

Provisional Diagnostic Criteria for Depression of Alzheimer Disease

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The authors, a group of investigators with extensive research and clinical experience related to both late-life depression and Alzheimer disease (AD), propose provisional affective and behavioral inclusion and exclusion diagnostic criteria for Depression of AD. (Am J Geriatr Psychiatry 2002; 10:125-128)

As a group of investigators with extensive research and clinical experience related to both late-life depression and Alzheimer disease (AD), we propose provisional diagnostic criteria for depression of AD. The purposes of these criteria are to 1) assist the field in facilitating hypothesis-driven research that can lead to a better understanding of the depression that co-occurs in AD, and 2) to provide a consistent target for treatment research. The need to establish diagnostic criteria is warranted by epidemiological data in AD indicating prevalence rates for significant depressive symptomatology ranging from 15 percent¹ to as high as 50 percent² (the background and rationale for these criteria are discussed in the accompanying review).

The development of diagnostic criteria describing behavioral symptom clusters has occurred in the context of efforts to garner a therapeutic claim from the Food and Drug Administration (FDA). A recent advance characterized behavioral symptoms under the term Behavioral and Psychological Symptoms of Dementia (BPSD).³ However, this was considered too broad an entity for a therapeutic claim by the FDA,⁴ resulting in a move toward characterizing individual syndromes in AD. Psychosis of AD was defined in this fashion in 2000⁵ and was accepted by the FDA as a potential specific target for intervention.⁶ Depression of AD is the next syndrome to be defined in this manner and is characterized in the present article.

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Currently, there are no criteria that define the depressive features that occur within the course of AD. Without standard criteria, clinical research must use inconsistently defined populations, making it difficult to interpret outcomes or to further the understanding of the syndrome itself. The introduction of standard criteria can facilitate clinical and pharmacological research in this area, and provide a systematic method for more focused inquiries into the depressive features that may be associated with AD.

Although the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV-TR)⁷ can be used to code depression as a separate Axis I diagnosis, co-existing as a separate condition from AD, the criteria for delineating such a separation are not specified. For example, a feature such as "loss of interest" is nonspecific and can be observed both in patients with clinically significant depression or in patients with dementia but no apparent disturbance of mood. Also, there are obstacles to using descriptive criteria, such as those found for Major Depressive Disorder or Minor Depressive Disorder, to characterize the depression found in patients with AD. DSM-IV-TR, like the DSMs before it, was developed for patients with idiopathic psychiatric conditions, and it depends to a great extent on subjects' verbal ability to report subjective depressive symptoms, such as changes in mood, loss of interest, or hopelessness. Such verbal expression often is impaired among patients with AD, however. Moreover, the withdrawal and social isolation that is observed in depressed individuals with AD must be differentiated from the behaviors that occur in the context of dementia.

Although the provisional diagnostic criteria were derived from those for Major Depressive Episode, there are several significant differences. First, Depression of AD requires the presence of three or more symptoms (vs. five or more for Major Depressive Episode). Second, it does not require the presence of symptoms nearly every day, as is the case for Major Depressive Episode. Third, criteria for the presence of irritability and for the presence of social isolation or withdrawal were added. Fourth, the criteria for loss of interest or pleasure were revised to reflect decreased positive affect or pleasure in response to social contact and usual activities.

An alternative approach to diagnosis might be based on the DSM-IV-TR diagnosis Mood Disorder Due to a General Medical Condition. Specifically, this condition requires that AD *causes* the depressive symptoms that are observed. Although this may be true for individual patients, there are scant data derived from rigorous studies to support this contention, and the extent

(or limits) of such a putative disorder remain to be defined. Moreover, there are no criteria to characterize the clinical nature of the patient's presentation, thus providing little application for planning treatment or determining prognosis.

Note that although these provisional diagnostic criteria are offered in the style of DSM-IV-TR, they are not meant as a model for future DSM terminology. Researchers are also cautioned that these criteria were developed on the basis of an iterative consensus process involving experienced investigators and clinicians. Future research is needed to confirm their validity.

Potentially relevant differences between Depression of AD and primary depression may involve incidence and prevalence, previous history, family history, severity, frequency of major depressive episodes, suicidality, duration of episodes, outcomes, and therapeutic responses. For example, Depression of AD may be less severe or persistent, with waxing and waning symptomatology. There may be less suicidal ideation and fewer suicide attempts, as well as fewer melancholic symptoms. Gender differences may not be apparent, and psychosocial factors may be less important. These issues are discussed further in the accompanying review article.

Clinical issues may also be different: for example, the overlap of depression-related and dementia-related signs and symptoms can lead to both different assessment demands and treatment needs. Note, too, that symptoms of depression such as weight loss, sleep disruption, or fatigue in dementia patients may result from coexisting general medical illnesses.

DIAGNOSTIC CONSIDERATIONS

The determination of Depression of AD is predicated primarily on careful clinical assessment, rather than symptom rating scales. The clinician must 1) establish the diagnosis of Dementia of the Alzheimer Type (DAT), and 2) identify that there are clinically significant depressive symptoms. This will involve thorough clinical assessment, with consideration of the temporal associations between the onset and course of the depression and the dementia. Finally, the clinician must judge that the depression is not better accounted for by a primary depression, other primary mental disorders, other medical conditions, or adverse effects of medication.

Thus, considerable clinical judgment is involved in making a diagnosis. The accompanying provisional criteria are meant to serve as a starting point in trying to

TABLE 1. Provisional Diagnostic Criteria for Depression of Alzheimer Disease

A. Three (or more) of the following symptoms have been present during the same 2-week period and represent a change from previous functioning; at least one of the symptoms is either 1) depressed mood or 2) decreased positive affect or pleasure.^a

Note: Do not include symptoms that, in your judgment, are clearly due to a medical condition other than Alzheimer disease, or are a direct result of non-mood-related dementia symptoms (e.g., loss of weight due to difficulties with food intake).

