Benchmarking a test of temporal orientation with data from American and Taiwanese persons with Alzheimer's disease and American normal elderly

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RUNNING HEAD: Benchmarking an Orientation Score
ABSTRACT

Orientation questions are readily incorporated into longitudinal population surveys, but their value as a screening tool for cognitive decline is uncertain. We evaluated the utility of four orientation-to-time items (TTO) from the Mini-Mental State Examination (MMSE) in screening by determining their association with full-scale MMSE scores. Data collected under protocols with strict eligibility criteria in the US (64 normal elderly, 242 persons with probable Alzheimer’s disease) and Taiwan (241 persons with probable Alzheimer’s disease) were analyzed. The TTO and full-scale MMSE scores were significantly correlated (p<0.05) in persons with Clinical Dementia Ratings (CDR) of 0 or 1; this was not significant in persons with CDR>1 (p>0.05). TTO had high sensitivity and specificity (both over 90%) for Alzheimer’s disease when dichotomized as 100%/0-75%. TTO may be a useful component of cognitive screening efforts.

Keywords: Elderly; measurement; orientation; dementia, longitudinal.
Introduction

The Mini-Mental State Examination (MMSE), originally intended to be a brief evaluation of cognitive status [1], has been used world-wide as a screening tool to identify individuals for more in-depth testing for dementia (e.g., [2-4]; see also [5]) or diagnosable cognitive impairment ([6]; see also [7]). The MMSE was designed for bedside evaluation of cognitive state as a brief but comprehensive alternative to the then-available test batteries ([1], p. 189) and not as a diagnostic instrument for dementia ([8], p. 232).

The MMSE was designed to be short (5-10 minutes to administer), but many researchers have developed shorter versions of it and of other, similar, instruments (reviewed in [9]). For example, recent efforts have described subsets of MMSE items in terms of their efficiency (e.g., [10]), discriminatory power for dementia severity (e.g., [11, 12]), and prediction of incident Alzheimer’s disease (AD) [4]; similar efforts have been carried out for other instruments (e.g., [13-15]) as well as in the creation of brief screening instrument composites (e.g., [9,16]).

Lezak (1995) [17] described a test of orientation to time (p. 336) and a scoring technique for such a test including five elements (date, month, year, day of week, and clock time, p. 337); Callahan et al. (2002) [9] derived a short cognitive screening test that included three of these items (day of the week, month, year), which are part of any temporal orientation test and are among the temporal orientation items included on the MMSE. Temporal disorientation is rare in persons with intact cognition [9, 17], so a test of temporal orientation (TTO) should have high specificity for cognitive impairment. Callahan et al. note that such a test (or test component), which can be administered over the phone and is easily scored, is ideal in large scale screening efforts such as in the identification of potential clinical research subjects or in the brief evaluation of survey participants. In the present study, we estimated the explanatory power of
the four orientation-to-time elements of the MMSE (date, month, year, day of week) for general
cognitive status as represented by the full-scale MMSE score. This study was undertaken as part
of an effort to estimate the utility of cognition-related items that are part of ongoing national
survey efforts (such as the Longitudinal Study on Aging (LSOA, National Center for Health
Statistics) and the Survey of Health and Living Status of the Elderly in Taiwan [18]). Our efforts
were focused on persons diagnosed with Alzheimer’s disease (AD), the most prevalent type of
dementia [19]; it increases in prevalence with age, and has very clear diagnostic criteria [20, 21].
We therefore sought both normal and AD-diagnosed elderly cohorts with full-scale MMSE
scores as well as MMSE item responses for the benchmarking analysis.

The TTO score used in these analyses was based on four items: date, month, year, and
day of week. By design these four items tap orientation [1]; this is reiterated by Lezak (1995)
[17], although she notes that a complete test of temporal orientation would also include a
question about the time of day. Recently Tierney et al. (1997) [22] found that each of the MMSE
items tended to associate to the same extent with neuropsychological tests specifically designed
to tap particular cognitive domains (e.g., orientation, attention, recent memory). They concluded
that the MMSE is actually a general indicator of cognitive function because each item is
associated with several cognitive domains. Thus we hypothesized that the TTO scores would
show significant correlation with full scale MMSE scores.

