

Cognitive neuroscience of delusions in aging

Anna EM Holt¹
Martin L Albert²

¹Brain and Cognitive Sciences
Department, Massachusetts Institute
of Technology, Boston, MA, USA;

²Department of Neurology, Boston
University School of Medicine,
Harold Goodglass Aphasia Research
Center, VA Boston Healthcare
System, Boston, MA, USA

Abstract: Assessments and clinical understanding of late-onset delusions in the elderly are inconsistent and often incomplete. In this review, we consider the prevalence, neurobehavioral features, and neuroanatomic correlations of delusions in elderly persons – those with documented cognitive decline and those with no evidence of cognitive decline. Both groups exhibit a common phenotype: delusions are either of persecution or of misidentification. Late-onset delusions show a nearly complete absence of the grandiose, mystical, or erotomanic content typical of early onset psychoses. Absent also from both elderly populations are formal thought disorders, thought insertions, and delusions of external control. Neuroimaging and behavioral studies suggest a frontotemporal localization of delusions in the elderly, with right hemispheric lateralization in delusional misidentification and left lateralization in delusions of persecution. We propose that delusions in the elderly reflect a common neuroanatomic and functional phenotype, and we discuss applications of our proposal to diagnosis and treatment.

Keywords: delusions, aging, dementia, cognitive neuroscience

Introduction

Late-onset delusions in the elderly (occurring for the first time after age 60) have received little treatment in the literature relative to the severity of the problem. Unlike attention paid to dementia, confusional states, and hallucinations in the elderly, geriatric neurology and neuropsychiatry do not focus on delusions. Appropriate identification and adequate treatment of delusional ideation have the potential to make a simple but important contribution to patient care and caregiver quality of life. Caregivers bear the brunt of accusations stemming from such delusions, and rate psychotic signs as more stressful than cognitive deterioration (Haupt 1996). Consequently, psychotic signs in the elderly are one of the best predictors of early placement in care facilities (Steele et al 1990). A clinical imperative exists to identify those at risk for the phenomenon and to isolate the underlying mechanisms.

In this review, we consider studies of late-onset delusions in the course of normal aging and in dementia, as indexed in a medical database (PubMed) in the last two decades. While earlier studies supporting the findings of this review exist, the period of the past 20 years coincides with the increasing use of neuroimaging in clinical and experimental research in cognitive neuroscience, and provides more complete documentation of inclusion criteria in observational studies. Our review reveals four principal themes. 1) Delusions in both populations share a common content, which distinguishes them from those in early onset psychoses. 2) Sustainability of delusions appears to require a minimum threshold of cognitive functioning. 3) Delusions reflect abnormalities of frontotemporal systems. 4) Increasing evidence suggests cerebral lateralization of delusions in the elderly, determining delusional content. In this paper we detail a clinical profile of late-onset delusions, and discuss its usefulness for diagnosis and treatment.

Correspondence: Martin L Albert
Harold Goodglass Aphasia Research
Center, 150 S. Huntington Ave (12A),
Boston, MA 02130, USA
Tel +1 617 232 9500
Fax +1 617 739 8926
Email malbert@bu.edu

Prevalence and classification

Late-onset delusions occur in two broad populations of the elderly: those with documented cognitive impairment, defined in this review as those with Mini Mental Status Exam (MMSE) scores below 27, and those with no measurable cognitive decline (MMSE 27 or greater). The explicit choice of 27 as a stringent requirement reflects concerns over the cognitive status of those in MMSE range 24–27 as potentially in preclinical stages of dementia. A less stringent criterion of 24 (as baseline) shifts a larger population into the category of nondemented delusional elderly.

Patients classified by National Institute of Neurological and Communicative Diseases and Stroke–Alzheimer’s Disease and Related Disorders Association (NINCDS–ADRDA) criteria (McKann et al 1984) for probable or possible Alzheimer’s disease (AD) are often given the diagnosis of Biological and Psychological Symptoms in Dementia (BPSD). This is a broad category, however, because it also includes verbal and auditory hallucinations, mood disorders and generalized anxiety, sleeplessness, wandering, and/or noisemaking.

Relative to patients with AD, those patients presenting with delusions and well-preserved cognition and premorbid personality have received even murkier classification; they are coded in a suite of possibilities by preference and custom. Foremost among these have been late-onset schizophrenia (LOS), very-late onset schizophrenia (VLOS), or delusional disorder (DD) (APA 2000; WHO 1994), and paraphrenia, late-paraphrenia, or late-onset paranoia colloquially.

In early observational studies, delusions were reported in 10%–73% of patients with AD (Rao and Lyketsos 1998; see also review by Fischer et al 2004). More recent studies now converge on a figure closer to 30% (Rao and Lyketsos 1998; Bassiony and Lyketsos 2003; Fischer et al 2004). A review by Henderson and Kay (1997) reported rates of around 5% in populations with MMSE scores 24 or above. Kay et al (1985) found rates of 6% for paranoid symptoms in Australian elderly over age 70 (Kay et al 1985). Additionally, population studies reveal an affected segment of the nondemented, independently living elderly population. Ostling and Skoog (2002) found rates of 5.5% for fully-fledged delusions and 6.6% for paranoid ideation in a 3-year observational study of elders aged 85 and above in Goteborg, Sweden. Livingston et al (2001) and Henderson et al (1998) found results comparable with those of Ostling and Skoog for the presence of any psychotic symptom, but more modest rates, 2.5% and 1.7%, for the presence of

delusions alone, in elderly aged 65 and above. Roughly speaking, therefore, we estimate delusions to be present in about 30% of persons with AD and about 5% of presumably normal elderly persons.

