

Aggression in the Elderly

Henry Brodaty, M.D., F.R.A.N.Z.C.P.,
and Lee-Fay Low, B.Sc. (Hons) (Psyc)

Aggression is a common behavioral symptom of dementia. Aggression is associated with fronto-temporal dementia, greater dementia severity, cognitive decline, and other behavioral and psychological disturbances. It is influenced by the environment and has been correlated with neuropathologic changes and certain polymorphisms. Aggression in dementia patients results in higher psychotropic use and distress to family caregivers and nursing home staff; it is predictive of institutionalization. There is empirical evidence for the efficacy of pharmacotherapy and more limited evidence for psychosocial interventions in the successful management of aggression in persons with dementia. Management of aggression should include comprehensive assessment of medical, psychological, and environmental variables.
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In the elderly, aggression occurs in a variety of contexts, including psychiatric disorders such as schizophrenia and psychotic depression, delirium, and dementia.

There appears to be no literature specific to the effects of old age on aggression occurring in schizophrenia and depression, nor could we locate any studies focusing on aggression in the delirious elderly. There have been no published randomized controlled medication trials for delirium in the elderly. We refer readers to the American Psychiatric Association Practice Guideline for the Treatment of Patients With Delirium, which includes a section on the elderly.¹ In this article, we focus on aggression in dementia.

DEFINITION OF AGGRESSION IN DEMENTIA

Aggression in dementia has been defined as “an overt act involving delivery of a noxious stimulus to another person which was clearly not accidental.”^{2(p457)} Aggression can be physical, verbal, and sexual. Verbal aggression, also called “vocally disruptive behavior,” includes screaming, swearing, and calling out. Physical and verbal aggression are highly correlated,³ although verbal aggression usually

occurs more often than physical aggression.^{4,5} Both types of aggression are commonly included in definitions of agitation. Because of this overlap, we report research on agitation when aggression specifically has not been similarly investigated.

Aggression is a symptom that may exist independently or in conjunction with other disturbances such as psychosis or depression. Evidence of independence from other behavioral and psychological symptoms of dementia, including nonaggressive agitation, comes from factor analyses of the Present Behavioural Examination (PBE), which yielded an aggression as well as other factors,^{6,7} and the Cohen-Mansfield Agitation Inventory (CMAI), which produced physical and verbal aggression and nonaggression factors.⁸ However, in a cluster analysis, agitated/aggressive behaviors were present in both a class with predominantly depressive symptoms and a class with psychotic features.⁹

PREVALENCE AND NATURAL HISTORY

The prevalence of aggression in dementia varies with the severity of the condition (see Dementia Characteristics), the population being studied, and the method of measurement. In an epidemiologic study of community dwellers and nursing home residents, 23.7% of those with dementia were rated as being agitated or aggressive.¹⁰ Verbal aggression in community samples has been reported to range from 33% to 59%,^{11,12} and physical aggression, from 11% to 46%.^{11,13} Studies in nursing home samples have found rates of reported verbal aggression between 51% and 52%, rates of physical aggression between 31% and 42%, and a rate of sexual aggression of 4%.^{14,15} Over a 3-day observation period, 45% of older hospitalized patients (71% with dementia and 13% with chronic schizophrenia)

From the School of Psychiatry, University of New South Wales (Dr. Brodaty), and the Academic Department for Old Age Psychiatry, Prince of Wales Hospital (both authors), Sydney, Australia.

