Depression and Cognitive Impairment
Impact on Daily Functioning
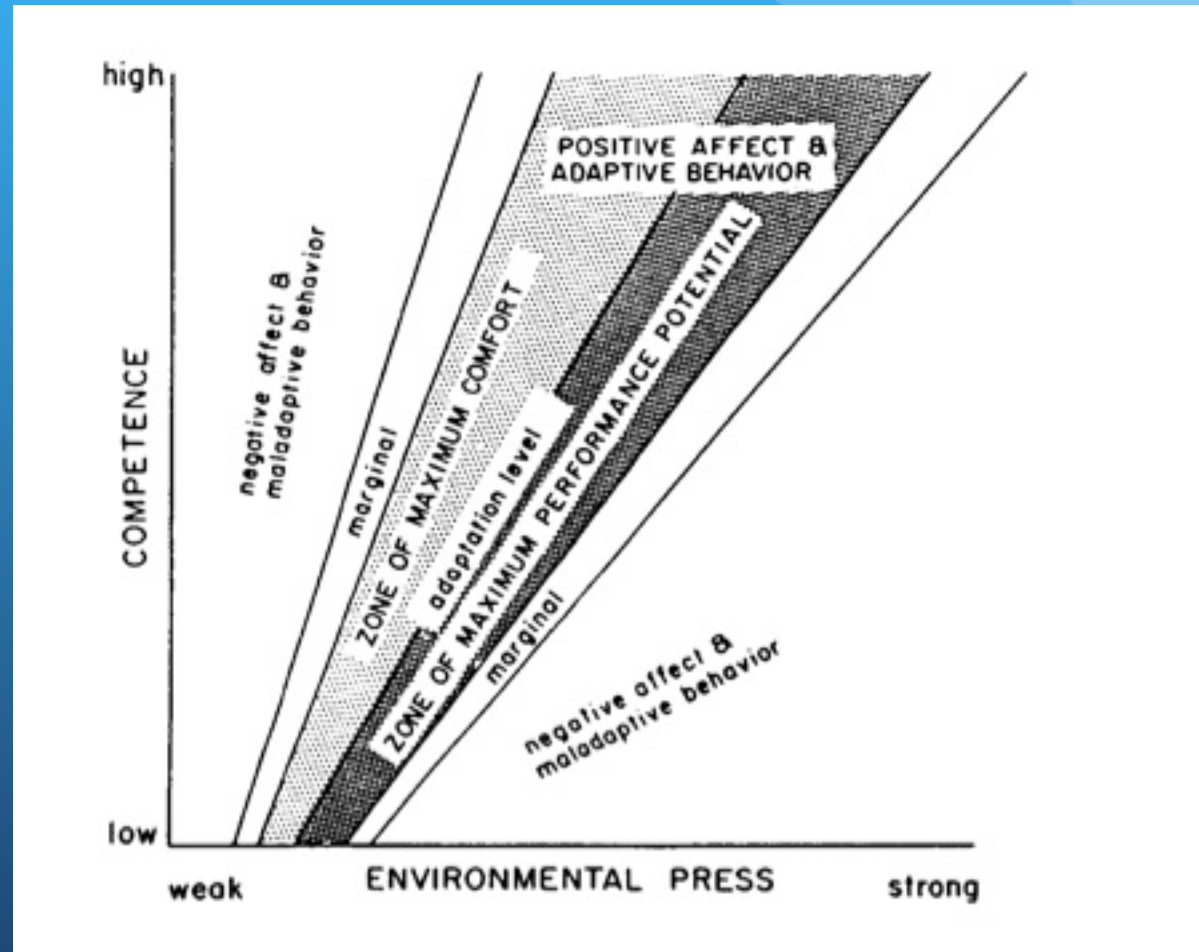
