Delusions in Alzheimer's Disease: A Literature Review

Delusions are common symptoms in AD. While much of the literature reveals inconsistencies, certain trends have emerged. Delusions occur in approximately one third of AD patients. They appear to be more common among older patients while the impact of other demographic variables is less clear. Certain types of delusions have been identified as being more common among AD patients. While some interesting associations exist, no compelling risk factors have been identified.

by Corrine Fischer, MD, FRCPC

Delusions are common symptoms in psychiatric practice and are often seen in illnesses such as schizophrenia, bipolar disorder and delirium. In Alzheimer's disease (AD), the literature suggests that these symptoms are not only common, but also associated with a number of adverse outcomes, including increased caregiver stress[1] and earlier institutionalization.[2-5] Despite the prevalence and severity of these symptoms in AD, the literature reveals many inconsistencies suggesting they are poorly understood. Some of the reasons may be that previous studies did not distinguish AD patients from patients with other forms of dementia and failed to separate delusions from hallucinations. This paper will review the existing literature on delusions in AD with respect to epidemiology, classification systems, etiology, neurocognitive findings and behaviour to familiarize the reader with what is known about these common symptoms.

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Epidemiology of Delusions in AD

Recent studies show delusions are present in approximately one third of patients with AD.[6-9] Previous studies examining the prevalence of delusions in dementia have quoted a prevalence range[10] from 10% to 73%, but most of these studies failed to separate delusions from hallucinations and were done in patients with different dementia diagnoses. It has been established that delusions occur more commonly in certain types of dementia, such as Lewy-body disease, and less commonly in other types, such as frontotemporal dementia,[11] although the mechanism of this is unclear. Paulsen and Salmon *et al*[12] showed the prevalence of delusions to increase 20% by year one and 50% by year four from the time of diagnosis, suggesting these symptoms may have to be evaluated over time.

The role of demographic variables including age, gender, education and race is not clear.

Most studies have shown AD patients with delusions and other psychotic symptoms are older than those without these symptoms,[6,13-15] but some have shown a lower prevalence[16] while others have shown no changes.[9,17] The role of gender is equally unclear, with some studies showing a higher prevalence of delusions and psychotic features among men with AD,[2,18-19] others showing a higher prevalence among women,[16,20] and still others showing an equal distribution among the sexes[9,17,21-23]. In terms of education, some studies have suggested an association between lower levels of education and the presence of delusions and psychotic features in AD,[24] while others have shown an association with higher levels of education[22-23] and still others have shown no difference.[9] The lack of consensus as to the role of demographic variables in the development of delusions in AD may reflect the poor differentiation between delusions and hallucinations, each of which may have separate associations.

Classification of Delusions in AD

Delusions are commonly referred to as "fixed false beliefs that are not culturally bound." Delusions exist in many psychiatric disorders, including bipolar disorder, schizophrenia and delirium. Classification systems exist for delusions in illnesses such as schizophrenia, where delusions are subtyped into persecutory, erotomanic, grandiose, etc. In AD patients, the challenge is to differentiate these symptoms from other memory-based symptoms such as confabulation or disorientation.

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There have been several attempts at developing classification systems for delusions in AD patients. One system[9] divided delusions into five different categories: paranoid, hypochondrical, Capgras syndrome, house misidentification and grandiosity. Capgras syndrome refers to the belief that someone close to the person is an imposter, and house misidentification refers to the belief that one's house is not one's home. Gormley *et al*[7] identified four common delusions in AD patients: delusions of theft (belief someone has stolen something), phantom boarders (belief an intruder is in the house), spousal infidelity (fear their spouse is having an affair) and delusions of abandonment (fear their caregiver is going to leave). Cummings[25] examined delusions in 20 patients with organic brain syndrome and found that four subtypes were most common, including simple persecutory delusions, complex persecutory delusions, grandiose delusions and delusions associated with a specific neurological deficit. He determined that simple persecutory delusions were most common in AD and that the other subtypes tended to occur more often in other types of organic brain syndromes.

While delusions of theft may be most common in patients with AD,[7] it has been suggested that multiple delusions may co-exist at one time.[9] Finally, there is some evidence that different types of delusions may emerge at different stages of the disease, with delusions of theft being most common and presenting early in AD and Capgras syndrome[26] being rarer and occurring late in the course of the disease.

Risk Factors for Delusions in AD

There is little consensus as to known risk factors for delusions in

AD. In terms of psychiatric symptoms, adverse life events[27] and premorbid personality[28] do appear to play a minor role, but the impact of depression is less clear. Other studies have looked at other variables and have found no relationship with apolipoprotein E (ApoE),[29] conflicting information around the role of extrapyramidal symptoms,[6,8,20,30,31] a possible link with antihypertensive medications[6] and a possible link with sensory changes.[32] In summary, no discrete risk factor has been identified to play a major role in delusion formation.

