

# Aggression in the Elderly

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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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**I**n 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.<sup>1</sup> 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.”<sup>2(p457)</sup> 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,<sup>3</sup> although verbal aggression usually

occurs more often than physical aggression.<sup>4,5</sup> 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,<sup>6,7</sup> and the Cohen-Mansfield Agitation Inventory (CMAI), which produced physical and verbal aggression and nonaggression factors.<sup>8</sup> However, in a cluster analysis, agitated/aggressive behaviors were present in both a class with predominantly depressive symptoms and a class with psychotic features.<sup>9</sup>

## 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.<sup>10</sup> Verbal aggression in community samples has been reported to range from 33% to 59%,<sup>11,12</sup> and physical aggression, from 11% to 46%.<sup>11,13</sup> 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%.<sup>14,15</sup> Over a 3-day observation period, 45% of older hospitalized patients (71% with dementia and 13% with chronic schizophrenia)

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

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.<sup>16</sup> Other types of aggressive behavior preceded the onset of physical aggression in 90% of those who were physically aggressive.<sup>16</sup> Physical aggression in nursing home residents with dementia is usually preceded by verbal aggression.<sup>17</sup> Physical aggression developed in 62% of 48 subjects with autopsy-confirmed pure AD, a mean  $\pm$  SD of  $6.3 \pm 3.2$  years from onset of dementia and  $2.6 \pm 1.8$  years before death.<sup>7</sup> 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.<sup>18</sup> In a 5-year prospective longitudinal study of initially community-dwelling AD patients, rates of physical aggression tripled in the sample over 3 years.<sup>19</sup>

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).<sup>16</sup> 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,<sup>19</sup> 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.<sup>20</sup> Patients with dementia and aggression may experience accelerated decline. Teri and colleagues<sup>21</sup> 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,<sup>22</sup> and aggression in particular,<sup>23,24</sup> is a significant predictor of institutionalization. Paradoxically, people with dementia and behavioral disturbances have more difficulty getting a place in a nursing home.<sup>25</sup>

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

### 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),<sup>30</sup> Neuropsychiatric Inventory,<sup>31</sup> Manchester and Oxford Universities Scale for the Psychopathological Assessment of Dementia (MOUSEPAD),<sup>32</sup> PBE,<sup>33</sup> and CERAD Behavior Rating Scale for Dementia.<sup>34</sup> Agitation rating scales such as the CMAI also have items measuring aggression.<sup>8</sup>

Scales specifically measuring aggression include the Rating Scale for Aggressive Behavior in the Elderly (RAGE),<sup>35</sup> Overt Aggression Scale,<sup>36</sup> and Ryden Aggression Scale.<sup>37</sup> 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 Instrument<sup>38</sup> 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,<sup>13,39</sup> but not in others,<sup>40</sup> male gender has been found to increase likelihood of aggressive behavior. No relationship has been found between age and aggression.<sup>16,41,42</sup>

## 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<sup>3,39,43</sup> or between those with AD and Lewy body dementia (LBD).<sup>44</sup> Frontotemporal dementia, however, is viewed by some primarily as a neurobehavioral disorder rather than a neuropsychological one.<sup>45</sup> Significantly higher rates of assault and other anti-social behaviors are reported in FTD compared with AD,<sup>46</sup> especially in subjects with right-variant FTD.<sup>47</sup>

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.<sup>3,39,40</sup> Impaired communication is also associated with aggression.<sup>20</sup>

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

## 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.<sup>50</sup> 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.<sup>51</sup> 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.<sup>52</sup>

## Biochemical Correlates

Low serotonin levels have been implicated in aggression in psychiatric disorders such as schizophrenia<sup>53</sup> and may also play a role in aggression in dementia.<sup>54</sup>

## 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.<sup>55</sup> 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.<sup>56</sup>

## Psychological Factors

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

## Environmental Factors

Aggression in nursing homes usually occurs in response to intrusions into the resident's personal space by staff or other residents<sup>14,17</sup> or during personal care.<sup>16,41,60</sup> In 2 psychogeriatric wards, a moderately strong correlation was found between aggression and how close staff reported feeling emotionally to the patient.<sup>61</sup> In a day care center, physical aggression was also found to be predicted by poorer relationships with staff and other participants.<sup>62</sup> 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.<sup>63</sup>

