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A Comparison Between Number And Letter Acuities Among Patients

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A COMPARISON BETWEEN NUMBER AND LETTER ACUITIES AMONG PATIENTS WITH DEMENTIA

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ABSTRACT

Purpose: Previous studies have shown that there is an association between visual acuity and Alzheimers' disease. Untreated visual problems may contribute to cognitive impairment and more progressive cognitive decline. This study investigates the association of chart design, specifically comparing charts using letters versus numbers, to accuracy and repeatability among patients with dementia.

Methods: 23 English-speaking subjects diagnosed with moderate to advanced levels of dementia were recruited from two local Birmingham nursing homes. Visual acuities were measured in a randomly selected eye and timed from six different charts: Back-illuminated ETDRS chart with letters, Back-illuminated ETDRS chart with numbers, HOTV cards with single, isolated letters, Lea cards with numbers, HOTV cards with single crowded letters, Lea cards with single crowded numbers. Acuities were re-measured and timed using the same subjects and same charts in random order, one week later. Non-parametric tests were used to evaluate differences between measured chart acuities. Intra class correlation coefficients between administrations were calculated using a linear mixed model.

Results: The best acuities were achieved with single letter (20/25 median) and single number charts (20/25 median). The poorest acuity was achieved with both the ETDRS number (20/50) and letter charts(20/50). Differences between ETDRS number and letters acuities were poorer ($p<0.005$) than comparable single letter acuities and between crowded versus uncrowded single

letter ($p<0.05$). Best agreement between first and second acuities on the same chart was with insert

a section single letter acuity with intraclass correlation coefficient of 0.79, followed by ETDRS letter ICC 0.55 and single number 0.55.

Conclusion: Single letter charts provided the best and most repeatable acuity among this group of subjects with dementia. There appears to be no number or letter bias for better acuity among this group. The worsening acuity with increasing chart complexity suggests a crowding effect or global distraction factor with chart type.

Keywords: visual acuity, dementia, Alzheimer's, repeatability

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BACKGROUND

Dementia is defined as a group of symptoms that involves memory, thinking, and social aptitude that can negatively impact daily functioning. It is caused by irreversible damage to brain cells typically from brain disease or injury. The most important risk factor is increasing age (>65). Other known risk factors include a family history and genetics. No link between gender, socioeconomic status, ethnicity, or geographical residence has yet been confirmed.[1]

According to the most recent Centers for Disease Control and Prevention (CDC) statistics from 2014, about 50% of nursing home residents have a form of dementia.[2] There are various forms of dementia including Alzheimer's disease, vascular dementia, dementia with Lewy bodies, frontotemporal dementia, and mixed dementia. The most common cause of progressive dementia in the elderly population is Alzheimer's disease. It makes up between 60 and 80% of dementia case. The International Classification of Diseases characterizes Alzheimer's as: "a deterioration of memory and thinking which gradually affects self-sufficiency in daily activities. Memory is affected in all its parts and its disorder is connected with disorders of behavior and thinking".[3]

Symptoms of dementia vary and can be difficult to unequivocally diagnose premortem. Standard of care requires that practitioners document two or more of the following to be compromised in order to consider diagnosing dementia: memory, communication, ability to focus, reasoning or judgment abilities, and visual perception.[4] Additionally, diagnostic changes due to dementia can be separated into cognitive and psychological changes. Cognitive changes among patients with dementia may include confusion and disorientation, coordination difficulties, difficulty in planning and problem solving, problems with communication, and

memory loss. Psychological changes typically include personality shifts, depression, anxiety, agitation, hallucinations, paranoia or inappropriate behavior.[1]

There is no one test to diagnose dementia or Alzheimer's. A definite diagnosis of can only be made through postmortem examination in which case the presence of tau-neurofibrillary tangles, amyloid plaques, and cortical atrophy would be noted.[4] If suspect during a patient's life, patients typically go through a series of mental status testing and neurological testing to analyze their cognitive function. Memory, orientation, reasoning, attention, balance and other senses and skills are evaluated. Brain scans such as computed tomography (CT), magnetic resonance imaging (MRI) or positron emission tomography (PET) scans may be useful in revealing any evidence of strokes, hemorrhages, tumors or unusual brain activity or deposits. Lab tests, such as simple blood tests, can rule out a possible vitamin B-12 deficiency or hypothyroidism that may be the ultimate cause of dementia-like symptoms such as depression, memory loss, behavioral changes, or coordination difficulties. Psychological evaluations may also be useful to eliminate mental health conditions.[1]

Alzheimer's is clinically divided into two categories: mild and major neurocognitive disorders. Mild neurocognitive disorders affects memory and learning while major neurocognitive disorders also involve problems with language and visual perception. Alzheimer's disease also tends to follow a three-phase course. The early (mild) phase involves the decline of short- and medium-term memory. These symptoms can affect an individual's professional life and productivity and may cause depression secondarily. The longest phase is the second (moderate) phase. Here, memory loss occurs and speech skills worsen. Individuals become unable to properly react to questions, attention spans tend to decrease, and verbal, mathematical, reading, and writing skills decline. Also during this phase, Alzheimer's patients become increasingly disoriented in time and space. Finally, the late (severe) stage occurs with difficulty in eating, walking and recognizing friends and family. Judgment, logical reasoning, and social skills also become impaired at this time. Communication is very reduced.[4]

Dementia is a public health concern for eye care providers. Nearly 5 million people in the United States alone have Alzheimer's and in the next thirty years this number is expected to triple.[3] Multiple studies, such as Rogers and Langa's study, have shown that there is an association between visual acuity and Alzheimer's disease, and that untreated vision problems may contribute to cognitive impairment and more progressive cognitive decline.[5] Finding an accurate, reliable, and repeatable visual acuity assessment to use among our elderly population with dementia in order to properly treat their visual needs is crucial.

