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Alzheimer Patient Evaluation and the Mini-Mental State: Item Characteristic Curve Analysis

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To develop a tool for precisely assessing dementia severity, items should be selected according to their relationship to the overall progression of the disease. Using an item characteristic curve analysis (ICC), items were examined from the Folstein Mini-Mental State Exam (MMSE), a useful clinical tool for evaluating dementia. MMSE data were available for 86 patients who met DSM-III criteria for primary degenerative dementia — possible or probable Alzheimer's disease (AD). A logistic regression analysis of the probability of correct performance on an item, given the total MMSE score, yielded statistics for difficulty and discrimination. These statistics were interpreted respectively as indicators of the point in the progression of the illness at which the mental function tested by that item is lost and the rapidity of that loss. The data indicated a systematic progression of the development of symptoms in AD related to decline of memory function. Temporal orientation was lost before spatial and object orientation, and recollection of words was lost before ability to repeat them. ICC can help to delineate the loss of mental functions during the course of AD.

MEMORY dysfunction in elderly individuals is an indication of dementia and the most common initial symptom of Alzheimer's disease (AD). The most recent diagnostic criteria for dementia (DSM-III-R) recognizes memory as the primary impairment of dementia (American Psychiatric Association, 1987). In very mild cases, neuropsychological evaluation focuses on determining whether memory, especially recall of recently obtained information, is affected. Dementia can be caused by several different diseases. Therefore, psychological status is carefully measured to determine if the pattern of dysfunction is characteristic of AD (Fuld, 1983), multi-infarct dementia (Hachinski, Lassen, & Marshall, 1974), left-hemisphere stroke (Benson, Cummings, & Tsai, 1982), or another disorder. Although the clinical validity of such determinations is still in doubt (Erkinjuntti, Laaksonen, Sulkava, Syrjaiainen, & Palo, 1986), specific differences in the nature of memory impairment between different diseases can be discriminated (Moss, Albert, Butters, & Payne, 1986). Clinical progression is helpful in confirming the diagnostic impression of AD (McKhann et al., 1984).

AD begins with mild symptoms of forgetfulness and progresses over years, highlighted by deterioration of memory, to cause total cognitive dysfunction. For patients with suspected AD, evaluation is also aimed at assessing the severity of the disease. AD generally progresses in a typical fashion, certain cognitive and social functions usually being lost before others. Therefore, the clinician assesses the patient's psychosocial function to determine severity. Such assessments of severity are useful in management of the patient because of their relation to the level of daily living function (Vitaliano, Breen, Albert, Russo, & Prinz, 1984a). However, these assessments currently have little value in predicting future decline. Measurement of disease severity must become more precise and reliable for use in estimating prognosis or for research applications.

The importance of determining dementia severity has led to the development of many assessment tools (Nelson, Fogel, & Faust, 1986). Because dementia is associated with such a broad spectrum of decline, very brief sets of questions can give reliable information about severity (MSQ: Kahn, Goldfarb, Pollack, & Peck, 1960; SPMSQ: Pfeiffer, 1975). Such brief tests also correlate well with the severity of AD pathology in the brain (Blessed, Tomlinson, & Roth, 1968). The Mini-Mental State Exam (MMSE) (Folstein, Folstein, & McHugh, 1975) has gained wide acceptance because of its ease of administration, its assessment of a popular variety of standard mental state items, and the broad range over which it can usefully assess dementia severity (Anthony, LeResche, Niaz, Von Korff, & Folstein, 1982). The Blessed Information-Memory-Concentration Test and the MMS show a correlation ranging between $-.73$ and $-.83$ (Thal, Grundman, & Golden, 1986). Other authors, feeling uncomfortable with such brief assessments, have advocated the use of a battery of tests to assess dementia severity (Pfeffer et al., 1981; Eslinger, Damasio, Benton, & Van Allen, 1985; Klein et al., 1985). However, none of the currently used tests has been examined on an item-by-item basis to validate the utility of each item for judging dementia severity or for providing a precise picture of the progression of AD.

Item analysis techniques are widely used to assess individual test items when groups of students are being quizzed regarding their knowledge or aptitude for a given subject. After initial usage, each test item can be evaluated to determine the level of performance at which the item dis-

criminates and the sharpness of that discrimination. Items used to test the performance of demented patients can be similarly analyzed. The level of severity at which specific items discriminate could suggest which functions were lost before others during the progression of the disease. To the extent that AD is a uniformly progressive disease, item analysis techniques could be used to assess uniformity and construct a more reliable scale for patient assessment.

