Phenomenological Distinctions Needed in DSM-V: Delirium, Subsyndromal Delirium, and Dementias

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Prior to DSM-III, the diagnostic criteria to distinguish delirium and dementia were lacking. Research using DSM-III and subsequent versions has highlighted substantial comorbidity between these two major cognitive disorders with up to 89% of hospitalized dementia patients experiencing delirium.[1] Though delirium negatively affects subsequent functional capacity and the trajectory of cognitive decline and is associated with increased morbidity and mortality, it is frequently underdiagnosed, especially in older patients, in whom symptoms overlapping with dementias can present diagnostic challenges. Neuropsychiatric symptoms are almost ubiquitous during the course of dementia,[2] but the role of unrecognized comorbid delirium in causing or exacerbating these symptoms has received limited attention, despite the heightened vulnerability to deliriogenic factors (e.g., anticholinergic medication effects) in dementia populations.

Various evidence suggests that psychotic symptoms in dementia may be due to unrecognised superimposed delirium. Two patterns in the course of psychotic symptoms in Alzheimer's disease contrast: persistence with treatment resistance versus relative transience, the latter consistent with delirious states.[3] Recent factor analytical studies indicate distinct phenomenological patterns to psychosis in Alzheimer's disease—hallucinations and misidentifications which correlate with cognitive impairment, and persecutory delusions that relate more closely to mood disturbances or other factors, such as delirium.[4,5] The risk of psychosis in both delirium and Alzheimer's disease is related to the magnitude of medical morbidity[6,7]—a risk factor for delirium, as well as with COMT (catechol-O-methyltransferase) genetic variations.[8,9] Moreover, dementia complicated by psychosis evidences generalized slowing on electroencephalography (EEG) comparable to that in delirium and is independent of dementia severity.[10]

The traditional distinction between delirium and dementia, according to acuteness of onset and temporal course, is less clear in those elderly who develop "persistent cognitive impairment" following an episode of delirium[11] or experience the fluctuating symptom pattern of Lewy Body Dementia (LBD). Delirium may be the harbinger of an underlying undiagnosed dementia,[12] or persistent cognitive deficits may relate to medical problems that caused delirium (e.g., hypoxemia, encephalitis), medication effects, consequences of inability to cooperate with treatments, or direct neurotoxicity of delirium. DSM-IV describes a circularity in delirium-dementia differentiation: delirium is the suggested diagnosis when cognitive changes "are not better accounted for by a preexisting, established or evolving dementia;" dementia is the suggested diagnosis when "deficits do not occur exclusively during the course of a delirium." Further, subsyndromal delirium is not recognized in DSM-IV-TR, nor are guidelines offered for when post-delirium cognitive impairment is better attributed to dementia.

DSM-V can provide more clarity regarding differential diagnosis and comorbidity by addressing relative frequencies and characteristics of individual symptoms, including further phenomenological delineation of dementia types, and by increasing awareness of symptoms possibly related to subsyndromal delirium. It is underappreciated that delirium symptoms predominate dementia symptoms when they are comorbid, but present with more impaired cognitive scores[13] or more disorganized thinking and disorientation.[14] These studies lend credence to the clinical dictum to "assume delirium until proven otherwise." Careful history-taking and use of sensitive and specific delirium assessment instru-

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ments (e.g., DRS-R98) can reliably distinguish delirium from dementia.

Neuropsychiatric symptom patterns also assist differentiation. In Alzheimer's disease, attentional abilities are relatively spared compared with LBD and delirium.[15] Blinded ratings of delirium and dementia cases found greater impairment in delirium for disturbances of attention, visuospatial ability, the sleep-wake cycle, perception, thought process, affective lability, motor agitation, comprehension, and acuity of onset and fluctuation of symptoms.[16] EEG findings can further aid differential diagnosis, especially with prion-induced dementias and LBD.

Criteria exist for differentiating psychosis of Alzheimer's disease from functional psychoses[17] but are less clear regarding delirium, although differences exist. Delusions in delirium typically involve paranoia about immediate well-being or perceived danger in the environment, whereas delusions in Alzheimer's disease commonly reflect themes of being robbed or abandoned or are really misidentifications.[4] Formal thought disorder in delirium frequently involves illogicality and derailment compared with the poverty of thought in dementia.[18] Visual illusions and hallucinations are most common in delirium and LBD, compared with Alzheimer's disease where careful interviewing is needed to differentiate complex visual hallucinations from delusions or confabulations. Tactile hallucinations and formication are highly suggestive of delirium.

Psychosis in Alzheimer's disease correlates with the rate and severity of cognitive decline, especially seen in disturbances of attention, construction, and fluency.[19] In contrast, studies of delirium suggest no correlation between cognition and psychosis.[20] Moreover, psychosis is related to structural neuropathological changes in Alzheimer's disease,[21] whereas psychosis in delirium may reflect neurochemical changes associated with particular etiologies. APOE genotype and premorbid schizotypal features are risk factors for psychosis in Alzheimer's disease but not in delirium.[22–24]

Psychotic symptoms in delirium respond well to neuroleptics,[25,26] but less so in Alzheimer's disease, reflecting the relatively greater increase in central dopaminergic function that occurs with delirium.[27] Cholinergic agents are mainstays for Alzheimer's disease treatment, and chronic prophylaxis with rivastigmine in vascular dementia reduces delirium incidence.[28] Cholinergic agents show some promise in treating delirium.[29] We hypothesize that neuropsychiatric symptom improvement in dementia using neuroleptics or cholinergic agents may be partly attributable to treating or preventing a component of delirium.

DSM remains the gold standard for research diagnoses and therefore its specificity in differentiating delirium and dementia is crucial to efforts to illuminate the neuropsychiatry of these disorders. We propose that 1) dementia research needs to assess more carefully any delirium component and utilize instruments that capture characteristics that differentiate these disorders (e.g., the Delirium Rating Scale–Revised); 2) the differing courses of delirium symptoms (acute transient versus recurring versus persistent improving/not improving) should be categorized; 3) DSM-V should include phenomenological detail about syndromal and subsyndromal delirium, including relative frequency of all core and associated symptoms; 4) DSM-V should include phenomenological detail and relative frequency of symptoms for major types of dementias; and 5) DSM-V should more strongly encourage differential diagnosis of delirium and subsyndromal delirium in the dementia sections as possible reasons for the clinical presentation during the course of illness or responsiveness to treatments.

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