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Dementia Status related to Presence of Type II Diabetes, APOE-e4, and Neurocognitive Losses

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Introduction

- For the 60 and over age group, the estimated prevalence of diagnosed and undiagnosed diabetes in the US is 12.2 Million or 23.1% (NIH, 2007).
- Type II diabetes as a risk factor to cognitive decline has been well-documented (e.g., Hassing et al., 2004; Arvanitakis, Wilson, & Bennett, 2006)
- There is conflicting information on which domains are affected (e.g., Iwata & Munshi, 2009), though new comprehensive investigations such as work by Yeung, Fischer, and Dixon (2009) have found lower performance by those with diabetes on measures of executive functioning and semantic speed.

Objectives

- Utilizing a statistical model of cognitive domain factors (*Revell & Schaie, in preparation*) we wanted to investigate the contribution of diabetes, dementia, and APOE-e4 subgroups
- Past published research from our group (*Revell, Caskie, Willis, & Schaie, 2009*) has found multi-group confirmatory factor analytic models valuable for differentiating health-related domains, such as quality of life

SLS Neuropsychological Study

- Objective: Follow participants from the Seattle Longitudinal Study (SLS; *Schaie, 1996, 2005*) over time for the early detection of dementia
- Participation criteria:
  - Must be 60 years of age or older
  - Previous participation in at least one previous SLS wave
- A comprehensive battery was created for this purpose, composed of 17 test measures, including the CERAD battery (*Morris et al.,1989*)

SLS Neuropsychological Battery

CERAD

Boston Naming Test, modified (Kaplan et al.,1984)

MMSE (Folstein, Folstein, & McHugh, 1975)

Verbal Fluency of Animals (Borkowski et al., 1967)

Word List Memory Recall (Atkinson & Shiffrin, 1971)

Word List Recognition (Mohs et al.,1984)

Constructional Praxis (Rosen et al., 1984)

Additional Assessment

Dementia Rating Scale (DRS; Mattis, 1988)

WAIS-R; Wechsler, 1981)
Selected Subtests: Voc, Compreh., Block Design, Digit Span, Digit Symbol

WMS-R (Wechsler, 1981)
Subtests: Logical Memory Immediate and Delayed Recall only

Trail Making Test, A & B (Reitan & Wolfson, 1985)

Fuld Object Memory Evaluation (Fuld, 1977)

Other Measures (not primarily cognitive)

IADL and PSMS Scale (Lawton & Brody, 1969)

Memory Functioning Questionnaire (Gilewski & Zelinski, 1988)

Quality of Life in Alzheimer's Disease Scale (Logsdon, 1997)

McMaster Problem Solving Scale (Epstein et al., 1983)

CES-D (Radloff, 1977)

Services Use; Caregiver Questionnaire

Measuring Risk Factors

- Type II Diabetes
- Dementia Status
- Apolipoprotein ε-4 status

Health Measures

Diabetes Type II	Dementia Status	APOE-e4
Measure Characteristics		
Presence/ Absence	Unimpaired or Impaired	Non-e4, e-4
Patient Medical Records; Code 250 from ICD-9	Binary grouping created from 4 ratings by Consensus Assessment Team	Whole blood processed via DNA Cryopreservation at Northwest Lipid Research Laboratory

Selection Criteria

- Cross-sectional, neuropsychological data, complete at Time 1
- Presence of APOE-e4 genotyping
- Rating of Dementia Status
- Medical Record information on presence/absence of Type 2 Diabetes
  - Presence=physician's report of ICD-9 Code 250

Sample Characteristics

Variable	Mean	SD
Age	73.21	7.92
Education	15.18	2.79
Gender (n)	207 Males	243 Females
Dementia Status	336 unimpaired	114 impaired
Allele Group	334 non-e4	116 e4 group
Diabetes Group	398 absence	52 presence

Factors

- Confirmatory three-factor structure for neuropsychological summary and subtest scores:

Spatial Orientation

- Trails B (Halstead-Reitan)
- Boston Naming (CERAD Total)
- Constructional Praxis (Delayed Total)
- Block Design (WAIS-R)
- Digit Symbol (WAIS-R)

Verbal Reasoning

- Vocabulary (WAIS-R)
- Comprehension (WAIS-R)
- Verbal Fluency of Animals

Memory Recall

- Logical Memory (LM) immediate (WMS-R)
- LM Delayed (WMS-R)
- Fuld Memory Scale (Rapid Retrieval Total)
- Word List Memory Recall

Procedure

- All measures within our factor analytic model were standardized to the T-score metric (*M*=50, *SD*=10), except where skew >2, whereupon the McCall correction (Garrett, 1966) was employed.

- We regressed dementia rating on our three continuous latent factors (Spatial Orientation, Verbal Reasoning, and Memory Recall), diabetes status, and allele grouping

- All factor analyses were conducted using the *Mplus* statistical package, Version 5.1 (Muthén & Muthén, 1998-2008).

Results

- Full-information, structural equation models indicated that:
  1) Cognitively-impaired individuals had significantly lower mean levels of performance on spatial orientation and verbal reasoning factors;
  2) Those with impaired dementia status were more likely to have Type II diabetes (p=.035), as well to have one or more APOE-e4 alleles (p=.019)
- Model met criteria for acceptable, though not ideal, fit (CFI=.93; RMSEA=.079), and all indicators were statistically significant at $p < .05$.

- Next two slides will be altered slightly to include diabetes, dementia, and allele type loadings

Item Loadings by Factor

Factor	Item	Standardized Loading
Memory Recall		
	WMS-R Logical Memory immediate recall	0.696***
	WMS-R Logical Memory delayed recall	0.746***
	Fuld Object Memory Scale, Rapid Retrieval	0.789***
	Word List Memory Recall	0.761***
Verbal Reasoning		
	WAIS-R Vocabulary	0.880***
	WAIS-R Comprehension	0.838***
	Verbal Fluency of Animals	0.243***
Spatial Orientation		
	Trails B	0.783***
	Modified Boston Naming	0.469***
	Constructional Praxis	0.605***
	WAIS-R Block Design	0.719***
	WAIS-R Digit Symbol	0.767***

Latent Factor Correlations

	Memory Recall	Spatial Orientation	Verbal Reasoning
Memory Recall	1.000		
Spatial Orientation	0.736	1.000	
Verbal Reasoning	0.533	0.532	1.000

Discussion

- Other vascular and non-vascular measures should be investigated to provide support across similar cognitive measures from other studies
- It may be that our Spatial Orientation factor is really Executive Functioning, as Trails B has the highest loading of all the measures in this factor, which would support the VLS findings of Yeung, Fischer, and Dixon (2009)
- This investigation may uncover differential patterns of cognitive functioning that aid in identifying additional risk factors for diabetes