In the present study, MMS items were analyzed from an item characteristic curve (ICC) analysis perspective. The relationship between performance on any given item and ability as assessed by overall test performance is described by a plot of the probability of success on the item as a function of overall test performance. A mathematical model fit to these plotted data results in an ICC from which the difficulty and discriminability of each item can be determined.

Difficulty describes the location of an item along the scale of overall test performance (ability). A measure of difficulty is defined as the score at which the expected probability of correct response is 0.5. A small value indicates an easy item and a large value indicates a difficult item. An easy item is one for which the probability of correct response is high for low-ability examinees (or, in this case, severely impaired patients) and approaches 1 for high-ability examinees (in this case, mildly impaired patients). An item of medium difficulty is one for which the probability of correct response is low for low-ability examinees, intermediate for those in the middle of the ability scale, and near 1 at the highest ability levels. A difficult item is one for which the probability of correct response is low even for high-ability examinees (Baker, 1985, p. 5).

Discrimination describes how well an item can differentiate between examinees having abilities below the item location and those having greater capabilities. Essentially, the slope of the ICC is a measure of discrimination, because the probability of correct response would change more rapidly within a narrower range of ability levels for a curve with a steeper slope. The flatter the curve, the less the item discriminates, as the probability of correct response at low-ability levels approaches the probability of correct response at high-ability levels (Baker, 1985, pp. 5–6). In other words, the probability of correct response changes more slowly over a wider range of ability levels.

Applied to the MMS, difficulty is an indicator of the point at which the mental function assumed to underlie performance on the item is lost in the progression of AD; discrimination is an indication of how quickly that function is lost. An item with high difficulty and high discrimination would indicate an early loss and a loss that occurs quite quickly in the progression of the disease. High difficulty and less discrimination would indicate early loss, but a loss that occurs over a longer range of progression. An item with low difficulty and high discrimination would indicate loss of function late in the progression of the disease, but a loss that occurs quickly. An item with low difficulty and low discrimination would indicate late loss and a loss occurring more slowly over the progression of the disease.

The purpose of this study was to examine these item statistics in order to identify: (a) the level or degree of severity of AD, as indicated by MMS total score, at which particular items are lost in the progression of AD; and (b) the rapidity or rate with which they are lost at that level. Level of severity at which particular functions are lost is, in this case, indexed by item difficulty, and the rate of loss by item discrimination. Specific items are considered to represent particular underlying mental functions, and loss of performance on an item presumably indicates impairment of that function.

METHODS

Subjects. — All patients in this study were evaluated in the UCLA Geriatric Psychiatry Outpatient Clinic. Patients presenting with complaints including memory difficulty were given complete dementia evaluations including psychiatric and neurologic examinations and CT scans and EEG (Wells, 1977). Between July 1982 and March 1984, 112 patients had received complete dementia evaluations that included a Mini-Mental State Exam (MMS). Of this group, 86 met DSM-III criteria for a clinical diagnosis of primary degenerative dementia (PDD). Subsequent studies involving this group of 86 patients indicated that 60% met NINCDS-ADRDA criteria for probable AD (McKhann et al., 1984) and 40% for possible AD (Ashford, Rosenblatt, Bekian, & Hayes, 1987) [National Institute of Neurological and Communicative Disorders and Stroke–Alzheimer's Disease and Related Disorders Association]. The present study focused on these 86 patients.

The average age of these patients was 74 years (SD = 8; range = 53–91). There were 23 males and 63 females. Average education was 11 years (SD = 3; range = 0–20). For 81 of these patients a significant other was available to provide information to assess Activities of Daily Living (ADLs, using the format of the OARS; Duke University, 1975).

Measures of dementia severity. — MMS scores (mean = 18.0; SD = 7.1; Range = 1–29) were computed according to the rule that the best score of serial 7's or "WORLD backward" was used for the total (this is an acknowledged weakness of this test, as the serial 7's task is more difficult). The ADL scores were totaled (scale range = 0–29) and the average score of the group was 21.1 (SD = 5.7; range = 4–29). ADL scores and MMS scores were highly correlated (r = .76; n = 81; $p < .0001$), both for males (r = .57; n = 20; $p < .0001$). and females (r = .77; n = 61; $p < .0001$). Both ADL scores and MMS scores were negatively correlated with age ($r = -.35$; n = 81; $p < .002$ and $r = -.36$; n = 86; $p < .001$, respectively), possibly reflecting a greater tolerance for social and cognitive dysfunction in more elderly individuals; older patients thus seem to be brought to clinical attention for the first time at a more advanced stage of the dementing process. No relationship was noted between educational status and either age (r = .10; n = 65; p = .43) or ADL (r = .13; n = 61; p = .32) or MMS (r = .19; n = 65; p = .13) scores.