It is well known that full-scale MMSE performance is strongly influenced by education
([23; see [7] for review; see also [24] for discussion of age, education and orientation). Not only
the MMSE score (high vs. low) but also its interpretation (cognitive impairment/no cognitive
impairment) can be affected by the respondent’s education level (see, e.g., [25]). Education-
based adjustments to full-scale MMSE performance, for purposes of identifying individuals with,
or at risk for, cognitive impairment, have been developed with American subjects (e.g., [23, 26,
27]). Whether adjustments (e.g., [27]) or cutoff scores (e.g., [23]) are employed, it is certain that
these methods are based on the performance of persons who have had some level of formal
education, typically completion of some high school education. The elderly in Taiwan,
particularly women, are more likely than younger persons to have had little or no education
[28]), making adjustments or norms difficult to implement [25]. Thus, it was also important to
document the influence of education on all of the MMSE items for comparison with the four
items incorporated into the TTO score and particularly for persons with 0-7 years of education.
This was a secondary objective for this study.

Two sources for benchmarking TTO scores against full-scale MMSE were identified.
One was a yearlong study of cognitively normal elderly (ANE, N=64) and probable-AD
diagnosed (AAD, N=242) Americans carried out by the Alzheimer’s Disease Cooperative Study
(ADCS) [29]. The other was a cohort of Taiwanese AD outpatients (TAD, N=241) seen in a
University hospital. These groups are described below.

We sought to determine if the TTO scores have descriptive power for general cognitive
function by ascertaining whether they are significantly correlated with full MMSE scores across
three cohorts where both full scale MMSE and the derivative TTO scores were available. We
evaluated the association between a correct answer on each MMSE item and education in the
TAD patients and particularly those with 0-7 years of education to determine if the items in the
TTO score represent a score less biased against individuals with little or no education than the
full-scale MMSE. Sensitivity and specificity of TTO for differentiating AAD and ANE were
estimated, and the influences of education and sex on TTO were explored.

Methods
Subjects:

Three groups of older individuals with full-scale (0-30) MMSE scores and MMSE item-level responses were used in the benchmarking effort.

**ANE**: A cohort of 64 elderly Americans with no clinical evidence of dementia or AD was recruited at AD clinics across the United States for a one-year study of the utility of new instruments for the study of AD [30].

**AAD**: A cohort of 242 elderly Americans recruited to AD clinics across the United States for a one-year study of the utility of new instruments for the study of AD [30] constituted the AAD group. These participants had National Institute of Neurological and Communicative Disorders and Stroke-Alzheimer’s Disease and Related Disorders Association (NINCDS-ADRDA) diagnosis of probable AD [20]. Roughly 50 individuals were recruited to each of five AD severity (not dementia stage) levels based on baseline full-scale MMSE: 21+ (mild), 16-20, 10-15, 5-9, and 0-4 (severe). Their Clinical Dementia Ratings (CDR, [31]) ranged from 1 (mild) to 3 (severe). These American clinical cohorts have been extensively described elsewhere [30].

**TAD**: A cohort of AD patients from Taiwan (TAD) was comprised of 241 outpatients with DSM-III-R [32] diagnoses of AD and severity ranging from mild (CDR=1) to severe (CDR=3). This cohort, seen in a VA hospital, was of particular interest for this analysis because it included many individuals with low (1-7 years) levels of, or no, formal education.

Instruments:

**CDR**: Dementia severity was staged with the Clinical Dementia Rating (CDR) scale [31]. This is a prominent instrument based on semi-structured interviews with the patient and a knowledgeable informant (see [33] for current scoring rules). Patients are rated on six domains: judgment and problem solving, memory, community affairs, home and hobbies, personal care
and orientation. The domain ratings are 0 (no impairment), .5 (questionable impairment), 1, 2, or 3 (mild, moderate and severe impairment, respectively). The personal care domain has no .5 rating. The CDR global rating, which represents the dementia severity, is based on a weighted combination of these domain scores. The individuals in the three benchmarking cohorts had CDR stages ranging from none (ANE) to severe; no individuals with questionable dementia (CDR = .5) were included in these cohorts.