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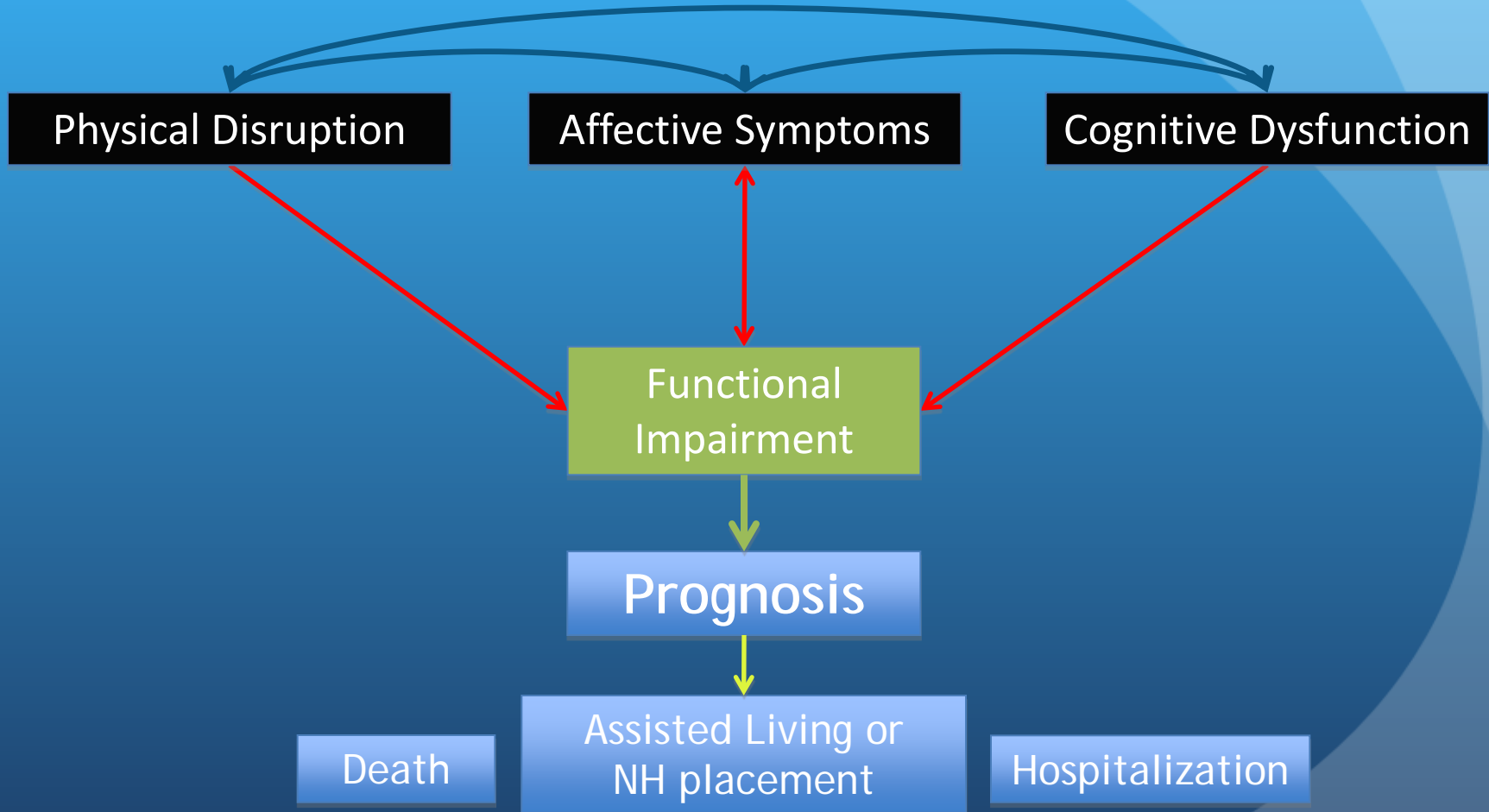New York State Psychiatric Institute