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Corresponding author and reprints: Henry Brodaty, M.D., Academic Department for Old Age Psychiatry, Prince of Wales Hospital, Randwick, 2031, New South Wales, Australia.

were mildly aggressive, 15% were moderately to severely aggressive, and 6% inflicted an injury on another person.⁴

An extraordinary finding was reported from a 10-year longitudinal, prospective study: 96% of subjects with Alzheimer's disease (AD), vascular dementia, or mixed dementia (AD plus vascular dementia) demonstrated severe or persistent aggressive behavior at some time during the course of the dementia.¹⁶ Other types of aggressive behavior preceded the onset of physical aggression in 90% of those who were physically aggressive.¹⁶ Physical aggression in nursing home residents with dementia is usually preceded by verbal aggression.¹⁷ Physical aggression developed in 62% of 48 subjects with autopsy-confirmed pure AD, a mean \pm SD of 6.3 ± 3.2 years from onset of dementia and 2.6 ± 1.8 years before death.⁷ In a retrospective medical review of 100 autopsy-confirmed AD patients, aggression was documented in over 40% of patients, with a mean onset of 23 months after diagnosis.¹⁸ In a 5-year prospective longitudinal study of initially community-dwelling AD patients, rates of physical aggression tripled in the sample over 3 years.¹⁹

Aggression does not endure for the entire period of dementia when it occurs. Median overall duration of physical aggression has been reported to be 16 months (interquartile range, 8–32 months).¹⁶ In another longitudinal study, physical aggression was the least persistent behavioral disturbance, occurring in only 2.8% of subjects over 4 consecutive assessments conducted every 6 months,¹⁹ although Markov analyses indicated a 53% probability for physical aggression persisting from one assessment to the next. The authors suggested that physical aggression may persist in more advanced stages of dementia.

EFFECTS OF AGGRESSION

Aggression has adverse effects on the patients, family caregivers, and nursing staff. People with dementia who display aggression are more likely to be given antipsychotic medication or be physically restrained than those who are nonaggressive.²⁰ Patients with dementia and aggression may experience accelerated decline. Teri and colleagues²¹ found that patients with AD and agitation (defined as extremely active: excited, frenzied, unable to sit still) declined on average 1.4 points faster per year on the Mini-Mental State Examination than subjects who were not agitated.

The presence of difficult behaviors in general,²² and aggression in particular,^{23,24} is a significant predictor of institutionalization. Paradoxically, people with dementia and behavioral disturbances have more difficulty getting a place in a nursing home.²⁵

Behavioral disturbance in patients with dementia is the single largest predictor of distress in family caregivers, robustly accounting for 25% of caregiver psychological morbidity across many different Western countries and

different measures of morbidity.^{26,27} Aggression is perceived by caregivers as more distressing than other behavioral and psychological symptoms of dementia including hallucinations, delusions, and depression.¹¹ Nursing home staff also find aggressive behavior in residents with dementia to be stressful, particularly if the aggression is perceived as threatening.²⁸ Staff report that physical abuse causes distress 92% of the time and verbal abuse causes distress 90% of the time.²⁹

MEASUREMENT

Aggression in dementia is usually measured from informant reports. Measurements of aggression are included in many general behavioral and psychiatric rating scales, such as the Behavioral Pathology in Alzheimer's Disease Rating Scale (BEHAVE-AD),³⁰ Neuropsychiatric Inventory,³¹ Manchester and Oxford Universities Scale for the Psychopathological Assessment of Dementia (MOUSEPAD),³² PBE,³³ and CERAD Behavior Rating Scale for Dementia.³⁴ Agitation rating scales such as the CMAI also have items measuring aggression.⁸

Scales specifically measuring aggression include the Rating Scale for Aggressive Behavior in the Elderly (RAGE),³⁵ Overt Aggression Scale,³⁶ and Ryden Aggression Scale.³⁷ RAGE was designed for completion by ward-based nursing staff and measures aggressive behavior over the past 3 days. It includes 19 aggression items, a rating of injury inflicted on others or self, whether the patient has been isolated or physically or chemically restrained, and an overall aggression rating. The Overt Aggression Scale is designed to allow staff to quantify the severity of specific aggressive episodes in psychiatric settings. It consists of 16 aggressive items divided into 4 categories (verbal aggression, physical aggression against self, physical aggression against objects, and physical aggression against other people), a record of the time and duration of the incident, 11 possible interventions, and comments. The Ryden Aggression Scale is an informant-completed scale designed to measure aggressive behavior in the community. It consists of 25 items (physical, verbal, and sexual aggression) rated on a 6-point Likert scale (0 = never to 5 = 1 or more times daily).

