23 The Utility of Global versus Domain-specific Neuropsychological Test Score Dispersion as Markers of Cognitive Decline

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Objective: Higher baseline dispersion (intra-individual variability) across neuropsychological test scores at a single time-point has been associated with more rapid cognitive decline, onset of Mild Cognitive Impairment (MCI) and Alzheimer's disease (AD), faster rates of hippocampal and entorhinal atrophy, and increased AD neuropathology. Comparison between predictions made from test score dispersion within a cognitive domain versus global, cross-domain dispersion is understudied. Global dispersion may be influenced by ability- and test-specific characteristics. This study examined the performance of global versus domain-specific dispersion metrics to identify which is most predictive of cognitive decline over time.

Participants and Methods: Data for baseline and five follow-up visits of 308 participants with normal cognition (Mage=73.90, SD=8.12) were selected from the National Alzheimer's Coordinating Center (NACC) Dataset. Participants were required to have no focal neurological deficits, or history of depression, stroke, or heart attack. Diagnoses and progression to MCI and/or dementia were determined at each visit through consensus conferences. Raw neuropsychological scores were standardized using NACC norms. Global baseline dispersion was defined as the intraindividual standard deviation (ISD) across the 10 scores in the NACC battery. Domain-specific dispersions were calculated by constructing composites and ISD was computed

Table 1. Mean Dispersion Differences and Model Fit Statistics for Models 1-4

	Model 1 (Global Dispersion, Age, Education, Sex,Race, Ethnicity, ApoE)	Model 2 (EFAS Dispersion, Age, Education, Sex, Race, Ethnicity, ApoE) ISD calculated across: Digit Span Forwards & Backwards, WAIS-R, Trail Making Test A & B	Model 3 (Language Dispersion, Age, Education, Sex, Race, Ethnicity, ApoE) ISD calculated across: Boston Naming Test-30 Item, Animals & Vegetables Fluency	Model 4 (Memory Dispersion, Age, Education, Sex, Race, Ethnicity, ApoE) ISD calculated across: Logical Memory Story A Immediate & Delayed Recall
Mean Dispersion		1.121		
No conversion	1.069	1.132	.903	.292
MCI conversion	1.079	1.311**	.921	.303
Dementia conversion	1.276*		.949	.375
Model Fit Statistics				
AIC	513.046	527.564	527.366	519.268
-2LogL	477.046	491.564	491.366	483.268
Final Model Significance	p=.000	p=.000	p=.000	p=.000
Goodness-of-Fit				
Pearson	.502	.359	.346	.647
Deviance	.877	.755	.694	.739

*Statistically significant mean dispersion differences between no conversion and dementia conversion groups (p<.001)

*Statistically significant mean dispersion differences between no conversion and dementia conversion groups (p<.05)

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Table 2. Parameter Estimates for Models 1-4

	Model 1 (Global Dispersion, Age, Education, Sex, Race, Ethnicity, ApoE)	Model 2 (EFAS Dispersion, Age, Education, Sex, Race, Ethnicity, ApoE)	Model 3 (Language Dispersion, Age, Education, Sex, Race, Ethnicity, ApoE)	Model 4 (Memory Dispersion, Age, Education, Sex, Race, Ethnicity, ApoE)
		MCI Conversion		
P-value	p=.527	p=.405	p=.753	p=.930
Exp (B)	-	-	-	-
B	-	-	-	-
95% CI for Exp (B)	-	-	-	-
		Dementia Conversion		
p-value	p<.001	p=.015	p=.982	p=.069
Exp(B)	11.475	2.431	-	-
B	2.440	.888	-	-
95% CI for Exp(B)	3.510-37.512	1.191-4.960	-	-

across tests sampling their respective domains (executive functioning/attention/processing speed [EFAS], language, and memory; see Table 1 for details on these tests). Higher values on each of these metrics reflect greater dispersion. Multinomial logistic regression model fit statistics and parameter estimates were compared across four different models (global, EFAS, Language, and Memory dispersion) covarying for age, years of education, sex, race, ethnicity, and ApoE4 status. Models were compared using the Likelihood Ratio Test (LRT) and the Akaike Information Criteria (AIC) of Models statistics.

Results: Of the 308 participants, 70 (22.7%) progressed to MCI, and 82 (26.6%) progressed to dementia. Tables 1 and 2 show the results of the logistic regressions for the four models. All models fit the data well, with statistically significant predictions of conversion. Model 1 (global dispersion) showed a better fit than domain-specific models of dispersion per LRT and AIC values. Consistent with the results from mean differences between groups, parameter estimates showed that only global dispersion and EFAS dispersion significantly predicted conversion to dementia (when included with other covariates in models), with higher dispersion reflecting a greater risk of conversion.

Conclusions: In this sample, baseline global and EFAS dispersion measures significantly predicted conversion to dementia. Although global dispersion was a stronger predictor of dementia progression, findings suggest that executive functioning performance may be driving this relationship. A single index of global variability, from the calculation of standard deviation across test scores, may be supplementary for clinicians when distinguishing individuals at risk for dementia progression. None of the models were predictive of conversion to MCI. Further research is required to examine cognitive variability differences among patients who progress to MCI and patient-specific factors that may relate to test score dispersion and its utility in predicting the progression of symptoms.

Categories: Dementia (Alzheimer's Disease)
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Keyword 2: dementia - Alzheimer's disease
Keyword 3: mild cognitive impairment
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