Brief report

Automated neuropsychological assessment metrics (ANAM) measures of cognitive effects of Alzheimer’s disease

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Abstract

Eight individuals with Alzheimer’s disease, and eight age-matched controls, were administered the MMSE, the Yesavage GDS, and a customized subset of the Automated Neuropsychological Assessment Metrics (ANAM) Battery. Accuracy (percent correct) and efficiency (number of correct responses per minute) of performance on six ANAM tasks were assessed. The patients’ GDS scores indicated no depression. Although their MMSE scores (mean ~ 25) were significantly lower than those of the controls, they nonetheless indicated that the patients were still functioning at a fairly high level. Analysis of ANAM accuracy scores indicated that the patients were significantly impaired on three tasks measuring working memory. A discriminant function analysis revealed 93.8% correct classification. Analysis of ANAM efficiency scores revealed that except for simple reaction time, the patients were significantly impaired on all tasks. A discriminant function analysis correctly classified 100% of the participants. Given the small size of the groups in the present study, this finding especially underscores the sensitivity of ANAM to the cognitive effects of Alzheimer’s disease, as indicated by the large effect sizes. The findings further indicate that ANAM might be capable of detecting more subtle effects of the disease at an earlier stage in its progress.

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Contemporary computerized cognitive assessment batteries, such as Cogscreen (Kay, 1995) and Microcog (Powell et al., 1993), have been in use for a number of years; they feature standardized administration and scoring, as well as ease and speed of administration. They measure accuracy and response speed in milliseconds. Further, they may be used with an elderly population. The Automated Neuropsychological Assessment Metrics (ANAM) Battery (Reeves, Kane, & Winter, 1995) also measures both accuracy and response speed on all tests in the battery, and these are used to evaluate cognitive performance. However, unlike most other computerized batteries, ANAM uses accuracy and response speed to calculate a measure known as throughput (Thorne, 1990). Throughput represents correct responses/minute, and since it is based on both accuracy and speed, it reflects efficiency of performance. ANAM measures accuracy and efficiency of performance on a “library” of tests, from which customized subsets may be constructed.

Subsets of ANAM have been used in studies on a variety of neurological conditions, resulting from either traumatic brain injury (Levinson & Reeves, 1997; Levinson, Reeves, Wild, & Lewandowski, 1998), stroke (Goldstone, Reeves, Levinson, & Pelham, 1995), heat exhaustion (Gestaldo, Reeves, Levinson, & Winger, 2001), exposure to ionizing radiation (Gamache, Levinson, Reeves, Bidyuk, & Brantley, 2005), or use of drugs such as cocaine and marijuana (Gottschalk, Bechtel, Maguire, Katz, Levinson, Harrington, Nakamura & Franklin, 2002).

In general, all of these investigations have found that both accuracy and, to a much greater degree, efficiency of performance on ANAM tasks are very sensitive to the cognitive effects of these conditions. In addition to its ease and speed of administration and scoring, ANAM has been found to have great utility in studies requiring repeated testing, such as those measuring recovery from injury and/or monitoring progress in treatment of neurological conditions. It has been shown to have high test–retest reliability; e.g., for efficiency on the simple reaction time task, $r = .85$; on the running memory continuous performance (CPT) task, $r = .81$; and on the matching-to-sample task (MSP), $r = .66$ (all $P$’s < .001; Bleiberg, Garmoe, Halpern, Reeves, & Nadler, 1997). It has also been shown to have validity, as assessed by correlational analyses with performance on Trails B (Reitan & Wolfson, 1995); e.g., for efficiency on MSP, $r = .66$, and on CPT, $r = .51$ (both $P$’s < .01; Bleiberg, Kane, Reeves, Garmoe, & Halpern, 2000). The purpose of the present study, performed as a pilot, was to determine if patients with Alzheimer’s disease could perform ANAM, and, if they could, to evaluate the extent of their cognitive impairment as measured by ANAM.

1. Method

1.1. Participants

Data were obtained on 16 participants: eight patients with Alzheimer’s disease, and eight age-matched controls. Each of these groups consisted of five females and three males. Mean age of the patients was 77.88 years; of the controls, 75.63 years. All patients and six of the controls were tested in the Center for Aging Research and Evaluation (CARE) unit at Granada Hills Hospital; the other two controls were tested at a seniors’ apartment complex.
The diagnosis of Alzheimer’s disease included a variety of tests. The patients underwent standard neurological testing, including CT or MRI scans, and, on occasion, an EEG. There were laboratory analyses performed on blood samples; these included CBC, metabolic tests, thyroid, TSH, folate, B12, and UA. The patients were also tested by a clinical neuropsychologist at the CARE unit, at which point they were given a comprehensive battery which included several tests for memory (e.g., California Verbal Learning Test or Rey Auditory Verbal Learning Test, and Logical Memory I and II from the Wechsler Memory Scale—III). After all testing was complete, the CARE neurologist made a diagnosis.

