Comparison of Consensus Alzheimer's Criteria Using the National Institute on Aging Alzheimer's Association (NIA-AA) Criteria as the Comparator Standard

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Background

- Diagnosis of Alzheimer's disease (AD) has undergone significant revision, largely in response to advances in biomarker research and the understanding of AD's syndromic complexity
- As a major update to the former NINCS-ADRDA Criteria[1], the NIA-AA Criteria[2] is quickly becoming the new research standard for the diagnosis of Alzheimer's disease (AD)
- Other new concensus criteria include:
  - International Working Group (IWG)[3,4]
  - International Classification of Disease (ICD-10)[5]
  - DSM-5[6]
- Although sharing features in common, these criteria differ in how the core cognitive syndrome is defined, what co-pathologies are permitted (if any), and how investigations including biomarkers are used[7]
- Differing operationalization schemes for these elements in the clinical setting further complicates the process of diagnosis, and introduces further discordance in disease classification amongst these consensus criteria
- Comparisons among Vascular Cognitive Impairment criteria in the past indicate such elements result in significant disagreements in the diagnostic classification of individual patients; however, comprehensive, systematic comparison among AD consensus criteria remains to be done

Purpose and Hypothesis

To conduct a comprehensive comparison of diagnostic classification by five major consensus criteria in a group of well-characterized AD subjects, using the NIA-AA as the criterion standard.

Methods

- Clinical history and imaging for 100 individuals from the Sunnybrook Dementia Study were reviewed; this was a consecutive sample of patients from a tertiary referral clinic who were felt to have either probable or possible AD
- Permitted diagnoses included:
  - Clinically diagnosed probable or possible AD
  - AD plus small vessel disease (SVD) and AD plus Dementia with Lewy Bodies (DLB) were allowed
- Consensus criteria were applied by three experienced neurologists: BL, AK and KH
- Checklists and standard procedures were developed to improve diagnostic consistency
- Tc^{99}-SPECT was used lieu of FDG-PET for the NIA-AA and IWG-1 criteria

Results

- 54 subjects met NIA-AA criteria for probable AD, while 46 met criteria for possible AD
- Among probable AD cases, percentage agreement was perfect with the DSM-V (100%), excellent with the NINCDS-ADRDA (90.7%), and fair with the IWG-1 (74.1%) and ICD-10 (64.8%)
- Among possible AD cases, percentage agreement was perfect with the DSM-V (100%), fair with NINCDS-ADRDA (76.1%), but poor with the IWG-1 (8.7%) and ICD-10 (17.4%)
- All 42 cases that met NIA-AA criteria but which failed to meet IWG-1 were disqualified due to co-occurring disease (including SVD and DLB)
- Probable AD cases were younger than possible AD cases (mean age 68.3 vs. 74.4; p = 0.01), but had an equal percentage of women (64.8% vs. 57.3%, NS) and years of education (14.3 vs. 13.8 years, NS)
- In the absence of amyloid biomarker evidence; the IWG-2 does not permit for the diagnosis of AD resulting in dramatic discordance.

	Probable AD by NIA-AA (n=54)	Possible AD by NIA-AA (n=46)	P
Age	68.3 (13.2)	74.4 (8.4)	0.01
Gender (% female)	64.8% (0.5%)	57.3% (0.5%)	NS
YOE	14.3 (3.0)	13.8 (3.5)	NS

Table 1: Subject characteristics; means (standard deviations).

NIA-AA (2011)	NINDS-ADRDA (1984)		IWG-1 (2007)	IWG-2 (2014)	ICD-10 (2010)	DSM-V (2013)	
Probable AD N = 54	AD	Probable AD 49	AD 40	0	AD 35	Probable AD — Major	54
		Possible AD 3				Probable AD — Mild	0
	Not AD 2		Not AD 14	54	Not AD 19	Possible AD — Major	0
						Possible AD — Mild	0
						Not AD	0
NIA-AA (2011)	NINDS-ADRDA (1984)		IWG-1 (2007)	IWG-2 (2014)	ICD-10 (2010)	DSM-V (2013)	
Possible AD N = 46	AD	Probable AD 3	AD 4	0	AD 8	Probable AD — Major	0
		Possible AD 35				Probable AD — Mild	0
	Not AD 8		Not AD 42	46	Not AD 38	Possible AD — Major	0
						Possible AD — Mild	46
						Not AD	0

Table 2: Breakdown of Diagnostic Categorization by consensus criteria, using the NIA-AA as the comparator standard. Note that ICD-10 and DSM-V diagnosis refers to AD-subtype only. Cases were unclassifiable by IWG-2 due to strict requirements for amyloid biomarkers.

Discussion and Conclusions

There was perfect agreement between the NIA-AA and the DSM-V, within our cohort. However, individuals presenting with multiple non-memory domain impairments would conceivably meet NIA-AA criteria but not meet DSM-V requirements for AD. This did not occur as all subjects had memory deficits.

Similarly, differences could arise if plateaus in progression were present (disallowed in DSM-V), though none of our cases had such plateaus.

Disagreement between NIA-AA and IWG-1 arose entirely due to the latter's exclusion of co-pathology.

In conclusion, although there is excellent concordance between the NIA-AA and DSM-V, differences in exclusions and cognitive construct resulted in notable disagreement with the IWG-1 and ICD-10. These findings demonstrate that AD criteria cannot be taken as equivalent, and should be carefully selected according to the requirements of individual clinicians and researchers.

References and Acknowledgements

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