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Genesis of functional impairment

- <u>Ecology of Aging</u>

- Ecology: "…interdependence of one element in a system upon every other element."

Lawton & Nahemow, 1973

Pathways to functional impairment

| Physical Disruption | Affective Symptoms | Cognitive Dysfunction |

Functional Impairment

Prognosis

Death

Assisted Living or NH placement

Hospitalization

Physical correlates of function

- <u>Acute disruptions:</u>
  - <u>Metabolic syndrome</u>: Increased waist circumference, hypertension, BP, etc.
    - Increased risk of mobility disturbance (Penninx et al., 2009)
  - <u>Stroke</u>: Level of function post stroke predicts discharge to acute care from inpatient rehab (Chung et al., 2012)
  - <u>Fractures</u>: Usual care leads to increased risk of death, nursing home admissions, and decreases in ADLs in hip fracture patients (Singh et al, 2012)
- <u>Syndromal marker:</u>
  - <u>Frailty</u>: "decreased resiliency and reserves"
    - Increased risk of BADL/IADL impairment, institutionalization, and death (Fried et al., 2001; Bandeen-Roche et al., 2006)

Depression and function

- Leading cause of disability in the US
  - 2nd highest cause in world, 50% take short-term disability; Kessler et al. 1999, 2003
  - Increased health care utilization and institutionalization
- Cyclical relationship:
  - Baseline depression in nonADL impaired sample predicted incident ADL impairment at follow-up (Bruce et al., 1994)
  - Baseline and incident ADL impairment predicted incident depression (Kennedy et al., 1990)
- Treatment of depression:
  - Mixed at best for the improvement of functional impairment in older depressed patients (Heilingenstein et al, 1995; Karp et al., 2009)

Cognitive impairment and function

- Dementia criteria – includes function
  - Clinical Dementia Rating Scale
    - Memory, Orientation, Personal Care, Home and Hobbies, Community Affairs, Judgment and Problem Solving
      - Informant-based interview, largely of function, accurately stages and 'diagnoses' dementia (autopsy; Morris, 1993)

- Original MCI criteria:
  - No "substantial interference with work, usual social activities or other activities of daily living." (Petersen et al, 1999)
    - Studies have shown IADL impairment in MCI stage
      - Episodic memory, Executive function, Processing speed (Wadley et al., 2008; Cahn-Weiner et al., 2000; Pereira et al., 2008; Tomaszewski-Farias et al., 2009)

MCI criteria and function: revisited

- New criteria: "preservation of independence in functional abilities", "persons with MCI commonly have mild problems performing complex functional tasks…" (Albert et al., 2011)
  - We have and continue to publish a line of research consistent with the new MCI criteria and the role that function plays in the dementia process.

Type of functional impairments in MCI

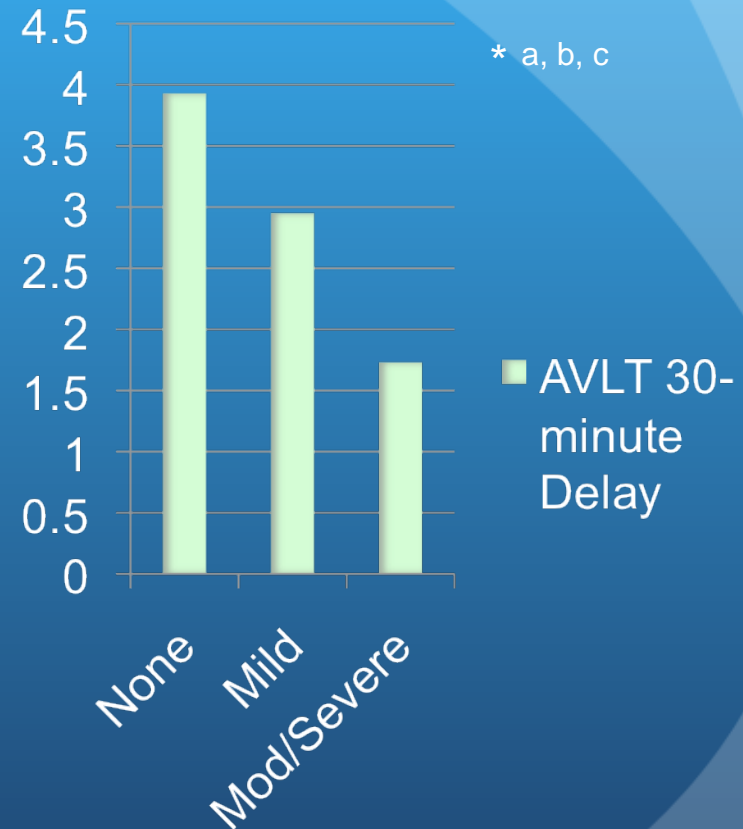| FAQ item	Normal n = 229	aMCI n = 394	AD n = 193	Trend test z-score
1. Writing checks, paying bills, or balancing checkbook.	2%	34%	88%	17.97
2. *Assembling tax records, business affairs, or other papers.*	2%	43%	91%	18.47
3. Shopping alone for clothes, household necessities, or groceries.	< 1%	19%	71%	16.19
4. Playing a game of skill such as bridge or chess, working on a hobby.	< 1%	22%	62%	14.27
5. Heating water, making a cup of coffee, turning off the stove.	0%	8%	28%	9.14
6. Preparing a balanced meal.	< 1%	20%	65%	14.98
7. Keeping track of current events.	< 1%	23%	67%	15.23
8. Paying attention to and understanding a TV program, book, or magazine.	< 1%	21%	59%	13.83
9. *Remembering appointments, family occasions, holidays, medications.*	4%	55%	91%	18.01
10. Travelling out of the neighborhood, driving, or arranging to take public transportation.	1%	26%	76%	16.39

