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The Basis for Choice Reaction Time Slowing in Alzheimer's Disease

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Slowed reaction time has been suggested as an early feature of Alzheimer's disease (AD), but the basis for this slowing has not been established. Patients with mild AD were compared with controls on a choice reaction time task, both cued (CCRT) and uncued (CRT). Initial and 1-year followup data were analyzed both as mean reaction times and as parameters of a fitted two-component quantitative model (the ex-Gaussian model). Slowing of CRT proved to be a sensitive test for AD. Slowing was due to changes in both the sensory/motor and the decisional components of the CRT model. However, these changes were found in both AD and slower, older controls. The modeling of CRT in AD is discussed.

Slowed response speed is one of the common concomitants of cerebral disease. Slowing, typically measured with simple or choice reaction time (RT) tasks, has been found with generalized disease, as well as with focal lesions at almost any site in either hemisphere (Benton, 1986; Tartaglione, Bino, Manzino, Spadavecchia, & Favale, 1986; Tartaglione, Oneto, Manzino, & Favale, 1987).

The theoretical framework used to understand the basis for this slowing has generally been one that divides processing for such tasks into two

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components: a lumped sensory input/motor output component, and a decisional process (Teichner & Krebs, 1974; Dawson, 1988). The time consumed by the decisional process can be estimated when uncued choice RT is compared to cued choice RT, in which the decision is removed or facilitated, as well as when the decision is made more difficult by increasing the number of alternatives on the task (Benton, 1986).

On this basis, it has been concluded that the slowing with cerebral disease is mostly the result of slowing in the decisional phase. Patients show greater slowing on tasks requiring choices than those that do not (Benton, 1986; Elsass & Hartelius, 1985), and slowing is in general more pronounced on choice tasks with more alternatives (Benton, 1986; Cerella, 1985; Welford, 1988). Slowness of the decision phase also seems to account for most of the slowing seen with aging (Cerella, 1985; Welford, 1988).

Slowed reaction time is also a feature of Alzheimer's disease (AD) (Ferris, Crook, Sathanathan, & Gershon, 1976; Pirozzolo & Hansch, 1981; Pirozzolo, Christensen, Ogle, Hansch, & Thompson, 1981; Vrtunski, Patterson, Mack, & Hill, 1983). It has even been suggested that slowing is one of the earlier markers of the condition (Vrtunski et al., 1983), and the best correlate of overall cerebral glucose metabolism in the disease (Foster, Chase, Fedio, Patronas, Brooks, & DiChiro, 1983).

However, the basis for the slowing in AD has not been convincingly established. Since choice RT is slowed more than simple RT in AD (Ferris et al., 1976; Pirozzolo et al., 1981), the decision component has been assumed to be the site of pathology. However, Loring, Mahurin, and Pirozzolo (1984) have suggested on the basis of their data that the overall slowing in AD is actually the result of an admixture of some responses of normal speed with some that are abnormally long. In this view, the problem in AD might not be in the sensory/motor and decisional processes directly involved in the RT tasks. Vrtunski and his colleagues (Vrtunski et al., 1983) have argued that slowing in AD is due to both an impairment in the processes involved in execution of the task per se, and to a "virtual psychomotor disintegration" which affects all of the organization and preparation required to set up the processes involved in actual execution.

The study reported here was primarily planned to address two interrelated questions: whether slowing in AD can be attributed to an intrinsic disorder of the RT mechanism(s); and, if so, whether this slowing represented an alteration of normal RT processes, or not. These questions were studied within the context of the two-component model of RT cited earlier.

For extra rigor, two special analytic techniques were used: a comparison of group reaction time distributions (Ratcliff, 1979), and a quantitative comparison of each component of the two-component model of

choice reaction time. In order to estimate each component of the choice reaction time model, a widely accepted quantitative two-component model was used, the ex-Gaussian model (Dawson, 1988; Luce, 1986). In the ex-Gaussian model, the two components of reaction time have different statistical characteristics: the durations of the lumped sensory input/motor output component have a Gaussian (normal) distribution, while the durations of the decisional phase of choice RT have an exponential distribution. The sum of the durations of these two components gives the observed reaction times; the distribution of observed RTs is therefore given by the product (convolution) of the exponential and the Gaussian distributions of the durations of the processing stages. The ex-Gaussian distribution has been shown to accurately model the empirical distribution of reaction times under many experimental manipulations (Ashby, 1982; Dawson, 1988; Hockley, 1984; Hohle, 1965; Luce, 1986; Ratcliff, 1978, 1979; Ratcliff & Murdock, 1976; Townsend & Ashby, 1982).

The resulting ability to compare reaction time distributions across groups, and to compare the durations of basic sensory/motor processing and of decision-making separately for the ADs and the controls, permitted a much more exact determination of how the ADs differed from controls in RT tasks that have otherwise been only compared qualitatively.

METHOD

Subjects

Subjects were 29 patients with AD, selected from a pool of 209 followed as part of Johns Hopkins' Alzheimer's Disease Research Center (ADRC), and 52 controls followed as part of the same study. The patients were age 50 or older, who met the NINCDS-ADRDA (McKhann, Drachman, Folstein, Katzman, Price, & Stadlan, 1984) criteria for Possible or Probable AD. Controls were largely the spouses of enrolled AD patients, who met the same criteria, except for not having evidence of AD, nor having any first-degree relative with AD. All were followed every 6 months as part of the study, with comprehensive physical exams and neuropsychologic testing. Some of the neuropsychologic tasks are given in Table 2. The data reported here are from the initial testing, and from reaction time testing done at least 1 year later.