Trained observers can use the Agitated Behavior Mapping Instrument³⁸ to directly quantify agitation (including verbal and physical aggression) in a nursing home setting. This instrument requires extensive rater training and time to complete.

RISK FACTORS AND ETIOLOGY

Demographics

In some studies,^{13,39} but not in others,⁴⁰ male gender has been found to increase likelihood of aggressive behavior. No relationship has been found between age and aggression.^{16,41,42}

Dementia Characteristics

Apart from frontotemporal dementia (FTD), it does not appear that dementia type influences the rate of aggression. No differences have been found between rates of aggression in subjects with AD, vascular dementia, and mixed or alcohol-induced dementia^{3,39,43} or between those with AD and Lewy body dementia (LBD).⁴⁴ Frontotemporal dementia, however, is viewed by some primarily as a neurobehavioral disorder rather than a neuropsychological one.⁴⁵ Significantly higher rates of assault and other anti-social behaviors are reported in FTD compared with AD,⁴⁶ especially in subjects with right-variant FTD.⁴⁷

Aggression increases with dementia severity until the very end stages of the disease. Decreased cognition and greater impairment of activities of daily living are associated with greater severity of physical aggression.^{3,39,40} Impaired communication is also associated with aggression.²⁰

Aggression has been found to be associated with the occurrence of other behavioral and psychological disturbances. Psychoses are significantly associated with aggression in dementia,^{39,48,49} explaining 22% of variance in aggression scores after excluding patients on treatment with psychotropics.¹² Depression has been correlated with physical aggression,^{20,39} and disorientation has been correlated with verbal aggression.²⁰

Neuropathologic Correlates

In subjects with dementia, a positive correlation has been found between the magnitude of loss of neurons in the rostral locus ceruleus (the major nucleus of origin of noradrenergic fibers in the brain) and aggressive behavior.⁵⁰ In dementia patients matched for demographics, cognitive impairment, and other behavioral disturbance, patients with aggression had significant hypoperfusion in the left anterior temporal cortex, additional bilateral dorsofrontal, and right parietal cortex compared with nonaggressive patients.⁵¹ At autopsy, the best predictor in AD patients of lowered choline acetyltransferase activity (ChAT) was aggressive behavior over the course of the disease. In the midfrontal and superior frontal cortex, ChAT has a curvilinear relationship to aggression, with higher ChAT levels in patients with moderate aggression than patients with mild or severe aggression at some stage during the dementia.⁵²

Biochemical Correlates

Low serotonin levels have been implicated in aggression in psychiatric disorders such as schizophrenia⁵³ and may also play a role in aggression in dementia.⁵⁴

Genetic Risk Factors

The homozygous long variant (*l*) genotype and the *l* allele of an identified biallelic polymorphism of the serotonin transporter promoter region (5-HTTPR) have been found to be significantly associated with an increased

risk of aggressive symptoms in patients with AD.⁵⁵ The *ll* genotype is also associated with increased expression of the transporter protein and increased speed of response to serotonin reuptake inhibitor treatment. There is some evidence to suggest that the 5-HTTPR *l* allele increases risk for psychosis and aggression in AD patients.⁵⁶

Psychological Factors

Physical aggression during dementia has been associated with higher premorbid neuroticism,⁵⁷ although this finding has not been replicated.^{58,59} Retrospective ratings of personality may not be reliable and may be biased by current behavioral symptoms.⁵⁹