**MMSE**: The MMSE [1] is a widely used instrument for the general characterization of cognitive status. Full-scale MMSE scores are calculated as the sum of correct (= 1 point) answers to 30 questions, so scores range from 0-30 (worst to best). Scores at every point on this range were observed in the reference cohorts (ANE range: 22-30). The MMSE was administered as part of the screening visit according to the study protocols. The TTO score was based on four items: date, month, year, and day of week, ranging from 0-4 (worst to best). Because temporal disorientation is so rare in persons without cognitive impairment [9, 17], we also dichotomized the TTO score to reflect “normal” performance (TTO=4) and “not normal” performance (TTO =0-3).

Statistical methods:

To control for deviations from normality in the score distributions, nonparametric statistics were employed where appropriate; tests were carried out for each of the three cohorts separately. After TTO scores (0-4) were computed, Spearman’s rank correlations between MMSE and TTO (adjusted as described below) were calculated. The educational bias of each of the MMSE items and performance on TTO were explored by independent samples t-tests or Wilcoxon rank sum tests comparing mean educational achievement across individuals in the TAD cohort answering correctly and incorrectly (MMSE items) and across individuals with TTO
scores of 4 (100% correct) or 0-3 (0-75% correct). Inflation of type I error rates was corrected for multiple comparisons according to the Holm method [34] which, due to sequential correction, provides a protective, yet less conservative, approach than Bonferroni’s method; adjusted p-values < 0.05 were considered significant.

**Correlations:** Cohen et al. (2003) [35] noted that, even if there were no real association between the MMSE items, there would still be a degree of correlation between TTO and full-scale MMSE simply because the former is a subset of the latter (p. 59). Thus, the correlation between MMSE and TTO is inflated due to their relationship. Nunnally (1971) [36] suggested adjusting inflated correlations such as that between MMSE and TTO by subtracting the correlation between TTO and (MMSE-TTO) (p. 281). Therefore, to evaluate whether the observed correlation between MMSE and TTO was statistically significant, we entered the adjusted coefficient, i.e., $r_{\text{MMSE/TTO}} - r_{\text{TTO/(MMSE-TTO)}}$, into the t-score test for significance of a Spearman’s (nonparametric) correlation coefficient ($r = \frac{n-2}{\sqrt{1-r^2}}$; [37]) to determine significance (alpha = 0.05).

After calculating adjusted correlations between full-scale MMSE and TTO, we compared educational attainment in ANE and AAD participants with TTO=4 vs. those with TTO 0-3 and examined the association between TTO=4 or TTO=0-3 with sex. In the TAD cohort, we compared years of education in individuals who succeeded or failed in answering each of the full-scale MMSE items correctly. If the TTO score has less of a relationship with education than the full-scale MMSE, then we would find that at least some of the MMSE items excluded to form the TTO have significant association with education after adjustment for multiple (26

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1 There were only 26 items in these analyses of the TAD cohort because in place of one of the MMSE items, “WORLD” spelled backwards, the clinician used either serial sevens or a five-word Chinese proverb (instead of
comparisons [34]. These comparisons were carried out for the full TAD cohort and replicated for individuals with 0-7 years of education. We also compared educational attainment in TAD participants with TTO=4 vs. those with TTO 0-3 and examined the association between TTO=4 or TTO=0-3 with sex.

All analyses were carried out using SPSS 11.5 (SPSS, 2002) for the PC.

Results

Descriptive statistics:

The descriptive statistics for the three cohorts are shown in Table 1. The two American cohorts were younger and better educated than the Taiwanese AD cohort, and had roughly 50% more women. The degree of cognitive impairment (MMSE) and dementia severity (CDR) were worse for the AAD (median rating = moderate severity) than for the TAD (median rating = mild severity). Performance on the TTO was much better in the TAD than the AAD, probably a reflection of the greater level of dementia in the AAD.

As shown in Table 1, only 1.2% (3/242) of the AAD cohort and no member of the ANE cohort had fewer than 7 years of education, compared with 44.7% (92/206 with non-missing education) of the TAD. The TAD cohort shows clearly that persons with less education performed worse on the MMSE and TTO, and although only three individuals in the AAD cohort had 1-6 years of formal education, the patterns suggest that worse MMSE and TTO performance were also observed in these individuals relative to those with more education.