Of the total group of AD patients, approximately half were felt to be potentially capable of RT testing (based on a Mini-Mental State Exam (MMSE) (Folstein, Folstein, & McHugh, 1975) score of ≥ 15, established through pilot work) and were tried on the tasks. Only 33 were able to perform at least one of the RT tasks on initial testing. Furthermore, for purposes of this study, the patient and control groups were matched as closely as possible post hoc on age, sex, education, and handedness, resulting in the exclusion of 4 of the 33 patients whose age at entry was greater than 80. The mean characteristics of the final group of 29 AD patients and 52 controls are given in Table 1. As can be seen from Table 1, most demographic variables were well-matched between patients and controls. The only exception was entry age. The AD patients as a group were somewhat older than the controls (69.6 years old versus 65.3, respectively, $p < .01$). (To anticipate the later data, this difference was not the basis for the difference in mean reaction times between the groups, as the older AD patients were the ones with the faster RTs, on the average. See Table 1.)

TABLE 1
DESCRIPTIVE CHARACTERISTICS OF THE SUBJECT GROUPS AND SUBGROUPS

	N	Entry age	Sex M/F	Handedness R/L/Ambi	Education (years)	MMSE[a]	Years ill
Alzheimer's	29	69.6*	17/12	28/1/0	12.4	21.5	3.8
CCRT task							
Subgroup 1 (Fast)	10	72.0	4/6	10/0/0	12.2	20.9	3.1
Subgroup 2 (Slow)	19	68.3	13/6	18/1/0	12.2	21.8	4.1
CRT task							
Subgroup 1 (Fast)	10	70.1	5/5	10/0/0	12.2	20.6	3.1
Subgroup 2 (Slow)	18	69.1	11/7	17/1/0	12.5	22.0	3.8
Controls	52	65.3*	23/29	46/2/4	13.2	29.1	n/a
CCRT task							
Subgroup 1 (Fast)	24	62.2	12/12	20/1/3	13.1	29.4	n/a
Subgroup 2* (Slow)	28	67.9	11/17	26/1/1	13.2	28.8	n/a
CRT task							
Subgroup 1 (Fast)	22	60.7	7/15	20/0/2	12.8	29.3	n/a
Subgroup 2*** (Slow)	30	68.6	16/14	26/2/2	13.4	28.9	n/a

Note. The age difference between the AD patients and the controls was also significant ($p < .01$).
[a] Mini-mental State Exam (Folstein et al., 1975) score.
* $p \leq .01$.
*** $p \leq .0001$.

Procedures

A standard digit-key choice reaction time task (Teichner & Krebs, 1974) was used. There were two versions, otherwise identical except that in one, the choices were *cued* in advance of each trial (cued choice reaction time, henceforth abbreviated as CCRT), while there was no such cuing in the other (the choice reaction time, or CRT, task).

For the uncued choice RT test (CRT), subjects were seated in front of a short-persistance high resolution video display screen, holding a microswitch in each hand. One trial was given at a time. Between each trial, a fixation message ("Ready?") was continuously present in the center of the screen. Each trial was initiated manually, after the subject indicated he was ready. Upon initiation, the fixation message disappeared. Four hundred milliseconds later, the numeral "1" or "2" was displayed in the center of the screen. The subject had to press the microswitch in the dominant hand if the number was a "1," and press the one in the nondominant hand if the number was a "2." Subjects were encouraged to respond as quickly and as accurately as possible.

The procedure for the cued choice RT task (CCRT) was identical, except that the fixation message gave the number that was to be presented on the trial (e.g., "Are you ready for the number One?", with the "One" on a separate line). Subjects were informed of this precuing and what it signified. All were able to read and understand the words "One" and the "Two" shown as cues. As with the uncued condition, this message disappeared 400 msec before the presentation of the critical stimulus.

There were 200 trials on each task, during each session. All stimulus display, timing,

and recording (of response and reaction time, to the nearest millisecond) were done by a microcomputer modified for laboratory work (Gordon & Field, 1985). Subject compliance and memory for the instructions were ensured by written cue cards in front of each subject during the entire time, and by experimenter monitoring. For right-handed subjects, a cue card on the right, in front of the subject, had a large "1," under which were the words "Right hand"; a cue card on the left had a "2" and the words "Left hand" as reminders.

The cued CRT task (CCRT) was always given first, in order to guarantee that patients understood the task. The two tasks (cued and uncued) were clearly differentiated from each other, and were separated in time by a rest break and by the experimenter's changing of the computer program.

All subjects with MMSE ≥ 15 were first tried on the CCRT task. If the task could not be accomplished with >95% accuracy after 94 trials, the subject was considered unable to do the task, and was not given the CRT task. The 94-trial criterion was also used with the CRT task. In practice, there was a clear distinction between those subjects who were able to learn the task, and those who could not. Only one subject who was considered unable to do the tasks required this many trials to demonstrate that fact; in the others, it was apparent much earlier, usually within the first 30 trials. All subjects were able to do the CCRT task to these criteria, but one AD patient was not able to learn the CRT task adequately.