Common delusional content

Demented and nondemented delusional elderly show commonality of delusion content. Delusions can be categorized within two subgroups: delusions of misidentification, associated with auditory (Ballard et al 1995a; Cook et al 2003) and visual hallucinations (Ballard et al 1995a; Cook et al 2003), and delusions of persecution. Patients with delusions often suffer from multiple persecutory or misidentification delusions, and both types of delusions may be present concurrently. Brune and Shroder (2003), in presentation of two cases of erotomanic delusions in AD, could find only three other such cases in the literature. LOS patients further failed to show erotomanic delusions. Bassiony and Lyketsos (2003) noted a rate of somatic delusions of 20% in AD patients. All other reviewed studies do not indicate a rate higher than 4% (see Table 1 for delusion type and frequency in elderly persons).

Delusions in the elderly are reality-based, unlike the fantastic delusions of early onset schizophrenia. Furthermore, delusions in the elderly do not share other characteristic symptoms of schizophrenia. Thought withdrawal, thought insertion, and thought broadcasting are not typically seen in patients with LOS, either on systematic observation or from admission notes in geriatric psychiatry wards (Webster and Grossberg 1998; Hafner et al 2001; Alici-Evcimen et al 2003). Literature surveyed in this review does not find early-onset schizophrenia-type delusions in AD, vascular dementia, or normal aging.

Delusions of persecution

Delusions of persecution predominate in both demented and nondemented elderly populations. Persecutory delusions are often difficult to identify due to their typically nonfantastic content and, also, due to real concerns about mistreatment of impaired elderly persons. A delusional belief that a patient’s neighbors seek to have them evicted, for example, must be disentangled from prior interpersonal conflict and legitimate conflict resulting from the sustaining of that belief. Delusions of persecution make up about 45%–60% of delusions in dementia (Binetti et al 1993; Webster and Grossberg 1998). Rates are comparable by dementia type (Bianchetti et al 1992; Binetti et al 1993; Webster and

Table 1 Delusions in the elderly

	Delusion type	Delusion content	Percentage of delusions
Delusions of theft	Persecutory	Patient is being robbed of possessions	20–75
Delusions of suspicion–physical anger	Persecutory	Harm to patient or patient's loved ones	11–30
Delusions of jealousy	Persecutory	Spouse is unfaithful	3–16
Misidentification of familiar persons	Misidentification	Familiar person is misidentified	16
Misidentification of objects	Misidentification	Familiar object is misidentified	10–20
Capgras delusion	Misidentification	Familiar person replaced by identical imposter	6–36
Phantom boarder syndrome	Misidentification	Phantom residents inhabit patient home	20–30
Mirror sign	Misidentification	Misidentifies mirror image	3
TV sign	Misidentification	Misidentifies television image as real	7–8
Nurturing syndrome	Misidentification	Deceased family members still living	No range reported

Grossberg 1998; Leroi et al 2003). Late-onset schizophrenics and nondemented elderly patients typically show only persecutory delusions. Howard et al (1994) alone found persecutory delusions mixed with misidentification delusions in LOS patients. Their group of LOS patients had significantly higher age at onset (mean onset age 74.1 years), and poor to total failure of anti-psychotic medication. Other studies group both medicated and naïve patients together in studies of delusions, noting the generally poor response rate to medication treatment.

Most common are delusions of theft (20%–75% of persecutory delusions), wherein the patient believes that others are stealing property (Binetti et al 1993; Cohen-Mansfield et al 1998; Rao and Lyketsos 1998; Bassiony et al 2000; Ikeda et al 2003; Leroi et al 2003). In about half such cases (Bassiony et al 2000), this belief takes the form of theft of money by caregivers, though others (including doctors) may be accused of theft of other objects. Other common persecutory delusions are of suspicion or physical danger (10%–30% of persecutory delusions: Leroi et al 2003; Hwang et al 1999; Konakanchi et al 1999; Shinosaki et al 2000; Ikeda et al 2003). In independently living patients, these delusions are commonly expressed as belief that neighbors or landlords are trying to have patients removed from their property, and may bring them into conflict with such persons. Other common delusions include intent of physical harm or mistreatment of patient or patient's family by their caregivers, and belief the patient has been abandoned. Delusions of jealousy (2%–16% of persecutory delusions) typically involve belief that the spouse has been unfaithful, and patients often take extraordinary measures to limit the spouse's contact with others (Tsai et al 1997; Rao and Lyketsos 1998; Ikeda et al 2003; Leroi et al 2003).

Persecutory symptoms appear to require a threshold level of preserved cognitive function to sustain. Delusions in

dementia typically begin early in the course of illness, and dissipate as the disease reaches moderate to severe severity (Bassiony and Lyketsos 2003). The majority of studies find comparable (Hwang et al 1997; Tsai et al 1997; Hwang et al 1999; Targum and Abbott 1999; Shinosaki et al 2000) or higher (Binetti et al 1993; Ikeda et al 2003) MMSE scores in Alzheimer's patients with persecutory delusions when compared with matched Alzheimer's patients without delusions. This pattern also holds for vascular dementia and multi-infarct dementia (Binetti et al 1993). Generally, LOS patients demonstrate very minor cognitive impairment, with MMSE scores of 24–27. In evaluating elderly patients for delusions, a good rule of thumb may be to look for mild (rather than severe) overall cognitive impairment and specific deficits in executive functioning, as discussed further in this review.