2-item
3.5% of Controls, 66% of aMCI, and 96.4% of AD
had one deficit (86% of AD had both)

Controls vs. aMCI/AD
Sensitivity: 2 vs. 10-item FAQ (.76 vs .81)
Specificity: 2 vs. 10-item FAQ (.95 vs .92)

NACC: 10/6/12

Brown et al., 2011

Severity of Functional Impairment in older adults with aMCI

[a] Denotes a significant difference in post hoc comparisons between no deficits and mild or few;
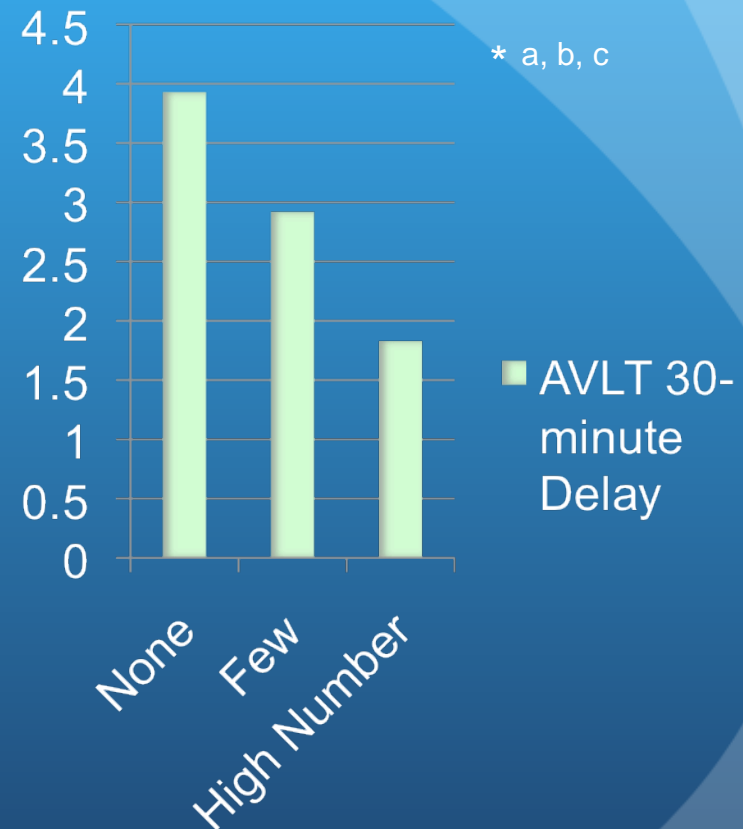[b] Denotes a significant difference in post hoc comparisons between no deficits and moderate/severe or high;
[c] Denotes a significant difference in post hoc comparisons between mild or few and moderate/severe or high.
Severity Groups: No deficits = 0; mild severity $\geq$ 1 and $\leq$ 4; moderate/severe $\geq$ 5. $p < .0167$ (Bonferroni corrected).