TTO in American cohorts:

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WORLD) backwards, whichever one the patient did better on. In all samples, full scale MMSE score ranged from 0-30, but for these item-level t-tests, a score of 0-3 was rescored as 0 and a score of 4-5 was rescored as 1.
TTO scores were calculated for the ANE and AAD from their baseline visit MMSE item level responses. Full scale MMSE and TTO scores were correlated as described above. The Spearman’s correlation coefficient for MMSE and TTO in the ANE was .41, and after adjusting for shared elements, this was significant (t(62)=2.12, p=0.025). The correlation coefficient for MMSE and TTO in the AAD was .71, but after adjusting for shared elements, this failed to reach significance (t(240)=1.24, p > .10).

We dichotomized TTO as described above (4 correct = 1, else =0) and evaluated its association with education and sex separately for ANE and AAD. Full-scale MMSE scores were significantly higher for those with four correct (ANE: t(62)= -2.1, p<0.05; AAD: t(16.4)= -9.3, p< 0.001). Education was not associated with the dichotomized TTO variable for ANE (Wilcoxon rank-sum test: W=186.5, p=.32) or for AAD (t(13.04) =-1.58, p=.14). The association between the dichotomized TTO variable and sex was marginally not significant for ANE (all four correct, men: 97.5%, women: 83.3%, p =.061) and virtually the same proportion of men and women in the AAD cohort had all four correct (men: 5.4%, women: 5.3%; p=1.0).

INSERT TABLE 2 ABOUT HERE.

TAD: TTO and MMSE, education and MMSE item responses:

The TTO and full-scale MMSE scores in the TAD were strongly and positively correlated (Spearman’s rho=.768), to a degree similar to that observed in the AAD cohort. After correcting for shared components, the correlation was significant (t(232)=2.56, p<.01). Independent samples t-tests were carried out to compare the mean educational level attained by TAD participants who were correct or incorrect on each of the 26 (see footnote 1) full-scale MMSE items. These 26 analyses were corrected for multiple comparisons [34]. Table 3 presents...
the mean educational attainment for individuals who responded correctly or incorrectly to each of the full-scale MMSE items.

**INSERT TABLE 3 ABOUT HERE**

In these Alzheimer’s disease patients, significantly lower education was associated with incorrect responses on 46% (12/26) of the full-scale MMSE items. The easiest items were naming watch and pencil (95.5% correct) and the hardest items were “what room are we in” (17.4% correct) and delayed recall of item 3 (19.9% correct). Of the four items included in the TTO score, significantly greater education was observed in those answering two of these correctly (today’s date and the year). Significantly greater educational attainment was also observed in persons with correct responses to ten other MMSE items (all adjusted \( p \leq 0.05 \)). We then limited the TAD cohort to only those with 0-7 years of formal education (n=92), and repeated t-tests comparing the mean level of education in respondents who were correct and incorrect for each full-scale MMSE item (data not shown). After Holm adjustment, four of the full-scale items showed a significant difference in mean educational attainment (all adjusted \( p<0.05 \)): what city are we in; what hospital are we in; serial 7s/WORLD spelled backwards (see footnote 1); and following the command to close your eyes (i.e., none of the TTO items and four of the twelve where significantly greater education was associated with correct answer in the full sample). When the analyses were replicated including only those with more than seven years of education, no differences were observed (one unadjusted \( p=0.045 \) [adjusted \( p>0.50 \)]; all other unadjusted \( p>0.055 \)).