Delusions of misidentification

Delusions of misidentification appear at a somewhat later age than persecutory delusions and reflect greater cognitive decline. Only in AD do delusions of misidentification show a rate equal to that of persecutory delusions. Delusions of misidentification make up 25%–47% of delusions in AD (Burns et al 1990; Mendez et al 1992; Binetti et al 1993; Forstl et al 1994a). Delusions of misidentification and hallucinations appear earlier and with greater frequency in dementia with Lewy bodies than in other forms of dementia (Ballard et al 1999). Patients suffering from delusions of misidentification show lower MMSE scores at onset and higher Blessed Dementia Scale ratings than matched nondelusional dementing controls (Forstl et al 1994a).

Misidentification of familiar persons (in which patients insist that familiar persons are not who they really are), the Capgras delusion (in which patients believe that familiar persons have been replaced with imposters), and the

phantom boarder syndrome (in which patients believe their house is inhabited by unwelcome guests), make up the majority of delusional misidentifications at 16% (Mendez et al 1992; Ballard et al 1999; Harwood et al 1999), 6%–36% (Cohen-Mansfield et al 1998), and 20%–30% (Ikeda et al 2003; Mendez et al 1992; Harwood et al 1999; Hwang et al 2003) of delusions of misidentification, respectively. Patients with phantom boarder syndrome complain their guests eat their food or make excessive noise, and can usually detail the daily routines of these phantoms. Misidentification of objects makes up 9%–18% (Ikeda et al 2003; Leroi et al 2003; Shinosaki et al 2000). Most commonly, patients insist their residence is not their home, and must be watched closely lest they attempt to relocate to their “real” home. Mirror sign (3%) (Mendez et al 1992) and tv sign (5%–7%) (Mendez et al 1992; Leroi et al 2003) are phenomena in which the patient misidentifies his or her own mirror image or treats television characters and events as reality. Finally, nurturing syndrome is an increasingly recognized (Schlimme et al 2002) delusion, clustering with phenomena of misidentification, in which the patient believes a dead family member to be alive. These patients often request the police to search for their missing relatives and feed and sleep with pictures of the dead family members.

Risk factors

Both major types of delusional content show a similar risk profile and progression. Overall, it appears the risk for paranoid or delusional ideation increases linearly with age after age 65 (Schlimme et al 2002), delusional patients in both groups are generally older than nondelusional controls (Bassiony et al 2000) or patients suffering from hallucinations only (Devanand et al 1992; Bassiony et al 2000). Predominant symptom onset is usually in the seventies. Significant risk factors include impaired hearing (Bassiony et al 2000; Leroi et al 2003) but not impaired vision, use of anti-hypertensive medication (Ballard et al 1995b), myocardial infarction, and congestive heart failure (Idiaquez et al 2002; Ostling and Skoog 2002). Elderly patients suffering from hallucinations often live alone, are unmarried or without children, tend to be African-American, and have a lower level of education; however none of these alone appears to be a significant risk factor for delusions in the elderly (Henderson et al 1998; Ostling and Skoog 2002; Cook et al 2003); or the association is unclear given general confounding in the literature of delusional and hallucinatory states. Delusions in the elderly are not generally associated with early or family history of psychiatric illness (Bassiony

et al 2000), although some studies (Gurian et al 1992; Fuchs 1994; Targum and Abbott 1999) have found an increased risk for late-life paranoia from early drastic life changes. Rate of admission (Ikeda et al 2003) and population (Leroi et al 2003) studies found an additional risk for delusions from female gender. Rates grouped by delusional content (Tsao et al 1997; Harwood et al 1999; Bassiony et al 2000; Hwang et al 2003) failed to find any gender differences, except for the study of Burns et al (1990) which found an increased risk of persecutory delusions in men. Conflicting studies cast doubt on the role of gender, but the issue of gender as a risk factor should be addressed formally. Cohen and others suggest that women may suffer more frequent multiple BPSD symptoms, for example, delusions and hallucinations or delusions and aggression (Cohen et al 1993).

Neuropsychological features and neuroanatomic considerations

Herlitz and Forsell (1996) found that 33 elderly persons diagnosed with delusional disorder were impaired in recall memory, but not recognition memory, on a Swedish version of the Famous Faces test and for a list of concrete nouns (Almeida et al 1995). Unlike patients with mild AD, their patients were able to use retrieval cues to improve performance, though the improvement was less than that of 66 normal controls.

Almeida et al (1995) were able to identify 2 clusters of delusional patients within a group of 47 based on tests of executive functioning. One of their study groups, distinguished by simple persecutory delusions and significantly older age at onset, showed increased initiation times and deficits in digit span, working memory, face recall, verbal fluency, extra-dimensional set shift, and the Tower of London task (starting at the 3-move stage) relative to other groups. These findings are consistent with those of deficient verbal fluency and conceptualization in AD patients (Jeste et al 1992) and verbal fluency and executive functioning deficits in nondemented elderly with persecutory delusions (Ostling et al 2004). Another group in the Almeida et al study, with earlier onset and traditional schizophrenic symptoms, had difficulty only with extra-dimensional set shift, and the Tower of London task at high difficulty levels, and normal performance on other tasks. These two groups were also distinguished electrophysiologically among a group of 81 subjects diagnosed with paranoid psychosis by Forstl et al (1994c). Their subjects with late paranoid psychosis and no Schneiderian

first rank symptoms showed slower posterior dominant alpha EEG rhythm (closer to AD) than the groups with traditional schizophrenic symptoms (Forstl et al 1994c).