Statistical methods. — MMS items are scored as either correct or incorrect. Therefore a logistic regression model

was applied, in this case, regression of the binary outcome, correct or incorrect, on the total MMS score. Logistic regression is a practical method of calculating a sigmoid curve to fit the data. The logistic regression resulted in an expected probability of success on an item given a particular MMS score. Specifically, the regression estimated the parameters of the model:

$$E(p) = \frac{e^{c + b(MMS)}}{1 + e^{c + b(MMS)}} \quad (1)$$

where c is the regression constant and b the regression coefficient. MMS represents the total MMS score.

Severity at loss (difficulty) was defined as the score at which the expected probability of correct response is .50. Maximum rate of loss (discrimination) was indicated by the slope of the curve at the 0.5 probability level; the steeper the slope, the greater the rate and the better the item served as discriminator between more severely and less severely affected patients.

A chi-square goodness-of-fit test was used to determine whether the fit of the logistic regression model to the ICC was statistically significant. In addition, a measure of goodness-of-fit was calculated by correlating the predicted probability of success with the observed proportion of success (R). The square of the correlation coefficient (R^2) indicated the proportion of variance in the ICC data explained by the logistic regression model. These statistics are indicators of the validity of the model.

RESULTS

Table 1 presents the item analysis statistics for each item. Items are arranged arbitrarily into four groups based on the rate of loss index (discriminability), the first group having the highest rate and the last group the lowest rate. Within each group, individual items were ordered from earliest lost to latest lost (difficulty). The chi-square goodness-of-fit tests indicated that for all items, the fit of the logistic regression model to the ICC was statistically significant (data not presented). However, from the R^2 value, it can be seen that the degree of fit was much better for some items than for others.

The first group of items in Table 1 were those with the highest rate of loss index. Figure 1 presents the ICCs for four of these items with the logistic regression curve overlaid. The high rate of loss index indicates that there was a sharp cutoff of ability level at which the item was answered correctly or incorrectly. For example, the ICC for the easiest item, "pencil," indicated that a patient with an MMS score of about 10 or more would have virtually a 100% chance of getting the item correct. These statistics indicate that the mental function assessed by the item "pencil" is lost at an advanced stage of the disease and that it is lost quite quickly at this stage. At the other extreme, "date" had a very high severity at loss index. An individual with a score of 20 or lower would have a very small chance of getting the item correct. This indicates that the mental function assessed by "date" is lost very early in the progression of AD and is lost quickly.

Figure 2 presents the ICCs for four items from the second group. These items have a fairly high rate of loss, although not as great in degree as the first group. Interpretation of the sequence and rapidity of loss of mental function would be essentially the same as for the first group.

Figure 3 presents four examples of the ICCs from the third group of items. It is readily apparent that rate of loss of these items was not nearly as great as the first two groups of items. In other words, there was a wider range of MMS scores in which subjects answered the item either correctly or incorrectly. This can be interpreted to mean that the mental functions underlying these items are lost more gradually or more variably than those underlying the first two groups of items or that mental functions are tested less succinctly by these items.

The four ICCs presented in Figure 4 are for those items at the extremes of the MMS for this sample, that is, the items lost first and the items lost last. The items lost first, "flag-memory" and "tree-memory," were answered correctly by less than 17% of the sample, whereas the items lost last,

