having longer naming times.[10] Naming form required significantly longer time than naming colors, especially in older men. The study did not detect a significant age-related difference in dual-dimension naming times. This might have been due to the small sample (n=60). The study groups were healthy younger women 30.6±7.2 years (mean±SD), older women 52.2±8.4, younger men 27.0±7.1 and older men 55.0±7.6.[10] A later study including healthy volunteers ranging from 15-85 years (n=144) found that age correlated significantly with reading time for single dimension color naming and for dual-dimension naming and that there was a linear relationship between increasing reading times and increasing age. This study found that color naming time could be expected to slow by 1 s every 16 years, other single-dimension naming times could be expected to slow by 1 s every 25 years and dual-dimension naming time could be expected to slow by 1 s every

10 years.[9] In the current study there was no significant difference in age between the studied groups.

The aim of our article was not to compare the AQT with other tests of cognitive speed but rather to compare the performance in AQT between different types of dementia and thereby explore the use of a new instrument to measure cognitive speed. There are however other tests that measure reading times. The Stroop test is a test of inhibition and executive function control by frontal lobe activation. The AQT was developed to avoid the frontal component of the Stroop test and therefore we believe that it may be a better instrument to measure cognitive speed in these patients. An article comparing a neuropsychological battery between DLB and PDD found that DLB patients had a poorer performance in reading names of colors in the Stroop test. No significant differences were detected in the recognition of colors.[17]

In a study including 103 PD patients, dementia was diagnosed in 27 subjects at follow-up after 4 years and 42(55%) had mild cognitive impairment. Within the cognitively impaired PD group, three different types of cognitive profiles were identified. One group of patients showed only executive dysfunction, a second group impaired visual memory and/or visuospatial abilities, and a third group a more widespread cognitive impairment affecting visual memory, executive and visuospatial skills.[18] A recent study, which assessed the cognitive profiles of patients with PDD in comparison with DLB and AD, identified four subgroups. Two subgroups exhibited a subcortical cognitive profile, one subgroup exhibited global impairment, and one subgroup a cortical cognitive profile. More than half of the patients with PDD (56%) and DLB (55%) showed a subcortical profile, whereas the majority of the patients with AD showed a cortical cognitive profile. Thirty percent of the PDD patients and 26% of the DLB patients exhibited a cortical cognitive profile, suggesting that

there are two subtypes of cognitive impairment in PDD and DLB.[19] Our findings of longer reading times in the DLB group could then be postulated to be explained by a more subcortical profile in this group. The larger variation in this group regarding reading times could then also be explained by the different cognitive profiles within the group rather than by fluctuating cognition.

DLB and PDD have relative sparing of memory functions in the beginning of the disease, as compared to AD. Furthermore, neuropsychological findings suggest that visuospatial function is more severely impaired in DLB than in AD.[2] AQT has been shown to result in a brain activation pattern of increased parietal cerebral blood flow and thus has been postulated to reflect parietal lobe dysfunction.[10] We therefore suggest that AQT might have an even higher sensitivity in detecting early DLB than in detecting early AD. Moreover, studies have shown a subcortical profile in neuropsychological testing in DLB and PDD, that might also influence cognitive speed.[19]

The AQT color-form naming test has in earlier studies been shown to have potential for providing quick, objective, reliable and sensitive screening to identify decreases in cognitive function associated with AD. Furthermore, test administration requires minimal equipment and training.[7] Here we compared two groups with equal performance on MMSE since this is the most used test in the clinic and a practical conclusion of the paper is that a patient with a relatively high MMSE score and slow performance on AQT should lead the clinician to ask questions relevant to the detection of DLB. Determining if AQT can be used to identify decreases in cognitive function associated with DLB is important, as this may have clinical implications for treatment as well as for understanding the neuropathological properties of the

disease. Further studies are needed to determine if AQT can play a more important role in the diagnosis of DLB.