An open question in the literature is the long-term cognitive status of the nondemented and LOS-diagnosed delusional elderly. Cohen-Mansfield et al (1998), in a study of delusions and hallucinations among elderly in day facilities, found 20% of their elderly sample to show caregiver reports of delusions and Brief Cognitive Rate Scale scores in the nondemented range. At 1-year follow up, a greater percentage had proceeded to dementia than nondelusional controls; however, the extremely small sample size prevented meaningful statistical analysis. At 7-year follow up, LOS patients were no more likely to progress to dementia than was a group of elderly persons with depression (Rabins and Lavrisha 2003) and have comparable life-expectancies to nondemented elderly at 5- to 10-year follow up. A case study by Schlimme et al (2002) and others suggests normal cognition at first symptom onset with moderate cognitive decline over the 20-year span of study in a nondemented elderly man.

The striking commonality of delusional content with age provokes several intriguing questions. First among these is the interplay of progressive brain disease with the natural changes of aging. The separate contributions of both executive functioning deficits and memory impairment to delusions of theft and delusions of misidentification can and should be further tested with targeted use of existing behavioral paradigms.

Temporal lobe atrophy occurs early in AD. As such, researchers must be careful to dissociate temporal lobe abnormalities in dementia associated with delusions from the generalized cerebral atrophy of dementia without delusions. Temporal lobes show less decline than that of other cerebral regions in normal aging, and thus may be a good place to search for what distinguishes delusional patients from elderly persons without delusions. Hirono et al (1998) studied a group of 26 patients with delusions (24/26 suffering from one or more persecutory delusions and 12/26 suffering from misidentification alone or with persecutory delusion) and found increases in cerebral glucose metabolism in left inferior temporal gyrus and a decrease in left medial temporal occipital region. An early SPECT study of 16 AD patients with mixed persecutory and misidentification delusions and 29 matched AD patients without delusions found bilateral hypoperfusion of superior and inferior temporal lobes in subjects with delusions. This area of hypoperfusion corresponds with location of the

fusiform face area and parahippocampal place area, which show increased activation after viewing faces and physical locations, respectively. The authors suggest potential disruption of these regions in Capgras delusion, house misidentification, and reduplicative paramnesia for houses (Starkenstein et al 1994).

Despite the probable involvement of temporal lobes in delusions of the elderly, it is likely that the frontal lobes may be the only region preferentially associated with delusions in both demented and nondemented populations. Executive function deficit on neuropsychological testing suggests a frontal mechanism, involving regions known to show selective atrophy in normal aging. Binetti et al (1995) compared a group of 24 AD and multi-infarct dementia patients' delusions with nondelusional controls. Delusion content in the group was split 54.4/45.6 simple persecutory beliefs/delusions of misidentification. The authors found the presence of isolated frontal white matter lesions to be independently associated with active delusions. These results did not correlate with dementia severity, and lesion number increased with age. The authors speculate on the interplay of dementia and age-related neuroanatomic changes. Mega et al (2000) found significant hypoperfusion of left and right dorsolateral frontal and left paralimbic regions in 10 delusional AD patients compared with an equal number of controls matched for Alzheimer's severity and severity of psychiatric symptoms excluding delusions and hallucinations.

Corey-Bloom et al (1995) and Howard (1992a, 1992b) found larger lateral ventricle size in LOS patients relative to both early-onset schizophrenics and controls, and late-onset schizophrenics did not show the thalamic volume decrease of early-onset schizophrenia (Howard et al 1992a). Staff et al (1999) found right frontotemporal hypoperfusion in 11 AD patients split 60/40 delusions of misidentification/delusions of persecution. Kotrla et al (1995) found that delusional patients with AD without hallucinations showed hypoperfusion of the left frontal regions; patients with hallucinations showed significant hypoperfusion of left parietal and summed total parietal lobes. Interestingly, those patients with delusions and hallucinations showed hypoperfusion of left frontal region, while hallucinations alone did not differ in frontal profile from control. Given the evidence for cerebral lateralization, it is unfortunate that the Kotrla et al patients were not reported by delusion content.

Intriguingly, a preponderance of the evidence suggests that localization of abnormality is, in fact, lateralized by delusion content. Delusions of persecution appear to be left lateralized, while delusions of misidentification right

lateralized. This is in keeping with evidence from delusions presenting after traumatic brain injury (Malloy 1994; Elie et al 1996). Forstl et al (1991) found a larger right anterior horn in the lateral ventricles and a larger volume of left anterior regions in a study of 40 patients with at least one type of delusional misidentification, suggesting accentuated atrophy of right frontal lobes and unusually well-preserved left frontal regions. Case study suggests right frontoparietal infarcts for Capgras delusion in dementia (Forstl et al 1991, 1994b; Diesfeldt and Troost 1995; Staff et al 2000). Right frontal hypoperfusion is also found in nurturing syndrome (Edelstyna et al 2001; Venneri et al 2000), phantom boarder syndrome (Jenkins et al 1997), and mirror sign (Breen et al 2001). Staff et al (2000) found this hypoperfusion to include Brodmann's area 9 and 10, which they hypothesize suggests a failure of episodic memory retrieval (Forstl et al 1994c). Delusions of misidentification, more common by far in AD than in other delusional syndromes, alone show a loss of cell count in CA1 regions of hippocampus (Jenkins et al 1997; Edelstyna et al 2001). Hippocampal volume in LOS with persecutory delusions (Forstl et al 1994c) was significantly greater than in that of paranoid schizophrenia (Howard et al 1992a).