## 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."<sup>64</sup> Other factors reported by clinicians as being important for the development of aggression include pain.<sup>62</sup> 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.<sup>16</sup>

## 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,<sup>65</sup> 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.<sup>66</sup> 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.<sup>67</sup> 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.<sup>68</sup> 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.<sup>69–71</sup>

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.<sup>72</sup> 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/aggression<sup>73</sup> and continued to be effective and well tolerated in the open-label extension.<sup>74</sup> 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.<sup>75</sup> A double-blind controlled trial with zuclopenthixol produced improvement on aggressive behavior in hospitalized elderly patients with dementia.<sup>76</sup>

**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.<sup>77–81</sup>

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.<sup>82</sup> A small (N = 9) double-blind pilot study suggested that carbamazepine improves aggression, depression, and cerebral efficiency in patients with frontal lobe dysfunction.<sup>83</sup>

**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.<sup>66</sup> Behavioral improvement on the Neuropsychiatric Inventory was demonstrated in 1 double-blind placebo-controlled trial<sup>84</sup> and 2 open-label studies of

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

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

**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.<sup>90</sup> Lorazepam and alprazolam both reduced agitation in demented patients, although no control group was used. Lorazepam produced more serious side effects.<sup>91</sup>

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

**Others—lithium, estrogens, anti-androgens.** Double-blind placebo-controlled trials have demonstrated that  $\beta$ -adrenergic receptor blocking agents ( $\beta$ -blockers) have some efficacy in treating aggression in schizophrenia.<sup>95,96</sup> A case series of 12 demented patients has shown that low-dose propranolol effectively reduced physical and verbal aggression in 8 of those patients.<sup>97</sup> 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.<sup>98</sup>

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.<sup>99</sup> 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.<sup>100</sup> A case series of 4 demented male patients showed that medroxyprogesterone acetate treatment was associated with a decrease in sexual aggression.<sup>101</sup>

### 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.<sup>102</sup> A daily gentle ex-

ercise program, also with 11 confused nursing home residents, decreased agitated behaviors.<sup>103</sup>

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.<sup>104</sup> 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.<sup>105</sup>

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.<sup>106</sup> 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.<sup>107</sup> 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.<sup>108</sup>

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.<sup>109</sup> 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.<sup>110</sup> 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,<sup>111</sup> 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.<sup>112</sup>

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.<sup>113</sup>

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,<sup>114</sup> but not others.<sup>25</sup> 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.<sup>115</sup>

## 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.<sup>116</sup> 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.

## REFERENCES

1. American Psychiatric Association. Practice Guideline for the Treatment of Patients With Delirium. *Am J Psychiatry* 1999;156(suppl 5):1-20
2. Patel V, Hope T. Aggressive behaviour in elderly people with dementia:

