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# Review of delusions in dementia

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## Abstract

*Although delusions are common symptoms in dementia and are associated with a number of adverse outcomes, research in this area has been limited. This article attempts to summarize the existing literature on delusions in dementia with respect to known risk factors, etiology, pathogenesis, neurocognitive findings, behavioral symptoms, and treatment. This study reviews all relevant abstracts and articles pertaining to delusions and dementia. The reviewers found that the studies were limited by confusion concerning phenomenology. However, consistent findings show that delusions are associated with certain demographic variables, neuropathologic and neurocognitive findings, adverse behavioral outcomes, and limited treatment response. The authors conclude that further longitudinal studies with better clarification of terminology are required to clarify inconsistencies and shed light on future treatment options.*

*Key words: Alzheimer's, dementia, delusions*

## Introduction

Delusions are a common manifestation of dementia and were reported in the first documented case of Alzheimer's disease (AD).<sup>1</sup> Delusions in dementia are significant for many reasons. Patients with dementia and delusions exhibit accelerated cognitive decline,<sup>1-3</sup> increased aggressive behavior,<sup>4,5</sup> higher caregiver stress,<sup>6</sup> and earlier institutionalization<sup>7-10</sup> than those without delusions. Despite the significance of the symptoms and their relative prevalence in dementia, delusions have not

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been studied extensively. This paper reviews the existing literature on delusions in dementia and provides suggestions for future study.

## Epidemiology

Several studies have examined the prevalence of delusions in dementia. However, samples used in early studies were clinically heterogeneous. The studies defined delusions differently and did not take into account confounding factors and known risk factors. Some studies did not differentiate delusions from other symptoms of psychosis, such as hallucinations.

The first extensive review of this area<sup>11</sup> examined 21 studies and found a prevalence ranging from 10 to 73 percent. This large range is not surprising, given the limitations of previous studies. More recent studies show that approximately one-third of dementia patients suffer from delusions.<sup>5,12-14</sup> Paulsen and Salmon<sup>15</sup> assert that the prevalence of delusions increases over time—20 percent by year one and 50 percent by year four—suggesting these symptoms may need to be evaluated longitudinally as opposed to cross-sectionally.

## Phenomenology

A delusion, according to DSM-IV criteria, is a fixed false belief that is not culturally bound. Delusions in dementia may resemble other phenomena, such as confabulation (an explanation for a missing or absent memory). Confabulation tends to be most prevalent in amnesic disorders such as Wernicke-Korsakoff's syndrome. Delusions also differ from memory-based cognitive symptoms, such as disorientation.

Migliorelli et al.<sup>14</sup> estimated five subtypes of delusions, including paranoid, hypochondriacal, Capgras syndrome, house misidentification, and grandiosity. They noted that, while paranoid delusions were most prevalent, 76 percent of patients had more than one subtype. Gormley et al.<sup>5</sup> found,

on the contrary, that delusions of theft were most common. Other subtypes include phantom boarders, spousal infidelity, and fear of the caregiver plotting to leave. Hwang et al.<sup>16</sup> studied delusions of theft in geriatric psychiatry inpatients and found that they occurred in the early stages of the disease. He also examined persecutory delusions, which were common and associated with physical aggression. Harwood et al.<sup>17</sup> found Capgras' syndrome to be present in 10 percent of patients with AD and to be most common in the later stages of the disease.

Cummings<sup>18</sup> examined delusions in 20 patients with organic brain syndrome and found that four subtypes were most common: simple persecutory delusions, complex persecutory delusions, grandiose delusions, and delusions associated with a specific neurological deficit. He determined that simple persecutory delusions, such as the delusions of theft, were most common among patients with AD and vascular dementia, while other subtypes tended to be rarer and associated with other organic brain pathology.

## Risk factors

Many studies have examined risk factors for the development of delusions in dementia. According to Hirono et al.,<sup>19</sup> most of these studies suffered from methodological limitations, such as small sample sizes, lack of statistical power, confusion around dementia diagnosis, lack of clarity when defining psychotic symptoms, and limited consideration of interaction among the various risk factors.

## Demographics

The role of demographic variables, which include age, gender, education, and race, is not clear. Most studies have shown patients with delusions and dementia to be older than those without delusions.<sup>12,20-22</sup> To the contrary, Chen et al.<sup>23</sup> found a lower prevalence of delusions, affective symptoms, and aggressive behavior among older patients with dementia when compared with their younger counterparts. Some studies<sup>14,24</sup> show no difference.