Environmental Factors

Aggression in nursing homes usually occurs in response to intrusions into the resident's personal space by staff or other residents^{14,17} or during personal care.^{16,41,60} In 2 psychogeriatric wards, a moderately strong correlation was found between aggression and how close staff reported feeling emotionally to the patient.⁶¹ In a day care center, physical aggression was also found to be predicted by poorer relationships with staff and other participants.⁶² When age, gender, and cognitive function were controlled for, a higher resident-to-bedroom ratio and being in a home with more functionally impaired residents significantly predicted higher levels of aggressiveness.⁶³

Multifactorial Etiology

It has been theorized that the interaction between neurobiological dysregulation, cognitive impairment, and aversive environmental stimuli cause aggressive behavior in dementia. This interaction has been called the "additive model."⁶⁴ Other factors reported by clinicians as being important for the development of aggression include pain.⁶² Despite all of these potential etiologic factors, aggression cannot always be attributed to an obvious reason or precipitant; no causal factor could be attributed in 11% of subjects in one study.¹⁶

TREATMENT

Treatment for aggression can be considered using a biopsychosocial model. In reviewing the literature, we found that intervention studies for aggression have often confounded aggression and agitation. The term *agitation*, which strictly refers to motor restlessness reflecting inner mental perturbation,⁶⁵ is often used as a catch-all for all behavioral disturbances occurring in dementia.

Prevention

Specific pharmacologic interventions to prevent the development of aggression may be distant, as its etiology is not well understood. There is evidence that acetylcholine inhibitors may delay the emergence of neuropsychiatric

symptoms.⁶⁶ Caregiver training programs may be able to delay the emergence of behavioral problems, although this has not yet been proved.

Biological

Antipsychotics. Both typical and atypical antipsychotics have been shown to be efficacious in treating agitation/aggression in demented patients, although atypical antipsychotics have better side effect profiles in the elderly.⁶⁷ Most randomized placebo-controlled trials of antipsychotics have been conducted in nursing home samples. Standard-dose haloperidol (2–3 mg) was shown to be superior to low-dose haloperidol (0.5–0.75 mg) or placebo for disruptive behavior.⁶⁸ Three randomized double-blind placebo-controlled trials of risperidone in demented nursing home residents have demonstrated the efficacy of risperidone (mean dose = 1.03 mg/day) in reducing agitation and aggression.^{69–71}

In a randomized double-blind trial, tiapride and haloperidol performed equally over placebo in decreasing agitation and aggressiveness in hospitalized or institutionalized patients with dementia.⁷² A randomized double-blind nursing home trial found that olanzapine (5 and 10 mg, but not 15 mg) was significantly better than placebo in treating agitation/aggression⁷³ and continued to be effective and well tolerated in the open-label extension.⁷⁴ A randomized double-blind trial of intramuscular olanzapine (2.5 mg, 5.0 mg) showed significant improvement over intramuscular lorazepam (1.0 mg) or placebo in improving agitation in patients with AD and/or vascular dementia.⁷⁵ A double-blind controlled trial with zuclopenthixol produced improvement on aggressive behavior in hospitalized elderly patients with dementia.⁷⁶

Anticonvulsants. One randomized double-blind, placebo-controlled trial; 3 open-label trials; and 1 case series review of sodium valproate with demented subjects suggest that valproate is better than placebo in reducing agitated behaviors and physical aggression, but not verbal aggression.^{77–81}

In a randomized double-blind trial in nursing home residents with dementia and agitation, carbamazepine was significantly better than placebo in global improvement and decreasing psychopathology. Secondary analyses showed that changes were due to reductions in agitation and aggression.⁸² A small (N = 9) double-blind pilot study suggested that carbamazepine improves aggression, depression, and cerebral efficiency in patients with frontal lobe dysfunction.⁸³