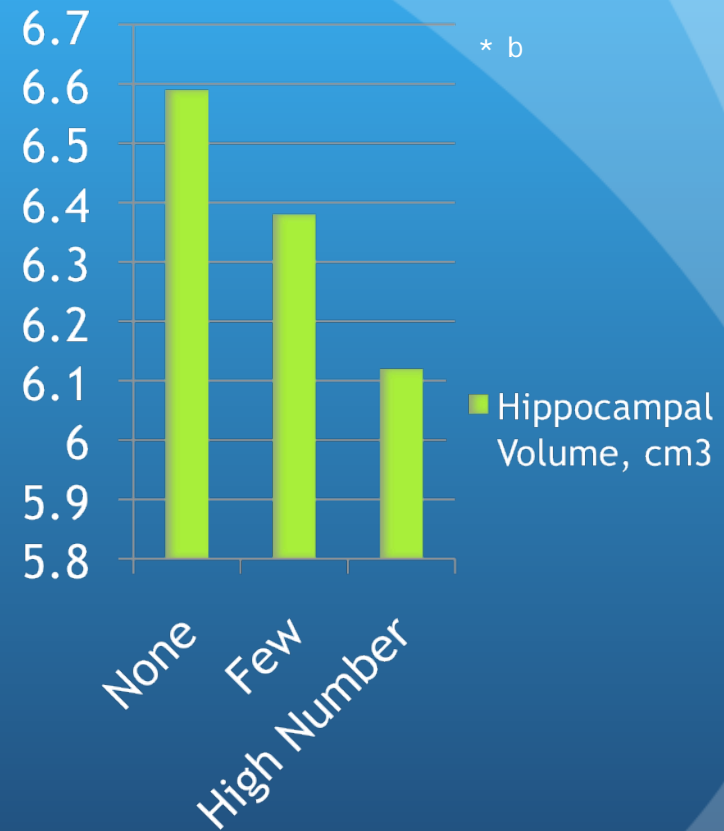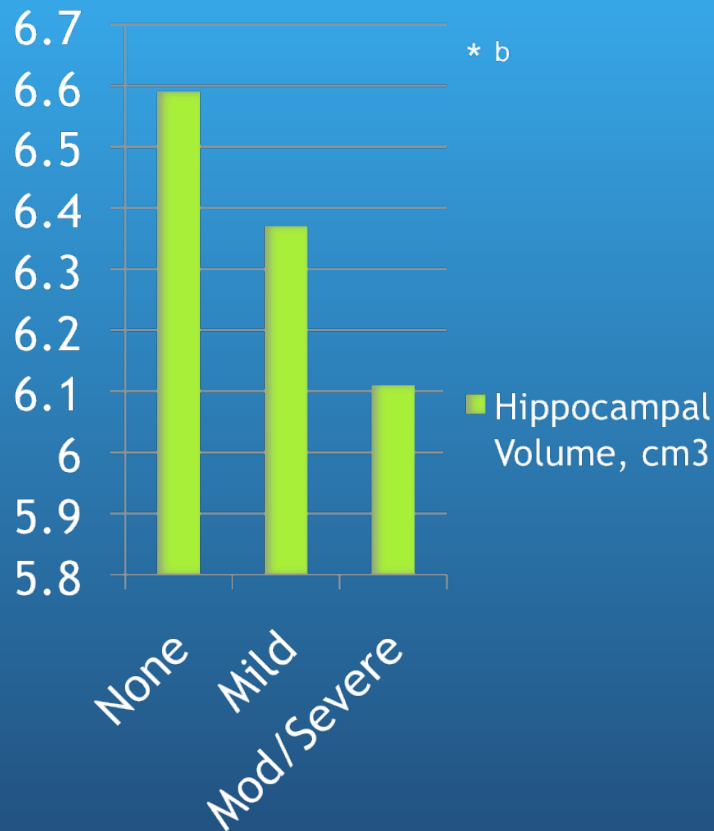NACC: 10/6/12 (Covariate adjusted means (age, sex, and education; ICV for hippocampal volume)

Brown et al., 2011

Numbers of Functional Impairments

* b, c — Trails A chart (None, Few, High Number)

* a, b, c — AVLT 30-minute Delay chart (None, Few, High Number)

[a] Denotes a significant difference in post hoc comparisons between no deficits and mild or few;
[b] Denotes a significant difference in post hoc comparisons between no deficits and moderate/severe or high;
[c] Denotes a significant difference in post hoc comparisons between mild or few and moderate/severe or high.
No deficits = 0; few deficits $\geq$ 1 and $\leq$ 3; high number $\geq$ 4 . $p < .0167$ (Bonferroni corrected).