When we dichotomized TTO performance as 100%/0-75%, 15% of TAD had correct answers on all four orientation items, nearly three times the proportion observed in the AAD cohort. It can be seen in Table 2 that greater full scale MMSE and educational attainment were
observed in individuals in the TAD cohort with all four TTO items correct (both p<0.001); the latter finding also reached significance when education was categorized as 0, 1-6 or 7+ years (Kendall’s tau –b = .235, p<0.001). More than twice as many men (20.1%) as women (8.8%) in the TAD cohort were able to answer all four correctly (chi square = 6.6, p=.01). We observed that all four items on the TTO were correct in 92.2% of ANE and 5.4% of AAD (see Table 4). Based on these proportions and the size of each cohort, we calculated the sensitivity (proportion of AAD with 0-3 correct on TTO) and specificity (proportion of ANE with 4 correct on TTO) of this dichotomized variable. Both were high; sensitivity was 94.6% and specificity was 92.2%. We also calculated the positive and negative predictive values for the two outcomes “TTO=4” and “TTO=0-3” to be 97.9% and 81.9%, respectively.

ANE (CDR=0) and the two AD cohorts were stratified by dementia severity level (CDR) and their performances on MMSE (0-30), TTO (0-4) and on the dichotomous TTO variable (% with all 4 correct) are shown in Table 4.

The means and ranges for both MMSE and TTO can be seen to decrease as dementia severity (CDR) increases. Correlation coefficients were calculated for MMSE and TTO for the stratified samples and their p-values were adjusted as described. Only the coefficient for individuals with CDR=1 was significant (AAD: rho=.558, p<0.005; TAD: rho = .597, p<.001; all other rho ranged from .160-.488, all other p>0.05). Similar to the means and ranges, the correlation coefficients weakened monotonically with dementia severity (data not shown).

Discussion

We found that the TTO score correlated strongly and positively with full-scale MMSE for each of the clinical samples. Although this did not reach significance (α =.05) after
correcting for shared components for the full AAD sample, of particular importance to screening for incident dementia is the finding that the association between MMSE and TTO was strongest (and significant) in individuals with CDR=0, and in individuals with CDR=1 in both AAD and TAD.

In a group of Taiwanese persons with AD, significant differences in education were observed between individuals with correct and incorrect answers on 12 of 26 MMSE items (see footnote 2); correct answers on two of the four items making up the TTO were associated with significantly more education in this cohort. Thus, both scores were sensitive to education, with roughly 50% of items associated with this variable. When analyses were limited to individuals with 0-7 years of education, the association was limited: 4 of 26 MMSE items and none of the TTO items were associated with education.

The finding of an association between education and orientation (TTO and dichotomous TTO) replicates those of Natelson, Haupt, Fleischer and Grey (1979) [38] and Sweet, et al. (1999) [24] and extends these earlier results to a non-Western cohort. It is unclear why orientation to time (date, month, year, day of week) would be associated with education. Although Liu et al. (1994) [3] pointed out that in some cultures the quality of education for males is higher than for females, this finding was observed in all three groups and in both men and women (when analyzed separately; data not shown). Employment and lifestyle, which tend to be determined by educational attainment, may in turn influence perception of time; for example, farmers or persons growing up in rural communities may not complete much school due to the demands of their work. A lifetime of seven-day workweeks or other non-standard schedules (i.e., not five 8-hour days per week) could lead to a limited appreciation for the four elements of
the TTO. Similarly, more education might lead to more familiarity with the Western calendar and greater temporal orientation.

In the Taiwanese cohort, more men than women were correct on all four orientation items; by contrast, in the AAD group, men and women did equally poorly (data not shown). In the ANE cohort six times as many men as women missed at least one orientation item. Evidence for an association between sex and TTO performance is thus equivocal.

The MMSE is a useful screening instrument and has established validity and reliability [2-7], especially with respect to identifying mild AD and cognitive impairment quickly and efficiently. A disadvantage of this instrument is its lack of sensitivity to changes in individuals with severe dementia [17, 39], although this concern is not particularly applicable in the survey context. A second drawback is the sensitivity to education [7, 25]; however, the four-item TTO is also not immune to this influence.

