Longitudinal Course of Behavioral Problems During Alzheimer’s Disease: Linear Versus Curvilinear Patterns of Decline

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Background. Patients with Alzheimer’s Disease (AD) are commonly assumed to experience a linear decline in behavioral functioning that parallels progressive cognitive decline. However, some researchers have suggested that specific behavioral problems either decline at different rates or improve in late dementia.

Methods. The present analyses examined 150 AD patients at an initial assessment, 61 of whom were also evaluated annually on two additional occasions. Measures of cognitive impairment and behavioral problems were obtained.

Results. Cross-sectional results indicated curvilinear associations between dementia severity and certain behavioral problems (forgetful behaviors, and emotional and impulsive behaviors). Longitudinal analyses further indicated trends for curvilinear rates of behavioral disturbance across time, with some problem areas showing improvement as AD progresses through the most severe stages.

Conclusions. Even though Alzheimer’s disease is a progressive dementia characterized by increasing cognitive deterioration, it appears to be inaccurate to expect behavioral functioning to show the same linear decline across time.

Cognitive decline in Alzheimer’s disease (AD) has been well researched and documented (1,2). However, the course of behavioral dysfunction is less well understood (3–6). Increases in behavioral problems and psychiatric symptoms are reported to be more distressing to caregivers than cognitive problems (7,8) and mapping the course of these difficulties across time could be of great benefit to clinicians who must advise patients and caregivers.

Some researchers have suggested that patient cognitive impairment and behavioral problems increase in a linear fashion throughout the course of Alzheimer’s disease (3,9–11). Conversely, other studies have reported that certain behavioral problems are not associated with progressive cognitive decline (6,12,13). Studies that have relied on a single global index of behavioral difficulty have generally not been sensitive to possible changes over time (14).

Any global characterization of cognitive and behavioral decline during AD potentially masks the more complex relationships that may exist between dementia severity and specific types of behavioral difficulties. Some domains of functioning may be quickly impaired during the early stages of AD, without significant changes over the subsequent disease course. Conversely, other domains may remain relatively preserved until the more severe stages of AD. Still other domains may be minimally problematic at the mild and severe stages, but more severely impaired during moderate stages of disease severity. When distinct clusters of behavior problems were examined cross-sectionally, some domains were found to increase with severity, whereas others were found to decrease with increasing severity; still other domains were found to remain stable across levels of severity (3,5,9,11,13).

Although much of the existing work on memory and behavioral problems has focused on cross-sectional data (3,5,9,10,15), researchers have attested to the importance of longitudinal research in the study of AD (16). For the tracking of behavioral dysfunction, even a full 1-year time period has been questioned as possibly being insufficient for identifying significant longitudinal progression (14). Thus, in order to more fully evaluate the progression of memory and behavioral problems across the course of AD, it is necessary to collect data longitudinally for more than 1 year, and to examine change on meaningful clusters of behavioral problems.

The purpose of the present study was to investigate cross-sectional and longitudinal changes in behavioral problems in relation to cognitive impairment for a large sample of AD patients. Utilizing caregiver reports of the frequency of patient memory and behavioral problems, we employed factor analytic techniques to identify subsets of these problems to use as potentially more sensitive indicators of changes over the course of AD. It was hypothesized that subscales based on these subsets of memory and behavioral problems would exhibit distinct patterns of association with disease severity when evaluated cross-sectionally. Furthermore, the longitudinal patterns of change over a 2-year time period on the subscales were expected to resemble the cross-sectional association patterns.
METHODS

Subjects
Alzheimer’s disease patients were recruited through the Memory Disorders Clinic at the University of Alabama at Birmingham as part of a larger, longitudinal project that focuses on stress and coping in African American and white caregiving families (17–19). Patients were diagnosed by neurologists from the Alzheimer’s Disease Center as having Alzheimer’s disease by the use of criteria from the National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer’s Disease and Related Disorders Association (20). The present patients are the subsample from our larger project who have the diagnosis of AD, rather than other dementias.