Howard et al (1995) compared 16 patients with late-onset delusional disorder (persecutory delusions and lack of other diagnostic schizophrenia criteria) with 31 late-onset schizophrenics (classified in his study by presence of grandiose or fantastic delusions) and normal controls. They found all groups to show right-biased frontal/temporal lobe asymmetry (1.7% controls, 0.3% schizophrenics, and 8.5% delusional disorder). Both aged schizophrenics (5.9%) and delusional disorder (8.4%) showed significant temporal lobe asymmetry relative to that found in normal aging (2.6%). However, the delusional disorder group showed significantly greater asymmetry than the two other groups. The subjects with delusional disorder further showed a trend, just short of statistical significance, for overall smaller left temporal lobe volume.

Lopez et al (2001) found resting left medial temporal and left dorsolateral prefrontal cortex abnormalities. Of four AD patients studied using positron emission tomography imaging, two with persecutory delusions and two with hallucinations, all had frontotemporal hypoperfusion relative to nonpsychotic AD patients (Geroldi et al 2000a). Patients with hallucinations had, in addition, right parietal hypoperfusion and those two with aggression showed right orbital, right cingulate, and right dorsolateral activation

(Lopez et al 2001). The authors suggest that frontotemporal abnormalities are involved in both persecutory delusions and hallucinations, with hallucinations further requiring parietal lobe dysfunction

Geroldi et al (2000, 2002) found right frontal and left temporal horn atrophy in AD patients with delusions of persecution. Interestingly, though, they found a lessening of usual asymmetry in their nonAD elderly controls. Brain asymmetry within the delusional group was on par with that of normal aging, while those AD patients without delusions showed a relative lack of asymmetry. Cloud et al (1996) found the same pattern of atrophy in a case study of an unusual LOS woman showing phantom boarder syndrome and delusions of suspicion. Their subject showed long-standing delusions of suspicion changing to phantom boarder syndrome after an attempted burglary and progressive executive functioning.

In a paper advising against overinterpretation of neuroimaging studies in dementia, Mentis et al (1996) studied 9 AD patients with misidentification delusions and found general hypoperfusion of bilateral orbitofrontal and cingulate regions and left medial temporal area and hyperperfusion of superior temporal and inferior parietal regions. Sultzer et al (2003) found right superior dorsolateral frontal cortex, right inferior frontal pole, and right lateral orbitofrontal perfusion in groups of AD patients with mixed delusion content. The Sultzer et al patients were interestingly biased toward delusions of leadership (of a group) or employment (at a company they had never previously worked for). Fukuhara et al (2001), uniquely, found right medial posterior parietal hypoperfusion in AD patients who had delusions of theft. Further work would be needed to distinguish clearly the role of parietal lobe dysfunction in delusions in dementia.

In sum, these studies lead to speculation that impairment of frontotemporal systems may underlie delusions in the elderly, and that delusional content in the elderly may be influenced by factors of cerebral dominance, such that delusions of persecution emerge with dysfunction of left hemisphere, while delusions of misidentification emerge with dysfunction of right hemisphere. These speculations must be constrained by serious limitations and cautions, as we discuss in the next section.

Limitations and cautions

Efforts to extract a neuroanatomic correlate for delusions in the elderly suffer from inconsistency in previous research as to three fundamental research design issues:

Criteria—diagnosis

Patients with multiple delusion types (that is, persecution and misidentification concurrently in dementia) are routinely grouped together in a generic “delusional” group. Studies may look predominantly at delusion types rare in the elderly, or delusion content may not be reported. Further, the difference between delusional disorder and psychosis—psychotic symptoms is poorly delineated. Patients experiencing both delusions and hallucinations are frequently not excluded from studies of delusions. Others group delusions of various content, including those referred to as “fantastic delusion” throughout this review, and hallucinations into the single category of Schneiderian first-rank symptoms. Such studies are often controlled only by conducting neuroimaging when no visual hallucinations are present.

Definition of delusional

No consistent standard has been set for presence of active delusions in available neuroimaging studies. Some studies administer neuropsychiatric evaluations at various times prior to brain scanning while others require symptom presence at time of scanning. This variability in methodology confounds the ability to determine whether, for example, depressed regional cerebral blood flow (rCBF) is transient during active delusion or reflects ongoing brain state. Studies also vary in their inclusion criteria for presence or absence of treatment – prior to or during neuroimaging. Studies of somatic delusions suggest an increase in rCBF in left temporoparietal regions following treatment with medication and/or modified electroconvulsive therapy (Ota et al 2003). Thus the role of treatment in obscuring significant differences is potentially relevant.

Lack of clarity in or lack of control group

Most studies in AD compared patients with AD with BPSD to AD patients without BPSD. Most in LOS compare either to aged early-onset schizophrenics or to normal nondemented elderly. Debate remains as to the degree of asymmetry present in these normal controls. We suggest future neuroimaging studies, sensitive to these methodological concerns, in attempts to test the proposals of this paper more rigorously.