Many previous studies have analyzed the effects dementia has on vision and visual processing. Armstrong and Kergoat[6] report in their study that visual acuities, color vision, visual fields, and eye movements were affected. Kirby et al found more complex visual functioning such as reading ability, object recognition, and spatial localization are negatively impacted among patients suffering from dementia.[7]

The reasons that visual impairment occurs in dementia, and Alzheimer's more specifically, is not yet well understood, but it is thought to be due in part to a reduced number of retinal ganglion cells as well as impaired dorsal and ventral streams of the visual pathway that occur along with the disease.[7] Bowen and Hancock found that visual impairment is considerably higher in people with dementia living in assisted living and nursing homes. Nearly half of these residents that had visual impairments were correctable with glasses with even more than half by cataract surgery.[8] The Prevalence of Visual Impairment in People with Dementia (PrOVIDe) study found that 32.5% of patients with dementia had vision worse then 20/40. Additionally, 16.3% had vision worse than 20/60, a standard for visual impairment. Other findings included that 16% of their tested subjects could not read standard newspaper-size print with their current corrective glasses. Nearly one-fourth of them had not had their vision tested within the last 2 years.[9]

It is well known that dementia, especially severe dementia, can affect the ease with which vision tests are administered. Patients with dementia tend to have a poorer ability to focus, follow instructions, and communicate clearly.[10] It is also known through various studies that visual acuity *can* be measured among patients with dementia and should therefore be attempted allowing more time than with patients without cognitive impairments.[11]

It is crucial that acuities and eye exams be attempted and stressed on patients with dementia because an improvement in vision has been associated with a better quality of life. Amstrong and Kergoat found that when vision was corrected in patients with dementia, daily living improved, incidence of depression decreased, and frequency of falls and injury decreased.[6] Spierer et al.'s study also found that good near VA was significantly correlated with a better Mini Mental State Examination- score, and therefore better cognitive ability.[12] Although the actual relationship between vision and cognitive function is not currently well understood, it is possible that treating visual impairment could prevent further cognitive decline. Ong et al, have shown that under-corrected refractive error may contribute to cognitive impairment, suggesting that something as simple as acquiring a more accurate glasses prescription may improve cognitive function.[13] Rogers and Langa found through their research that people with dementia, and in particular those with Alzheimer's disease, had poorer vision and less frequent eye examinations before being diagnosed with dementia than those with normal cognition.[5] This suggests that vision treatment may affect the development of Alzheimer's and that "underdiagnosis or undertreatment of visual problems in the elderly may contribute to cognitive decline."[5]

Chriqui et al. attempted a study relevant to our own, that evaluated visual acuities among patients with dementia regardless of whether it was mild, moderate or severe dementia. Their study population included young participants, older subjects without a known cognitive impairment, and older persons with various levels of dementia living in long term care facilities. They incorporated six different acuity charts: Snellen charts, Teller cards, (ETDRS)-letters, (ETDRS)-numbers, (ETDRS)-Patty Pics, and (ETDRS)-Tumbling Es. Among the patients with

known dementia, the worst acuity scores were with Teller cards (20/65) and Patty Pics (20/62), and this was true whether or not the patient had early or advanced stages of dementia. The best acuities were achieved using the Snellen (20/35) and ETDRS-letter (20/36) charts.[11] This study not only suggests which charts may be more suitable to test vision on cognitively impaired adults, but it reveals that although VA measurements may not be as easy to take when dealing with dementia, it most certainly can be done.

In contrast to the previously mentioned study, Morse et al. found in their study that Snellen-type charts like ETDRS charts are generally inadequate and inaccurate protocols in measuring visual acuities in patients with dementia.[14] So while visual acuities are not always easy to measure in dementia, particularly in the advanced stages when communicative skills and focusing abilities have greatly declined, it might be that we do not have the proper tool or chart to measure visual acuities as accurately in a person with dementia.[6] This study hopes to identify an acuity chart with letters or numbers that is repeatable among patients with dementia and Alzheimer's, and that allows a more accurate assessment of their vision.

SPECIFIC AIMS AND STUDY HYPOTHESIS

Our hope is to find an accurate and consistent way of determining these patients' visual levels and, therefore, visual needs, in order to improve their day-to-day quality of life.

Specific Aim 1

Determine whether patients with dementia can achieve a higher level of visual acuity and faster response while using numbers as compared to using letters.

Numbers may be learned even earlier in life than letters, thus may be even more easily retrieved.

Specific Aim 2

Determine whether acuities taken with numbers are more consistent (using correlation coefficients) than acuities using letters.

Study Hypothesis 1

Patients with dementia respond better and elicit better visual acuity consistency when presented with numbered charts rather than lettered charts.

Null Hypothesis 1

There are no differences in acuities between numbers and letters among patients with dementia.

Study Hypothesis 2

Additionally, we expect that patients will have the most difficulty with the crowded letters/numbers on Lea Cards and will have the easiest/shortest time and best acuities with single number un-crowded Lea cards.

Null Hypothesis 2

There are no differences in average times when completing numbered and lettered charts.

JUSTIFICATION OF AIMS

Untreated poor vision was found to be associated with a nine-fold greater risk of developing Alzheimer's disease and a five-fold greater risk of developing cognitive impairment with no dementia.[5] Rogers and Langa's study revealed an association between visual acuity and Alzheimer's disease as well as the likelihood that untreated vision problems may contribute to cognitive impairment. [5] Therefore, early intervention and accurate visual acuity assessment may be important in reducing the risk of dementia or worsening existing dementia.