Each patient was being cared for at home by a primary caregiver. In this project, each caregiver completed an extensive structured interview and a series of questionnaires. The details of the data collection procedures are described in other papers from the project (17, 18). In the present study, the hypotheses focused on initial cognitive impairment and changes in patient functioning (behavioral problems) across time, so only these variables were included in the analyses. At baseline, data were collected from the caregivers of 150 patients. Where possible, annual follow-ups were conducted, and caregivers of 61 patients provided complete data at baseline and at 1- and 2-year follow-up sessions. We did not include data for patients who had moved to nursing homes or who had experienced a change in caregiver to enhance the reliability of follow-up reports by the caregiver. Of the 89 patients who did not provide 2 full years of follow-up data, 16 died, 29 were placed in nursing homes, 24 were ineligible (e.g., had a change of caregiver or moved out of the area), and 20 withdrew from the study or were unavailable for other reasons.

Subject Characteristics
The baseline sample of 150 AD patients included 42 men and 108 women. The sample was mostly Caucasian (67%), but it contained 49 African American patients (33%). Patient age ranged from 56 to 95 years (M = 74.2; SD = 8.6). The subsample of 61 patients who provided 2 years of follow-up data consisted of 18 men and 43 women. African Americans composed 36% of this sample.

Measures

Cognitive status.—The Mini-Mental State Exam (MMSE, 21) was administered during the neurological exam. The MMSE is a brief measure of cognitive status that yields a summary score from 0 to 30, with lower scores indicating greater overall cognitive impairment. For the purposes of the longitudinal analyses, patients were categorized into one of four initial severity levels based on MMSE scores (21–30, 11–20, 1–10, and 0). Similar methods of categorization have been used in other studies (4,5,12).

Behavior problems.—The Memory and Behavior Problem Checklist-Revised (MPBC-R; 22) was used to assess the patient behavioral problems associated with Alzheimer’s disease. The MPBC-R is a 30-item instrument that assesses the frequency of occurrence of memory and behavioral problems exhibited by the patient during the past week. Items were scaled from 0 to 3, with 0 indicating no occurrence of the problem and 3 indicating occurrence of the problem on a daily basis or more often. It should be noted that this instrument has been subsequently revised again (15), but the present project began before publication of the 1992 revision. Because our focus in the present study is on patient behavioral problems, we do not address longitudinal changes in caregivers’ subjective reactions to behavioral problems, which we have reported in a separate article (19).

RESULTS

Factor Analysis of MPBC Items
In order to identify meaningful clusters of behavioral problems for further analysis, a principal components analysis was conducted on the intercorrelation matrix from the MPBC-R items for the 150 participants who provided complete data at baseline. The scree test (23) indicated that four factors should be retained for interpretation. These four factors accounted for 44.8% of the total variance of the items. A varimax rotation was applied, and each item that shared 10% or more of its variance with a factor (i.e., varimax factor loading of 0.32 or greater) was identified as a meaningful contributor to that factor (23). These varimax factor loadings are presented in Table 1.

