Crières diagnostique de Maladie d'Alzheimer

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Déficit Cognitif

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Altération de l'autonomie dans la vie quotidienne

⬇

DEMENCE

(Major Neuro-Cognitive Disorder

pour le DSM V)

Alzheimers Dement. 2011

The diagnosis of dementia due to Alzheimer's disease: Recommendations from the National Institute on Aging - Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease

Guy M. McKhann, David S. Knopman , Howard Chertkow, Bradley T. Hyman, Clifford R. Jack Jr., Claudia H. Kawash, , William E. Klunk , Walter J. Koroshetz , Jennifer J. Manlym, Richard Mayeux, Richard C. Mohs, John C. Morris, Martin N. Rossor, Philip Scheltens , Maria C. Carrillo, Bill Thies, Sandra Weintraub and Creighton H. Phelps

Core clinical criteria

Dementia is diagnosed when there are cognitive or behavioral (neuropsychiatric) symptoms that:
1.Interfere with the ability to function at work or at usual activities
2. Represent a decline from previous levels of functioning and performing
3.Are not explained by delirium or major psychiatric disorder
4.Cognitive impairment is detected and diagnosed through a combination of

1. history-taking from the patient and a knowledgeable informant and
2. an objective cognitive assessment, either a "bedside" mental status examination or neuropsychological testing.

5. The cognitive or behavioral impairment involves a minimum of two of the following domains :

a. Impaired ability to acquire and remember new information...
b. Impaired reasoning and handling of complex tasks, poor judgment...
c. Impaired visuospatial abilities...
d. Impaired language functions (speaking, reading, writing) ...
e. Changes in personality, behavior, or comportment symptoms

Probable AD dementia is diagnosed when the patient

1. Meets criteria for dementia described earlier

2. has the following characteristics:
   A. Insidious onset. Symptoms have a gradual onset over months to years, not sudden over hours or days;
   B. Clear-cut history of worsening of cognition by report or observation
   C. The initial and most prominent cognitive deficits are evident on history and examination in one of the following categories :
      - amnestic presentation
      - non amnestic presentation

a. Amnestic presentation: It is the most common syndromic presentation of AD dementia. The deficits should include impairment in learning and recall of recently learned information. There should also be evidence of cognitive dysfunction in at least one other cognitive domain, as defined earlier in the text

b. Non amnestic presentations:
   - Language presentation: The most prominent deficits are in word-finding, but deficits in other cognitive domains should be present.
   - Visuospatial presentation: The most prominent deficits are in spatial cognition, including object agnosia, impaired face recognition, simultanagnosia, and alexia. Deficits in other cognitive domains should be present.
   - Executive dysfunction: The most prominent deficits are impaired reasoning, judgment, and problem solving. Deficits in other cognitive domains should be present

D. The diagnosis of probable AD dementia should not be applied when there is evidence of
(a) substantial concomitant cerebrovascular disease, defined by a history of a stroke temporally related to the onset or worsening of cognitive impairment; or the presence of multiple or extensive infarcts or severe white matter hyperintensity burden
(b) core features of Dementia with Lewy bodies other than dementia itself
(c) prominent features of behavioral variant frontotemporal dementia;
(d) prominent features of semantic variant primary progressive aphasia or nonfluent/ agrammatic variant primary progressive aphasia;
(e) evidence for another concurrent, active neurological disease, or a non-neurological medical comorbidity or use of medication that could have a substantial effect on cognition.

Probable AD dementia with increased level of certainty

1. Probable AD dementia with documented decline

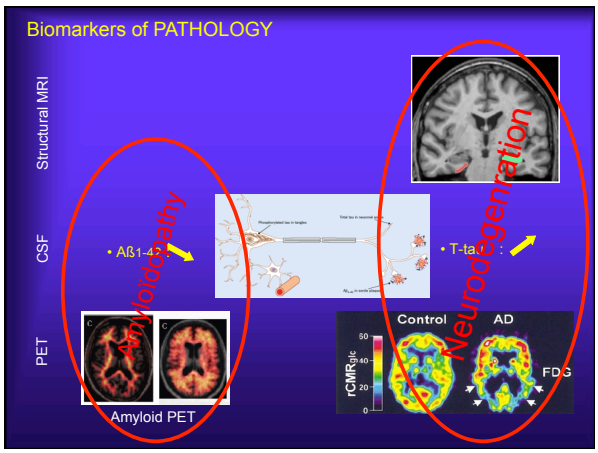
2. Probable AD dementia in a carrier of a causative AD genetic mutation (in APP, PSEN1, or PSEN2)

Possible AD dementia:

Core clinical criteria

Atypical course

Etiologically mixed presentation



Probable and Possible AD dementia with evidence of the AD pathophysiological process

Tableau 3 – Critères de démence par maladie d'Alzheimer (MA) utilisant les biomarqueurs.
AD dementia criteria incorporating biomarkers.