- (1) Clinically significant depressed mood (e.g., depressed, sad, hopeless, discouraged, tearful)^b
- (2) Decreased positive affect or pleasure in response to social contacts and usual activities^c
- (3) Social isolation or withdrawal^d
- (4) Disruption in appetite
- (5) Disruption in sleep
- (6) Psychomotor changes (e.g., agitation or retardation)^e
- (7) Irritability
- (8) Fatigue or loss of energy
- (9) Feelings of worthlessness, hopelessness, or excessive or inappropriate guilt
- (10) Recurrent thoughts of death, suicidal ideation, plan or attempt^f

B. All criteria are met for Dementia of the Alzheimer Type (DSM-IV-TR).^g

C. The symptoms cause clinically significant distress or disruption in functioning.

D. The symptoms do not occur exclusively during the course of a delirium.

E. The symptoms are not due to the direct physiological effects of a substance (e.g., a drug of abuse or a medication).

F. The symptoms are not better accounted for by other conditions such as major depressive disorder, bipolar disorder, bereavement, schizophrenia, schizoaffective disorder, psychosis of Alzheimer disease, anxiety disorders, or substance-related disorder.^h

Specify if:

Co-occurring Onset: if onset antedates or co-occurs with the AD symptoms

Post-AD Onset: if onset occurs after AD symptomsⁱ

Specify:

With Psychosis of Alzheimer Disease

With Other Significant Behavioral Signs or Symptoms

With Past History of Mood Disorder^j

Note: ^aThe criteria are in the style of DSM-IV-TR, with the goal being to identify from among all affectively disturbed individuals with Alzheimer disease, those with predominant depression. As with DSM-IV-TR, either depressed mood or anhedonia is a required feature (anhedonia is considered a required feature because it can be considered an alternative expression of depressed mood). The remaining criteria are included because they are features of depression that occur with Alzheimer disease. The duration requirement is similar to that of a Major Depressive Episode and consistent with consensus of experts. Many patients show significant variability in their presentation; clinicians may need to consider information from informants to obtain a better appreciation of the symptomatology. ^bTearfulness may be an expression of depressed mood, particularly in less verbal individuals with Alzheimer disease. (Tearfulness that may occur spontaneously, or that in the judgment of the clinician is caused by other physiological mechanisms should not be considered a manifestation of depression). ^cAnhedonia is usually defined as the inability to enjoy what is usually pleasurable or to experience pleasure from activities that usually produce pleasurable feelings. The proposed criterion above is a behavioral descriptor that attempts to capture the anhedonia seen in Depression of Alzheimer disease. ^dPatients with uncomplicated Alzheimer disease may tend to withdraw from social contacts and their customary activities, presumably because of their diminished ability to cope with tasks that challenge cognition. Clinical judgment is required to distinguish social isolation that is due to the loss of interest associated with depression. ^ePsychomotor agitation is excessive motor activity often attributed to "internal tension," and can include the "inability to sit still; pacing, hand-wringing . . . (DSM-IV-TR)." Psychomotor agitation in this case does not imply disruptive behavior or combativeness, nor does it necessarily refer to resisting assistance from others, shouting, or attempting to hurt others. Similarly, stereotypies or repetitive motor activities are not intended to be included under agitation here. In DSM-IV-TR, psychomotor retardation is described as "slowed speech, thinking, and body movements; increased pauses before answering; speech that is decreased in volume, inflection, and amount, or variety of content, or muteness." Clinical judgment is needed to decide the extent to which agitation or retardation are components of depression or of the dementia. ^fSuicidal ideation is less commonly observed in patients with Depression of Alzheimer disease as compared with primary depression, but when it occurs is likely to be specific for depression. ^gDSM-IV-TR criteria are used because they are consistent with NINCDS-ADRDA criteria. Thus, the need to make an often tenuous distinction between Possible and Probable Alzheimer disease, per NINCDS-ADRDA criteria, especially in the context of depression is avoided. ^hMajor Depressive Disorder, as well as other disorders, may be diagnosed in patients with Alzheimer disease or other medical conditions. In this section, it is acknowledged that some subjects will be assessed as having these disorders rather than Depression of Alzheimer disease. For example, a depressed individual who, long before the onset of Alzheimer disease, had Major Depressive Disorder, recurrent, might not be considered by the clinician to have Depression of Alzheimer disease. One item for discussion is whether Major Depressive Disorder and Depression of Alzheimer disease need to be mutually exclusive. ⁱThese specifiers are included to help document the frequency of depression relative to the diagnosis of Alzheimer disease. ^jThere will be cases where subjects with a history of mood disorder will meet, in the judgment of the clinician, criteria for Depression of Alzheimer disease. This specifier is included so these subjects can be documented as such.

define minimal, operational criteria that do not overspecify a condition, yet are both suitably broad and specific that they can be used for future research and for assessing the efficacy of specific treatments. They are meant to be as simple as possible. Annotations are provided to explain our reasoning.

CONCLUSIONS

The provisional diagnostic criteria for depression of AD form an attempt to define a group of individuals with

AD whose depression is distinguishable from Major Depressive Disorder and Minor Depressive Disorder. The criteria are broad and rely on clinical judgment. Admittedly, there remains overlap between these syndromes, which, in fact, is a reflection of the state of knowledge in this area. Nevertheless, these criteria accomplish the goal of being a starting point that allows investigators to study and treat a relatively homogeneous group of individuals with both AD and depression. Ultimately, we hope that research using these criteria will lead to a better understanding of Depression in AD and the development of more specific criteria.

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NOTICE

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