- a review. *Int J Geriatr Psychiatry* 1993;8:457–472
3. Swearer JM, Drachman DA, O'Donnell BF, et al. Troublesome and disruptive behaviors in dementia: relationships to diagnosis and disease severity. *J Am Geriatr Soc* 1988;36:784–790
  4. Patel V, Hope RA. Aggressive behaviour in elderly psychiatric inpatients. *Acta Psychiatr Scand* 1992;85:131–135
  5. Snowdon J, Miller R, Vaughan R. Behavioural problems in Sydney nursing homes. *Int J Geriatr Psychiatry* 1996;11:535–541
  6. Hope T, Keene J, Gelding K, et al. Behaviour changes in dementia, 1: point of entry data of a prospective study. *Int J Geriatr Psychiatry* 1997;12:1062–1073
  7. Hope T, Keene J, Fairburn RJ, et al. Natural history of behavioural changes and psychiatric symptoms in Alzheimer's disease. *Br J Psychiatry* 1999;174:39–44
  8. Cohen-Mansfield J. Agitated behaviors in the elderly, 2: preliminary results in the cognitively deteriorated. *J Am Geriatr Soc* 1986;34:722–727
  9. Lyketos CG, Sheppard J-ME, Steinberg M, et al. Neuropsychiatric disturbance in Alzheimer's disease clusters into three groups: the Cache County study. *Int J Geriatr Psychiatry* 2001;16:1043–1053
  10. Lyketos CG, Steinberg M, Tschanz JAT, et al. Mental and behavioral disturbances in dementia: findings from the Cache County study on memory in aging. *Am J Psychiatry* 2000;157:708–714
  11. Nagaratnam N, Lewis-Jones M, Scott D, et al. Behavioral and psychiatric manifestations in dementia patients in a community: caregiver burden and outcome. *Alzheimer Dis Assoc Disord* 1998;12:330–334
  12. Aarsland D, Cummings JL, Yenner G, et al. Relationship of aggressive behavior to other neuropsychiatric symptoms in patients with Alzheimer's disease. *Am J Psychiatry* 1996;153:243–248
  13. Eastley R, Wilcock GK. Prevalence and correlates of aggressive behaviours occurring in patients with Alzheimer's disease. *Int J Geriatr Psychiatry* 1997;12:484–487
  14. Ryden MB, Bossenmaier M, McLachlan C. Aggressive behavior in cognitively impaired nursing home residents. *Res Nurs Health* 1991;4:87–95
  15. Brodaty H, Draper B, Saab D, et al. Psychosis, depression and behavioural disturbances in Sydney nursing home residents: prevalence and predictors. *Int J Geriatr Psychiatry* 2001;16:504–512
  16. Keene J, Hope T, Fairburn CG, et al. Natural history of aggressive behaviour in dementia. *Int J Geriatr Psychiatry* 1999;14:541–548
  17. Bridges-Parlet S, Knopman D, Thompson T. A descriptive study of physically aggressive behavior in dementia by direct observation. *J Am Geriatr Soc* 1994;42:192–197
  18. Jost BC, Grossberg GT. The evolution of psychiatric symptoms in Alzheimer's disease: a natural history study. *J Am Geriatr Soc* 1996;44:1078–1081
  19. Devanand DP, Jacobs DM, Tang M-X, et al. The course of psychopathologic features in mild to moderate Alzheimer disease. *Arch Gen Psychiatry* 1997;54:257–263
  20. Talerico KA, Evans LK, Strumpf NE. Mental health correlates with aggression in nursing home residents with dementia. *Gerontologist* 2002;42:169–177
  21. Teri L, Hughes JP, Larson EB. Cognitive deterioration in Alzheimer's disease: behavioral and health factors. *J Gerontol Psychol Sci* 1990;45:P58–P63
  22. Yaffe K, Fox P, Newcomer R, et al. Patient and caregiver characteristics and nursing home placement in patients with dementia. *JAMA* 2002;287:2090–2097
  23. Hamel M, Gold DP, Andres D, et al. Predictors and consequences of aggressive behavior by community-based dementia patients. *Gerontologist* 1990;30:206–211
  24. O'Donnell BF, Drachman DA, Barnes HJ, et al. Incontinence and troublesome behaviors predict institutionalization in dementia. *J Geriatr Psychiatry Neurol* 1992;5:45–52
  25. Maslow K. Special care units for persons with dementia: expected and observed effects on behavioral symptoms. *Alzheimer Dis Assoc Disord* 1994;8:122–137
  26. Brodaty H. Caregivers and behavioral disturbances: effects and interventions. *Int Psychogeriatr* 1996;8:455–458
  27. Brodaty H, Hadzi-Pavlovic D. Psychosocial effects on carers of living with persons with dementia. *Aust N Z J Psychiatry* 1990;24:351–361
  28. Rodney V. Nurse stress associated with aggression in people with dementia: its relationship to hardiness, cognitive appraisal and coping. *J Adv Nurs* 2000;13:172–180