Because they are based on two American cohorts that may not be representative of persons in the age group and also excluded any persons with mild cognitive impairment, our estimates of sensitivity and specificity are preliminary. Despite these caveats, our results seem promising. We hope to capitalize on this benchmarking exercise in future analyses of relationships among social factors, biomarkers and cognition in survey data. Moreover, in the analysis of survey data, it may be desirable to adjust or control for “cognitive function” or “cognition”; we propose that a score of 100% on the four elements of the orientation score (TTO) could be utilized to identify individuals as having “intact orientation” [40]. Change in this status over time in longitudinal social or epidemiologic surveys might be used to identify the hallmark symptom of dementia, namely, a significant change in cognition [8].
In contrast to other efforts to derive a shorter MMSE (e.g., [9, 10, 12]), our emphasis on the orientation-to-time questions was a combination of factors related to suitability for the survey context, where cognitive status is clearly difficult to assess. Guilmette, Tsoh and Malcolm (1995) [41] found that problems with orientation and memory were not associated in neurologic patients, suggesting that the use of TTO plus a memory task might be useful for describing the cognitive status of survey participants (or in other contexts where neuropsychological and/or neurologic evaluations cannot be done). Klein et al. (1985) [11] found that orientation alone was specific, but not sensitive. Individuals with both normal orientation and memory performance (assessed by word list recall) might be considered normal, and tracked over time to identify incident changes from this status; individuals with non-normal performance on both tasks could be considered to have cognitive impairment\(^2\). This dichotomy will not account for all participants in a survey, but may be useful in the evaluation of existing survey data.

Word count: 3731.

\(^2\) This approach is currently under investigation; contact the first author (RET) for details of this analysis.
References


Table 1. Descriptive statistics by cohort: mean ±SD/median or percent: overall and by education.

<table>
<thead>
<tr>
<th></th>
<th>ANE (n=64)</th>
<th>AAD (n=242)</th>
<th>TAD (n=241†)</th>
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<td>Education (years)</td>
<td>13.8 (2.9)</td>
<td>13.1 (2.9)</td>
<td>8.7 (5.4)</td>
</tr>
<tr>
<td>Age (years)</td>
<td></td>
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<tr>
<td>Overall</td>
<td>70.3±8.8</td>
<td>72.3±9.0</td>
<td>76.6±7.1</td>
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<td>(n=0)</td>
<td>79.2±7.2 (n=33)</td>
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<td>1-6 years educ:</td>
<td>(n=0)</td>
<td>87.0±5.3 (n=3)</td>
<td>74.7±7.3 (n=59)</td>
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<td>7+ years educ:</td>
<td>70.3±8.8 (n=64)</td>
<td>72.1±8.9 (n=239)</td>
<td>76.6±6.8 (n=114)</td>
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<tr>
<td>Gender (% female)</td>
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<tr>
<td>Overall</td>
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<td>79%</td>
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<td>1-6 years educ:</td>
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<td>67 **</td>
<td>64%</td>
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<td>MMSE (full-scale) *</td>
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<td>1.2±1.5</td>
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<tr>
<td>7+ years educ:</td>
<td>3.9±0.3</td>
<td>0.8±1.2</td>
<td>1.9±1.5</td>
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</table>

### Table 2. Mean (±SD) of MMSE and education for TTO = 4 vs. TTO = 0-3 by cohort.

<table>
<thead>
<tr>
<th>TTO Score</th>
<th>ANE mean MMSE (±sd)</th>
<th>ANE mean education (±sd)</th>
<th>AAD mean MMSE (±sd)</th>
<th>AAD mean education (±sd)</th>
<th>TAD mean MMSE (±sd)</th>
<th>TAD † mean education (±sd)</th>
</tr>
</thead>
<tbody>
<tr>
<td>4 correct (=1)</td>
<td>29.4 ± 1.3 *</td>
<td>13.7±2.9 **</td>
<td>24.2 ± 4.3 **</td>
<td>14.5±3.3 **</td>
<td>24.1 ±3.6 **</td>
<td>11.9 ± 4.4 **</td>
</tr>
<tr>
<td>0-3 correct (=0)</td>
<td>28.2 ± 0.8</td>
<td>15.0±3.2 **</td>
<td>12.2 ± 7.6 **</td>
<td>13.1±2.8 **</td>
<td>15.6 ±6.6 **</td>
<td>8.1 ± 5.4 **</td>
</tr>
</tbody>
</table>

Notes: TAD: Taiwanese DSM-diagnosed probable Alzheimer’s disease. † 33 missing education values. AAD: American NINCDS-ADRDA-diagnosed probable Alzheimer’s disease. ANE: American normal elderly (controls). * significantly higher than for individuals in the cohort scoring 0-3; p<0.05; ** significantly higher than for individuals in the cohort scoring 0-3, p<0.001.
Table 3. Taiwan Alzheimer’s disease patients (TAD): proportion with correct response per item and mean (SD) education for correct/incorrect responses on MMSE items. Items shown in **bold** were included in the TTO score.

