Comparison of Four New Consensus Criteria Against the 1984 NINCDS-ARDRA Criteria for Alzheimer's Disease

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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.
- New criteria include: (1) International Working Group (IWG; Dubois et al. Lancet Neurol 2007 and Dubois et al. Lancet Neurol 2010), (2) International Classification of Disease (ICD-10; WHO 2010), (3) National Institute on Aging – Alzheimer's Association (NIA-AA; McKhann et al. Alzheimers Dement 2011), and (4) DSM-5 (APA 2013).
- These differ in requirements for memory impairment, functional decline, biomarkers, and allowance for disease subtypes and mixed pathologies (Visser et al. Alzheimers Dement 2012).
- Comprehensive, systematic comparison in a group of well-characterized AD subjects remains to be done.

Purpose and Hypothesis

To compare the ascertainment of AD by four new and one established criteria. We hypothesize there will be greater agreement on AD diagnosis among criteria for typical presentations (prototypic AD cases), and less for individuals presenting with non-amnestic symptoms or co-occurring pathology (AD variants cases).

Methods

- Clinical history and imaging for 101 participants from the Sunnybrook Dementia Study who met 1984 NINCDS-ARDRA criteria (McKhann et al. Neurology 1984), for probable AD were reviewed.
- New criteria were applied by three experienced neurologists: BL, AK and KH.
- Tc^{99}-SPECT was used instead of FDG-PET for NIA-AA and IWG criteria.

Results

- The NIA-AA and NINCDS-ARDRA criteria had excellent agreement, with 90% (n=91) of those meeting the original 1984 McKhann criteria also satisfying the revised NIA-AA criteria.
- Among those that did not, 7 had insufficient functional decline to fulfill dementia criteria, and would be classified as MCI.
- By contrast, 47% (n=47) of those meeting the 1984 McKhann criteria failed to meet the IWG criteria, similar to the results from a prior study comparing it to the ICD-10/DSMIV (Oksengard et al. Dement Geriatr Cogn Disord 2010).
- This may reflect the IWG's strict requirement for biomarkers and predominantly amnestic course, and disallowance of co-pathology. Indeed, all atypical individuals from our cohort and those with mild-to-moderate white matter disease were rejected.
- Similarly, only 44% (n=44) of those meeting the 1984 McKhann criteria met the ICD-10 criteria, likely reflecting construct differences , namely, ICD-10's unique requirements for functional impairment and behavioural symptoms.
- 85% (n=86) of those meeting the 1984 McKhann also met the DSM-V. Both allow for non-amnestic presentations and are largely based on a similar combination of cognitive and functional factors.

Discussion and Conclusions

Differences in syndrome construct (including functional decline), biomarker use, and allowance for co-pathology within criteria significantly affect the diagnostic classification of individuals with dementia. Going forward, such differences merit careful validation to ensure that criteria can accurately and meaningfully ascertain AD, both prototypic and variant cases, as they exist in the general population.

McKhann 1984	NIA-AA 2011		IWG 2007	ICD-10	DSM-V
AD (n=101)	**AD or MCI** (n=98)	**Probable AD** (n=52)	**AD** (n=54)	**AD** (n=57)	**Major ND-AD** (n=86)
		Possible AD (n=39)			
		MCI due to AD (n=7)			**Minor ND-AD** (n=8)
	Did not meet new criteria (n=3)		(n=47)	(n=44)	(n=7)

Table 1: Breakdown to Diagnostic Categorization by Criteria. Individuals that did not meet the NIA-AA criteria had memory symptoms in isolation, while those that did not meet the IWG criteria generally had co-morbidities or lacked of imaging biomarker support. Those not meeting ICD-10 had a mix of reasons including lack of the specific behavioural and functional symptoms required by its criteria.

References and Acknowledgements

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