Table 1. Varimax Rotated Factor Loadings

<table>
<thead>
<tr>
<th>MBPC-R Item Content</th>
<th>Factor 1</th>
<th>Factor 2</th>
<th>Factor 3</th>
<th>Factor 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Repetitive questions</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>0.73</td>
</tr>
<tr>
<td>Memory of recent events</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>0.56</td>
</tr>
<tr>
<td>Memory of significant past</td>
<td>0.61</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Confusing past and present</td>
<td>0.45</td>
<td>0.38</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Losing things</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>0.77</td>
</tr>
<tr>
<td>Hiding things</td>
<td>0.36</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Can’t find way indoors</td>
<td>0.64</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Can’t find way outdoors</td>
<td>0.63</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Wandering/lost</td>
<td>0.42</td>
<td>0.37</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Recognition of familiar places</td>
<td>0.69</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Recognition of familiar people</td>
<td>0.67</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Recognition of familiar objects</td>
<td>0.62</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Forgetting day</td>
<td>—</td>
<td>—</td>
<td>0.45</td>
<td>0.50</td>
</tr>
<tr>
<td>Can’t self-start activities</td>
<td>—</td>
<td>—</td>
<td>0.74</td>
<td>—</td>
</tr>
<tr>
<td>Unable to keep busy</td>
<td>—</td>
<td>—</td>
<td>0.72</td>
<td>—</td>
</tr>
<tr>
<td>Following people</td>
<td>0.44</td>
<td>—</td>
<td>0.34</td>
<td>—</td>
</tr>
<tr>
<td>Restless/agitated</td>
<td>—</td>
<td>0.61</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Spends time inactive</td>
<td>—</td>
<td>—</td>
<td>0.70</td>
<td>—</td>
</tr>
<tr>
<td>Constantly talkative</td>
<td>0.45</td>
<td>0.43</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Talking little or none</td>
<td>—</td>
<td>—</td>
<td>0.69</td>
<td>—</td>
</tr>
<tr>
<td>Suspicious/accusative</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>0.35</td>
</tr>
<tr>
<td>Embarrassing in public</td>
<td>0.32</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Waking people</td>
<td>0.32</td>
<td>—</td>
<td>0.36</td>
<td>—</td>
</tr>
<tr>
<td>Sad/depressed</td>
<td>—</td>
<td>—</td>
<td>0.59</td>
<td>0.39</td>
</tr>
<tr>
<td>Anxious/worried</td>
<td>—</td>
<td>—</td>
<td>0.53</td>
<td>—</td>
</tr>
<tr>
<td>Angry</td>
<td>—</td>
<td>0.71</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Striking out</td>
<td>—</td>
<td>0.57</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Destroying property</td>
<td>—</td>
<td>0.47</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Dangerous behavior</td>
<td>—</td>
<td>0.58</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Hallucinations</td>
<td>0.48</td>
<td>—</td>
<td>—</td>
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</tr>
</tbody>
</table>
The factor loading pattern suggested that the four symptom clusters represent problems with general cognitive disturbance, emotional and impulsive behaviors, apathy, and forgetful behaviors, respectively. Subscale scores representing each factor were calculated by determining the mean response of the items that loaded on each factor. The magnitude of these subscale scores, therefore, was independent of the number of items contributing to each factor, allowing for comparisons of severity across factors.

Initial Impairment

Initial scores on the measures of cognitive and behavioral impairment are shown in Table 2. Briefly, although patients in the sample are generally moderately to severely impaired, the sample has a wide range of impairment, and the scores suggest little problem with floor and ceiling effects.

Simple t tests were used to compare African American and white caregiver ratings of frequency of memory and behavioral problems at baseline. For total frequency, no ethnic differences were observed. Subscale scores for frequency of memory and behavioral problems did not differ for general cognitive disturbance, emotional and impulsive behavior, or apathy, but African American caregivers reported a lower frequency of forgetful behaviors than did white caregivers; T(148) = 2.63, p < .01, and M = 1.32 and 1.60, respectively. We have previously reported that African American caregivers appraise behavioral problems and self-care problems as less stressful, and they report a higher self-efficacy in managing these problems, when compared with white caregivers (18).

Cross-Sectional Analyses

Hierarchical regression analyses were conducted to test the linear and possible curvilinear associations between MMSE and the MBPC-R total and subscale frequency scores. For each dependent variable, the linear trend was entered and tested for significance first, and a quadratic term was then added on a subsequent step to determine if a significant curvilinear effect was evident. These results are summarized in Table 3.

For the MBPC-R total score, a significant linear effect was found such that, as expected, memory and behavioral problems were more evident for patients with a greater severity of dementia. The curvilinear effect was not statistically significant for the MBPC-R total score. As expected, different patterns were observed on the subscales across severity. For the general cognitive disturbance and apathy subscales, only linear effects were statistically significant, but significant quadratic effects were found for emotional and impulsive behaviors and for forgetful behaviors. Both linear and quadratic effects were statistically significant for emotional and impulsive behavior problems, whereas only the quadratic effect was statistically significant for forgetful behaviors.