EXPERIMENTAL DESIGN AND METHODS

English-speaking patients were recruited for this study with the help of two nursing homes in the Birmingham area of Alabama. Social workers and medical staff were asked to identify potential candidates based on the Clinical Dementia Rating Scale.[15] To be included in the study, subjects had to have been clinically diagnosed with moderate to severe dementia. If mental status had been previously tested, patients with Saint Louis University Mental Status (SLUMS) test scores <21, and Brief Interview for Mental Status (BIMS) test scores <13 were included in our study. Saliba, et al. found that BIMS is a quick and straightforward test with a sensitivity of 83% and specificity of 92%.[16] It consists of three sections testing immediate recall, attention, orientation, and short-term memory. Scores below 13 indicate moderate to severe dementia.[16] Although the SLUMS test is more extensive and can be more difficult for subjects with more severe dementia, Tariq, et al. have found that it is an effective test for detecting neurocognitive disorders. The SLUMS test has a sensitivity of 100% and specificity of 83%.[17] It includes 11 items involving orientation, short-term memory, calculation skills, naming of animals, the clock drawing test, and recognition of geometric figures. Scores below 21 are indicative of dementia.

After selecting potential participants based on cognitive testing, letters were sent to the patients' guardians explaining our study, and including its aims and protocol. The patients' guardians were given the opportunity to sign consent forms with provided stamps and return envelopes in order to include the patient in the study.

There is some controversy as to whether reading performance depends heavily on cognitive, linguistic, and motivational factors.[18] However, we used only letters and numbers that required very low reading levels, in order to reduce any cognitive influence. We used standard testing distances based on the chart type and manufacturer recommendations. Halving the testing

distance was done only if subjects were unable to cooperate or read the acuity charts. Closer proximity is thought to increase visual attention.[19] Numerous attention studies have found improved visual performance when the test targets were placed closer to the subject.

The order of visual acuity charts presented was determined for each subject through a random order generator in Matlab, version R2017a.[20] Each subject was tested monocularly two times, at two separate visits, testing the same eye one week apart. In addition to recording their measured visual acuity at each visit, we also observed and recorded the speed at which the patients were able to perform each individual test.

First visit

Before proceeding with the six acuity charts, each subject was first asked whether they assented to having their vision checked. Each participant's BIMS or other mental status results were requested from the nursing home. If mental status testing had not been done within the last six months, we administered either the SLUMS test or BIMS. We required that patients score between 0 and 20 on SLUMS and score between 0 and 12 on BIMS to confirm moderate to severe impairment.

If assent was obtained from the subjects to check vision, we asked each patient to identify the largest number (~20/1400 size) on the Feinbloom chart and an equivalent 20/1400 "E" from 5 feet away using both eyes to ensure patient cooperation as well as the ability to identify numbers and letters. An abbreviated clinical acuity was measured to determine the eye with the better visual acuity to be used for testing. If the patient had similar acuities in both eyes, a coin was flipped to randomly select the eye to be tested. Retinoscopy was used to determine the corrective power needed by the subjects' better seeing eye to accomplish the best visual acuity measurement possible. The opposite eye was patched to eliminate any binocular influence in case one eye had significantly worse acuity.

In random order, we tested each subject individually with the 6 charts (described below).

1a. Back-illuminated ETDRS chart with letters

1b. Back-illuminated ETDRS chart with numbers

2a. HOTV cards with single, isolated letters

2b. Lea cards with numbers

3a. HOTV cards with single crowded letters

3b. Lea cards with single crowded numbers

Testing was done in a designated “common” space chosen by the facility or in the patient’s bedroom, if deemed necessary.

When administering the back-illuminated ETDRS chart with letters or numbers, subjects were instructed to start at the top of the chart (20/400) and to read down the chart as far as they could. The subject read down the chart until he or she reached a row where a minimum of three letters/numbers on a line could not be read. The patient was scored by how many letters/numbers could be correctly identified. We used the letter by letter method.

The HOTV-optotype single letter acuity chart was tested at 10 feet from the patient, and we started at the 20/100 acuity level. During this test, we showed one card of letters in each decreasing letter size asking the subject to identify a single letter (covering the other four available letters at the same acuity level). The visual acuity threshold was recorded at the level where the subject correctly identified at least 3 out of 5 symbols. If the subject correctly identified only two of the five symbols, the acuity was recorded at the previously larger number size. If the patient was unsuccessful at 10 feet, we attempted acuities again at 5 feet to see if responses improved and noted that accordingly in the data. Standard illumination (85 candelas/m^2) was provided with the John Nash Ott light.

The LEA single number card acuity chart was tested at 10 feet from the subject, starting at 20/100. During this test, we showed one page in each decreasing number size asking the subject to identify a single number (covering the other three available numbers at the same acuity level). The visual acuity threshold was recorded at the level where the subject correctly identified

at least 3 out of 5 symbols. If only two out of the four symptoms were identified correctly, we proceeded to show one of the symbols a second time to provide a fifth choice. If the subject correctly identified only two of the five symbols, the acuity was recorded at the previously larger number size. If the patient was unsuccessful at 10 feet, we attempted acuities again at 5 feet to see if responses improved and noted that accordingly in the data. Standard illumination (85 candelas/m^2) was provided.