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**LEGENDS**

**Table 1**

* p<0.001 DLB vs. controls, AD vs. controls, † p<0.001 DLB vs. controls, DLB vs. AD, ‡ p<0.001 AD vs. controls, § p<0.001 DLB vs. controls, 0.043 DLB vs. AD, ‖ p<0.001 AD vs. controls, ¶ p<0.001 DLB vs. controls, 0.003 DLB vs. AD, ** p<0.001 AD vs. controls.

**Figure 1**

Median reading times for color (seconds) together with interquartile range and range are shown for the three study groups.

**Figure 2**

Median reading times for color-form (seconds) together with interquartile range and range are shown for the three study groups.

Table 1

| | DLB (n=23) | AD (n=18) | Controls (n=24) |
|---|---|---|---|
| Age(years) (mean±SD) | 76±4 | 78±6 | 77±3 |
| Men n, (%) | 13 (57) | 8 (44) | 11 (45) |
| MMSE score (mean±SD) | 22±5 | 22±4 | 29±1* |
| AQT color(s) (mean±SD) | 76±50† | 39±12‡ | 25±5 |
| AQT form(s) (mean±SD) | 87±56§ | 62±30‖ | 36±8 |
| AQT color-form(s) (mean±SD) | 151±63¶ | 103±40** | 66±15 |