<table>
<thead>
<tr>
<th>ITEM</th>
<th>% correct</th>
<th>Mean education, correct</th>
<th>Mean education, incorrect</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 * today’s date</td>
<td>26.0%</td>
<td>11.0 (4.8)</td>
<td>7.9 (5.4)</td>
</tr>
<tr>
<td>2 * year</td>
<td>42.3</td>
<td>10.9 (4.9)</td>
<td>7.0 (5.3)</td>
</tr>
<tr>
<td>3 month</td>
<td>46.3</td>
<td>9.8 (5.2)</td>
<td>7.7 (5.5)</td>
</tr>
<tr>
<td>4 day of week</td>
<td>37.3</td>
<td>9.8 (5.2)</td>
<td>8.0 (5.5)</td>
</tr>
<tr>
<td>5 season</td>
<td>36.8</td>
<td>9.3 (5.4)</td>
<td>7.6 (5.4)</td>
</tr>
<tr>
<td>6 * ‡ name of hosp</td>
<td>71.6</td>
<td>9.7 (5.3)</td>
<td>6.2 (5.1)</td>
</tr>
<tr>
<td>7 * floor we’re on</td>
<td>37.3</td>
<td>10.6 (5.2)</td>
<td>7.5 (5.3)</td>
</tr>
<tr>
<td>8 * ‡ city we’re in</td>
<td>64.2</td>
<td>9.9 (5.0)</td>
<td>6.5 (5.6)</td>
</tr>
<tr>
<td>9 * department</td>
<td>51.7</td>
<td>10.0 (4.9)</td>
<td>7.3 (5.7)</td>
</tr>
<tr>
<td>10 * room we’re in</td>
<td>17.4</td>
<td>11.6 (4.6)</td>
<td>8.1 (5.4)</td>
</tr>
<tr>
<td>11.immed recall 1</td>
<td>93.5</td>
<td>8.8 (5.5)</td>
<td>7.7 (5.7)</td>
</tr>
<tr>
<td>12. † immed recall 2</td>
<td>93.0</td>
<td>8.6 (5.5)</td>
<td>9.3 (4.2)</td>
</tr>
<tr>
<td>13. † immed recall 3</td>
<td>85.1</td>
<td>8.6 (5.4)</td>
<td>9.3 (5.6)</td>
</tr>
<tr>
<td>14-18 * WORLD/serial 7s</td>
<td>41.3</td>
<td>11.4 (4.2)</td>
<td>6.8 (5.5)</td>
</tr>
<tr>
<td>19 delayed recall 1</td>
<td>27.3</td>
<td>9.8 (5.7)</td>
<td>8.3 (5.3)</td>
</tr>
<tr>
<td>20. delayed recall 2</td>
<td>23.9</td>
<td>9.8 (5.4)</td>
<td>8.4 (5.5)</td>
</tr>
<tr>
<td>21 delayed recall 3</td>
<td>19.9</td>
<td>10.1 (5.2)</td>
<td>8.3 (5.5)</td>
</tr>
<tr>
<td>22. † name item 1</td>
<td>95.5</td>
<td>8.7 (5.5)</td>
<td>9.1 (3.8)</td>
</tr>
<tr>
<td>23. name item 2</td>
<td>95.5</td>
<td>8.8 (5.4)</td>
<td>5.3 (5.1)</td>
</tr>
<tr>
<td>24. repeat phrase</td>
<td>78.0</td>
<td>9.0 (5.4)</td>
<td>7.7 (5.4)</td>
</tr>
<tr>
<td>25 obey directions: rt hand</td>
<td>72.6</td>
<td>9.2 (5.2)</td>
<td>7.4 (6.0)</td>
</tr>
<tr>
<td>26 obey directions: fold paper</td>
<td>57.2</td>
<td>9.1 (5.3)</td>
<td>8.1 (5.7)</td>
</tr>
<tr>
<td>27. ** obey directions: floor</td>
<td>51.7</td>
<td>9.8 (5.0)</td>
<td>7.5 (5.6)</td>
</tr>
<tr>
<td>28 * close eyes</td>
<td>72.3</td>
<td>11.1 (4.2)</td>
<td>6.2 (5.0)</td>
</tr>
<tr>
<td>29 * write sentence</td>
<td>52.9</td>
<td>11.4 (4.1)</td>
<td>7.8 (5.3)</td>
</tr>
<tr>
<td>30 * pentagons</td>
<td>61.7</td>
<td>10.2 (4.9)</td>
<td>6.4 (5.4)</td>
</tr>
</tbody>
</table>