With respect to gender, some studies show a higher prevalence of psychosis among men with dementia,<sup>25-27</sup> while others show a higher prevalence among women.<sup>23,28</sup> Other studies have shown an equal distribution among the sexes.<sup>14,24,29-31</sup>

Some studies have suggested an association between lower levels of education and the presence of psychosis,<sup>32</sup> while others have not.<sup>14,30,31</sup> Two of these studies have shown an association between the presence of delusions and lower education.<sup>30,31</sup>

Ethnicity has been explored in some studies. Two studies have demonstrated a higher association of delusions

with AD among African Americans.<sup>33,34</sup> Chow et al.<sup>35</sup> demonstrated that patients with AD and delusions who lived in China tended to be referred for treatment later in the course of the disease and less in response to caregiver stress than those in the US.

## Psychiatric symptoms

Some studies have explored the relationship of psychiatric symptoms to the presence of delusions in dementia. Two studies<sup>3,36</sup> showed higher depression rating scores among patients with AD and delusions versus those without, while other studies<sup>5,14,37</sup> showed no difference. Ballard et al.<sup>38</sup> explored the role of anxiety among patients with psychotic features and found that the presence of psychosis, including delusions, increased levels of anxiety among patients with dementia.

Ballard et al.<sup>39</sup> found an association between adverse life events and delusions in dementia. Low et al.<sup>40</sup> examined premorbid personality and its relationship to psychosis in dementia and concluded that patients with delusions had higher rates of neuroticism.

## Medications and extrapyramidal symptoms

Bassionny et al.<sup>12</sup> found an increased probability of dementia and delusions in patients taking antihypertensive medications but no association with neuroleptics, antidepressants, cholinesterase inhibitors, oral hypoglycemics, or insulin. Two studies<sup>41,42</sup> have shown an association between extrapyramidal symptoms and delusions, while other studies<sup>13,14,29,44</sup> failed to show an association. Ballard et al.<sup>39</sup> found an association with sensory impairment among delusional patients with dementia.

## Disease course

There is little consensus as to what, if any, role the disease stage plays in the presence of delusions in dementia. Some studies have shown a relationship between the presence of psychosis and severity of dementia,<sup>13,45-46</sup> while others have not.<sup>30,47</sup>

Eustace et al.<sup>48</sup> conducted a retrospective chart review of patients with AD and behavioral symptoms. They found that, while activity disturbance was a common and persistent symptom, delusional ideation was moderately persistent and affective symptoms seldom lasted longer than a year.

## Etiology

The existence of delusions and psychosis in dementia suggests that these symptoms may reflect underlying disease pathology. Hirono et al.<sup>19</sup> compared patients with

frontotemporal dementia, AD, and Lewy body disease and found significantly higher rates of psychosis among the latter two diagnoses.

Several theories have been proposed regarding the etiology of delusions in dementia. The theory of hypofrontality states that delusional symptoms are related to selective frontal lobe dysfunction. Studies have shown impaired frontal lobe metabolism, higher density of senile plaques in the frontal cortex, and deficits in frontosubcortical circuits.<sup>15</sup> Neuroimaging studies, including SPECT, have supported this as well.<sup>49,50</sup>

In 1991, Flynn<sup>51</sup> proposed that delusions were independent noncognitive manifestations of the neurobiology of AD and vascular dementia. Supporting this theory, Sweet et al.<sup>52</sup> examined the density of neuritic plaques and tangles in the brains of 25 patients with AD and 25 controls and found no difference in density.

A contrary theory<sup>11,53</sup> proposes that affective and psychotic symptoms arise as a manifestation of the common pathophysiology attributable to AD. This is substantiated by Farber et al.,<sup>54</sup> who examined 100 cases post-mortem and found those with psychosis had two times the density of neurofibrillary tangles than those without psychosis. Edwards-Lee et al.<sup>55</sup> used quantitative electroencephalogram (EEG) and found more severe brain dysfunction among patients with psychosis and dementia than among patients with psychosis without dementia.

Forstl et al.<sup>56</sup> looked at a cohort of patients with AD and misidentification delusions. Using neuroimaging, he was able to establish accentuated degeneration of the right frontal lobe relative to the left. Ballard et al.<sup>57</sup> found that delusions in a cohort of Lewy body patients were related to up-regulation of postsynaptic muscarinic receptors.