Analysis

The first 10 trials of each task were considered practice and were excluded from the analyses. In addition, trials that might have been corrupted for any reason apparent to the experimenter (e.g., overt lack of subject attention, or an interruption) were also excluded.

Mean RTs. For the purpose of calculating mean RTs, the individual RTs were log transformed to normalize their distribution (e.g., Gordon, 1983). Individual RTs which were greater than ± 3.0 standard deviations from the mean of the log-transformed times for each subject, for each task and session, for "1" and "2" responses separately, were considered to be outliers and were eliminated. No more than 1–2 data points per subject (out the 190 critical trials) were eliminated this way. Mean true positive and true negative RTs using the logarithmically transformed values were then calculated for each subject, for each task, for each session, and converted back to milliseconds for group comparisons.

Subgroup selection. The analysis of correct mean RTs, to be described below, demonstrated that the controls were generally faster than the patients, but with appreciable overlap. Therefore, to facilitate comparisons, for each of the two tasks, we further distinguished two subgroups within the AD and the control groups, on the basis of mean RTs. One subgroup was that of "fast" responders, the other of "slow" responders. "Fast" and "slow" were defined with reference to how their mean RTs compared to those of the other subject group. The fast Controls (Control subgroup 1) were all those controls whose mean correct RT was *faster* than the mean correct RT of the fastest AD subject. The slow controls (Control subgroup 2) were all the rest (whose RTs were at least as fast as that of the slowest ADs). The fast ADs (Patient subgroup 1) were all those who were at least as fast as the slowest control. The slow ADs (Patient subgroup 2) were all those who were slower than the slowest control subject. Therefore, for each task, we established three major contrasts between AD patients and controls: controls whose mean RT was faster than any patient's (Control subgroup 1); controls and patients with the same range of RTs (Control subgroup 2 and Patient subgroup 1), henceforth referred to as the Overlap Controls and the Overlap ADs; and patients with RTs slower than any control's (Patient subgroup 2). Table 1 also gives the descriptive characteristics of these subgroups.

For the overlap subgroups, for the CRT task there were no significant differences in mean reaction times or error rates between the AD and control subjects. For this task,

the matching was quite close both for reaction times[1] (e.g., for "1" responses, mean RTs of 460.5 and 466.2 msec, respectively) and for error rates (proportion of false negatives 0.023 and 0.016, n.s., and of false positives 0.014 and 0.012, n.s.). For the CCRT task, the matching by reaction time ranges gave a less accurate matching, with a slight difference in mean RTs (402 versus 361 msec for the patients and controls, respectively), although not in error rates (for false negatives, 0.009 versus 0.003, n.s.; for false positives, 0.015 versus 0.008, n.s.). Particularly for the CRT task, then, the matching of the overlap subgroups permits a direct comparison of the effects of AD on the RT distributions, apart from any differences due to different mean RT and error rates.

RT distributions. In addition to the analysis by mean RT, the distributions of correct response times were analyzed. These distributions were compared graphically, and also through a comparison of their parameters, as estimated from the ex-Gaussian model of choice reaction time (Dawson, 1988). As noted, only sessions with more than 96 valid data points (of the maximum possible total of 190) were analyzed in this fashion, to ensure adequate sampling. Outliers were then excluded using the log-transformed RTs compared against the mean RT calculated as described above, but with the limits set at -3 and $+8$ standard deviations.

Reaction time distributions were then computed using the Vincentizing procedure described by Ratcliff (Ratcliff, 1979), which preserves the shape of the RT distribution across the averaging process (Ratcliff, 1979; see also Thomas & Ross, 1980). Details of this computation are given in Appendix 1. RT distributions were compared graphically by overlay and visual inspection, with particular attention to the intersections of their maxima and their minima, as described by Ashby (1982).

The quantitative model of choice reaction time, the ex-Gaussian model (Dawson, 1988) described in the Introduction, was used to derive estimates of each of the two assumed components of choice reaction time from the group reaction time distributions. In this model, the time spent in basic sensory/motor transduction is assumed to be normally distributed (with a mean of *mu* and standard deviation of *sigma*). The time spent in the decisional phase is assumed to be exponentially distributed (with a mean of *tau*). These parameters of the ex-Gaussian model—*mu*, *sigma*, and *tau*—were estimated from the empirical subgroup reaction time distributions. More details about this estimation procedure are given in Appendix 1. Quantitative fitting was done for both group-averaged distributions and individual distributions. In both cases, particularly for the group data, the fits were quite close (see Table 3 for an example). The χ^2 of the fit to the group data was always ≤ 2.5 (for 19 degrees of freedom), and in most cases was ≤ 0.45, with associated probabilities of >0.999. The plausibility of each fit was also checked graphically.

Subject selection differences between cross-sectional, subgroup, and longitudinal analyses. It should be noted that, depending upon the issue examined, different sets of subjects and combinations of tasks must be used. In the subgroup comparisons, for example, a given subject's CCRT performance may qualify him/her for the "fast" group, while his CRT performance may place him/her into the "slow" group. These considerations will be given in detail with each section, but the reader should be warned in advance that this is why subject *n*'s are in each table, and why the *n*'s in the different categories vary.

RESULTS

General Considerations

There was no evidence of a speed–accuracy tradeoff that would com-

[1] *t* tests and significance values are not reported for the comparison of subgroups by reaction times, because mean RT had been used as the basis for the subgroup selection. Therefore, subgroup RTs could not be presumed to be distributed as the *t*-statistic requires. This caveat does not apply, of course, to comparisons of the groups as wholes.