Table 1. MMS Item Analysis Statistics

#	Item	Difficulty	Discriminability	R^2
Group I				
1	Date	23.1	0.51	0.731
3	Month	18.2	0.55	0.815
2	Year	17.6	0.49	0.931
31	Sentence	10.3	0.55	0.939
24	Watch	8.5	0.51	0.876
30	Close I's	7.2	0.44	0.661
25	Pencil	6.6	0.62	0.863
Group II				
19	65	24.2	0.37	0.744
17	79	23.3	0.32	0.643
21	Ball-M	22.7	0.37	0.757
16	86	20.8	0.35	0.681
6	Place	16.6	0.34	0.724
10	State	10.6	0.35	0.671
Group III				
18	72	22.1	0.27	0.635
4	Day	19.0	0.17	0.597
9	County	18.7	0.25	0.556
15	93	18.0	0.24	0.571
5	Season	17.2	0.21	0.661
7	Floor	16.5	0.27	0.771
8	City	14.6	0.23	0.817
32	Pentagon	14.4	0.17	0.508
26	No-Ifs . . .	10.0	0.25	0.479
29	Paper-Of	7.6	0.23	0.495
12	Flag-R	7.0	0.24	0.561
11	Ball-R	6.1	0.29	0.488
13	Tree-R	5.0	0.21	0.320
Group IV				
23	Tree-M	31.8	0.12	0.366
22	Flag-M	30.1	0.23	0.283
27	Paper-RH	2.0	0.11	0.336
28	Paper-IH	0.3	0.14	0.502

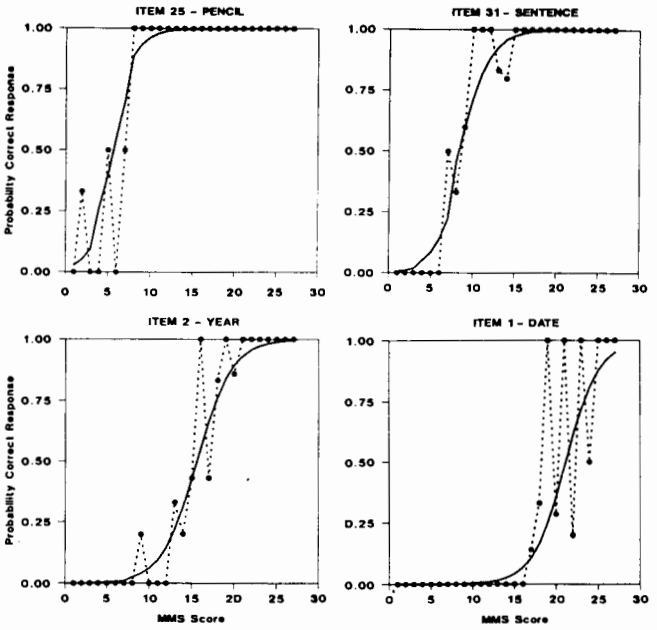

Figure 1. ICCs of four items from Group I. MMS scores (0 = all wrong; 30 = all correct) plotted against probability of correct response. Observed proportion correct (dashed line) overlaid with expected probability curve (solid line).

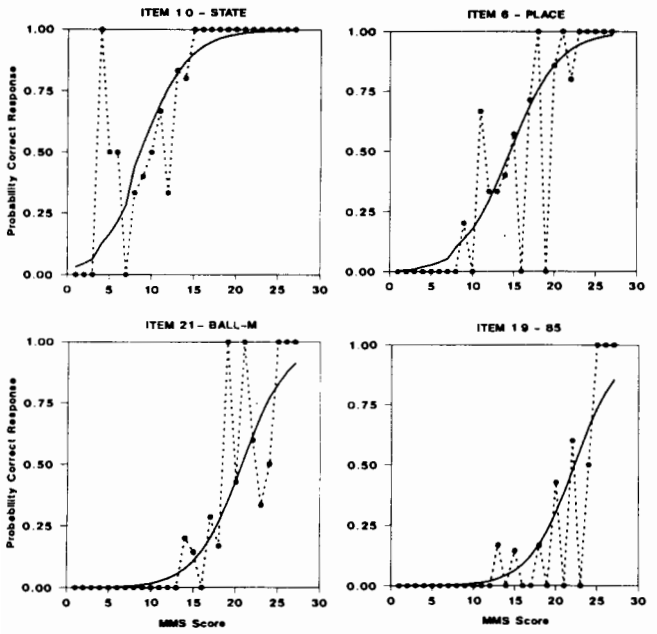

Figure 2. ICCs of four items from Group II. Same parameters as Figure 1.