Clinical relevance

The relative homogeneity of delusional content between both demented and nondemented elderly populations

suggests a common neuroanatomic phenotype. Patients with this phenotype may be suspicious of caregivers and medical professionals and, as a result, may not present for treatment until the family is unable to deal with the problem (Gurian et al 1992). Ostling and Skoog (2002) found that, in nondemented patients, only 28% of delusional patients were detected in formal medical evaluation, and suggest that key informant interview is crucial for identifying these cases. Patients with late-onset delusions may respond poorly to antipsychotic medications relative to patients in younger groups with delusional symptoms. Commonality of delusion content may suggest need for a separate diagnostic classification and different course of treatment to reflect the clear differences of these patients from those with early-onset delusions. Structured long-term study of late-onset delusions in nondemented and mildly demented patients would provide necessary information to help prepare families for expected changes and potential complications, and help answer whether delusions in the elderly are an early warning sign of future dementia or reflect additional potential complications of aging separate from dementia.

Acknowledgments

The authors would like to acknowledge the support of the Medical Research Service, Department of Veterans Affairs, Washington DC and the National Institutes of Health (R01 AG 14345 05).

References

- Alici-Evcimen Y, Ertan T, Eker E. 2003. Case series with late-onset psychosis hospitalized in a geriatric psychiatry unit in Turkey: experience in 9 years. *Int Psychogeriatr*, 15:69–72.
- Almeida OP, Howard RJ, Levy R, et al. 1995. Clinical and cognitive diversity of psychotic states arising in late life (late paraphrenia). *Psychol Med*, 25:699–714.
- [APA] American Psychiatric Association. 2000. Diagnostic and Statistical Manual of Mental Disorders DSM-IV-TR, 4th ed. Washington DC: APA.
- Ballard C, Bannister C, Graham C, et al. 1995a. Associations of psychotic symptoms in dementia sufferers. *Br J Psychiatry*, 167:537–40.
- Ballard CG, Bannister CL, Patel A, et al. 1995b. Classification of psychotic symptoms in dementia sufferers. *Acta Psychiatr Scand*, 92:63–8.
- Ballard C, Holmes C, McKeith I, et al. 1999. Psychiatry morbidity in dementia with Lewy bodies: a prospective clinical and neuropathological comparative study with Alzheimer's disease. *Am J Psychiatry*, 156:1039–45.
- Bassiony MM, Lyketsos CG. 2003. Delusions and hallucinations in Alzheimer's disease: a review of the brain decade. *Psychosomatics*, 44:388–401.
- Bassiony MM, Steinberg MS, Warren A, et al. 2000. Delusions and hallucinations in Alzheimer's disease: prevalence and clinical correlates. *Int J Geriatr Psychiatry*, 15:99–107.