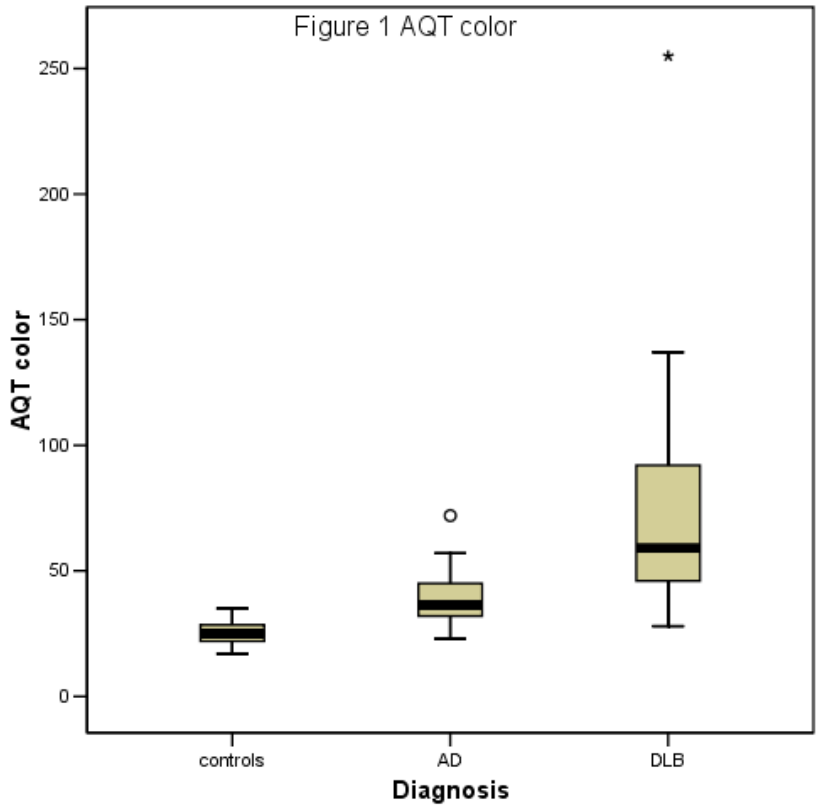


Figure 1 AQT color
AQT color
250
200
150
100
50
0
controls
AD
DLB
Diagnosis

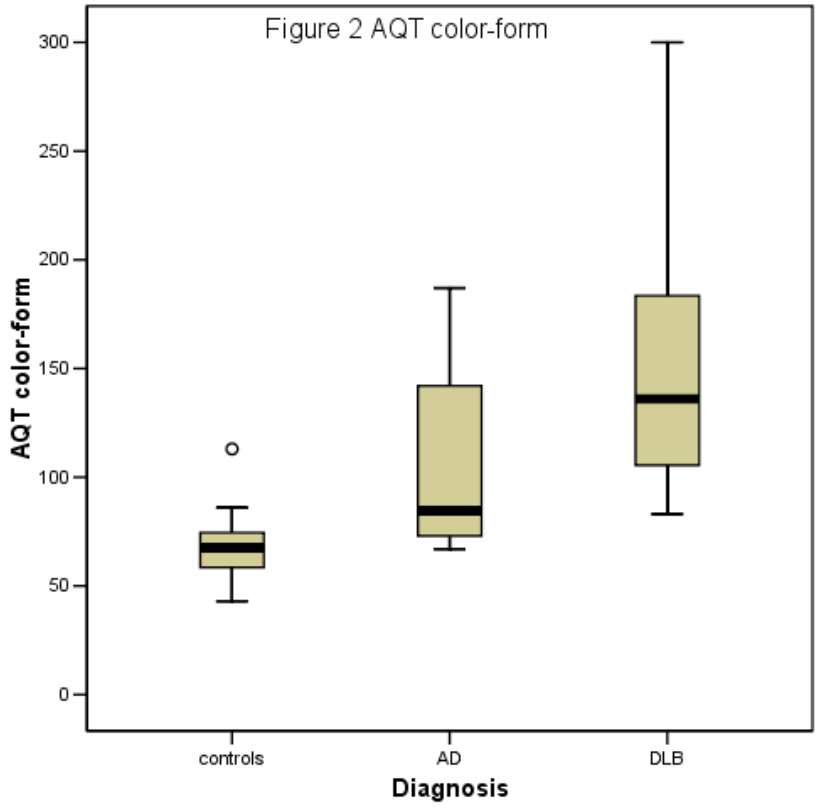
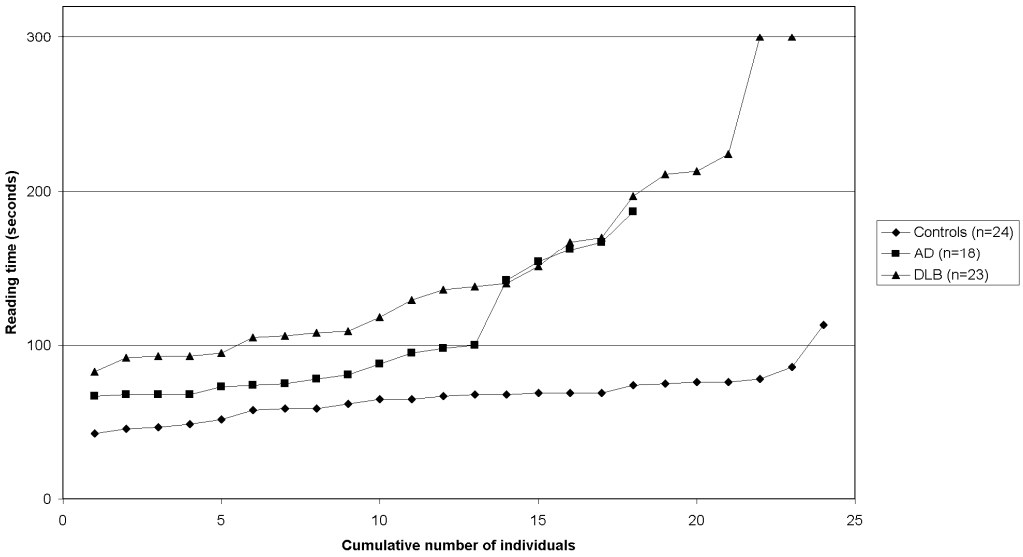


Figure 2 AQT color-form
AQT color-form
300
250
200
150
100
50
0
controls
AD
DLB
Diagnosis

**Figure 3 Color-Form**



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