Figure 1 depicts the predicted subscale scores for the total MBPC score and each factor-analytic-derived subscale score as a function of MMSE score. Predicted scores were generated from the full model (linear and quadratic) only when the quadratic effect reached statistical significance. Otherwise, the simple linear model is depicted. For patients with mild and moderate dementia, forgetful behaviors are reported to be the most problematic, but these symptoms peak at an MMSE score of 14 and then decrease as the MMSE score further declines. Conversely, emotional and impulsive behavior problems are reported less often, but these problems begin to increase once the MMSE score drops below 19, and this increase continues to accelerate as the MMSE score further declines.

Longitudinal Analyses

For the 61 patients and their caregivers who provided longitudinal data, test-retest correlations indicated that the factor-analytic-derived MBPC-R frequency subscales showed moderate to high temporal stability (r = 0.50–0.72; p < .01). Patients were categorized into four severity levels based on initial MMSE score: severity 1, MMSE = 21–30, n = 13; severity 2, MMSE = 11–20, n = 26; severity 3, MMSE = 1–10, n = 12; and severity 4, MMSE = 0, n = 10. A series of 4 (severity level) by 3 (initial, 1 year, 2 year) mixed model analyses were conducted for the MPBC-R to-
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These results are displayed in Figures 2–6. If memory and behavior problems increase at a steady rate across time for all severity groups, then the main effect for year of assessment should be statistically significant. However, this effect was not statistically significant for any MBPC-R scale (all \( p > .14 \)). Instead, the total score and each subscale showed a significant severity Group \( \times \) Year interaction effect: MBPC-R total score \( F(6,114) = 8.19, \) Huynh-Feldt (HF) \( p < .001, \) Huynh-Feldt epsilon (HF-\( \epsilon \)) = 1.00; general cognitive disturbance \( F(6,114) = 5.91, \) HF \( p < .001, \) HF-\( \epsilon \) = 0.93; emotional and impulsive behaviors \( F(6,114) = 4.63, \) HF \( p = .003, \) HF-\( \epsilon \) = 1.00; apathy \( F(6,114) = 2.60, \) HF \( p = .02, \) HF-\( \epsilon \) = 1.00; and forgetful behaviors \( F(6,114) = 2.73, \) HF \( p = .02, \) HF-\( \epsilon \) = 1.00.

As Figures 2–6 indicate, the patterns are similar for all MBPC-R scales. Those with initial MMSE scores ranging from 11 to 30 (severity levels 1 and 2) tended to show increased memory and behavioral problems across time, whereas those with initial MMSE scores ranging from 1 to 10 (severity 3) tended to show stable scores across time. Caregivers of those with initial MMSE scores equal to zero (severity 4) reported fewer problems across time on all scales.

Regarding the curvilinear trends observed from the cross-sectional analyses, it is interesting to note that the means from the longitudinal analysis generally fit the same pattern. In particular, caregivers of those with mild dementia (MMSE = 21–30, severity 1) actually reported fewer problems on the emotional and impulsive behaviors subscale from baseline \( (M = 0.50) \) to 1-year follow-up \( (M = 0.40) \), but this decrease was not statistically significant. Also, mean scores on the forgetful behaviors subscale for those with moderate dementia (MMSE = 11–20, severity 2) showed an inverted U shape as predicted by the cross-sectional results, but again pairwise contrasts of these specific means failed to achieve conventional levels of statistical significance.

DISCUSSION

This study combined cross-sectional and longitudinal approaches to characterize the progression of behavior problems during the course of Alzheimer’s disease. Dementia severity, as measured by patients’ scores on the MMSE,
was found to have a linear relationship with a global index of the frequency of memory and behavioral problems in a cross-sectional analysis, but this finding masked significant curvilinear relationships between dementia severity and specific types of behavioral problems. A factor analysis of the MBPC-R was used to empirically identify four meaningful categories of behavior problems, and subscales derived from the factor analysis were found to show different patterns of association with dementia severity.