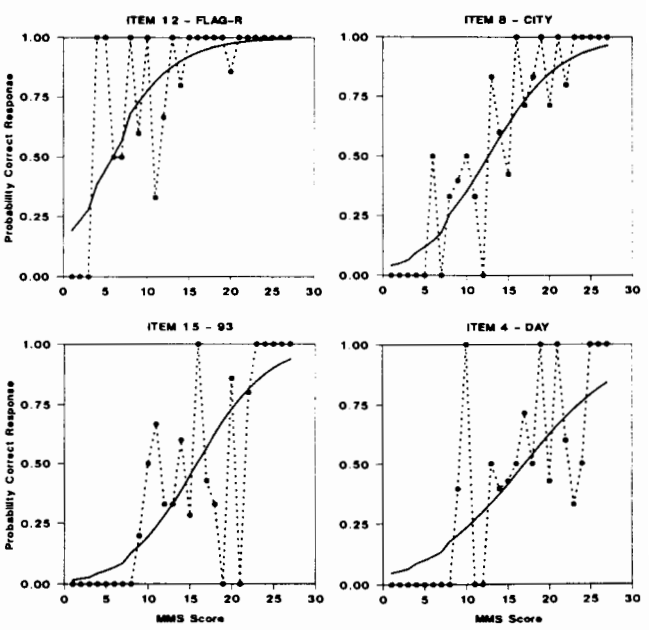

Figure 3. ICCs of four items from Group III. Same parameters as Figure 1.

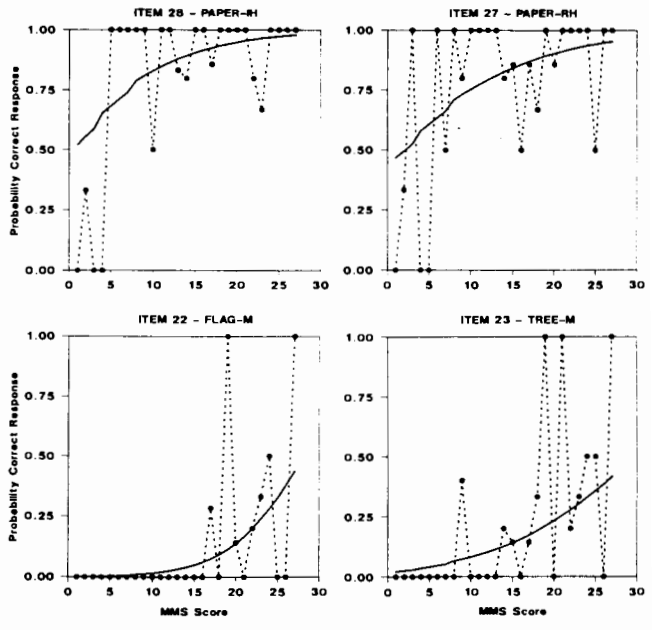

Figure 4. ICCs of the two least difficult items, 28 and 27, and the two most difficult items, 22 and 23, constituting Group IV. Same parameters as Figure 1.

"paper-ih" and "paper-rh," were answered correctly by over 80% of the sample. The rate of loss indices for these items cannot be interpreted in quite the same way as for the other items. Because responses were mostly correct for the items lost last and incorrect for items lost first, the ICCs are very flat over most of the scale; therefore the rate of loss indices is necessarily low. In other words, because these items are lost almost immediately or not until the end, a concept of rate of loss is not meaningful. These items are of considerable potential utility because they measure function at the extremes of the MMS state.

While Table 2 presents the same information as in Table 1, the items in the former are ordered by severity at loss. The

Table 2. MMS Items Ordered by Difficulty

#	Item	Difficulty	Discriminability	R^2
Most difficult				
23	Tree-M	31.8	0.12	0.366
22	Flag-M	30.1	0.23	0.283
19	65	24.2	0.37	0.744
17	79	23.3	0.32	0.643
1	Date	23.1	0.51	0.731
21	Ball-M	22.7	0.37	0.757
18	72	22.1	0.27	0.635
16	86	20.8	0.35	0.681
Intermediate difficulty				
4	Day	19.0	0.17	0.597
9	County	18.7	0.25	0.556
3	Month	18.2	0.55	0.815
15	93	18.0	0.24	0.571
2	Year	17.6	0.49	0.931
5	Season	17.2	0.21	0.661
6	Place	16.6	0.34	0.724
7	Floor	16.5	0.27	0.771
8	City	14.6	0.23	0.817
32	Pentagon	14.4	0.17	0.508
10	State	10.6	0.35	0.671
31	Sentence	10.3	0.55	0.939
26	No-Ifs . . .	10.0	0.25	0.479
Least difficult				
24	Watch	8.5	0.51	0.876
29	Paper-Of	7.6	0.23	0.495
30	Close I's	7.2	0.44	0.661
12	Flag-R	7.0	0.24	0.561
25	Pencil	6.6	0.62	0.863
11	Ball-R	6.1	0.29	0.488
13	Tree-R	5.0	0.21	0.320
27	Paper-RH	2.0	0.11	0.336
28	Paper-IH	0.3	0.14	0.502