Etiology of Delusions in AD

There are three major theories regarding the etiology of delusions in AD. The theory of hypofrontality states that delusional symptoms are related to selective frontal lobe dysfunction. This theory has been substantiated by both neuroimaging and neuropathologic studies with Single-Photon Emission Computed Tomography (SPECT) scans showing diminished frontal lobe perfusion[22,33] and neuropathologic studies showing a higher density of senile plaques in the frontal lobes.[12] An alternative theory proposed by Flynn *et al* in 1991 is that delusions arise as an independent non-cognitive manifestation of AD, a theory substantiated by Sweet[34] who was able to demonstrate no difference in the density of neuritic plaques and tangles when comparing the brains of delusional and non-delusional AD patients. Finally, it has been proposed that delusions in AD patients may arise as a manifestation of the pathophysiology attributed to AD,[10,35] a theory substantiated by Farber[36] who examined 100 cases of AD post-mortem and found that patients with psychosis had twice the density of neurofibrillary tangles.

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Other investigators have found that delusions may be secondary to neuroanatomical changes such as isolated degeneration of the right frontal lobe[37] and temporal lobe asymmetry,[38] neurotransmitter changes—including a reduction in serotonin in the prosubiculum[39] and upregulation of postsynaptic muscarinic receptors,[40] genetic factors[41] and an altered sense of familiarity[42].

Neurocognitive and Behavioural Changes in AD Patients with Delusions

Several investigators have examined the relationship of cognitive function to the development of delusions in AD. The evidence has been conflicting, with some studies showing that AD patients with psychosis have an increased rate of cognitive decline,[12,16] some showing only mild differences[34] and others showing the preservation of intellectual function.[43-45] It has been speculated that a certain degree of cognitive function may be required to develop a delusion[46], although what aspect of cognitive functioning needs to be preserved is less clear. The fact that delusions tend to occur in the mid-range of cognitive impairment (Mini-Mental State Examination 17-23)[47] suggests that patients who are moderately affected may be more vulnerable to developing delusions.

More consistent findings have been documented in the area of frontal lobe dysfunction, supporting the theory of hypofrontality. AD patients with delusions have been shown to have more signs of frontal lobe dysfunction on neurocognitive testing,[12] although the relationship of this to poor insight has been questioned.[29]

There is substantial evidence that Alzheimer patients with delusions are more aggressive[7,14,15,47-50] with rates of verbal

aggression[51,52] outmatching rates of physical aggression.[53,54] Eustace *et al*[55] hypothesized that verbal aggression among delusional AD patients is likely linked to a perceived environmental threat. He also determined that delusions, unlike other behaviours such as wandering, may have only moderate persistence. Delusions among AD patients have been linked to other behaviours such as wandering[20] and adverse outcomes such as early institutionalization.[5]

Conclusion

Delusions are common symptoms in AD. While much of the literature reveals inconsistencies, certain trends have emerged. Delusions occur in approximately one third of AD patients. They appear to be more common among older patients while the impact of other demographic variables is less clear. Certain types of delusions have been identified as being more common among AD patients. While some interesting associations exist, no compelling risk factors have been identified. There is evidence neuropathologically, radiologically and neurocognitively that delusions may be linked to frontal lobe dysfunction. Patients appear to be most vulnerable to developing delusions when they are moderately ill. Finally, delusions are associated with a number of adverse outcomes, including increased caregiver burden, aggressiveness and earlier institutionalization. Future research needs to focus on clarifying areas of inconsistency, so as to create a better understanding of these complex and interesting symptoms.