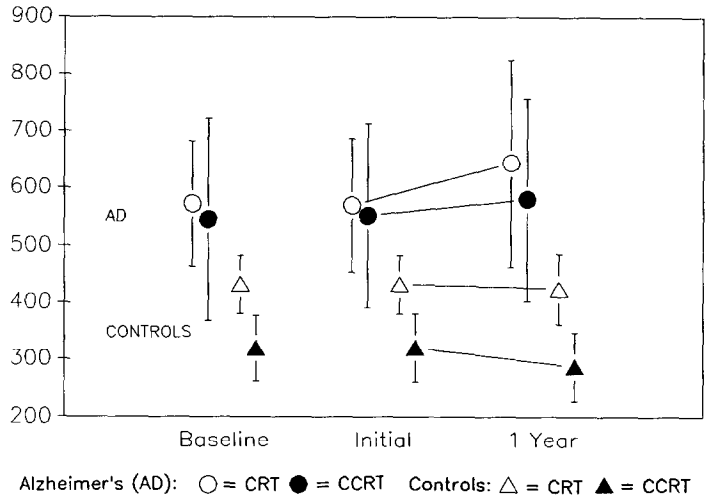

FIG. 1. Comparison of mean reaction times, by task (CCRT or CRT), subject group (AD patients or controls), and examination time. All subjects are included in the baseline comparison; only those with valid data on both tasks, both on initial exam and on exam after ≥1 year, are in the longitudinal group.

promise interpretation of the mean RT data. Mean error rates were relatively low (for the AD subjects, in the 2.4 to 4.0% range; for the controls, in the .4 to 1.5% range, for the CCRT and CRT tasks, respectively), and were in the same direction as the mean RTs.

The mean RT of correct responses made to the "1s" (with the dominant hand) did not significantly differ from that of correct responses made to the "2s" (with the nondominant hand) for three out of four comparisons of the subject groups as a whole (for the AD patients, on CCRT (t = 0.79, p = 0.44) or CRT (t = −1.30, p = .21), and the controls on CRT (t = 0.68, p = .50)). There was a statistically significant difference in the mean RT of "1" versus "2" responses for the controls on the CCRT task (with the "1" responses, made with the dominant hand, faster by 9.4 msec, t = 2.2, p = .03, uncorrected for multiple comparisons). For this reason, the mean RTs of the two types of responses were compared separately. However, for the purposes of the subgroup distributional analysis, the difference was so small and of such borderline significance that it was ignored, and "1" and "2" responses were pooled together to ensure more accurate quantization.

Correlations and Sensitivity of Baseline RT Measures

The correlations between mean RT on the CRT task and summary scores from the other neuropsychological tasks given to these patients were examined. The highest intercorrelations were with digit span (r = −.51, n = 28, p = .006), serial 7's (r = −.57, n = 28, p = .002),

spatial recognition span (Moss, Albert, Butters, & Payne, 1986) ($r = -.50$, $n = 28$, $p = .007$), and vocabulary ($r = -.45$, $n = 28$, $p = .02$). Correlations with all other tasks were generally below 0.30, and were not significant.

The sensitivity of the CRT testing relative to that of the other neuropsychologic tasks in the battery was compared using z scores based on the controls' performance. The results are given in Table 2. As can be seen in Table 2, even for just that subset of patients capable of taking almost all of the tasks, CRT was among the tasks showing the largest differences between patient and control performance, even though variance prevented it from being the one with the greatest discriminating power statistically.

Differences between the CCRT and the CRT tasks at baseline. Our expectation was that precuing (the CCRT task) would eliminate the de-

TABLE 2

COMPARISON OF SENSITIVITY OF CRT TASK TO OTHER NEUROPSYCHOLOGIC TASKS, IN DISCRIMINATING AD FROM CONTROL PERFORMANCE ON INITIAL EXAMINATION, ORDERED BY ABSOLUTE Z SCORES

Task	Mean Z score (absolute value)	t
Word recognition[1]	10.3	6.0[a]
Word recall[2]	6.5	11.3
Choice reaction time	5.2	4.7
Face recognition[1]	3.4	3.8[a]
Word recall[3]	2.9	19.1
Category retrieval[4]	2.8	17.5
Recognition span[5]	2.3	9.5
Paired associates, hard[6]	2.1	31.1[b]
Confrontation naming[7]	2.1	5.8
Block design[8]	1.9	7.6
Visual retention[9]	1.4	15.6
Vocabulary[10]	.6	2.0

Note. Z scores were computed based on the means and standard deviations of the controls. The t is Student's t value. $N = 28$, except where otherwise indicated.

[1] Warrington Recognition Tests (Warrington, 1984)

[2] From the MMSE (Folstein et al., 1975)

[3] From the Brief Cognitive Rating scale (Selnes et al., 1988)

[4] For foods, 3-min interval

[5] Spatial recognition span (Moss et al., 1986)

[6] Wechsler Memory Scale (Wechsler, 1972)

[7] Boston Naming Test (Kaplan, Goodglass, & Weintraub, 1976)

[8] WAIS-R (Wechsler, 1981)

[9] Benton Visual Retention Test (Benton, 1974)

[10] Selnes et al. (1988)

[a] $n = 11$.

[b] $n = 15$.