data are represented in this fashion to more clearly illustrate the progression of loss across all of the items. The items lost first were those where the patient was required to remember information after distraction, recall the date, and count backwards. Items lost last were those requiring the patient to perform an action immediately following some instruction or to repeat information immediately after presentation.

DISCUSSION

The results of the analysis of MMS items show a differential pattern of loss of items which implies that there is a pattern of deterioration of mental functions in the progression of AD. The items with the highest severity at loss index (MMS score above 20), indicating earliest loss, are recent memory items: the three detail memory items (ball, flag, and tree), recall of the date, and the serial 7 calculations beyond the first subtraction. The latter are difficult because they require a functional recent memory — the patient must recall what he or she is supposed to do next after being distracted by performing the first subtraction. Indeed, memory difficulty is the most common initial problem affecting patients (Liston, 1979a, 1979b), and memory is rapidly lost early in the course of the disease (Folstein & Whitehouse, 1983; Vitaliano, Breen, Russo, Albert, Vitiello, & Prinz, 1984b; Storandt, Botwinick, & Danziger, 1986). Items that became impaired in the middle category of severity level (MMS greater than 10 and less than 20) were time and place orientation items that utilize longer term memory functions and involve many more cues for developing acquisition. The item requiring the perception and reproduction of intersecting pentagons was affected quite variably, perhaps because it involves many different cerebral systems. The items lost late in the progression of AD (severity at loss index of 10 or less on the MMS) are those requiring use of the most solidly stored memories: early-learned verbal mimicking (the repetition of simple words), over-learned associations (the naming of simple objects), and frontal lobe procedural functions (the following of simple commands). Naming objects, writing, and reading are lost even later in AD progression than the repetition and command items. Indeed, expressive language deficits indicate late disease stage (Kaszniak et al., 1978; Folstein & Whitehouse, 1983; Heyman, 1984). Thus, the pattern of loss of performance on MMS items is consistent with the observed clinical course of AD.

A particularly striking and well-known comparison clearly documented by these results is the difference between the ability to repeat the names of three objects (ball, flag, tree) and to recall them later. Most of the patients in our group, particularly those with mild and moderate impairment, clearly perceived these items and could repeat them easily (87%, 84%, and 86% correct, respectively). Yet only a few of the patients were able to recollect these items after distraction (24%, 9%, and 16% correct, respectively). This clear example and the overall pattern of deficit development support the notion that the single underlying factor in Alzheimer dementia is a disorder of memory. The most recent, volatile memory storage is the first to be disrupted, followed by longer term memories, with the pathological process affecting over-learned associations and highly practiced motor skills appearing late in the disease.

The importance of memory dysfunction in Alzheimer's disease has been well documented. The disease affects both recent memory (Corkin, 1982) and remote memory (Wilson, Bacon, Fox, & Kasniak, 1983). Both recall and recognition memory is impaired (Moss et al., 1986). Numerous other functions have been documented to be impaired in this disease, including language function (Huff, Corkin, & Growdon, 1986; Cummings, Benson, Hill, & Read, 1985), object perception (Flekkoy, 1976), and motor skills (Foster, Chase, Patronas, Gillespie, & Fedio, 1986). However, the analysis of the present study supports an alternative clinical impression that aphasia, agnosia, and apraxia, which are frequently diagnosed in AD, are really difficulty in remembering words, what things are for, and how to do things. This leads to the hypothesis that Alzheimer's disease is quintessentially a disease of memory.