Finally, the crowded number and letter charts were administered at ten feet again and started on the 20/100 acuity level. We showed one page in each decreasing number size while asking the subject to identify a letter/number. We then flipped the page to a different letter/number on the same acuity level. The visual acuity threshold was recorded at the level where the subject correctly identified at least 3 out of 5 symbols. If only two out of the four symptoms were identified correctly, we showed one of the symbols a second time to give a fifth choice. If the subject correctly identified only two of the five symbols, the acuity was recorded at the previously larger number size. If the patient was unsuccessful at 10 feet, we attempted acuities again at 5 feet to see if responses were better and recorded that accordingly in the data. Standard illumination (85 candelas/m^2) was provided.

Second visit

Each patient, except one who did not agree to a second visit, was re-tested one week after the initial visit. Every attempt was made to see the patient at a similar time as the previous visit. At the beginning of the 1-week follow-up, each subject was again asked if they agreed to testing. In a new random order, we tested each subject individually with the 6 previously mentioned charts using the same protocol for each chart as the first visit. We tested the same eye and used the same retinoscopy measurement as the previous visit.

Data Analysis

We used parametric and nonparametric testing to evaluate acuity and time results between visit 1 and visit 2. We used repeated measures mixed model to test within subject and between subject variability. To measure repeatability, we used calculated coefficient of repeatability (smallest real difference) to show the relationship between first and second visit measurements as well as intraclass correlation coefficients.

The following assumptions were used for same size calculation. A power value of 0.8, an alpha value of 0.05, a correlation value of 0.8 and standard deviation of 0.12. Sample size for repeated measures gave us a sample size of 12. Based on sample size calculations for paired t test 13 subjects were needed to detect 1 line.

This research conformed to the tenets of the Declaration of Helsinki. This research was approved by the University of Alabama Birmingham Institutional Review Board and the legal counsel of each facility.

RESULTS

For this study we recruited a total of 23 subjects with 22 that consented to acuity testing during the second visit. The mean mental status was 8.8(std 3.6) ranging between 5 and 16(BIMS), signifying moderate to severe dementia. As seen by the range, there was one patient who scored too high on BIMS to meet our qualifications, so this patient was retested with SLUMS and successfully met our requirements for moderate to severe dementia. Of the 23 subjects, 2 were male and 21 were female. A total of 16 right eyes were tested and a total of 7 left eyes were tested. 18 participants were tested in the provided common room, 4 participants were tested in their bedroom, and 1 participant was tested in a hallway. Participants tested outside of a common room were re-tested at the second visit in the same location.

Visual Acuity Results

The mean overall visual acuity (VA) across all subjects and charts was 20/46.6(±30.0), median 20/40 with individual acuity measurements ranging between 20/16 to 20/250. The best acuities were achieved were with single letter (20/25 median) and single number charts (20/25 median) [Table 1]. The worst acuities were measured when testing with both the ETDRS number (20/50 median) and ETDRS letter charts (20/50 median).

Table 1

Visual Acuity by Visit and Chart Type

VISUAL ACUITY	**Visit 1**		**Visit 2**		**Paired T**	**Signed Rank**
	Mean(std)	Median	Mean(std)	Median	P	P
ETDRS Letters	54.0(23.4)	50	57.9(30.6)	45	0.72	0.73
ETDRS Numbers	65.3(51.2)	50	62.0(35.2)	50	0.88	0.49
HOTV Crowded	48.4(40.4)	40	46.3(24.2)	45	0.64	0.59
HOTV Single Letters	32.8(18.4)	25	33.5(20.5)	30	0.97	0.93
Lea Crowded Numbers	40.7(19.2)	40	38.3(16.6)	32	0.49	0.24
Lea Single Numbers	30.6(13.0)	25	34.4(16.7)	32	0.28	0.17

Subjects did not achieve better acuity with the number charts in comparison to all of the letter charts [Table 2]. The average visual acuity measurement with all of the letter charts combined was ~20/46 while the average visual acuity measurement with all three charts using numbers was ~20/45 ($P = 0.81$). When looking at the chart of similar design (eg. ETDRS number versus ETDRS letter) no significant differences in acuities was found between the ETDRS letter chart and the ETDRS number chart, between the HOTV single letter chart and the LEA single number chart, or between the crowded lettered HOTV chart and crowded number chart.

Table 2

Visual Acuity by Test Characteristics

Visual Acuities	**P**
Visit Number	0.87
Number vs. Letter Charts	0.81
ETDRS letter vs. ETDSR number	0.18
Crowded letter vs. crowded number	0.09
Single letter vs. single number	0.89
Where	*
Order	0.06
Chart Type	<0.001
Chart by visit	0.98
Chart by order	0.35
Time	<0.001

*Not enough test locations for evaluation

The majority of subjects were tested in common areas (recreation room or dining hall). While location may have impacted acuity for these subjects, too few were tested in other locations to allow for meaningful statistical analysis.

We assessed whether the order in which the charts were presented made a difference in acuities. There appears to be a possible influence of chart order (P =0.06), as the chart order approached significance. We compared the 6th chart presented to all of the other charts shown prior [Table 3]. If subjects became fatigued or lost concentration, we would have expected that the later charts produced poorer acuities. The opposite was true. The average visual acuity on the 6th chart presented averaged about 20/42, while the acuities on the first chart presented averaged 20/52, a difference of about 1 line in acuity. This difference approached statistical significance (P =0.08). However, the main contributing factor was chart type itself. The order no longer approaches significance (P =0.84) when chart design was controlled and no interaction between chart design and order of presentation was seen.