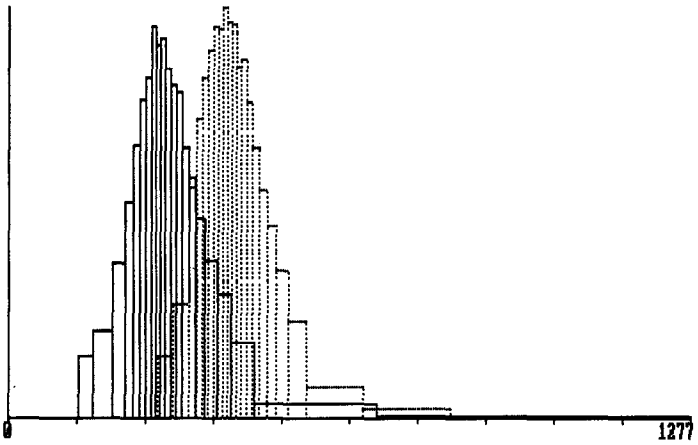

FIG. 2. RT distribution comparison of CCRT (solid lines) and CRT (dotted lines) tasks, for the Controls. In this and subsequent figures, the X axis is in milliseconds. For each figure, the X axis is individually scaled to the maximum for each plot, to maximize resolution. Each subdivision on the X axis is 1/10th of the maximum time given on the right. The Y axis is probability density (seconds^{-1}; see Gordon, 1983). The area under each curve has been normalized to unity.

cision requirements of the CRT task, resulting in faster responses and RT distributions akin to those of simple RT tasks. Correct responses on the CCRT task were in fact faster than those on the CRT task, for both patients and controls (see Fig. 1). This difference was highly significant for the controls (319 msec versus 432, $t = 10.4$, $p < .0001$), but not significant for the patients (545 versus 572, $t = 0.7$, n.s.).

However, upon examining the RT distributions rather than just the mean RTs, it did not appear as though either group treated the CCRT as a completely precued and predetermined form of the CRT task. This can be seen in comparing the RT distributions of the two tasks (for controls, Fig. 2; for the AD patients, Fig. 3), and the fitted parameters for the two tasks for the ex-Gaussian model (Table 3). (This analysis used only those subjects who had done both tasks [all but one of the AD patients], broken down only by AD versus Control groups; the subgroupings were not used.)

As Fig. 2 shows, for the Controls, the RT distributions for the CCRT and the CRT tasks resemble each other, except that the CCRT distribution appears to be shifted to a lower reaction time. For the AD patients (Fig. 3), the CCRT distribution also resembles that of the CRT task, but the downwards shift is not as great.

All the distributions could be well fit by the ex-Gaussian model. The fitted parameters given in Table 3 confirm that most of the difference between the two tasks can be accounted for by change in the percep-

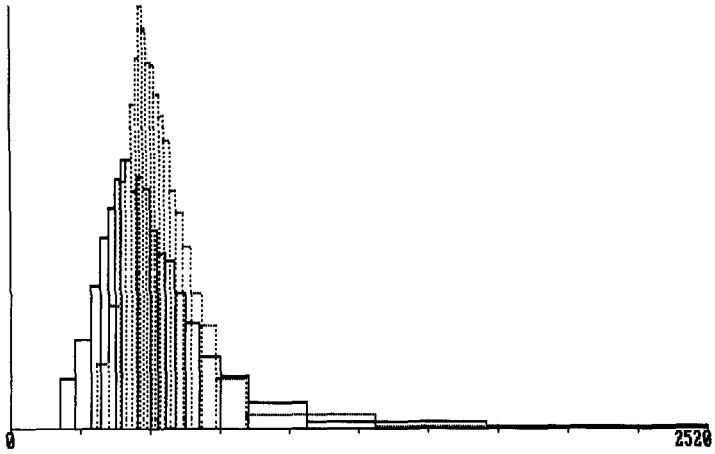

FIG. 3. RT distribution comparison of CCRT (solid lines) and CRT (dotted lines) tasks, for the AD patients.

TABLE 3
COMPARISON OF THE RT DISTRIBUTION PARAMETERS OF THE CCRT AND CRT TASKS

	Task	
	CCRT	CRT
Controls (n = 52)		
tau	.071	.070
mu	.24	.36***
sigma	.055	.046
Patients (n = 28)		
tau	.20	.14*
mu	.32	.42**
sigma	.085	.063

Note. Across subject groups (controls versus AD), using data from the initial testing of all subjects who could do both tasks (see text). Parameters fitted using the ex-Gaussian model. *Tau* is the estimated mean of the exponential (decision) component of the total distribution; *mu* is the estimated mean of the Gaussian (transduction, or sensory/motor) component; and *sigma* is the estimated standard deviation of the Gaussian component. All values have been rounded to 2 significant digits.

* $t = -2.2$; $p < .05$.
** $t = 5.4$; $p < .0001$.
*** $t = 17.7$; $p \ll .0001$.

tual/response component (*mu*), not by changes in the decision component (*tau*). *Mu* is greater for the CRT task than for the CCRT task for both controls ($t(51) = 17.7$, $p < .00001$) and for the AD patients ($t(27) = 5.37$, $p < .0001$); *tau* had a tendency to be less for the CRT than the CCRT task, but this difference was infinitesimal for the controls, and only significant for the AD patients ($t(27) = -2.22$, $p < .05$).