Catégories diagnostiques	Apport à la probabilité diagnostique de MA	Biomarqueur physiopathologique Amyloïde Aß (PET au PIB ou LCR)	Biomarqueur structurel (mort neuronale) (Tau dans le LCR, FDG-PET, IRM structurelle)
Démence par MA probable			
Basée sur les critères cliniques	Inchangé	Non contributif[a]	Non contributif[a]
Avec 3 niveaux de preuve du processus physiopathologique de MA	Modéré	Non contributif	Positif
	Modéré	Positif	Non contributif
	Élevé	Positif	Positif
Démence par MA possible (présentation clinique atypique)			
Basée sur les critères cliniques	Inchangé	Non contributif	Non contributif
Avec preuve du processus physiopathologique de MA	Élevé mais n'exclut pas une autre étiologie associée	Positif	Positif
Démence de type non Alzheimer	Très faible	Négatif	Négatif

D'après McKhann et al., 2011.
[a] Résultats discordants entre les biomarqueurs, ou résultats normaux, ou résultats indisponibles (examens non réalisés).

Mac Khann et al. (2011) : new criteria

Probable AD according clinical profile

Moderate Probability if
* one biomarker of amyloïdopathy
(amyloïd PET + or low rate of Abéta 42 in CSF)
OR
* one biomarker of neurodegeneration
(structural MRI, FDG PET, high rate of Tau in CSF)

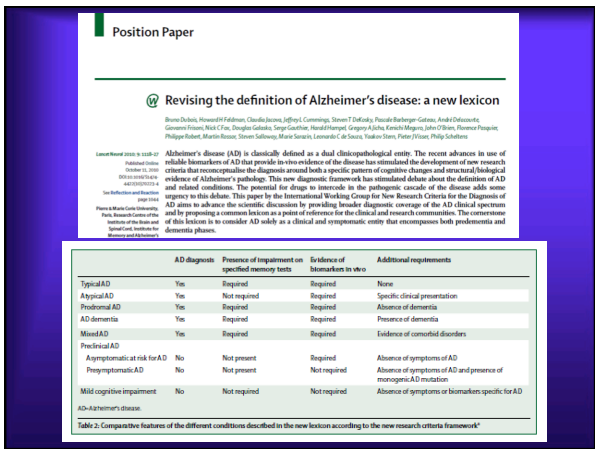
High Probability if
* one biomarker of amyloïdopathy
(amyloïd PET + or low rate of Abéta 42 in CSF)
AND
* one biomarker of neurodegeneration
(structural MRI, FDG PET, high rate of Tau in CSF)

The new 2011 recommendations of the National Institute on Aging and the Alzheimer's Association on diagnostic guidelines for Alzheimer's disease: Preclinal stages, mild cognitive impairment, and dementia

Pathophysiologically proved AD dementia

clinical and cognitive criteria for AD dementia
+
neuropathological examination demonstrating the presence of the AD pathology (Hyman & Trojanowski, 1997)

Dementia unlikely to be due to AD
1.Does not meet clinical criteria for AD dementia.
2.Regardless of meeting clinical criteria for probable or possible AD dementia, there is sufficient evidence for an alternative diagnosis such as HIV dementia, dementia of Huntington's disease, or others that rarely, if ever, overlap with AD
3.Regardless of meeting clinical criteria for possible AD dementia, both Aβ and neuronal injury biomarkers are negative



Position Paper

Revising the definition of Alzheimer's disease: a new lexicon

Bruno Dubois, Howard H Feldman, Claudia Jacova, Jeffrey L Cummings, Steven T DeKosky, Pascale Barberger-Gateau, André Delacourte, Giovanni Frisoni, Nick C Fox, Douglas Galasko, Serge Gauthier, Harald Hampel, Gregory A Jicha, Kenichi Meguro, John O'Brien, Florence Pasquier, Philippe Robert, Martin Rossor, Steven Salloway, Marie Sarazin, Leonardo C de Souza, Yaakov Stern, Pieter J Visser, Philip Scheltens

