Longitudinal Relationships Between Alzheimer Disease Progression and Psychosis, Depressed Mood, and Agitation/Aggression

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Objectives: *Behavioral and psychological symptoms of dementia (BPSD) are prevalent in Alzheimer disease (AD) and are related to poor outcomes such as nursing home placement. No study has examined the impact of individual BPSD on dependence, a clinically important feature that reflects changing patient needs and their effect on caregivers. The current study characterized independent cross-sectional and longitudinal relationships between three BPSD (psychosis, depressed mood, and agitation/aggression), cognition, and dependence to better understand the interplay between these symptoms over time.* **Design:** *The Predictors Study measured changes in BPSD, cognition, and dependence every 6 months in patients with AD. Cross-sectional and longitudinal relationships between individual BPSD, cognition, and dependence over 6 years were characterized by using multivariate latent growth curve modeling. This approach characterizes independent changes in multiple outcome measures over time.* **Setting:** *Four memory clinics in the United States and Europe.* **Participants:** *A total of 517 patients with probable AD.* **Measurements:** *Columbia University Scale for Psychopathology, modified Mini–Mental State Examination, and Dependence Scale.* **Results:** *Both psychosis and depressed mood at study entry were associated with worse subsequent cognitive decline. Independent of cognitive decline, initial psychosis was associated with worse subsequent increases in dependence. Rates of increase in agitation/aggression separately correlated with rates of declines in both cognition and independence.* **Conclusions:** *Although purely observational, our findings support the poor prognosis associated with psychosis and depression in AD. Results also show that agitation/aggression tracks declines in cognition and independence independently over time. Targeted intervention for individual BPSD, particularly psychosis, could have broad effects not only on patient well-being but also on care costs and family burden.* (Am J Geriatr Psychiatry 2013; ■:■–■)

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Behavioral and psychological symptoms of dementia (BPSD) are prevalent in Alzheimer disease (AD), occurring in 75% of patients.[1] They include symptoms such as agitation, depression, and psychosis. BPSD accelerate poor outcomes in AD, including nursing home placement. A recent review found that in 21 of 36 studies, the presence of BPSD predicted nursing home placement among individuals with dementia.[2] As is customary with research on BPSD and family outcomes,[3] most studies combined all BPSD into a single category despite evidence for disparate trajectories. A previous study on a subset of the current sample followed up over a shorter period of time suggests that agitation is common and persistent in AD, whereas psychotic symptoms are persistent but less common, and depressed mood rarely persists.[4]

Results from studies examining the impact of individual BPSD on nursing home placement have been mixed. Agitation/aggression is repeatedly associated with nursing home admission,[5–7] but results regarding psychosis and depression are inconsistent.[2,6,8,9] Unfortunately, many of these studies featured relatively short follow-up, did not control for other contributors to patient care needs (e.g., cognitive decline), and/or focused on only one BPSD. The current article sought to overcome these limitations by examining the impact of individual BPSD (i.e., psychosis, depressed mood, agitation/aggression) on patient care needs over 6 years in a sample of 517 patients with AD, controlling for other factors that influence disease outcomes (e.g., education, cognitive decline).

In addition, the current study used a dynamic, quantitative measure of patient dependence rather than nursing home placement to index patient care needs. Nursing home placement is influenced not only by patient care needs but also by caregiver factors and financial, cultural, and regional differences.[2,10,11] Racial differences in formal care service utilization exist,[12] and the number of in-home services covered by Medicaid differs according to geographic location. Nursing home placement may not fully capture a patient's needs or the impact of these needs on the family. Level of dependence correlates with dementia severity,[13] level of disability,[14] home health aide use,[15] longitudinal increases in medical and nonmedical costs,[16] overall resource utilization,[14] increases in caregiving time,[17] and caregiver burden.[14] Thus, identifying and treating specific contributors to dependence have the potential for wide-ranging effects not only on patient quality of life but also on care costs and family burden.

The goals of the current study were to characterize: 1) cross-sectional and longitudinal relationships between individual BPSD (i.e., psychosis, depressed mood, agitation/aggression) and cognition; and 2) cross-sectional and longitudinal relationships between dependence and individual BPSD independent of cognitive decline. Based on previous findings of disparate courses of individual BPSD[4] and effects of BPSD on nursing home placement,[2] we predicted that worsening agitation/aggression and psychosis would each relate to cognitive decline and increased dependence, whereas depression would only be associated with cognition and dependence cross-sectionally.

METHODS

Participants and Procedures

The sample included 517 patients with probable AD enrolled in The Predictors Study, a multicenter study of predictors of disease course in AD.[18] Local institutional review boards at all participating sites approved the study. Written informed consent was obtained directly from patients at study entry. All patients had mild dementia at enrollment and were deemed capable by a study physician of providing informed consent. Patient assent was documented at each subsequent visit in accordance with institutional review board requirements. Characteristics of the sample are shown in Table 1. Race and ethnicity were determined by using patient and caregiver report according to the format of the 2000 US Census.