Acetylcholinesterase inhibitors. There is some evidence that acetylcholinesterase inhibitors may reduce levels of aggression. Galantamine (16 and 24 mg) significantly improved behavioral symptoms in AD in a double-blind controlled trial.⁶⁶ Behavioral improvement on the Neuropsychiatric Inventory was demonstrated in 1 double-blind placebo-controlled trial⁸⁴ and 2 open-label studies of

donepezil (5 mg, 10 mg).^{85,86} However, in a randomized double-blind trial set in nursing homes, behavioral disturbance in both donepezil and placebo groups improved.⁸⁷

Rivastigmine (mean dose of 9.4 mg) significantly improved behavioral disturbance in patients with LBD, although agitation/aggression did not specifically change with treatment.⁸⁸ Donepezil improved behavior in a case series of LBD patients.⁸⁹

Benzodiazepines. Clonazepam (mean dose of 1.2 mg for 2 weeks) was shown in a retrospective consecutive case series to improve behavioral disturbance and agitation in demented hospitalized patients.⁹⁰ Lorazepam and alprazolam both reduced agitation in demented patients, although no control group was used. Lorazepam produced more serious side effects.⁹¹

Selective serotonin reuptake inhibitors. In a randomized double-blind trial, citalopram (10–20 mg) and perphenazine (mean dose of 6.5 ± 1.7 mg) were equally better than placebo in reducing behavioral disturbance in patients with dementia.⁹² Trazodone was equally as good as haloperidol in reducing agitated behaviors associated with dementia, although verbally aggressive behaviors responded preferentially to trazodone.⁹³ Improvement in agitation by trazodone-treated patients was associated with mild depressive symptoms in subjects with dementia at baseline.⁹⁴

Others—lithium, estrogens, anti-androgens. Double-blind placebo-controlled trials have demonstrated that β -adrenergic receptor blocking agents (β -blockers) have some efficacy in treating aggression in schizophrenia.^{95,96} A case series of 12 demented patients has shown that low-dose propranolol effectively reduced physical and verbal aggression in 8 of those patients.⁹⁷ Another case report described propranolol as effective in treating verbal and physical but not sexual aggression in a patient with dementia and Kluver-Bucy syndrome. Sexual aggression later responded to leuprolide.⁹⁸

There are case reports on the effectiveness of conjugated estrogens in managing physical and sexual aggression in males with dementia who were unresponsive to antipsychotics and other psychotropics.⁹⁹ One 4-week double-blind placebo-controlled trial with patients with moderate-to-severe dementia showed that estrogen therapy was associated with lower total aggression and decreased frequency of physical aggression, but not statistically significant differences in verbal, sexual, resistive, or self-directed aggressive behaviors.¹⁰⁰ A case series of 4 demented male patients showed that medroxyprogesterone acetate treatment was associated with a decrease in sexual aggression.¹⁰¹

Psychological

Psychological therapies can target patients directly or involve caregivers or staff. A walking program for 11 confused nursing home residents significantly decreased aggressive incidents on activity days.¹⁰² A daily gentle ex-

ercise program, also with 11 confused nursing home residents, decreased agitated behaviors.¹⁰³

A trial in which preferred music was played during the bath times of aggressive demented residents suggested that the music was beneficial in reducing the total number of aggressive behaviors and, more specifically, hitting.¹⁰⁴ A crossover, controlled trial was conducted of individualized versus classical relaxation music played for 30 minutes twice a week for 6 weeks for agitated demented nursing home residents. Results showed that both types of music reduced agitated behaviors compared with baseline, but individualized music was more effective than generic classical music.¹⁰⁵

Behavioral management training for caregivers can successfully reduce agitation and possibly aggression in patients with dementia, depending on the "dose" of intervention. A brief (4 sessions over 8 weeks) behavior management program produced a trend toward reducing aggressive behaviors.¹⁰⁶ A psychoeducational behavior management program for caregivers (90 minutes a week for 12 weeks) yielded a significant improvement in agitation and anxiety in dementia patients.¹⁰⁷ Behavioral management training (11 sessions over 16 weeks) for community caregivers was as efficacious as haloperidol, trazodone, and placebo in reducing agitation in AD patients.¹⁰⁸