Table 3

Effect of Presentation Order on Visual Acuity

Order	VA	Estimate	Standard Error	t Value	P
1	51.66	9.61	5.34	1.80	0.075
2	47.59	5.54	5.30	1.04	0.30
3	43.11	1.06	5.34	0.20	0.84
4	47.82	5.77	5.28	1.09	0.28
5	41.85	-0.20	5.34	-0.04	0.97
6	42.05	.	.	.	.

Using the LEA isolated numbers chart, as a comparison, the data suggests that subjects had significantly worse acuities on the HOTV crowded letters chart, ETDRS-letters chart, and ETDRS-numbers chart [Table 4]. Compared to the LEA single numbers chart, subjects, on average, performed about the same on the HOTV single letter chart and only did somewhat worse

on the crowded single number chart. Differences between LEA single numbers and LEA crowded numbers and HOTV single letters were not statistically significant.

Table 4

Visual Acuity by Chart Type

Effect	**VA**	**Estimate**	**Standard Error**	**t Value**	**P**
ETDRS Letters	55.95	24.91	4.72	5.28	<0.001
ETDRS Numbers	63.65	31.20	4.72	6.61	<0.001
HOTV Crowded Letters	47.35	14.87	4.72	3.15	0.002
HOTV Single Letters	33.15	0.64	4.72	0.14	0.89
Lea Crowded Numbers	39.50	7.02	4.72	1.49	0.14
Lea Single Numbers	32.50	.	.	.	.

Time Results

It is somewhat difficult to assess the differences in time taken between the charts accurately due to the variation in chart design. The necessary manipulation of the single number cards and HOTV letter and LEA number crowded cards was a factor contributing to the increased times compared to the single ETDRS chart which did not require card turning. Possibly for this reason, the acuity chart that took the longest was the isolated number chart (mean 138 sec, SD= 39.0) [Table 5]. The fastest time to acuity was achieved on the ETDRS letter charts, averaging 76 seconds, and the ETDRS number charts, averaging 70 seconds. All of the charts were read faster than the LEA single numbers [Table 7]. To account for varying chart design, we calculated time per letter read for each chart. Data shows that even the time it took per letter appears fastest on both ETDRS charts [Table 8].

Table 5

Time by Visit and Chart Type

TIME	Visit 1		Visit 2		Paired T	Signed Rank
	Mean(std)	Median	Mean(std)	Median	P	P
ETDRS Letters	79.2(36.7)	63	72.7(34.0)	69	0.21	0.11
ETDRS Numbers	68.6(23.6)	65	70.4(24.3)	71	0.87	0.93
HOTV Crowded	114.7(33.3)	114	96.7(28.6)	97	0.09	0.03
HOTV Single Letters	123.9(61.4)	110	91.5(18.1)	87	<0.001	0.02
Lea Crowded Numbers	98.8(24.3)	102	97.5(32.4)	94	0.83	0.61
Lea Single Numbers	143.3(35.6)	137	133.2(42.3)	118	0.24	0.29

Table 7

Time by Chart Type

Chart	Time	Estimate	Standard Error	t Value	P|
ETDRS Letters	76.0	-62.3	7.50	-8.30	<0.001
ETDRS Numbers	69.5	-68.8	7.50	-9.18	<0.001
HOTV Crowded	105.9	-32.4	7.50	-4.32	<0.001
HOTV Single Letters	108.4	-30.3	7.50	-4.04	<0.001
Lea Crowded Numbers	98.2	-40.1	7.50	-5.35	<0.001
Lea Single Numbers	138.3	0	.	-8.30	<0.001

Table 8

Letter Per Second by Chart-type

CHART	Time/Letter(std)
ETDRS Letters	1.7(0.9)
ETDRS Numbers	1.6(0.6)
HOTV Crowded Letter	5.9(2.9)
HOTV Single Letter	4.3(2.1)
Lea Crowded Number	5.2(2.2)
Lea Single Number	5.3(2.1)

There was no interaction between visit number and the actual chart-type in determining testing times [Table 6]. Individually, however, the visit number influenced the time ($P = 0.02$) and the actual chart-type influenced the time taken to measure acuities ($P < 0.001$) [Table 7].

Visit number played a significant role in the time it took patients to get through an acuity chart ($P = 0.02$) [Table 6]. On the first visit, patients took about 12 seconds longer on all charts

than on the second visit. During the first visit, the acuity testing took 105 seconds for each chart on average, while testing took only 93 seconds for each chart on average during the second visit. It appears the main learning curve occurred with the HOTV single letter chart where on average, patients improved by nearly 32 seconds on the second visit. This improvement may have been our own improvement and familiarity with testing procedures. We had one person in charge of recording time and acuities and one person in charge of chart manipulation. These roles were the same for both sessions. So there is a possibility that the individual responsible for chart manipulation improved in efficiency by the second visit. While the overall differences in time may be statistically significant, they differ by only a few seconds, which may not signify anything from a practical standpoint especially when looking at the difference in chart testing procedures (flipping cards vs displaying one chart).

Table 6

Time by Test Characteristics

Time	**P**
Chart	<0.001
Visit Number	0.02
Order	0.96
Where	*
Number vs. Letter chart	0.33
ETDSR numbers vs. letters	0.38
HOTV crowded letter vs. Lea crowded number	0.30
HOTV single letter vs. Lea number	0.001
Chart by visit number	0.12

*Not enough test locations for evaluation

Similar to the acuity assessment, the order in which the charts were tested did not make a difference in time ($P = .96$). When looking at the number charts and the letter charts, the only significant difference found was between the single numbers and the single letter charts [Table 6]. On average, it took patients about 30 seconds longer to read the single numbered charts than the single letter charts (138 sec vs 108 sec). There was no significant difference between the other letter or number charts. This could partly be due to the chart design; the single number chart

required much more chart manipulation than the single letter charts. Therefore, overall, there was no difference in time between letter and number charts.