NACC: 10/6/12

Brown et al., 2011

Neuroanatomical correlates of functional impairment

Means adjusted for age, gender, education, and intracranial volume.
[a] Denotes a significant difference in post hoc comparisons between no deficits and mild or few;
[b] Denotes a significant difference in post hoc comparisons between no deficits and moderate/severe or high;
[c] Denotes a significant difference in post hoc comparisons between mild or few and moderate/severe or high.
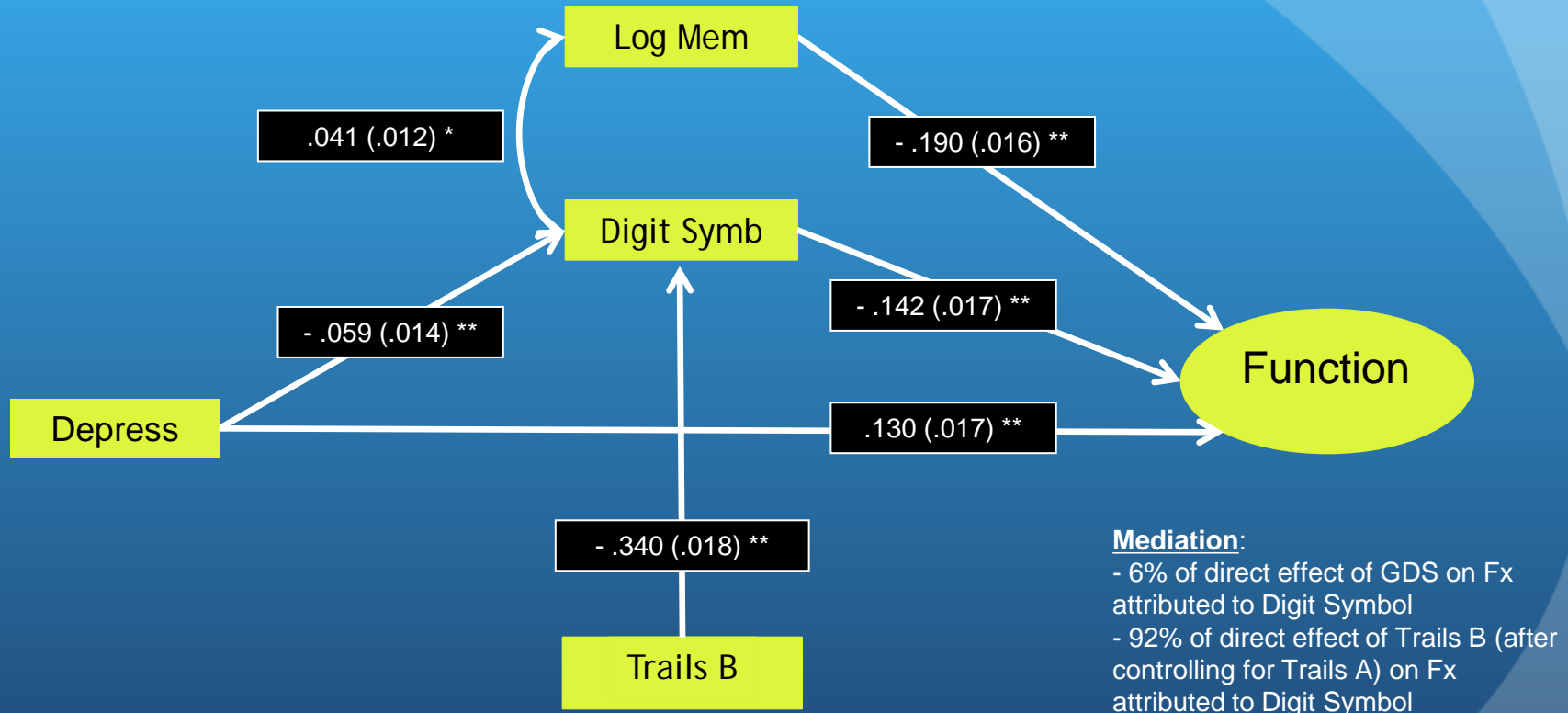$p < .0167$ (Bonferroni corrected).