That the CCRT task is not simply the CRT task with the exponential component removed is further supported by the graphical analysis suggested by Ashby (1982; see in particular p. 122). As he established, if one distribution differs from another only by the addition of an exponential stage, then the peak of the distribution with the additional exponential component must intersect the distribution of the one without. If this is not the case, then the two distributions do not differ by only an exponential stage. The curves in Fig. 2 (for the controls) clearly fail this test. Similar considerations apply to the data from the AD patients.

Therefore, it appears that for both groups, the precuing did not eliminate the decision phase. Instead, it appears to have facilitated stimulus encoding and/or response programming in some fashion. Moreover, judging by reduction in mean RTs, this precuing was more effective for the controls than for the AD patients.

Basis for the slowing in AD—cross-sectional data. Within-task comparisons show that the AD patients are slower than controls, on the average, for both tasks. For the CCRT, the AD patients were slower by 243 msec ($t = 7.1$, $p < .0001$); for the CRT, by 140 msec ($t = 6.4$, $p < .0001$). These differences were not unexpected, given the prior

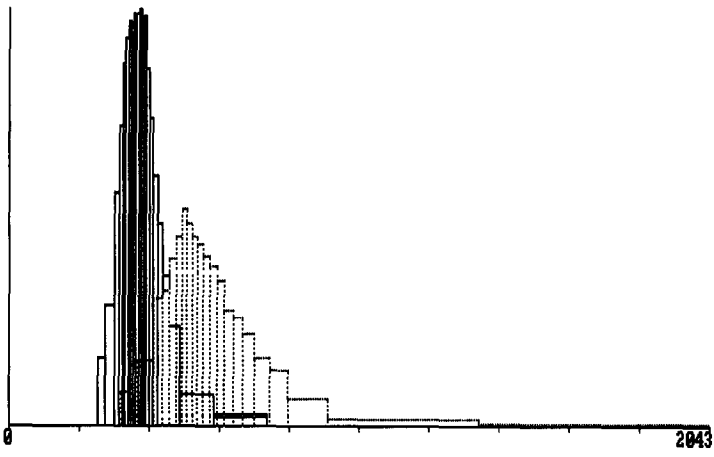

FIG. 4. Comparison of Controls (Control subgroup 1, "fast" normals [dotted lines]) and AD patients (AD Subgroup 2, "slow" ADs [solid lines]) on the CRT task, cross-sectional data.

literature. However, their basis cannot be easily discerned from the mean RTs, particularly in light of the problems with interpreting differences between the CCRT and the CRT tasks that the foregoing analysis revealed.

The source of these differences can, however, be seen in the parameters of the fitted RT distributions (Table 4). Increasing slowness is caused by changes in both *tau* and *mu*, as can best be seen with the CRT task data. For the CRT task, this was independent of subject type. When we compare the RT distributions on the CRT task for the "overlap" subgroups that were comparable in their mean RT and error rates, there is virtually no difference between ADs and controls, as can be seen in Fig. 5. This was also true statistically for the CCRT task, but the parameters are not as close as they were for the CRT task subgroup comparison. (We suggest this is due to the less-than-precise matching

TABLE 4
COMPARISONS OF SUBJECT DIFFERENCES (AD VERSUS CONTROLS) BY SUBGROUPS, ACROSS TASKS

	Control subgroup 1	Overlap controls	Overlap ADs	AD subgroup 2
CCRT				
n	24	28	10	19
RT range				
tau	.058	.081	.18	.23
mu	.20	.27	.22	.38
sigma	.039	.069	.063	.11
CRT				
n	22	30	10	18
RT range				
tau	.054	.081	.097	.16
mu	.33	.38	.37	.45
sigma	.042	.048	.047	.071
	| —*—	| —NS—	| —*—	
	| ——————— ** ———————			

Note. As described in the text, the subgroups were determined by mean RT, with the RT for Control subgroup 1 < Control subgroup 2 = Patient subgroup 1 (the Overlap subgroups) < Patient subgroup 2. Parameters from the fitted ex-Gaussian model, as described in the text. *Tau* is the estimated mean of the exponential (decision) component of the total distribution; *mu* is the estimated mean of the Gaussian (transduction, or sensory/motor) component; and *sigma* is the estimated standard deviation of the Gaussian component. The bottom of the table shows the results of the statistical comparisons between the *tau* and *mu* values in the columns. All values have been rounded to 2 significant digits.

* = borderline.

** = significant ($\leq .05$).

NS = not significant.

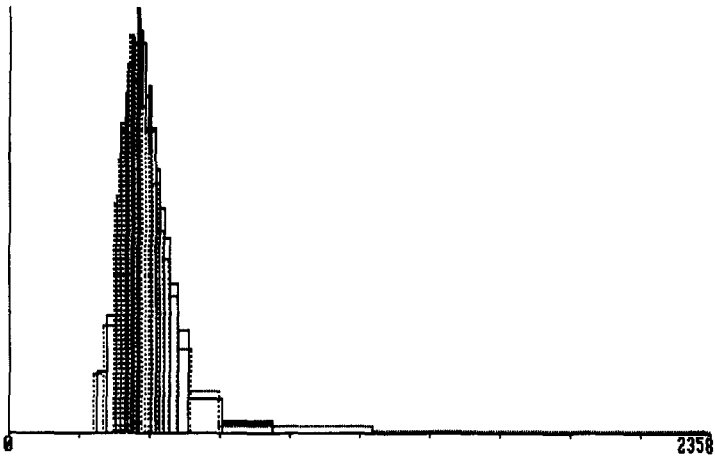

FIG. 5. Comparison of matched subgroups (Control subgroup 2, "slow" normals [dotted lines], and AD subgroup 1, "fast" ADs [solid lines]) on the CRT task, cross-sectional data.

for these subjects, but we cannot exclude a true difference for this task that is hidden by the small n and error variance.)