  29. Everitt DE, Fields DR, Soumerai SS, et al. Resident behavior and staff distress in the nursing home. *J Am Geriatr Soc* 1991;39:792–798
  30. Reisberg B, Borenstein J, Salob SP, et al. Behavioral symptoms in Alzheimer's disease: phenomenology and treatment. *J Clin Psychiatry* 1987;48(5, suppl):9–15
  31. Cummings JL, Mega M, Gray K, et al. The Neuropsychiatric Inventory: comprehensive assessment of psychopathology in dementia. *Neurology* 1994;44:2308–2314
  32. Allen NHP, Gordon S, Hope T, et al. Manchester and Oxford Universities Scale for the Psychopathological Assessment of Dementia (MOUSEPAD). *Br J Psychiatry* 1996;169:293–307
  33. Hope T, Fairburn CG. The Present Behavioural Examination (PBE): the development of an interview to measure current behaviour abnormalities. *Psychol Med* 1992;22:223–230
  34. Tariot PN, Mack JL, Patterson MB, et al. The Behavior Rating Scale for Dementia of the Consortium to Establish a Registry for Alzheimer's Disease. *Am J Psychiatry* 1995;152:1349–1357
  35. Patel V, Hope RA. A rating scale for aggressive behaviour in the elderly: the RAGE. *Psychol Med* 1992;22:211–221
  36. Yudofsky SC, Silver JM, Jackson W, et al. The Overt Aggression Scale for the objective rating of verbal and physical aggression. *Am J Psychiatry* 1986;143:35–39
  37. Ryden MB. Aggressive behavior in persons with dementia who live in the community. *Alzheimer Dis Assoc Disord* 1988;2:342–355
  38. Cohen-Mansfield J, Marx MS, Rosenthal AS. A description of agitation in a nursing home. *J Gerontol* 1989;44:M77–M84
  39. Lyketos CG, Steele C, Galik E, et al. Physical aggression in dementia patients and its relationship to depression. *Am J Psychiatry* 1999;156:66–71
  40. Beck C, Frank L, Chumbler NR, et al. Correlates of disruptive behavior in severely cognitively impaired nursing home residents. *Gerontologist* 1998;28:189–198
  41. Schreiner AS. Aggressive behaviors among demented nursing home residents in Japan. *Int J Geriatr Psychiatry* 2001;16:209–215
  42. Gormley N, Rizwan MR, Lovestone S. Clinical predictors of aggressive behaviour in Alzheimer's disease. *Int J Geriatr Psychiatry* 1998;13:109–115
  43. Kunik ME, Huffman JC, Bharani N, et al. Behavioral disturbances in geropsychiatric inpatients across dementia types. *J Geriatr Psychiatry Neurol* 2000;13:49–52
  44. Perry RJ, Irving D, Blessed G, et al. Senile dementia of the Lewy body type: a clinically and neuropathologically distinct form of Lewy body dementia in the elderly. *J Neurosci* 1990;59:119–139
  45. Perry RJ, Miller BL. Behavior and treatment in frontotemporal dementia. *Neurology* 2001;56:S46–S51
  46. Miller BL, Darby A, Benson DF, et al. Aggressive, socially disruptive and antisocial behaviour associated with fronto-temporal dementia. *Br J Psychiatry* 1997;170:150–155
  47. Mychack P, Kramer JH, Boone KB, et al. The influence of right frontotemporal dysfunction on social behavior in frontotemporal dementia. *Neurology* 2001;56:S11–S15
  48. Rapoport MJ, Reekun RV, Freedman M, et al. Relationship of psychosis to aggression, apathy and function in dementia. *Int J Geriatr Psychiatry* 2001;16:123–130
  49. Deutsch LH, Bylsma FW, Rovner BW, et al. Psychosis and physical aggression in probable Alzheimer's disease. *Am J Psychiatry* 1991;148:1159–1163
  50. Matthews KL, Chen CPL-H, Esiri MM, et al. Noradrenergic changes, aggressive behavior and cognition in patients with dementia. *Biol Psychiatry* 2002;51:407–416
  51. Hirono N, Mega MS, Dinov ID, et al. Left frontotemporal hypoperfusion is associated with aggression in patients with dementia. *Arch Neurol* 2000;57:861–866
  52. Minger SL, Esiri MM, McDonald B, et al. Cholinergic deficits contribute to behavioral disturbance in patients with dementia. *Neurology* 2000;55:1460–1467
  53. Cheung P, Schweitzer I. Correlates of aggressive behaviour in schizophrenia: an overview. *Aust N Z J Psychiatry* 1998;32:400–409
  54. Mintzer JE. Underlying mechanisms of psychosis and aggression in patients with Alzheimer's disease. *J Clin Psychiatry* 2001;62(suppl 21):23–25
  55. Sukonick DL, Pollock BG, Sweet RA, et al. The 5-HTTPR\**S*/\**L* polymorphism and aggressive behaviour in Alzheimer disease. *Arch Neurol* 2001;58:1425–1428
  56. Sweet RA, Pollock BG, Sukonick DL, et al. The 5-HTTPR polymorphism