Brown et al., 2011

Depression and cognitive impairment:
Impact on function

- What impacts functional impairment in a combined depressed, cognitively impaired group
  - ADNI has low comorbidity, no depressive symptoms
  - 3,117 patients with aMCI and nonaMCI from baseline NACC
    - The amnestic group was older, more educated, more functionally impaired, less independent, and had fewer ischemic problems than the nonaMCI group ($p < .01$)
    - The nonamnestic group had better memory but poorer executive function

Brown et al., 2012

Sample characteristics

Variable	Total MCI N = 3117	aMCI n = 2488	nonaMCI n = 629	*p*-value
Age	74.37 (9.37)	74.83 (9.33)	72.57 (9.33)	< .001
Education	14.91 (3.34)	14.97 (3.30)	14.67 (3.45)	.045
M/F (% F)	1407/1710 (54.9%)	1132/1356 (54.5%)	275/354 (56.3%)	.423
MMSE	27.27 (2.32)	27.14 (2.35)	27.80 (2.13)	< .001
Logical Mem Del	7.04 (4.76)	6.32 (4.61)	9.90 (4.21)	< .001
Trails A (sec)	45.16 (23.48)	45.13 (23.76)	45.30 (22.32)	.869
Trails B (sec)	142.66 (80.34)	140.41 (78.92)	151.57 (85.19)	.003
Digit Symbol	36.90 (12.27)	37.02 (12.34)	36.43 (12.01)	.279
CDR sum of boxes Mean Median (min/max)	1.28 (1.13) 1.00 (0/9)	1.33 (1.11) 1.00 (0/8)	1.11 (1.20) 0.50 (0/9)	< .001
GDS	2.49 (2.70)	2.44 (2.62)	2.65 (2.98)	.116
GDS ≥ 5, % (n)	17.3% (538)	16.6 % (414)	19.7 % (124)	.068
FAQ	3.31 (4.97)	3.46 (5.04)	2.71 (4.66)	.002

Brown et al., 2012

The relationship of depression, cognitive impairment, and function

Mediation:
- 6% of direct effect of GDS on Fx attributed to Digit Symbol
- 92% of direct effect of Trails B (after controlling for Trails A) on Fx attributed to Digit Symbol