Notes: t-tests comparing educational attainment in persons answering correctly vs. education in those answering incorrectly. * Holm-adjusted p-value < 0.05. † higher mean education in people with incorrect response. ‡ Majority of group had correct response AND Holm-adjusted p-value < 0.05. ** Adjusted p =0.05.
Table 4. Mean±SD and (range) for MMSE and TTO, and % with TTO=4 by group by CDR.

<table>
<thead>
<tr>
<th>GROUP:</th>
<th>N</th>
<th>MMSE Mean ± SD</th>
<th>Range</th>
<th>TTO Mean ± SD</th>
<th>Range</th>
<th>% TTO = 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>ANE (CDR=0) †</td>
<td>64</td>
<td>29.3 ± 1.3</td>
<td>22-30</td>
<td>3.9 ± 0.3</td>
<td>3-4</td>
<td>92.2%</td>
</tr>
<tr>
<td>AAD overall</td>
<td>242</td>
<td>12.8 ± 7.9</td>
<td>0-30</td>
<td>0.8 ± 1.2</td>
<td>0-4</td>
<td>5.4%</td>
</tr>
<tr>
<td>AAD CDR=1†</td>
<td>91</td>
<td>20.5 ± 4.5</td>
<td>8-30</td>
<td>1.8 ± 1.4</td>
<td>0-4</td>
<td>14.3%</td>
</tr>
<tr>
<td>AAD CDR=2</td>
<td>126</td>
<td>9.2 ± 5.4</td>
<td>0-19</td>
<td>0.3 ± 0.5</td>
<td>0-2</td>
<td>0%</td>
</tr>
<tr>
<td>AAD CDR=3</td>
<td>25</td>
<td>2.8 ± 2.3</td>
<td>0-9</td>
<td>0.04 ± 0.2</td>
<td>0-1</td>
<td>0%</td>
</tr>
<tr>
<td>TAD overall †</td>
<td>234*</td>
<td>16.9 ± 6.9</td>
<td>1-30</td>
<td>1.5 ± 1.5</td>
<td>0-4</td>
<td>15.5%</td>
</tr>
<tr>
<td>TAD CDR=1†</td>
<td>137</td>
<td>21.0 ± 4.9</td>
<td>7-30</td>
<td>2.3 ± 1.4</td>
<td>0-4</td>
<td>25.6%</td>
</tr>
<tr>
<td>TAD CDR=2</td>
<td>78</td>
<td>12.4 ± 4.5</td>
<td>2-23</td>
<td>0.6 ± 0.9</td>
<td>0-3</td>
<td>0%</td>
</tr>
<tr>
<td>TAD CDR=3</td>
<td>19</td>
<td>5.9 ± 3.3</td>
<td>1-12</td>
<td>0.05 ± 0.2</td>
<td>0-1</td>
<td>0%</td>
</tr>
</tbody>
</table>

Notes. MMSE: Mini-Mental State Examination; TTO: Test of Temporal Orientation. ANE: American normal elderly; AAD: American persons with Alzheimer’s disease; TAD: Taiwanese persons with Alzheimer’s disease; * The number of individuals (N) in the TAD group represents individuals with both MMSE and TTO scores. † After adjusting, correlation between TTO and MMSE was significant, p<0.05 (see text).