- confers liability to a combined phenotype of psychotic and aggressive behavior in Alzheimer disease. *Int Psychogeriatr* 2001;13:401–409
57. Kolanowski AM, Garr M. The relation of premonitory factors to aggressive physical behavior in dementia. *J Neurosci Nurs* 1999;31:278–284
  58. Low LF, Brodaty H, Draper B. A study of premonitory personality and behavioural and psychological symptoms of dementia in nursing home residents. *Int J Geriatr Psychiatry* 2002;17:779–783
  59. Swearer JM, Hoople NE, Kane KJ, et al. Predicting aberrant behavior in Alzheimer's disease. *Neuropsychiatry Neuropsychol Behav Neurol* 1996; 9:162–170
  60. Keatinge D, Scarfe C, Bellchambers H, et al. The manifestation and nursing management of agitation in institutionalised residents with dementia. *Int J Nurs Pract* 2000;6:16–25
  61. Bahareethan M, Shah A. Aggressive behaviour, staff attitude and staff perception of patients on two continuing care psychogeriatric wards. *Aging Ment Health* 2000;4:66–71
  62. Cohen-Mansfield J, Werner P. Predictors of aggressive behaviors: a longitudinal study in senior day care centers. *J Gerontol Psychol Sci* 1998;53B: P300–P330
  63. Brodaty H, Draper B, Low LF. What environment and staffing characteristics predict behavioural and psychological symptoms of dementia in nursing home residents? *Psychogeriatrics* 2002;2:47–53
  64. Raskind MA. Evaluation and management of aggressive behavior in the elderly demented patient. *J Clin Psychiatry* 1999;60:45–49
  65. Schatzberg AF, DeBattista C. Phenomenology and treatment of agitation. *J Clin Psychiatry* 1999;60(suppl 15):17–20
  66. Tariot PN, Solomon PR, Morris JC, et al. A 5-month, randomized, placebo-controlled trial of galantamine in AD. *Neurology* 2000;54:2269–2276
  67. Buckley PF. Broad therapeutic uses of atypical antipsychotic medications. *Biol Psychiatry* 2001;50:912–924
  68. Devanand DP, Marder K, Michaels KS, et al. A randomized, placebo-controlled dose-comparison trial of haloperidol for psychosis and disruptive behaviors in Alzheimer's disease. *Am J Psychiatry* 1998;155:1512–1520
  69. De Deyn PP, Rabheru K, Rasmussen A, et al. A randomized trial of risperidone, placebo, and haloperidol for behavioral symptoms of dementia. *Neurology* 1999;53:946–955
  70. Katz IR, Jeste DV, Mintzer JE, et al, for the Risperidone Study Group. Comparison of risperidone and placebo for psychosis and behavioral disturbances associated with dementia: a randomized, double-blind trial. *J Clin Psychiatry* 1999;60:107–115
  71. Brodaty H, Ames D, Snowdon J, et al. A placebo-controlled trial of risperidone for the treatment of aggression, agitation, and psychosis of dementia. *J Clin Psychiatry* 2003;64:134–143
  72. Allain H, Dautzenberg PH, Maurer K, et al. Double blind study of tiapride versus haloperidol and placebo in agitation and aggressiveness in elderly patients with cognitive impairment. *Psychopharmacology (Berl)* 1999;148: 361–366
  73. Street JS, Clark WS, Gannon KS, et al, for the HGEU Study Group. Olanzapine treatment of psychotic and behavioral symptoms in patients with Alzheimer disease in nursing care facilities: a double-blind, randomized, placebo-controlled trial. *Arch Gen Psychiatry* 2000;57:968–976
  74. Street JS, Clark WS, Kadam DL, et al. Long-term efficacy of olanzapine in the control of psychotic and behavioral symptoms in nursing home patients with Alzheimer's dementia. *Int J Geriatr Psychiatry* 2001;16:S62–S70
  75. Meehan KM, Wang H, David SR, et al. Comparison of rapidly acting intramuscular olanzapine, lorazepam and placebo: a double-blind randomized study in acutely agitated patients with dementia. *Neuropsychopharmacology* 2002;26:494–502
  76. Nygaard HA, Bakke K, Brudvik E, et al. Dosing of neuroleptics in elderly demented patients with aggressive and agitated behaviour: a double-blind study with zuclopenthixol. *Curr Med Res Opin* 1994;13:222–232
  77. Porsteinsson AP, Tariot PN, Erb R, et al. Placebo-controlled study of divalproex sodium for agitation in dementia. *Am J Geriatr Psychiatry* 2001;9: 58–66
  78. Kunik ME, Puryear L, Orengo CA, et al. The efficacy and tolerability of divalproex sodium in elderly demented patients with behavioral disturbances. *Int J Geriatr Psychiatry* 1998;13:29–34
  79. Porsteinsson AP, Tariot PN, Erb R, et al. An open trial of valproate for agitation in geriatric neuropsychiatric disorders. *Am J Geriatr Psychiatry* 1997;5: 344–351