Path analysis conducted in MPlus, model includes probit regression coefficients and SEs, and Function as a latent outcome variable. Covariates include age, gender, education, Hachinski and, in each model with Trails B, Trails A
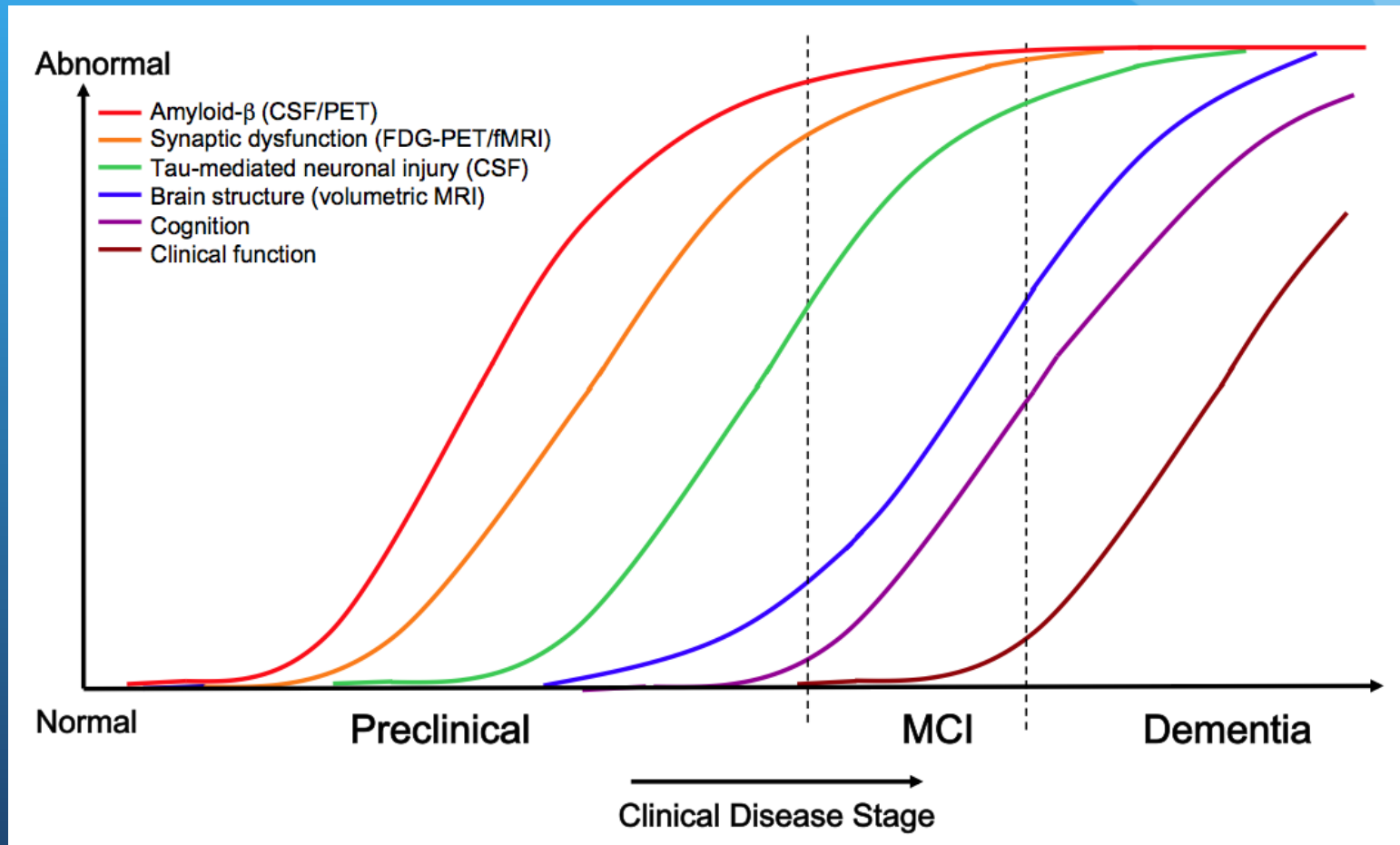* $p < .001$; ** $p < .0001$

Brown et al., 2012

Depression, cognitive impairment, and function in nonaMCI elders

Conclusions:
What we know about functional deficits in MCI?

- Subtle functional deficits occur early in the MCI stage
  - Marker for disease progression:
    - Early fx deficits are associated with deficits in episodic memory and processing speed
    - Fx deficits are associated with medial temporal atrophy
  - <u>Clinical utility</u>: Clinicians can assess specific informant-reported deficits commonly observed in the MCI stage
    - Medication management, remembering appointments, and managing one's finances.
    - Mindful that the impairment is a "change" from premorbid fx
- Depression appears to have a direct and indirect effect on function in cognitively impaired individuals
  - Slowing plays an important role in impaired daily activities

Clinical Disease Stage for Dementia

Sperling et al., 2011

Future Directions

- Despite its utility, how will research on function contribute to the field as the focus turns towards "the silent years" of the dementia process
  - Improvements in assessment may play a role
    - Increased breathe of assessment with deficits statistically shown to load on a specific cognitive domain
      - ECog; Farias, 2008
    - Performance measures
      - UPSA (Goldberg's group)
    - Technological advances:
      - Will improved technology identify subtle deficits in these "silent years" to expand the role of clinical measures as neuropathological techniques continue to advance?

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