Zubenko et al.<sup>37</sup> proposed that psychotic symptoms in dementia are related to a reduction of serotonin in the prosubiculum. Geroldi et al.<sup>58</sup> found temporal lobe asymmetry—where the right temporal lobe is larger than the left—may be related to the presence of delusions in dementia.

Genetic studies<sup>59</sup> have shown a relationship with a specific 102/C polymorphism on the gene regulating 5HT (serotonin) 2A receptor. Patients with AD and delusions, whether familial or nonfamilial, were significantly more homozygous for the C 102 allele than those who were not. Apo E has shown not to be a factor.<sup>44</sup>

According to Mendez et al.,<sup>60</sup> misidentification delusions may arise from an altered sense of familiarity based on misperceptions, and are sustained by confabulation.

## Neurocognitive and behavioral changes

The relationship of neurocognitive function in demented patients with delusions versus those without delusions is

unclear. Two studies<sup>13,15</sup> showed a relationship with more rapid cognitive decline, while another<sup>51</sup> showed only mild differences. Other studies<sup>3,61,62</sup> have shown that patients with AD and psychosis were less intellectually compromised and had higher Mini-Mental State Examination (MMSE) scores. Fleminger et al.<sup>63</sup> proposed an inverse relationship between organic brain damage and the presence of paranoid delusions, based on the assumption that cognitive capacity is needed to formulate delusions. Lachs et al.<sup>64</sup> found that delusions tended to occur in the mid-range of cognitive impairment (MMSE 17-23) and were less common in patients mildly and severely affected.

Studies show that AD patients with delusions are more uninhibited and have more frontal lobe dysfunction on neurocognitive testing.<sup>15</sup> Lopez et al.<sup>3</sup> looked at neuropsychological function and its relationship to symptoms of psychosis. He determined that patients with poor insight had more evidence of frontal or executive dysfunction but that this had no relation to the presence of psychosis.

Several studies have found an increased association between aggression and delusions among AD patients.<sup>4,21,22,25,51,64</sup> Verbal aggression rates have ranged from 33 to 67 percent<sup>65,66</sup> and have been documented to be more common than physical aggression.<sup>67,68</sup> Gilley et al.<sup>4</sup> looked at physical aggression prospectively and found a high association with delusions among patients with AD.

Eustace et al.<sup>69</sup> reported that 28 percent of patients with AD and delusions were verbally aggressive, and hypothesized that their behavior was the result of a perceived threat based on false beliefs. He also followed patients over a 24-month period and found delusions to be moderately present, while other symptoms, such as activity disturbance, were present more commonly. Wandering behavior was found to be more common among patients with dementia and psychosis.<sup>28</sup>

Magni et al.<sup>10</sup> found that delusions were predictive of early institutionalization when other confounding factors were not a cause.

## Treatment

The literature on treatment of delusional symptoms in dementia is sparse. Limitations of previous studies include the lack of diagnostic specificity around delusional symptoms and lack of good treatment options. Cholinesterase inhibitors have been used to treat these symptoms.<sup>70</sup> The mechanism of this is believed to be related to cholinergic dysfunction. In open label studies, risperidone has demonstrated a reduction in delusions of theft and the caregiver stress associated with it,<sup>71</sup> and it has reduced the frequency of delusions in general.<sup>72</sup> Olanzapine has been shown in two large placebo-controlled multicentered trials to reduce psychotic symptoms and

delay their emergence.<sup>73,74</sup> In two randomized separate placebo-controlled trials,<sup>31,75</sup> haloperidol has been effective in reducing psychosis and agitation, although the relationship of delusional symptoms to behavioral symptoms is not clear. The vast majority of these studies have suffered from the limitation that psychotic symptoms were not differentiated, and if they were, specific subtypes of delusions were not isolated.

## Conclusion

Delusions are common yet often under-recognized symptoms in dementia. There are many different kinds. Known risk factors include depression, advanced age, and limited education, while the role of gender and ethnicity is less clear. There appears to be an association with advanced neuropathology, selective frontal lobe dysfunction, preserved intellect, and rapid cognitive decline. Delusions in dementia are associated with adverse outcomes such as aggression, caregiver stress, and earlier institutionalization. Response to treatment remains poor. Limitations of existing research include the lack of longitudinal studies, poor understanding of phenomenology, and the need for more rigorous exclusion criteria. Before an effective treatment can be developed, further research must better characterize the prevalence, phenomenology, and etiology of symptoms.

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