  80. Lott AD, McElroy SL, Keys MA. Valproate in the treatment of behavioral agitation in elderly patients with dementia. *J Neuropsychiatry Clin Neurosci* 1995;7:314–319
  81. Mellow AM, Solano-Lopez C, Davis S. Sodium valproate in the treatment of behavioral disturbance in dementia. *J Geriatr Psychiatry Neurol* 1993;6:205–209
  82. Tariot PN, Erb R, Podgorski CA, et al. Efficacy and tolerability of carbamazepine for agitation and aggression in dementia. *Am J Psychiatry* 1998;155:54–61
  83. Foster HG, Hillbrand M, Chi CC. Efficacy of carbamazepine in assaultive patients with frontal lobe dysfunction. *Prog Neuropsychopharmacol Biol Psychiatry* 1989;13:865–874
  84. Feldman H, Gauthier S, Hecker J, et al. A 24-week, randomized, double-blind study of donepezil in moderate to severe Alzheimer's disease. *Neurology* 2001;57:613–620
  85. Matthews HP, Korbey J, Wilkinson DG, et al. Donepezil in Alzheimer's disease: eighteen month results from Southampton memory clinic. *Int J Geriatr Psychiatry* 2000;15:713–720
  86. Weiner MF, Martin-Cook K, Foster BM, et al. Effects of donepezil on emotional/behavioral symptoms in Alzheimer's disease patients. *J Clin Psychiatry* 2000;61:487–492
  87. Tariot PN, Cummings JL, Katz IR, et al. A randomized, double-blind, placebo-controlled study of the efficacy and safety of donepezil in patients with Alzheimer's disease in the nursing home setting. *J Am Geriatr Soc* 2001;49:1590–1599
  88. McKeith I, Del Ser T, Spano P, et al. Efficacy of rivastigmine in dementia with Lewy bodies: a randomised, double-blind, placebo-controlled international study. *Lancet* 2000;356:2031–2036
  89. Lanctot KL, Herrmann N. Donepezil for behavioural disorders associated with Lewy bodies: a case series. *Int J Geriatr Psychiatry* 2000;15: 338–345
  90. Calkin PA, Kunik ME, Orengo CA, et al. Tolerability of clonazepam in demented and non-demented psychogeriatric patients. *Int J Geriatr Psychiatry* 1997;12:745–749
  91. Ancill RJ, Carlyle WW, Liang RA, et al. Agitation in the demented elderly: a role for benzodiazepines? *Int Clin Psychopharmacol* 1991;6: 141–146
  92. Pollock BG, Mulsant BH, Rosen J, et al. Comparison of citalopram, perphenazine and placebo for the acute treatment of psychosis and behavioral disturbances in hospitalized, demented patients. *Am J Psychiatry* 2002;159:460–465
  93. Sultzer DL, Gray A, Gunay I, et al. A double-blind comparison of trazodone and haloperidol for treatment of agitation in patient with dementia. *Am J Geriatr Psychiatry* 1997;5:60–69
  94. Sultzer DL, Gray KF, Gunay I, et al. Does behavioral improvement with haloperidol or trazodone treatment depend on psychosis or mood symptoms in patients with dementia? *J Am Geriatr Soc* 2001;49:1294–1300
  95. Alpert M, Allan ER, Citrome L, et al. A double-blind, placebo-controlled study of adjunctive nadolol in the management of violent psychiatric patients. *Psychopharmacol Bull* 1990;26:367–371
  96. Pugh CR, Steiner J, Priest RG. Propranolol in schizophrenia: a double blind, placebo controlled trial of propranolol as an adjunct to neuroleptic medication. *Br J Psychiatry* 1983;143:151–155
  97. Shankle WR, Nielson KA, Cotman CW. Low-dose propranolol reduces aggression and agitation resembling that associated with orbitofrontal dysfunction in elderly demented patients. *Alzheimer Dis Assoc Disord* 1995;9:233–237
  98. Ott BR. Leuprolide treatment of sexual aggression in a patient with dementia and Kluver-Bucy syndrome. *Clin Neuropharmacol* 1995;18: 433–437
  99. Shelton PS, Brooks VG. Estrogen for dementia-related aggression in elderly men. *Ann Pharmacother* 1999;33:808–812
  100. Kymen HH, Satlin A, Hennen J, et al. Estrogen therapy and aggressive behavior in elderly patients with moderate-to-severe dementia: results from a short-term randomized double-blind trial. *Am J Geriatr Psychiatry* 1999;7:339–348
  101. Cooper AJ. Medroxyprogesterone acetate (MPA) treatment of sexual acting out in men suffering from dementia. *J Clin Psychiatry* 1987;48: 368–370
  102. Holmberg S. Evaluation of a clinical evaluation for wanderers on a geriatric nursing unit. *Arch Psychiatr Nurs* 1997;11:21–28
  103. Nazami KH, Gwinnup PB, Zadorozny CA. A low intensity exercise/movement program for patients with Alzheimer's disease: the TEMP-AD protocol. *J Aging Phys Activity* 1994;2:80–92
  104. Clark ME, Lipe AW, Bilbrey M. Use of music to decrease aggressive behaviors in people with dementia. *J Gerontol Nurs* 1998;24:10–17