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References

1. Haupt M, Romero B, Kurz A. Delusions and hallucinations in Alzheimer's disease: results from a two-year longitudinal study. Geriatr Psychiatry 1996; 11:965-72.
2. Rabins PV, Mace NL, Lucas MJ. The impact of dementia on the family. JAMA 1982; 248(3):333-5.
3. Steele C, Rovner B, Chase GA, et al. Psychiatric symptoms and nursing home placement of patients with Alzheimer's disease. Am J Psychiatry 1990; 147(8):1049-51.
4. Haupt M, Kurz A. Predictors of nursing home placement in patients with Alzheimer's disease. Int J Geriatr Psychiatry 1993; 8;741-6.
5. Magni E, Binetti G, Bianchetti, A et al. Risk of mortality and institutionalization in demented patients with delusions. J Geriatr Psychiatr Neurol 1996; 9:123-6.
6. Bassiony MM, Steinberg MS, Warren A, et al. Delusions and hallucinations in Alzheimer's disease: prevalence and clinical correlates. Int J Geriatr Psychiatry 2000; 15(2):99-107.
7. Gormley N, Rizwan MR, Lovestone S. Clinical predictors of aggressive behaviour in Alzheimer's disease. Int J Geriatr Psychiatry 1998; 13(2):109-15.
8. Jeste DV, Wragg RE, Salmon DP, et al. Cognitive deficits of patients with Alzheimer's disease with and without delusions. Am J Psychiatry 1992; 149(2):184-9.
9. Migliorelli R, Petracca G, Teson A, et al. Neuropsychiatric and neuropsychological correlates of delusions in Alzheimer's disease. Psychol Med 1995; 25(3):505-13.
10. Wragg RE, Jeste DV. Overview of depression and psychosis in Alzheimer's disease. Am J Psychiatry 1989; 146(5):577-87.
11. Hirono N, Mori E, Ishii K, et al. Alteration of regional cerebral glucose utilization with delusions in Alzheimer's disease. J Neuropsychiatry Clin Neurosci 1998; 10(4):433-9.
12. Paulsen JS, Ready RE, Stout JC, et al. Neurobehaviors and psychotic symptoms in Alzheimer's disease. J Int Neuropsychol Soc 2000; 6(7): 815-20.
13. Devanand DP, Brockington CD, Moody BJ, et al. Behavioral syndromes in Alzheimer's disease. Int Psychogeriatr 1992; 4 Suppl 2:161-84.
14. Cooper JK, Mungas D, Verm AM, et al. Psychoatic symptoms in Alzheimer's disease. Int J Geriatr Psychiatr 1991; 6:721-6.
15. Forstl H, Besthorn C, Geiger-Kabisch C, et al. Psychotic features and the course of Alzheimer's disease: relationship to cognitive, electroencephalographic and computerized tomography