- Bianchetti A, Binetti G, Zanetti O, Frisoni, et al. 1992. Delusions in multi-infarct dementia and in Alzheimer's disease. Third International Conference on Alzheimer's disease. 1992 July 12-17; Abano Terme, Italy. *Neurobiol Aging*, 13(Suppl 1):S9.
- Binchetti G, Bianchetti A, Padovani A, et al. 1993. Delusions in Alzheimer's disease and multi-infarct dementia. *Acta Neurol Scand*, 88:5-9.
- Binetti G, Padovani A, Magni E, et al. 1995. Delusions in dementia: clinical and CT correlates. *Acta Neurol Scand*, 91:271-5.
- Breen N, Caine D, Coltheart M. 2001. Mirrored-self misidentification: two cases of focal onset dementia. *Neurocase*, 7:239-54.
- Brune M, Shroder SG. 2003. Erotomania variants in dementia. *J Geriatr Psychiatry Neurol*, 16:232-4.
- Burns A, Jacoby R, Levy R. 1990. Psychiatric phenomena in Alzheimer's disease I: disorders of thought content. *Br J Psychiatry*, 157:72-6.
- Cloud, G, Carew T, Rothenberg H, et al. 1996. A case of late-onset psychosis: integrating neuropsychological and SPECT data. *J Geriatr Psychiatry Neurol*, 9:146-53.
- Cohen D, Eisdorfer C, Gorelick P, et al. 1993. Sex differences in the psychiatric manifestations of Alzheimer's disease. *J Am Geriatr Soc*, 41:229-32.
- Cohen-Mansfield J, Taylor L, Werner P. 1998. Delusions and hallucinations in an adult day care population: a longitudinal study. *Am J Geriatr Psychiatry*, 6:104-21.
- Cook SE, Miyahara S, Bacanu SA, et al. 2003. Psychotic symptoms in Alzheimer disease: evidence for subtypes. *Am J Geriatr Psychiatry*, 11(4):406-413.
- Corey-Bloom J, Jernigan T, Archibald S, et al. 1995. Quantitative magnetic resonance imaging of the brain in late-life schizophrenia. *Am J Psychiatry*, 152:447-9.
- Devanand DP, Brockington CD, Moody BJ, et al. 1992. Behavioral syndromes in Alzheimer's disease. *Int Psychogeriatr*, 4(Suppl 2):161-84.
- Diesfeldt HFA, Troost D. 1995. Delusional misidentification and subsequent dementia: a clinical and neuropathological study. *Dementia*, 6:94-98.
- Edelstyna, NMJ, Oyebodeb F, Barrettc K. 2001. The delusions of capgras and intermetamorphosis in a patient with right-hemisphere white-matter pathology. *Psychopathology*, 34:299-304.
- Elie M, Primeau F, Cole MG. 1996. Chronic subdural hematoma in the elderly: a case report. *J Geriatr Psychiatry Neurol*, 9:100-1.
- Malloy PF, Richardson ED. 1994. The frontal-lobes and content-specific delusions. *J Neuropsychiatry*, 6:455-66.
- Fischer C, Bozanovic-Sosic R, Norris M. Review of delusions in dementia. 2004. *Am J Alzheimers Dis Other Demen*, 19:19-23.
- Forstl H, Burns A, Jacoby R, et al. 1991. Neuroanatomical correlates of clinical misidentification and misperception in senile dementia of the Alzheimer's type. *J Clin Psychiatry*, 52:268-71.
- Forstl H, Besthorn C, Burns A, et al. 1994b. Delusional misidentification in Alzheimer's disease: a summary of clinical and biological aspects. *Psychopathology*, 27:194-9.
- Forstl H, Burns A, Levy R, et al. 1994a. Neuropathological correlates of psychotic phenomena in confirmed Alzheimer's disease. *Br J Psychiatry*, 165:53-9.
- Forstl H, Dalgalarrondo P, Riecher-Rossler A, et al. 1994c. Organic factors and the clinical features of late paranoid psychosis: a comparison with Alzheimer's disease and normal aging. *Acta Psychiatr Scand*, 89:335-40.
- Fuchs, T. 1994. Uprooting and late-life psychosis. *Eur Arch Psychiatry Clin Neurosci*, 244:126-30.
- Fukuhara R, Ikeda M, Nebu A, et al. 2001. Alteration of rCBF in Alzheimer's disease patients with delusions of theft. *Neurorep*, 12:2473-6.
- Geroldi C, Akkawi NM, Galluzzi S, et al. 2000. Temporal lobe asymmetry in patients with Alzheimer's disease with delusions. *J Neurol Neurosurg Psychiatry*, 69:187-91.
- Geroldi C, Bresciani L, Zanetti O, et al. 2002. Regional brain atrophy in patients with mild Alzheimer's disease and delusions. *Int Psychogeriatr*, 14:365-78.
- Gurian BS, Wexler D, Baker EH. 1992. Late-life paranoia: possible association with early trauma and infertility. *Int J Geriatr Psychiatry*, 7:277-84.
- Hafner H, Löffler W, Riecher-Rossler A, et al. 2001. Schizophrenia and delusions in middle aged and elderly patients. Epidemiology and etiological hypothesis. *Nervenarzt*, 72:347-57.
- Harwood DG, Barker WW, Ownby RL, et al. 1999. Prevalence and correlates of Capgras syndrome in Alzheimer's disease. *Int J Geriatr Psychiatry*, 14:415-20.
- Haupt M, Romero B, Kurz A. 1996. Delusions and hallucinations in Alzheimer's disease: results from a two year longitudinal study. *Geriatr Psychiatry*, 11:965-72.
- Henderson AS, Kay DW. 1997. The epidemiology of functional psychoses of late onset. *Eur Arch Psychiatry Clin Neurosci*, 247:176-89.
- Henderson AS, Korten AE, Levings C, et al. 1998. Psychotic symptoms in the elderly: a prospective study in a population sample. *Int J Geriatr Psychiatry*, 13:484-92.
- Herlitz A, Forsell Y. 1996. Episodic memory deficit in elderly adults with suspected delusional disorder. *Acta Psychiatr Scand*, 93:355-61.
- Hirono N, Mori E, Ishii K, et al. 1998. Alteration of regional cerebral glucose utilization with delusions in Alzheimer's disease. *J Neuropsychiatry*, 10:433-9.
- Howard R, Almeida O, Levy R. 1994. Phenomenology, demography and diagnosis in late paraphrenia. *Psychol Med*, 24:397-410.
- Howard RJ, Forstl H, Almeida O, et al. 1992a. Computer-assisted CT measurements in late paraphrenics with and without Schneiderian first-rank symptoms. *Int J Geriatr Psychiatry*, 7:35-8.
- Howard RJ, Forstl H, Burns A, et al. 1992b. First-rank symptoms of Schneider in late paraphrenia: Cortical structural correlates. *Br J Psychiatry*, 160:108-9.
- Howard R, Mellers J, Petty R, et al. 1995. Magnetic resonance imaging volumetric measurements of the superior temporal gyrus, hippocampus, parahippocampal gyrus, frontal and temporal lobes in late paraphrenia. *Psychol Med*, 25:495-503.
- Hwang JP, Cheng-Hong Y, Shih-Jen Tsai, et al. 1997. Delusions of theft in dementia of the Alzheimer type: a preliminary report. *Alzheimer Dis Assoc Disor*, 11:110-12.
- Hwang JP, Chen-Hong Y, Shih-Jen T. 2003. Phantom boarder symptom in dementia. *Int J Geriatr Psychiatry*, 18:417-20.
- Hwang JP, Tsai SJ, Yang Ch, et al. 1999. Persecutory Delusions in Dementia. *J Clin Psychiatry*, 60:550-3.
- Idiaquez J, Sandoval E, Seguel A. 2002. Association between neuropsychiatric and autonomic dysfunction in Alzheimer's Disease. *Clin Auton Res*, 12:43-6.
- Ikeda M, Shigenobu K, Fukuhara R, et al. 2003. Delusions of Japanese patients with Alzheimer's disease. *Int J Geriatr Psychiatry*, 18:527-32.
- Jenkins MA, Cimino C, Malloy PF, et al. 1997. Neuropsychiatric factors in the illusion of visitors among geriatric patients: a case series. *J Geriatr Psychiatry Neurol*, 10:79-87.
- Jeste DV, Wragg RE, Salmon DP, et al. 1992. Cognitive deficits of patients with Alzheimer's disease with and without delusions. *Am J Psychiatry*, 149:184-9.
- Kay DW, Henderson AS, Scott R, et al. 1985. Dementia and depression among the elderly living in the Hobart community: the effect of the diagnostic criteria on the prevalence rates. *Psychol Med*, 15:771-8.
- Konakanchi R, Grace JJ, Yap D, et al. 1999. Pimozide in the treatment of litigious delusions. *Psychiatr Serv*, 50:837.
- Kotrla KJ, Chacko RC, Harper RG, et al. 1995. SPECT findings on psychosis in Alzheimer's disease. *Am J Psychiatry*, 152:1470-5.
- Leroi I, Voulgari A, Breitner JCS, et al. 2003. The epidemiology of psychosis in dementia. *Am J Geriatr Psychiatry*, 11:83-91.