Repeatability

The mean visual acuity during visit 1 was ~20/46 while the mean visual acuity was ~20/45 on visit 2 ($P = 0.87$). In both parametric (paired t-test) and non-parametric(signed rank test) across all charts, there was no significant improvement in visual acuities after the initial visit suggesting subjects did not improve based on greater familiarity with the charts after the first visit [Table 1]. Differences across all charts were not different between first and second visit suggesting good repeatability.

Best agreement between first and second acuities on the same chart was with single letter acuities with an intraclass coefficient of 0.79 which is considered to be excellent correlation. Following the single letter chart were the ETDRS letter chart (ICC 0.56) and Lea single number chart (ICC=0.56), both scaled as "fair" correlation [Table 9].

Table 9

Repeatability of Charts

	Intraclass Correlation Coefficients
ETDRS letters	0.56
ETDRS Numbers	0.19
HOTV Crowded	0.49
HOTV Single Letter	0.79
Lea Crowded Number	0.35
Lea Single Number	0.56

We examined the smallest real difference between charts as another indicator of reliability [Table 10]. The single number charts had the best smallest real difference (±25), a value of about 3 lines of acuity, indicating the best reliability again. This value is consistent with what NIH clinical trials use on ETDRS charts when testing subjects with various eye conditions such as macular degeneration and diabetic retinopathy. The ETDRS number chart had a very

large smallest real difference. The reason for this was two very inconsistent subjects as seen in Figure 1.

Table 10

Smallest Real Difference by Chart

CHART	Mean Difference Acuity 1 and 2	Smallest Real Difference
ETDRS Letters	-2.0	±50.7
ETDRS Numbers	1.8	±111.5
HOTV Crowded	3.4	±67.2
HOTV Single Letters	0.1	±25.0
Lea Crowded Numbers	3.1	±40.3
Lea Single Numbers	3.3	±27.4

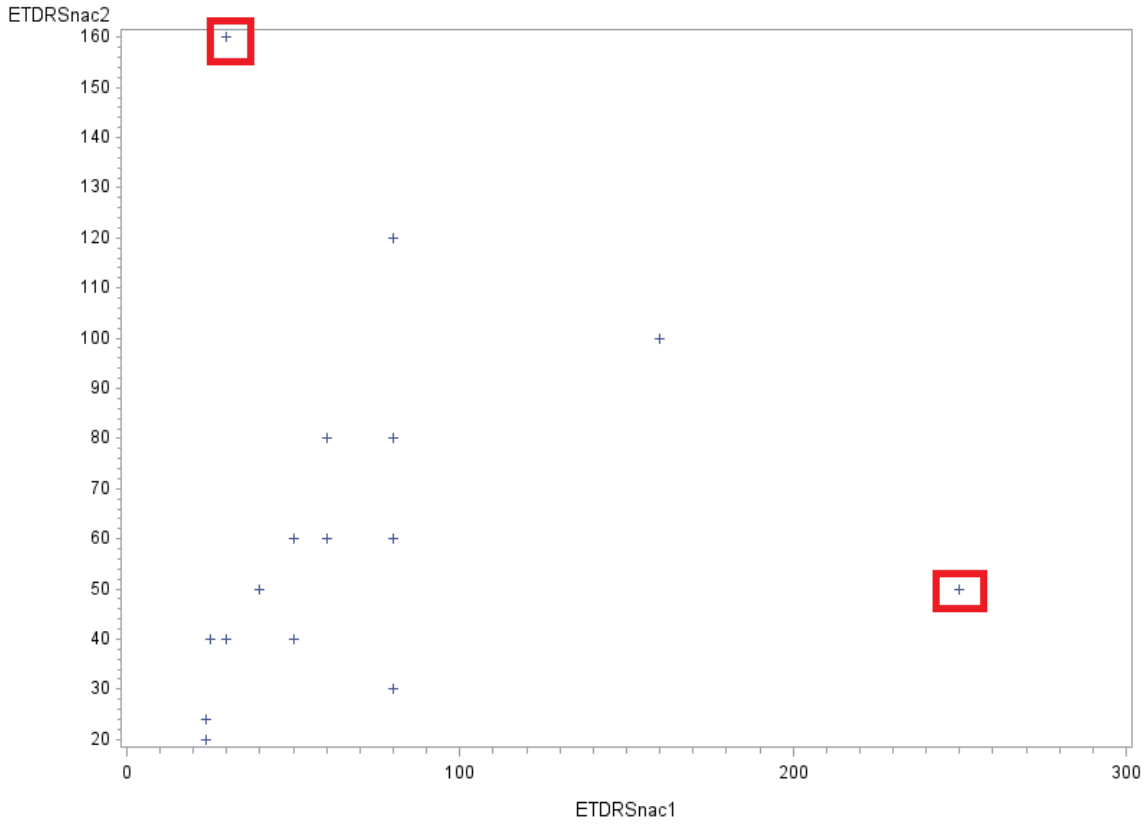

Figure 1 *Scatterplot of ETDRS Number Chart Visit 1 vs Visit 2*

Legend: ETDRSnac1-ETDRS number acuity chart first test, ETDRSnac2- ETDRS number acuity chart second test

When assessing how consistent and repeatable the times were between visits, the paired t and signed rank values show that times were only better on the second visit with HOTV single letter charts [Table 5]: This could have been the subjects getting better or the individual in charge of chart manipulation getting better at testing. Statistical significance was also approached with times using the HOTV crowded charts. We are not sure why this occurred. Otherwise, there was no difference in times with other charts between visits.