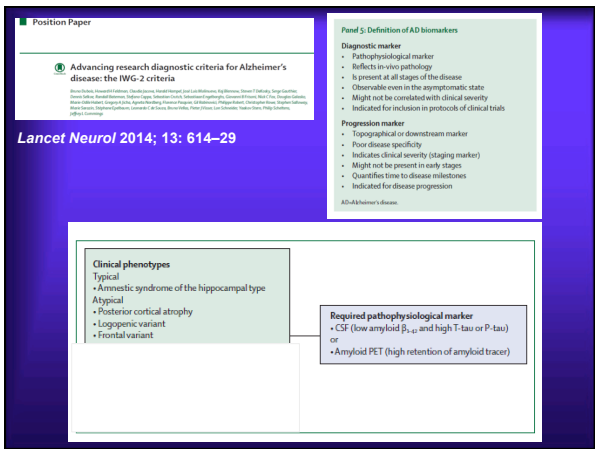
Lancet Neurol 2010; 9: 1118–27

Alzheimer's disease (AD) is classically defined as a dual clinicopathological entity. The recent advances in use of reliable biomarkers of AD that provide in-vivo evidence of the disease has stimulated the development of new research criteria that reconceptualise the diagnosis around both a specific pattern of cognitive changes and structural/biological evidence of Alzheimer's pathology. This new diagnostic framework has stimulated debate about the definition of AD and related conditions. The potential for drugs to intercede in the pathogenic cascade of the disease adds some urgency to this debate. This paper by the International Working Group for New Research Criteria for the Diagnosis of AD aims to advance the scientific discussion by providing broader diagnostic coverage of the AD clinical spectrum and by proposing a common lexicon as a point of reference for the clinical and research communities. The cornerstone of this lexicon is to consider AD solely as a clinical and symptomatic entity that encompasses both predementia and dementia phases.

	AD diagnosis	Presence of impairment on specified memory tests	Evidence of biomarkers in vivo	Additional requirements
Typical AD	Yes	Required	Required	None
Atypical AD	Yes	Not required	Required	Specific clinical presentation
Prodromal AD	Yes	Required	Required	Absence of dementia
AD dementia	Yes	Required	Required	Presence of dementia
Mixed AD	Yes	Required	Required	Evidence of comorbid disorders
Preclinical AD				
Asymptomatic at risk for AD	No	Not present	Required	Absence of symptoms of AD
Presymptomatic AD	No	Not present	Not required	Absence of symptoms of AD and presence of monogenic AD mutation
Mild cognitive impairment	No	Not required	Not required	Absence of symptoms or biomarkers specific for AD

AD=Alzheimer's disease.

Table 2: Comparative features of the different conditions described in the new lexicon according to the new research criteria framework[4]



Position Paper

Advancing research diagnostic criteria for Alzheimer's disease: the IWG-2 criteria

Lancet Neurol 2014; 13: 614–29

Panel 5: Definition of AD biomarkers

Diagnostic marker
- Pathophysiological marker
- Reflects in-vivo pathology
- Is present at all stages of the disease
- Observable even in the asymptomatic state
- Might not be correlated with clinical severity
- Indicated for inclusion in protocols of clinical trials

Progression marker
- Topographical or downstream marker
- Poor disease specificity
- Indicates clinical severity (staging marker)
- Might not be present in early stages
- Quantifies time to disease milestones
- Indicated for disease progression

AD=Alzheimer's disease.

Clinical phenotypes
Typical
- Amnestic syndrome of the hippocampal type

Atypical
- Posterior cortical atrophy
- Logopenic variant
- Frontal variant

Required pathophysiological marker
- CSF (low amyloid β_{1-42} and high T-tau or P-tau)
or
- Amyloid PET (high retention of amyloid tracer)

Specific clinical phenotype

Presence of an early and significant episodic memory impairment (isolated or associated)

- that includes the following features:
  * Gradual and progressive change in memory function reported by patient or informant over more than 6 months
  * Objective evidence of an amnestic syndrome of the hippocampal type,
  * based on significantly impaired performance on an episodic memory test with established specificity for AD, such as cued recall with control of encoding test

In-vivo evidence of Alzheimer's pathology (one of the following)
- Decreased Aβ1–42 together with increased T-tau or P-tau in CSF
- Increased tracer retention on amyloid PET
- AD autosomal dominant mutation present (in *PSEN1, PSEN2, or APP)*

Exclusion criteria for typical AD
History, Clinical features, Other medical conditions severe enough to account for memory and related symptoms, MRI

Specific clinical phenotype (one of the following)

- Posterior variant of AD
  - occipitotemporal variant
  - biparietal variant
- Logopenic variant of AD
- Frontal variant of AD
- Down's syndrome variant of AD

In-vivo evidence of Alzheimer's pathology (one of the following)
- Decreased Aβ1–42 together with increased T-tau or P-tau in CSF
- Increased tracer retention on amyloid PET
- Alzheimer' s disease autosomal dominant mutation present (in *PSEN1, PSEN2, or APP)*