- Livingston G, Kitchen G, Manela M, et al. 2001. Persecutory symptoms and perceptual disturbance in a community sample of older people: the Islington study. *Int J Geriatr Psychiatry*, 16:462–8.
- Lopez OL, Smith G, Becker JT, et al. 2001. The psychotic phenomenon in probable Alzheimer's disease: a positron emission tomography study. *J Neuropsychiatry Clin Neurosci*, 13(1):50–55.
- McKhann G, Drachman D, Folstein M, et al. 1994. Clinical Diagnosis of Alzheimer's disease: Report of the NINCDS-ADRDA work group under the auspices of department of Health and Human Services Task Force on Alzheimer's dDisease. *Neurology*, 34:939–44.
- Malloy PF. 1994. The frontal lobes and content specific delusions. *J Neuropsychiatry Clin Neurosci*, 6:455–66.
- Mega MS, Lee L, Dinov ID, et al. 2000. Cerebral correlates of psychotic symptoms in Alzheimer's disease. *Neuropsychiatry Neuropsychol Behav Neurol*, 13:163–70.
- Mendez MF, Martin RJ, Smyth KA, et al. 1992. Disturbances of person identification in Alzheimer's disease: a retrospective study. *J Nerv Ment Dis*, 180:94–6.
- Mentis MJ, Weinstein EA, Horwitz B, et al. 1996. Abnormal glucose metabolism in the delusional misidentification syndromes: a positron emission tomography study in Alzheimer's disease. *Biol Psychiatry*, 58:438–49.
- Ostling S, Johansson B, Skoog I. 2004. Cognitive test performance in relation to psychotic symptoms and paranoid ideation in non-demented 85-year-olds. *Psychol Med*, 34:443–50.
- Ostling S, Skoog I. 2002. Psychotic symptoms and paranoid ideation in a nondemented population-based sample of the very old. *Arch Gen Psychiatry*, 59:53–9.
- Ota M, Mizukami K, Katano T, et al. 2003. A case of delusional disorder, somatic type with remarkable improvement of clinical symptoms and single photon emission computed tomography findings following modified electroconvulsive therapy. *Prog Neuropsychopharmacol Biol Psychiatry*, 27:881–4.
- Rabins PV, Lavrisha M. 2003. Long-term follow-up and phenomenologic differences distinguish among late-onset schizophrenia, late-life depression and progressive dementia. *Am J Geriatr Psychiatry*, 11:589–94.
- Rao V, Lyketsos CG. 1998. Delusions in Alzheimer's disease: a review. *J Neuropsychiatry*, 10:373–82.
- Schlimme J, Bruggemann B, Haltenhof H, et al. 2002. Paranoia with late onset: psychopathology and psychodynamics. *Nervenarzt*, 73:289–92.
- Shinosaki K, Nishikawa T, Takeda M. 2000. Neurobiological basis of behavioral and psychological symptoms in dementia of the Alzheimer type. *Psychiatry Clin Neurosci*, 54:611–20.
- Staff RT, Shanks MF, Macintosh L, et al. 1999. Delusions and Alzheimer's disease: SPECT evidence of right hemisphere dysfunction. *Cortex*, 35:549–60.
- Staff RT, Venneri A, Gemmell HG, et al. 2000. HMPAO SPECT imaging of Alzheimer's disease patients with similar content-specific autobiographical delusion: comparison using statistical parametric mapping. *J Nucl Med*, 41:1451–55.
- Starkenstein SE, Vazquez S, Petracca G, et al. 1994. A SPECT study of delusions in Alzheimer's disease. *Neurology*, 44:2055–9.
- Steele C, Rovner B, Chase GA. 1990. Psychiatric symptoms and nursing home placement of patients with Alzheimer's disease. *Am J Psychiatry*, 147:1049–51.
- Sultzer DL, Brown CV, Mandelkern MA, et al. 2003. Delusional thoughts and regional frontal/temporal cortex metabolism in Alzheimer's disease. *Am J Psychiatry*, 160:341–9.
- Targum SD, Abbott JL. 1999. Psychoses in the elderly: a spectrum of disorders. *J Clin Psychiatry*, 60(Suppl 8):4–10.
- Tsai SJ, Hwang JP, Chen-Hong Y, et al. 1997. Delusional jealousy in dementia. *J Clin Psychiatry*, 58:492–4.
- Venneri A, Shanks MF, Staff RT, et al. 2000. Nurturing syndrome: a form of pathological bereavement with delusions in Alzheimer's disease. *Neuropsychologia*, 38:213–24.
- Webster J, and Grossberg GT. 1998. Late-life onset of psychotic symptoms. *Am J Geriatr Psychiatry*, 6:196–202.
- [WHO] World Health Organization. 1994. International Statistical Classification of Diseases and Related Health Problems, 10th Revision. Geneva: WHO.