105. Gerdner LA. Effects of individualized versus classical "relaxation" music on the frequency of agitation in elderly persons with Alzheimer's disease and related disorders. *Int Psychogeriatr* 2000;12:49–65
106. Gormley N, Lyons D, Howard R. Behavioural management of aggression in dementia: a randomized controlled trial. *Age Ageing* 2001;30:141–145
107. Haupt M, Karger A, Janner M. Improvement of agitation and anxiety in demented patients after psychoeducative group intervention with their caregivers. *Int J Geriatr Psychiatry* 2000;15:1125–1129
108. Teri L, Logson RG, Peskind E, et al. Treatment of agitation in AD: a randomized, placebo-controlled trial. *Neurology* 2000;55:1271–1278
109. Maxfield MC, Lewis RE, Cannon S. Training staff to prevent aggressive behaviour of cognitively impaired elderly patients during bathing and grooming. *J Gerontol Nurs* 1996;22:37–43
110. Moniz-Cook E, Woods RT, Richards K. Functional analysis of challenging behaviour in dementia: the role of superstition. *Int J Geriatr Psychiatry* 2001;16:45–56
111. Haffmans PMJ, Sival RC, Lucius SAP, et al. Bright light therapy and melatonin in motor restless behaviour in dementia: a placebo-controlled study. *Int J Geriatr Psychiatry* 2001;16:106–110
112. Lyketsos CG, Veiel LL, Baker A, et al. A randomized, controlled trial of bright light therapy for agitated behaviors in dementia patients residing in long-term care. *Int J Geriatr Psychiatry* 1999;14:520–525
113. Camberg L, Woods P, Ooi WL, et al. Evaluation of Simulated Presence: a personalised approach to enhance well-being in persons with Alzheimer's disease. *J Am Geriatr Soc* 1999;47:446–452
114. Bianchetti A, Benvenuti P, Ghisla K, et al. An Italian model of dementia special care unit: results of a pilot study. *Alzheimer Dis Assoc Disord* 1997;11:53–56
115. Sloane PD, Mitchell CM, Preisser JS, et al. Environmental correlates of resident agitation in Alzheimer's disease special care units. *J Am Geriatr Soc* 1998;46:862–869
116. Carrier L, Brodaty H. Mood and behaviour management. In: Gauthier S, ed. *Clinical Diagnosis and Management of Alzheimer's Disease*. London, United Kingdom: Martin Dunitz Ltd; 1996:205–220