A staff training program on application of behavioral management approaches during personal care reduced aggressive behavior, p.r.n. medication use associated with bathing, and staff injuries from patient aggression during personal care in a nursing unit in a psychogeriatric hospital.¹⁰⁹ In a case series of 5 nursing home residents with agitation and aggression, individualized systematic identification of triggers of these behaviors by researchers and training of staff to avoid them resulted in successful management.¹¹⁰ In summary, there appears to be some evidence, albeit from small or open trials, that psychological techniques can be effective in reducing aggression.

Environment

In a crossover study,¹¹¹ bright light therapy (30 minutes twice a day for 5 consecutive days) reduced agitation and increased cooperation in nursing home residents with dementia, although this positive effect was not found in another study.¹¹²

Personalized interactive audiotapes similar to a one-sided conversation with a family member or friend, called "Simulated Presence," have been compared with a tape of a person reading emotionally neutral newspaper articles or standard care for subjects with moderate dementia and agitation/aggression. Staff records showed a decrease in agitation in the Simulated Presence group, although this was not confirmed by direct observation of agitation.¹¹³

Special care units are parts of, or whole, nursing homes specifically designed and staffed for dementia care. Placement in special care units has decreased agitation in de-

menting residents in some studies,¹¹⁴ but not others.²⁵ In special care units, lower agitation level has been found to be associated with higher-rated physical environment and staff activities on a therapeutic environment scale, low rates of physical restraint use, a high proportion of residents in bed during the day, and small unit size.¹¹⁵

CONCLUSIONS

Data are accumulating for effective interventions for aggression and agitation in patients with dementia. While potential algorithms of treatment approaches have not been evaluated, common clinical practice has been articulated.¹¹⁶ A meticulous history, thorough physical and psychological examination, careful observation with good record keeping, and relevant investigations are the bases for any management approach. If medical causes, such as a urinary tract infection or pain; psychological factors, such as depression; and environmental triggers, such as overcrowded ward environment or insufficient or excessive stimulation, can be identified, further management clearly should be directed to this cause. A diary that documents the antecedents, behaviors, and consequences (ABC approach) will often pinpoint the precipitant for aggression.

As there are known brain changes underpinning aggression, it is hardly surprising that in a proportion of cases no external cause can be found, psychological and environmental interventions fail, and pharmacotherapy is indicated. No specific medication has been proven to be superior, although there are indications that cholinesterase inhibitors, anticonvulsants, and atypical antipsychotics have utility.

Drug names: alprazolam (Xanax and others), carbamazepine (Tegretol, Eptol, and others), citalopram (Celexa), clonazepam (Klonopin and others), donepezil (Aricept), estrogen (Premarin, Cenestin, and others), galantamine (Reminyl), haloperidol (Haldol and others), leuprolide (Lupron, Viadur, and others), lorazepam (Ativan and others), medroxyprogesterone acetate (Depo-Provera and others), olanzapine (Zyprexa), perphenazine (Etrafon and others), propranolol (Inderal and others), risperidone (Risperdal), rivastigmine (Exelon), trazodone (Desyrel and others).

Disclosure of off-label usage: The authors of this article have determined that, to the best of their knowledge, alprazolam, clonazepam, haloperidol, olanzapine, risperidone, trazodone, and tiapride are not approved by the U.S. Food and Drug Administration for the treatment of aggression and agitation in dementia; carbamazepine is not approved for the treatment of psychopathology in dementia; citalopram and perphenazine are not approved for the treatment of behavioral disturbance in dementia; estrogen, propranolol, valproate, and zuclopenthixol are not approved for the treatment of aggression in dementia; leuprolide and medroxyprogesterone acetate are not approved for the treatment of sexual aggression in dementia; and lorazepam is not approved for the treatment of agitation in dementia.

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