Crowding Results

We noticed in our subjective findings that the majority of our subjects had difficulty with charts that included crowding bars. During acuity testing, only about 17% were able to ignore the flanking bars around the target letter, while 83% verbally identified the laterally placed crowding bars either as a letter “I” or a number “1” or alternated between the two. Based on our data, it also appears that the percentage of subjects who read the crowding bars decreased from 89% on the first visit to 77% on the second visit, suggesting minimal improvement from familiarity.

We assessed whether or not reading the crowding bars had an adverse effect on the visual acuity. It appears subjects performed slightly better, by about a line of acuity, when they were able to ignore the crowding bars [Table 11]. However, there were no statistically significant differences between the average acuities on charts without bars, to acuities from charts with bars, to acuities from charts where bars were read, to acuities from charts where bars were ignored. The reason for this is obvious by the large standard errors. We did not have enough subjects who did not read the bars to make an accurate assessment.

Table 11

Crowding Bars and Acuity

	VA	EST	SE	t Value	P
Charts w/ bars vs. Charts w/o bars	43.5 vs 46.6	3.10	3.7	0.81	0.43
Read bars vs. no bars on chart	45.6 vs. 46.6	1.00	4.12	0.24	0.81
Ignored bars vs no bars on chart	32.7 vs 46.6	13.87	8.05	1.72	0.1
Ignored bars vs read bars	32.7 vs 45.6	12.87	8.47	1.52	0.14

LIMITATIONS

We did not have a perfectly controlled environment. Due to different subjects and their individual physical limitations, we varied our testing environment from a common room provided by the nursing home facility and the patients' bedroom. Only one patient was testing outside of their bedroom in the hallway. In addition, there were not enough subjects in each location to assess whether the testing environment made a difference in test results. Finally, variation in card manipulation could also be another limiting factor in having solid data analysis on times. We did not know each subjects full history or whether they had any retinal diseases, for instance.

DISCUSSION

There appears to be no number or letter bias for better acuity or better times among this group of subjects. The results support our null hypothesis 1, stating, “There is no difference in acuities between number and letter among patients with dementia.” There are no differences in average times when completing numbered and lettered charts. Single letter charts provided the best and most repeatable acuities among patients with dementia. Furthermore, the worsening acuity with increasing chart complexity suggests a crowding effect or global distraction factor with chart type.

It is thought that many aspects of vision and vision processing are affected in cases with Alzheimer’s and dementia. Contrast sensitivity, visual acuity, color and motion perception[7] as well as more complex processing such as visual-perceptual abnormalities, spatial agnosia, environmental disorientation, visual agnosia, facial identification problems, and visual hallucinations[21] have all been documented as secondary visual disturbances related to dementia. There is also supported evidence that Alzheimer's patients, who suffer from some of these visual processing difficulties, also have coexisting histologic and metabolic abnormalities in the parieto-occipital area of the brain, regions responsible for processing visual-spatial information.[21,22]

Overall, no statistically significant data supported our hypothesis that suggests a difference in acuity measurements and acuity times between numbered and lettered charts. However, our data supports the conclusion that chart type matters most in testing patients with dementia. Single lettered and single numbered charts consistently provided better acuities among these subjects with dementia. Although subjects seem to read letters and numbers in a standard ETDRS chart in less time, an accurate acuity level is sacrificed. We argue that the “busier” and

more cluttered the chart, whether it be crowded bars around single letters or having multiple rows of letters on a single chart, the poorer the visual acuity will be among patients with dementia.

Mendez, et al conducted a study with 30 elderly patients diagnosed with Alzheimer's disease in which all 30 patients had impaired figure-ground skills (identifying a figure from the background), and over half of them had difficulties recognizing familiar objects ("agnosia"). They found that patients with severe dementia also had the most complex visual disturbances.[23] Whitney and Levi note that crowding, or the inability to distinguish items in clutter, is the ultimate barrier to object identification.[24] Crowding is defined as the "increased difficulty in identifying a target object when it is surrounded by nearby objects," also known as flankers.[25] Not only does crowding impair object identification but it can also hinder reading, face recognition, navigation, and visual search.[24] Typically, crowding only affects peripheral vision in healthy individuals, but we are now discovering that crowding can affect central vision secondary to certain conditions and diseases.[26] Furthermore, the crowding affect is not a normal aging process. Astle's study found that uncrowded and crowded acuities did not change as a function of age.[25]

Through previous studies it has been established that patients with macular degeneration, amblyopia and dyslexia have problems with crowding, but Yong et al. suggests that patients with Posterior Cortical Atrophy also commonly have excessive crowding impairments in their central vision.[27] Posterior Cortical Atrophy (PCA) is a slowly progressive degenerative disease that affects the outer, posterior part of the brain, leading to impaired complex visual processing. Although there remains some debate, many believe that PCA is a possible form of Alzheimer's disease, since patients with PCA also commonly have amyloid plaques and neurofibrillary tangles similar to Alzheimer's disease, but located in different areas of the brain.[28]

Yong et al. did an extensive study analyzing how crowding plays a role in patients with PCA compared to patients with typical Alzheimer's disease and compared to healthy adults. Crowding is mostly understood to be a pre-attentive process and a likely effect of visual interactions. There are currently three ongoing hypotheses of where crowding originates. The first

hypothesis states that crowding is associated with “low level” masking, more specifically lateral masking, at the level of the retina, lateral geniculate nucleus, or primary visual cortex. The second hypothesis suggests that flankers create a “noisy” environment to the onlooker leading to a substitution effect, where the subject swaps the target for the distractor. Finally, the third hypothesis states that crowding is the result of “excessive feature integration,” which is explained as a process of pooling and averaging visual information over a large area that assembles the flanker and target stimuli information together.[27]