There have been numerous reports of diversity in the impairments associated with Alzheimer's disease. Many of these studies have stressed hemispheric asymmetries either in cerebral metabolic measurements (Foster et al., 1983; Benson et al., 1983; Friedland, Budinger, Koss, & Ober, 1985) or on neuropsychological testing (Martin, Cox, Brouwers, & Fedio, 1985; Filley, Kelly, & Heaton, 1986;

Grady, Haxby, Schlageter, Berg, & Rapoport, 1986). In our analysis of MMS data, the rate of loss index is a measure of the variability in the progressive loss of discrete functions. This variability accommodates observations of disproportionate cerebral involvement at any one phase of the disease, even if that means that one hemisphere is much more impaired than the other at that time. However, evidence that language or visuospatial functions may be selectively impaired at some point in the illness does not dispute that memory impairment is at the root of those deficits. On the contrary, across the full course of the disease a progressive pattern emerges in which functions dependent on more recent memory are lost before functions that are dependent on more solidly stored memories.

Identifying the progressive nature of AD as related to a sequential disruption of memory function rather than a deterioration of certain anatomical structures (Whitehouse, 1982) is relevant to understanding the diverse cellular neuropathology of AD. Several authors have proposed an anatomical spread of Alzheimer pathology (Saper & German, 1987), that the disease process affects cells because of their degree of connectivity (Gajdusek, 1985; Hyman, Van Hoesen, Kromer, & Damasio, 1986; Lewis, Campbell, Terry, & Morrison, 1987) or is related to olfactory connections (Pearson, Esiri, Hiorns, Wilcock, & Powell, 1985; Roberts, 1986). However, these hypotheses fail to account for the preservation of basic functions, such as perception, in regions that have totally lost the capacity to store new information [this point is based on the concept that memories are stored in the same area that information is originally perceived (Ashford & Fuster, 1985; Mishkin & Appenzeller, 1987)]. Further, these hypotheses do not explain why the temporo-parietal regions, where detailed memories are stored, are disproportionately affected compared to the frontal lobes (Brun, 1983). The solution to this dilemma of "what system is affected by AD" is that neural plasticity itself, the neural foundation of memory storage, predisposes to the development of Alzheimer pathology in a particular neuron (Ashford & Jarvik, 1985). Just as the cells with the highest cell division rates are the most vulnerable to cancer, those cells most vulnerable to neurofibrillary disruption are those cells which produce the most new neurofibrils. Neural plasticity has recently been conceived of as an active process involving continual production and loss of new synapses (Lee, Schottler, Oliver, & Lynch, 1980; Chang & Greenough, 1984; Cotman & Nieto-Sampedro, 1984). This process is a likely target for the etiological agent which causes AD, because the productivity of neural plasticity reaches its greatest extent in the human brain, and it is the human that is most vulnerable to AD.

The MMSE has two weaknesses, one at each extreme of test performance, which were particularly problematic for the logistic regression analysis (Table 1, group 4). First, the MMSE is not an adequate test to distinguish patients with very mild AD from normal patients. Problems in making this distinction include variation in educational and socioeconomic status (Cavanaugh, 1983). There may be too much variability early in the course of dementia to rely on any simple scale to reliably identify demented patients, and this task should be left to clinical judgment. However, usual clinical procedures have done poorly in detecting dementia (Klein et al., 1985), and PET scan data suggest that those patients who are examined early in the course of their illness already have substantial metabolic impairment (Kuhl et al., 1985, Haxby et al., 1986). Thus, there is a need to expand early patient evaluation with more difficult but still sharply discriminating test items that lack external bias, to assist the clinician in improving the early detection of dementia. The second difficulty with the MMSE is that the score reaches zero at a stage in the disease after which a patient may continue to deteriorate for several years. At this phase, there is little left to evaluate in the way of cognitive functions, and the more relevant measures are ADL scales (Katz, Ford, Moskowitz, Jackson, & Jaffe, 1963; Linn & Linn, 1983; Lawton, 1983), which follow a parallel sequence of functional loss but are more sensitive to severe impairment (Ashford, Hsu, Becker, Kumar, & Bekian, 1986).

The ICC analysis technique offers an approach for improving the measurement of dementia severity. A large number of items could be administered to AD patients, and those items displaying the best discrimination across the spectrum of deterioration could be used for developing an ever-expanding test to more accurately assess patients with early and late AD. More accurate assessment would lead to better measurement of rate of decline and improve prediction of future deterioration.

As is true with all AD studies, autopsy confirmation of AD in each case would strengthen the findings. However, quantification of pathology at late stage death and correlation with performance near that event (Blessed et al., 1968) does not imply validation of a test across a broad spectrum of function and the long course of AD (though the Blessed scale does correlate well with the MMS; Thal et al., 1986). Studies must focus on early detection, long-term follow-up, and autopsy confirmation to determine the course of AD.

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