Longitudinal changes. Over the course of a year (3 test sessions), the controls' mean RTs tended to get faster, while those of the AD patients slowed (see Fig. 1). These changes were significant only for the CCRT task for the controls (mean reduction = 32 msec, $t = 4.8$, $p < .0001$), and for the CRT task for the AD patients (mean increase = 81 msec, $t = -3.1$, $p = .006$).

The fitted parameters of the distributional model, given in Table 5, permit a more detailed examination of these changes. There was a trend for a smaller *tau* for the controls, and a longer *tau* for the patients. There was no consistent change or pattern for the *mu* parameter. (While *mu* for the CCRT tasks was slightly smaller after a year for the controls, this was of borderline significance, and there were no other consistent trends for *mu* in the other subconditions.)

DISCUSSION

We should first resolve a methodologic issue. It is clear that our expectations for the differences between the CCRT task and the CRT tasks were not fulfilled by these subjects. For the AD patients, making the answer available before the response was required, in the CCRT task, did not mean that they were going to make much use of it. Since use of the cue perhaps required some effort (e.g., to recode the word) and memory, it may not be surprising that the AD patients were not very much affected by it. However, we would have expected the controls at

TABLE 5
LONGITUDINAL COMPARISONS, BY SUBJECT AND TASK

	Initial exam	1-year exam
Controls		
CCRT (n = 49)		
tau	.073	.061
mu	.24	.21***
sigma	.055	.047
CRT (n = 49)		
tau	.071	.064
mu	.36	.36
sigma	.046	.049
AD patients		
CCRT (n = 21)		
tau	.20	.28**
mu	.32	.31
sigma	.089	.096
CRT (n = 19)		
tau	.14	.20*
mu	.42	.45
sigma	.066	.093

* $t = 2.1$; $p < .05$.
** $t = 2.4$; $p < .05$.
*** $t = -3.2$; $p < .001$.

least to make full use of the cue to preprogram their response. Instead, they seemed to use it to facilitate stimulus encoding or response generation (see Table 4), not to eliminate the decision phase, which took as long as it did without cuing. This does not mean that normals can not eliminate the decision phase with a cue, as this has been reliably established (Gottsdanker & Shragg, 1985). However, it does mean that use of a cuing technique to separate out the components of CRT must be independently justified whenever it is to be employed. This being noted, we can turn to the broader significance of these results.

Mean CRT proved to be a sensitive discriminator at the initial visit between controls' performance and that of AD patients, as can be seen in Table 2. This was true even though our sample was a relatively milder subset of the AD population, with mean MMSE score of 21.5 (Table 1), because only these individuals were able to accomplish the task. The differences between controls and ADs were magnified after 1 year, where the controls tended to show an improvement (probably due to practice effects), while the ADs declined (presumably because of the progression of their disease, and also because practice effects may have been less pronounced for them).

These results therefore confirm earlier suggestions that RT slowing is

a prominent feature even of early AD (Ferris et al., 1976; Pirozzollo & Hansch, 1981; Pirozzolo et al., 1981; Vrtunski et al., 1983). They help indicate that choice reaction time can be a useful diagnostic tool for the condition on initial evaluation, and is even more useful for discriminating patients from controls after 1 year.

One of this study's original intentions was to determine whether the slowing of CRT in AD represented a disorder of the processes directly involved in the task, or was a perturbation by external problems of an otherwise normal CRT mechanism. The slowing we found appears to be intrinsic to the RT process itself, in that there was no evidence from comparing the RT distributions between the patients and controls of any bimodality or additional component (see, for example, Fig. 5). Therefore, while it is certainly plausible that patients with AD may also have additional, extra-long-latency responses, as Loring and his colleagues (Loring et al., 1984) claimed, these are not the basis for the slowing in the mild phase of the disease. Similarly, we might expect that some AD patients, particularly those with more severe disease, might also show impairments of general organizational and preparatory abilities that contribute to slowness on the task (Vrtunski et al., 1983). However, this cannot explain the slowing seen in our patients. They were able to perform the relatively simply and highly practiced CRT task without appreciable disorganization, with high accuracy, and with good trial-to-trial consistency.

Having identified the CRT processes themselves as expressing the pathology in AD, what this study further establishes is that, even from the more refined perspective of the RT distributional analysis, there is no unique marker for the effects of AD on CRT. This is most conclusively demonstrated when mean RTs are nearly matched, as in the overlap subgroups on the CRT task. Then it can be seen that the form of the RT distributions for AD patients is almost identical to that of controls. This point is also apparent in tracking the changes in the fitted parameters from the fast control subgroup, through the overlap subgroups, to the slowest AD patients (Table 4).