Yong’s study found that the subjects with PCA were not only slower at identifying flanked letters, but also less accurate compared to typical Alzheimer’s patients and the healthy control group. Their data revealed that their accuracy was most heavily influenced by the flanker spacing condition (closely positioned flankers led to less accurate letter identification) rather than by flanker type (letter versus shape). Their imaging data also suggests that the findings were associated with significantly reduced grey matter in the right collateral sulcus between the fusiform and lingual gyri.[27] Of the errors made within the PCA group, whether it was no response, identifying the flanker rather than the target, or identifying a letter not present in the array, the overall errors suggested perceptual integration and averaging of the flanker and target. For instance if the target ‘M’ was presented between two different letters (YMT), the subject may incorrectly identify the target as ‘V,’ suggesting total integration of target and flanker information. This finding closely supports the third hypothesis, suggesting that identifying flanked letters are at least partially influence by averaging the target and flanker stimuli.[27]

Although Yong et al. found data revealing that patients with PCA suffered from crowding affects in their central vision and not typical Alzheimer’s patients, our data may suggest otherwise, despite not knowing the specific type of dementia each patient had. In addition to the crowding affect, higher order attentional deficits may also explain why our subjects did worse on the busy, more cluttered charts. Visual selective attention is the process that allows us to be selective in what we are focused on by sifting through visual information that is relevant and

suppressing irrelevant information in the current situation or environment.[29] Visual attention requires complex cognitive processing and visual perception. It involves detection of important sensory information, ignoring distracting information, and shifting attention from various details or locations. Peters et al. did a study that found both patients with Alzheimer's and Dementia with Lewy Bodies suffered from poor visual selective attention.[30]

Foldi et al. found after administering a multi-target visual cancellation test, that as similarity between targets and distractors increased, Alzheimer's patients not only slowed their visual searching, but also made more mistakes and failed to identify more targets. They found similar results when they increased the density, or clutter, of targets and distractors: Alzheimer's patients searched more slowly and had more errors. This suggests evidence of complex attentional deficits among patients with dementia and could be a potential reason for performing more poorly on crowded acuity charts.[31]

It is thought that the posterior parietal cortex is partially responsible for attention visual function. Severe pathology in this region has been seen to trigger problems interpreting the visual scenario in its entirety despite maintaining the ability to decipher individual portions. Therefore, patients with dementia may have more difficulty living and processing our naturally cluttered world, due to a declining ability to process the scene wholly and simultaneously.[32]

Although our findings did not support that patients with dementia can achieve a higher level of visual acuity and more consistent measurement using numbers rather than with letters, we were able to determine that the type of chart administered while testing vision among patients with dementia makes a significant difference. Additionally, our subjective findings reveal greater difficulty and confusion with "busy" ETDRS charts and charts using crowding bars. The majority of our patient base subjectively stumbled with crowded charts, often deciding verbally whether they should include the crowding bars as a potential number or letter. Additionally, multiple patients skipped and repeated lines while reading ETDRS charts, and were more likely to give up abruptly during testing. So although the actual timing did not reflect considerable difficulty while

testing crowding charts, it was documented subjectively.

Based on our results, the most accurate and consistent way of determining visual levels among patients with dementia was found to be with using the HOTV single letter chart. This chart was also one of the least crowded and least “busy” charts. This supports previous studies that have found the crowding effect and poorer visual selective attention among patients with various types of dementia.

While examining patients with dementia and assessing their acuities, we recommend using simpler charts and allotting more time in the exam chair. More research is needed to further assess visual testing, crowding effects, and visual attention among patients with various forms of dementia to further improve their day-to-day quality of life.

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APPENDIX A

IRB APPROVAL FORM

THE UNIVERSITY OF ALABAMA AT BIRMINGHAM

Institutional Review Board for Human Use

Form 4: IRB Approval Form
Identification and Certification of Research
Projects Involving Human Subjects

UAB's Institutional Review Boards for Human Use (IRBs) have an approved Federalwide Assurance with the Office for Human Research Protections (OHRP). The Assurance number is FWA00005960 and it expires on January 24, 2017. The UAB IRBs are also in compliance with 21 CFR Parts 50 and 56.

Principal Investigator:	SWANSON, MARK
Co-Investigator(s):	
Protocol Number:	**X160914007**
Protocol Title:	*A Comparison Between Number and Letter Acuity in Patients with Dementia*

The IRB reviewed and approved the above named project on 10-31-16 The review was conducted in accordance with UAB's Assurance of Compliance approved by the Department of Health and Human Services. This Project will be subject to Annual continuing review as provided in that Assurance.

This project received EXPEDITED review.

IRB Approval Date: 10-31-16

Date IRB Approval Issued: 10-31-16

IRB Approval No Longer Valid On: 10-31-17

Expedited Reviewer
Member - Institutional Review Board
for Human Use (IRB)

Investigators please note:

The IRB approved consent form used in the study must contain the IRB approval date and expiration date.

IRB approval is given for one year unless otherwise noted. For projects subject to annual review research activities may not continue past the one year anniversary of the IRB approval date.

Any modifications in the study methodology, protocol and/or consent form must be submitted for review and approval to the IRB prior to implementation.

Adverse Events and/or unanticipated risks to subjects or others at UAB or other participating institutions must be reported promptly to the IRB.

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