findings. Acta Psychiatr Scand 1993; 87(6):395-9.
16. Chen JC, Borson S, Scanlan JM. Stage-specific prevalence of behavioral symptoms in Alzheimer's disease in a multi-ethnic community sample. Am J Geriatr Psychiatry 2000; 8(2):123-33.
17. Doody RS, Massman P, Mahurin R, et al. Positive and negative neuropsychiatric features in Alzheimer's disease. J Neuropsychiatry Clin Neurosci 1995; 7(1):54-60.
18. Burns A, Jacoby R, Levy R. Psychiatric phenomena in Alzheimer's disease. IV: Disorders of behaviour. Br J Psychiatry1990; 157:86-94.
19. Eastley R. Wilcock GK. Prevalence and correlates of aggressive behaviours occurring in patients with Alzheimer's disease. Int J Geriatr Psychiatry 1997; 12(4):484-7.
20. Rockwood K, Stadnyk K. The prevalence of dementia in the elderly: a review. Can J Psychiatry 1994; 39(5):253-7.
21. Cohen CI, Carlin L. Racial differences in clinical and social variables among patients evaluated in a dementia assessment center. J Natl Med Assoc 1993; 85(5):379-84.
22. Kotrla KJ, Chacko RC, Harper RG, et al. Clinical variables associated with psychosis in Alzheimer's disease. Am J Psychiatry 1995; 152(9):1377-9.
23. Binetti G, Padovani A, Magni E, et al. Delusions and dementia: clinical and CT correlates. Acta Neurol Scand 1995; 91(4):271-5.
24. Devanand DP. The interrelations between psychosis, behavioral disturbance, and depression in Alzheimer disease. Alzheimer Dis Assoc Disord 1999; 13 Suppl 2:S3-8.
25. Cummings JL. Organic delusions: phenomenology, anatomical correlations, and review. Br J Psychiatry 1985; 146:184-97.
26. Hwang JP, Yang CH, Tsai SJ, et al. Delusions of theft in dementia of the Alzheimer type: a preliminary report. Alzheimer Dis Assoc Disord 1997; 11:110-2.
27. Ballard CG, Bannister CL, Patel A, et al. Classification of psychotic symptoms in dementia sufferers. Acta Psychiatr Scand 1995; 92(1):63-8.
28. Low LF, Brodaty H, Draper B. A study of premorbid personality and behavioural and psychological symptoms of dementia in nursing home residents. Int J Geriatr Psychiatry 2002; 17:779-83.
29. Gabryelewicz T, Religa D, Styczynska M, et al. Behavioural pathology in Alzheimer's disease with special reference to apolipoprotein E genotype. Dement Geriatr Cogn Disord 2002; 14:208-12.
30. Mayeux R, Marder K, Cote LJ, et al. The frequency of idiopathic Parkinson's disease by age, ethnic group, and sex in northern Manhattan, 1988-1993. Am J Epidemiol 1995; 142(8):820-7.
31. Pfeffer-Baczuk A, Barcikowska M, Karwanska A. Neurologia i Neurochirurgia Polska 1996; 30(3): 389-98.
32. Ballard C, Boyle A, Bowler C, et al. Anxiety disorders in dementia sufferers. Int J Geriatr Psych 1996; 11:987-90.
33. Mega MS, Lee L, Dinov ID, et al. Cerebral correlates of psychotic symptoms in Alzheimer's disease. J Neurol Neurosurg Psychiatry 2000; 69(2):167-71.
34. Sweet RA, Hamilton RL, Lopez OL, et al. Psychotic symptoms in Alzheimer's disease are not associated with more severeneuropathologic features.Int Psychogeriatr 2000; 12(4):547-58.
35. Lyketsos CG, Steinberg M, Tschanz JT, et al. Mental and behavioral disturbances in dementia: findings from the Cache County Study on Memory in Aging. Am J Psychiatry 2000; 157(5):708-14.
36. Farber NB, Rubin EH, Newcomer JW, et al. Increased neocortical neurofibrillary tangle density in subjects with Alzheimer disease and psychosis. Arch Gen Psychiatry 2000; 57(12): 1165-73.
37. Forstl H, Almeida OP, Owen AM, et al. Psychiatric, neurologic and medical aspects of misidenitification syndromes: a review of 260 cases. Psychol Med 1991; 21:905-10.
38. Geroldi C, Bresciani L, Zanetti O, et al. Regional brain atrophy in patients with mild Alzheimer's disease and delusions. Int Psychogeriatr. 2002; 14(4): 365-78.
39. Zubenko GS, Moossy J, Martinez AJ, et al. Neuropathologic and neurochemical correlates of psychosis in primary dementia. Arch Neurology 1991; 48(6):619-24.
40. Ballard C, Piggott M, Johnson M, et al. Delusions associated with elevated muscarinic binding in dementia with Lewy bodies. Ann Neuro 2000; 48:619-24.
41. Nacmias B, Tedde A, Forleo P, et al. Association between 5-HT(2A) receptor polymorphism and psychotic symptoms in Alzheimer's disease. Biol Psychiatry 2001; 50(6):472-5. Erratum in: Biol Psychiatry 2001 Nov15; 50(10):821.
42. Mendez MF. Delusional misidentification of persons in dementia. Br J Psychiat 1992; 160:414-6.
43. Lopez OL, Brenner RP, Becker JT, et al. EEG spectral abnormalities and psychosis as predictors of cognitive and functional decline in probable Alzheimer's disease. Neurology 1997; 48(6):1521-5.
44. Ballard C, O'Brien J, Coope B, et al. A prospective study of psychotic symptoms in dementia sufferers: psychosis in dementia. Int Psychogeriatr 1997; 9(1):57-64.
45. Jacoby RJ, Levy R. Computed tomography in the elderly. 2. Senile dementia: diagnosis and functional impairment. British Journal of Psychiatry 1980; 136:256-69.
46. Fleminger S. Delusional misidentification: an exemplary symptom illustrating an interaction between organic brain disease and psychological processes. Psychopathology 1994; 161-7.
47. 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(2):243-7.
48. Gilley DW, Wilson RS, Beckett LA, et al. Psychotic symptoms and physically aggressive behaviour in Alzheimer's disease. J Am Geriatr Soc 1997; 45: 1074-9.
49. Flynn FG, Cummings JL, Gornbein J. Delusions in dementia syndromes: investigation of behavioral and neuropsychological correlates. J Neuropsychiatry Clin Neurosci 1991; 3(4):364-70.
50. Deutsch LH, Bylsma FW, Rovner BW, et al. Psychosis and physical aggression in probable Alzheimer's disease. Am J Psychiatry 1991; 148(9):1159-63.
51. Ballinger BR, Reid AH, Heather BB. Cluster analysis of symptoms in elderly demented patients. Br J Psychiatry 1982; 140:257-62.
52. Reisberg B, Borenstein J, Salob SP, et al. Behvioural symptoms in Alzheimer's disease: Phenomenology and treatment. J Clin Psychiat 1987; 48:9-15.
53. Kumar A, Koss E, Metzler D et al. Behavioural symptomatology in dementia of the Alzheimer's type. Alzheimer Dis Assoc Disord 1988; 2:363-5.
54. Ryden MB. Aggressive behavior in persons with dementia who live in the community. Alzheimer Dis Assoc Disord 1988; 2(4):342-55.
55. Eustace A, Kidd N, Greene E, Fallon et al. Verbal aggression in Alzheimer's disease. Clinical, functional and neuropsychological correlates. Int J Geriatr Psychiatry 2001; 16(9):858-61.