What this examination reveals, in fact, is that the functional changes responsible for differences in RT among the controls can also be put on a plausible continuum with that of the AD patients. With increasing RT, regardless of whether it is found in a normal but still slower control, or in an AD patient, there is a smooth change in both the decisional and the sensory/motor components. Therefore, it seems that the processes giving rise to the RT distributions have a relatively nonspecific response to the malfunction(s) caused by AD in the patients or by, perhaps, aging, in the normal controls. (The only demographic variable distinguishing the fast from the slow Control subgroups [1 and 2, respectively] was that the slower subgroup was also the significantly older one [Table 1]).

The distributional analysis and parameter fitting make it possible to determine more precisely which of the processes underlying CRT, the decisional one or the lumped sensory/motor one, contributes to the observed slowing. As Tables 4 and 5 show, both do. Recall that *mu* is the mean of the Gaussian component, and *tau* the mean of the exponential component, which add together to give the observed mean RT (Luce, 1986). Given the empirical changes, the question of which is more responsible for the slowing actually becomes a question as to how the responsibility is to be measured. When assessed in terms of proportional changes in the parameters, the change in the decision component (*tau*) is the greatest. This is so whether the groups are compared at baseline (Table 4) (from the fast control group to the slow ADs, an almost 3-fold increase in *tau*, compared to a 1.4-fold increase in *mu*) or after 1 year (Table 5). However, when the roles of the two components are assessed in terms of magnitude of RT changes, then at initial exam, slowness in the lumped sensory/motor processes contributes a slightly larger absolute amount to the prolonged CRT with AD (.12 sec for *mu*, .11 sec for *tau*).

This question as to where the locus of pathologic changes can be found in terms of the two-component model also points to the larger question of where AD and normal aging (the latter subject to the caveat noted above) are exerting their influences on the CRT mechanism. While the exact neurophysiologic mechanisms of CRT have not been determined, from neurophysiologic investigations of simple RT (e.g., Glickstein, 1972) and choice tasks (e.g., Ashford & Fuster, 1985) in monkeys, it is clear that presentation of a visual stimulus elicits a complex chain of reactions. Processing of a stimulus proceeds from the occipital cortex, through the parastriate visual regions, into the inferotemporal region for stimulus identification, and then on to an equally complex motor control system (see, for example, Cheney, 1985), before the overt response is enabled. In the single-unit neuron studies, it has not been possible to identify an explicit decisional phase. This may be because there is instead, as some psychological evidence (e.g., Gratton, Coles, Sirevaag, Eriksen, & Donchin, 1988) suggests, simultaneous, parallel activation of all responses. That only one is overtly produced may be due to strength considerations that are continuously graded through the processing sequence, rather than in a single "decisional" stage.

The details of this outline may not prove to be correct. However, it is enough for our argument to note that the neurophysiologic basis for CRT is undoubtedly complex, with far greater overlap of "processing" and "decisional" aspects than has been assumed in the standard psychological models.

The effects of AD are likewise also not confined to a single neuronal system. AD is associated with cortical neuronal degeneration (Terry, Peck, DeTeresa, Schechter, & Horoupian, 1981), lesions of the white

matter (Brun & Englund, 1986), and alternations in a number of neurotransmitter systems (Perry, 1986), in many areas of the brain.

Given, then, that there are many steps involved in CRT, and that AD may be causing dysfunction in a large subset of these, it is not surprising that the effects of AD appear to be relatively nonspecific at the level of the overt response and distributional RT analysis. It is also plausible that normal aging (assuming that was the basis for the difference between the two control groups) should likewise have similar, overtly nonspecific, effects.

In summary, CRT slowing is a prominent feature even of mild AD. The slowing is due to impairment intrinsic to the CRT process, but it is not specific for AD. If the standard model of CRT is accurate, then slowing occurs both in the decisional and in the sensorimotor components of CRT that it identifies. Alternatively, the actual neuronal events underlying CRT, and the effects of pathology, may be so complex that they cannot be accurately modeled by separating them into these two lumped components.

APPENDIX 1

To Vincentize the data (Ratcliff, 1979; Thomas & Ross, 1980), for each subject, task, session, and correct response (whether "1" or "2," on the basis of lack of significant difference between them, as described below), the set of reaction times was sorted by magnitude of RT and divided into 20 quantiles. Each quantile was averaged with data from corresponding quantiles from other subjects in that subgroup to arrive at a subgroup quantile. From these subgroup quantiles, the height of the probability distribution of the group's reaction time distributions was then calculated, using the method of equal-area rectangles described in Ratcliff (1979) (modified to take into account the upper and lower portions of the distribution, which added two more rectangles). The total area of the distributions were normalized to the same value (a total probability of 1.0) for each of the subgroup conditions. Interested investigators may obtain the numeric data describing the RT distributions shown in Figs. 2–5 from the first author.

The estimates of the parameters of the ex-Gaussian model reported here were derived from group reaction time distribution data made using 22 quantiles. Estimates from 10- and 15-quantile distributions were also compared; the 22-quantile solution gave the best fit without excessive quantization noise.

Parameters were fit based on the criterion of minimization of the χ^2 difference between observed and predicted values, using the Simplex algorithm as described by Dawson (1988) with some modifications. The major difference from Dawson's (1988) method was that we treated the values obtained from the Vincentizing procedure as estimates of the

midpoints of RT values of the quantiles, as Ratcliff (1979) apparently did (judging from his graphs), rather than using the edges of the quantiles as the basis for the RT values, as Dawson (1988) apparently did. The estimated parameters reported represent the convergent solutions obtained from several different starting estimates for each set of three parameters, to ensure their robustness.

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