1.2. Instruments and procedure

Following completion of the Mini Mental State Exam (MMSE; Folstein, Folstein, & McHugh, 1975) and the Yesavage Geriatric Depression Scale (GDS-Short Form; Yesavage, 1986), each participant was administered a customized subset of ANAM: the Dementia Screening Battery (DEMBAT). It consists of six tasks. These include simple reaction time (SRT), two-choice reaction time (2CH), matching-to-sample (M2S), running memory-continuous performance test (CPT), Sternberg six-letter memory (ST6), and spatial discrimination (SPD). The SRT measure reflects response speed to presentation of a single stimulus. The 2CH task measures differential response speed to each of two stimuli and the M2S task entails matching one of two spatial patterns to a previously viewed sample pattern. The CPT consists of a series of letters presented one at a time, and the decision of whether or not a given letter is the same as the previous letter must be made. The ST6 task requires memorization of a set of six letters; one letter at a time is then presented and the decision of whether or not it is one of the previously memorized six-letter set is made. The SPD task requires a person to decide if two bar graphs are the same or not; one is upright and the other is on its side. Cognitive performance on the ANAM DEMBAT was assessed in terms of both accuracy (percent correct) and efficiency (number of correct responses per minute) of performance on the six tasks. The battery also includes the Stanford Sleepiness Scale, which requests an individual to rate their level of sleepiness at time of testing on a scale from 1 to 7 (1 = awake, alert, 7 = very sleepy).

As was the case in other studies using ANAM, an examiner was present throughout administration of the ANAM battery just in case the participants experienced any difficulties with the use of the mouse or with the instructions for the tasks (there are several “warm-up” trials preceding each task; however, it is still not uncommon for people to misunderstand the instructions). In this study, all eight patients and six controls were tested by a clinical neuropsychologist (J.W.). They were instructed on the use of the mouse, and the neuropsychologist ensured that they remembered how to use it correctly during the session. Most of the patients experienced some difficulty with this and required the careful observations of the neuropsychologist throughout the entire test session. This also occurred for one of the two control participants tested by the senior author (D.L.).

2. Results

No difference between the two groups was observed on the Stanford Sleepiness Scale (patients’ mean = 1.50, controls’ mean = 1.38). Mean MMSE scores (and standard deviations)
of the patients were 24.50 (3.55); of the controls, 29.59 (0.76). Although the patients scored significantly lower on the MMSE \( t(14) = 3.90, P < .01 \), it should be mentioned that an MMSE score of 24–25 nonetheless indicates a fairly high level of functioning.

On the GDS, the mean score of the patients was 3.13 (2.75), while that of the controls was 0.63 (1.19). Although the patients had a statistically significantly higher mean \( t(14) = 2.36, P < .05 \), their scores are still considered to be in the non-depressed range. Independent \( t \)-tests revealed that the age difference between the groups was not significant.

2.1. ANAM-accuracy

One patient scored 98\% correct on SRT accuracy; all other 15 participants scored 100\%. Mean accuracy scores for the two groups on the five other ANAM tasks are illustrated in Table 1. A multivariate analysis of variance (MANOVA) indicated that the patients were significantly impaired on the ANAM general indicator of brain function, Wilk’s lambda = .26; \( F(5, 10) = 5.64, P < .01 \) (see Levinson & Reeves, 1997). Univariate tests indicated that the patients were significantly impaired on three of the six tests: M2S, CPT, and ST6 (see Table 1). These require integrity of working memory. Using the guidelines of Keppel (1991) for evaluating magnitude of effect, a large effect size is equal to an omega squared of .15. The effect sizes for these three tasks were approximately .40. A discriminant function analysis revealed 93.8\% correct classification of participants in their respective groups (one patient was incorrectly classified as a control).

2.2. ANAM-efficiency

Mean efficiency scores for the two groups are also presented in Table 1. As with accuracy, a MANOVA revealed that the patients were significantly impaired on the ANAM general indicator of brain function, Wilk’s lambda = .25; \( F(6, 9) = 4.46, P = .02 \). Univariate tests indicated that with the exception of simple reaction time, the patients were significantly impaired on all ANAM tests; \( F(1, 14) > 4.75, P's < .05 \) (see Table 1). Omega squareds were large, range-