One subscale consisted of multiple cognitive complaints and was interpreted to reflect general cognitive disturbance. This construct might be expected to show a linear relationship with performance on a general measure of cognitive functioning, and the cross-sectional regression analysis confirmed such an association with the MMSE score. A linear association with MMSE was also found for the apathy subscale, which appeared to reflect concerns with initiating and maintaining basic activities. Statistically significant curvilinear associations were found for subscales that assessed emotional and impulsive behaviors and forgetful behaviors. For emotional and impulsive behaviors, problems were minimal and stable across the MMSE range for mild dementia, but began to intensify in moderate dementia and continued to worsen as the MMSE suggested more and more severe dementia. In contrast, forgetful behaviors, which were rated as the most severe of the four types of behavior problems by the caregivers of patients with mild and moderate dementia, clearly peaked in the moderate dementia range and then declined as the MMSE score indicated more severe dementia.

It is highly unlikely that memory improves as dementia severity increases. The curvilinear effect for the forgetful behaviors subscale might, therefore, appear to be counterintui-
tive at first glance. However, as problems with general cognitive functioning (e.g., recognition of familiar people and objects) and apathy increase, problems with forgetfulness and recent memory may not be as evident because more severe patients lack the initiative and organization to function in situations where recent memory is expected. In order to demonstrate forgetfulness, one must first be in a position to comprehend and understand new information. These opportunities become more limited as the general level of cognitive disturbance increases. Previous studies have observed that a decline in recent memory is particularly problematic in early AD, whereas impairment of remote memory and other cognitive functions becomes more severe in the later stages of the disease (2,24). The present pattern of results is consistent with this progression from the caregivers' point of view.

Prior to the longitudinal analyses, patients were divided into four severity groups based on initial MMSE score. In addition to mild (MMSE = 21–30), moderate (MMSE = 11–20), and severe (MMSE = 1–10) groups, a fourth group of patients whose initial MMSE scores were exactly equal to zero was included. Even though AD continues to progress across time in these most severe cases, changes across time cannot be predicted for this group with a cross-sectional approach because the MMSE score is already at its minimum. In general, the longitudinal results were consistent with the cross-sectional findings. Most behavior problems became more severe as time passed for those patients with mild and moderate dementia at baseline, but the caregivers of the most severely demented patients actually reported gradual improvements in behavior problems as the years passed and these patients became more globally incapacitated. Similar improvements across time for the most severely impaired patients were observed by

Figure 5. Mean apathy subscale scores across time for four severity groups.

Figure 6. Mean forgetful behaviors subscale scores across time for four severity groups.
Koss and colleagues (25) in their study of agitation frequency.

This study has several limitations. First, the behavioral problems were measured through caregiver reports. There may be caregivers who minimize the occurrence of certain behaviors or simply have difficulty remembering a number of problems over 1 week of providing care. In addition, although a range of impairment was represented in the sample, the patients in this study continued to be cared for at home. Thus, it is possible that patients in a nursing home may show differing patterns of behavioral problems.

Even though Alzheimer’s disease is a progressive dementia characterized by increasing cognitive and behavioral deterioration, it appears to be inaccurate to expect each of these domains to show the same linear decline across time. In fact, some of the behavioral problems that are often considered to be the most stressful by family caregivers actually decline in frequency over time once the patients become severely impaired. Thus, families and clinicians should be informed that caregivers may actually experience some relief from the problems of managing certain behavioral problems in late dementia, although problems with activities of daily living (ADL) continue to become increasingly more severe. Another important implication for longitudinal studies and intervention projects is that it is important to carefully assess different aspects of memory and behavioral problems, as they show different longitudinal courses of progression. Clinical trials of interventions for behavioral problems in AD that include patients with heterogeneous levels of dementia severity may unwittingly pool patients together who are likely to show both increased and decreased behavioral problems over time simply as a result of disease progression. Ideally, intervention studies should target patients within a relatively narrow range of severity, or consider severity level to be an important predictor variable that may interact with treatment in the analysis. Outcome measures should include indices of not only overall behavioral problems, but also specific domains of function.

By providing more specific information about the pattern of expected changes across time, clinicians should be able to better assist family caregivers to minimize their own distress and to improve the quality of care that they are providing to their loved ones. By considering the multiple domains of behavior disturbance, clinicians and family members should also gain greater insight into the true progression of symptom patterns over the course of this disease.

Acknowledgments

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