<table>
<thead>
<tr>
<th>Task</th>
<th>Patients</th>
<th>Controls</th>
<th>( F )</th>
<th>( P )</th>
<th>Omega squared</th>
</tr>
</thead>
<tbody>
<tr>
<td>2CHACC</td>
<td>92.75 (7.74)</td>
<td>97.50 (3.12)</td>
<td>2.59</td>
<td>.11</td>
<td>.23</td>
</tr>
<tr>
<td>M2SACC</td>
<td>59.50 (24.41)</td>
<td>90.88 (8.63)</td>
<td>11.74</td>
<td>&lt;.01</td>
<td>.40</td>
</tr>
<tr>
<td>CPTACC</td>
<td>45.63 (27.92)</td>
<td>84.50 (16.88)</td>
<td>11.36</td>
<td>&lt;.01</td>
<td>.39</td>
</tr>
<tr>
<td>ST6ACC</td>
<td>77.13 (14.46)</td>
<td>96.12 (3.83)</td>
<td>12.91</td>
<td>&lt;.01</td>
<td>.43</td>
</tr>
<tr>
<td>SPDACC</td>
<td>71.13 (24.84)</td>
<td>89.38 (6.78)</td>
<td>4.02</td>
<td>.05</td>
<td>.27</td>
</tr>
<tr>
<td>SRTEFF</td>
<td>194.50 (71.03)</td>
<td>165.38 (35.24)</td>
<td>1.08</td>
<td>.33</td>
<td>.60</td>
</tr>
<tr>
<td>CPTEFF</td>
<td>40.38 (10.61)</td>
<td>75.75 (23.09)</td>
<td>6.81</td>
<td>&lt;.05</td>
<td>.27</td>
</tr>
<tr>
<td>ST6EFF</td>
<td>28.75 (11.26)</td>
<td>60.75 (14.68)</td>
<td>23.92</td>
<td>&lt;.01</td>
<td>.60</td>
</tr>
<tr>
<td>SPDIEFF</td>
<td>12.00 (6.23)</td>
<td>18.13 (4.91)</td>
<td>4.77</td>
<td>&lt;.05</td>
<td>.23</td>
</tr>
</tbody>
</table>
ing from .23 for SPD to a whopping .60 for ST6. A discriminant function analysis correctly classified 100% of the participants.

3. Discussion

These findings indicate that accuracy of performance on the ANAM DEMBAT possesses a high degree of utility in detecting impairments of performance in patients with Alzheimer’s disease, especially in the area of working memory. All three of the tasks on which their accuracy of performance was significantly impaired (M2S, CPT, and ST6) measure integrity of this ability. In this regard, their performance is comparable to individuals with moderate traumatic brain injuries (Levinson & Reeves, 1997); it also parallels that of the Forestry workers observed in the longitudinal study of the neurocognitive effects of chronic exposure to the radiation emanating from the Chernobyl disaster (Gamache et al., 2005).

In concert with the findings of other studies (Gamache et al., 2005; Gottschalk et al., 2002; Levinson & Reeves, 1997), the results of the present study indicate that efficiency of performance was more sensitive than accuracy in detection of cognitive impairments. With the exception of SRT, efficiency of performance of these patients was significantly impaired on all tasks in the ANAM DEMBAT. The global impairment in efficiency of performance observed in these patients is remarkably similar to that shown by the Eliminators, who went into the reactor site to remove nuclear debris immediately following the Chernobyl disaster (Gamache et al., 2005). It is also reminiscent of that observed in survivors of moderate-to-severe traumatic brain injuries (Levinson & Reeves, 1997), who may have sustained subcortical (brainstem) injuries which would compromise their response speed. Unlike those individuals, however, these patients were actually faster (although not significantly) on the simple reaction time task. This suggests that their global impairment is more probably a result of generalized cerebral dysfunction. Given the small size of the groups (only eight participants in each group) in the present study, the finding of 100% correct classification in the discriminant function analysis especially reveals the sensitivity of the ANAM battery to the level of impairment shown by these patients. Since the group Ns were small, this is undoubtedly a result of the very large effect sizes (omega squareds) reflective of impairments in efficiency of performance.

Although this is a pilot study, the results are nonetheless very profound. The data indicate that although the patients showed fairly high levels of functioning on the MMSE (mean = 24.50), they exhibited gross impairments in cognitive performance as measured by ANAM, some of which were actually more severe than those shown by survivors of moderate-to-severe TBI and by the Chernobyl Eliminators. These findings illustrate the value of measures that reveal the presence of the disease at a much earlier stage. The ANAM DEMBAT has undergone modifications which include a separate section on instructions for the proper use of the mouse in performing the various tasks. Safeguards have been instituted that detect misunderstandings of instructions. In addition, a code substitution task that assesses both immediate and delayed recall has been added. These modifications will increase the ease of use and sensitivity of the battery in assessing effects of Alzheimer’s which appear earlier in the course of the disease. Although the medications and other treatments being presently used are helping patients in moderate or later stages of the disease, it is believed that if they are treated at earlier
stages, the medications will be even more effective. Also, the emphasis on development of ANAM for studies with repeated measures render it very useful for assessment in clinical trials of medications, and its sensitivity should prove valuable in detection of subtle changes in performance.

References


