Vascular Burden and the Relationship Between ADHD and Cognition in Older Adults

- 39 older adults with clinical ADHD and 50 age- and gender-matched older adults without ADHD.
- MRI was used to quantify periventricular (pWMH) and deep WMH (dWMH) volumes. (white matter hyperintensities)
- Cognition was measured using standardized tests of memory, processing speed, visuo-construction, language, and executive functioning.
- Relative to similarly aged adults without ADHD, the older ADHD sample experienced worse cognition in the presence of vascular pathology, despite lower levels of vascular pathology overall.

Callahan BL, et al. Am J Geriatr Psychiatry. 2024 Apr;32(4);427-442.

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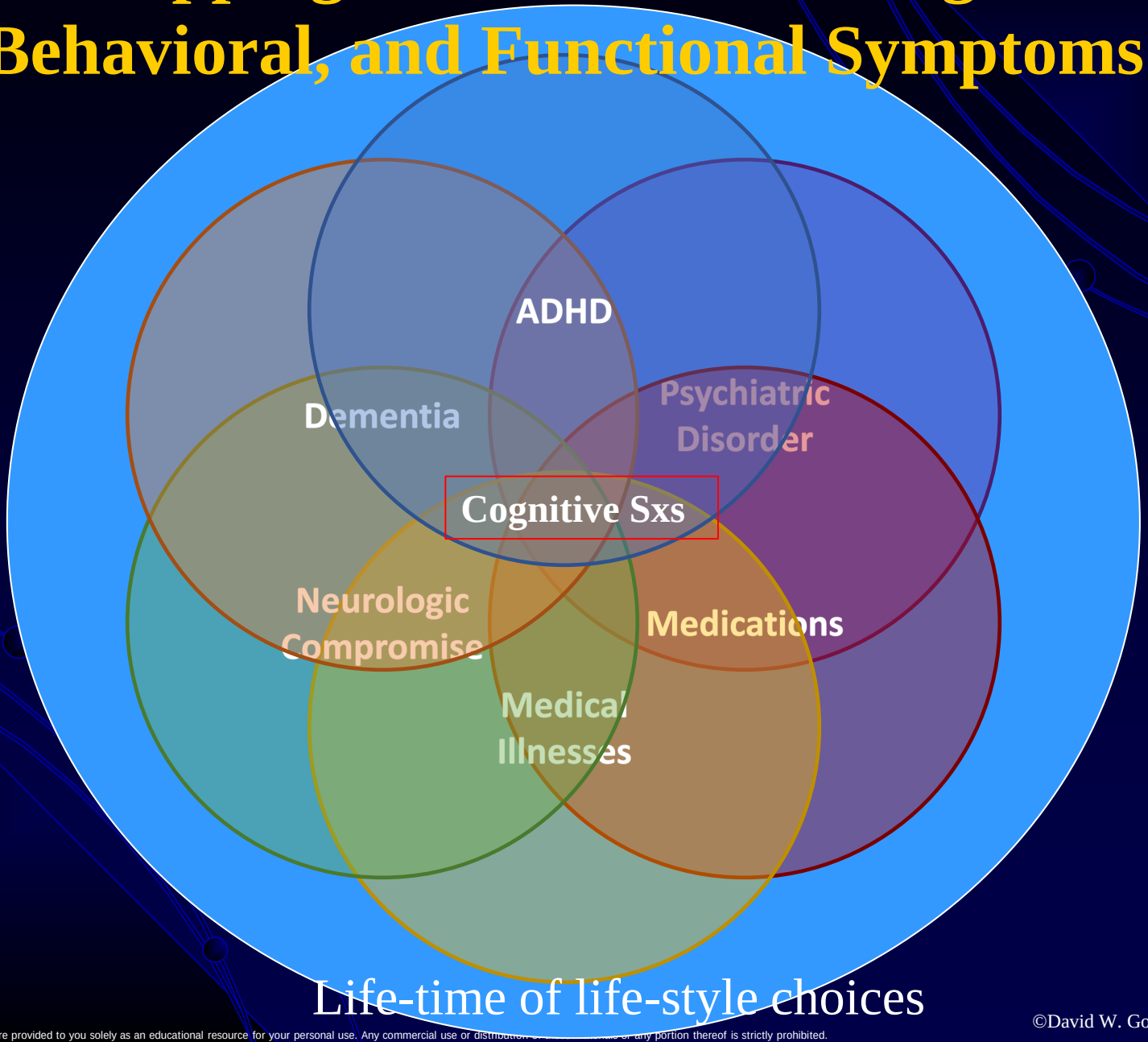
Overlapping Contributors to Cognitive, Behavioral, and Functional Symptoms



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Prevalence of MCI by Age

Mild Cognitive Impairment Criteria

-Memory complaint, preferably corroborated by an informant
-Objective memory impairment
-Normal general cognitive function
-Intact activities of daily living
-Not demented

Age (years)	Prevalence
60-64	6.7%
65-69	8.4%
70-74	10.1%
75-79	14.8%
80-84	25.2%

Petersen RC. J Intern Med 2004;256:183.

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ADHD or MCI? ADHD and MCI?

- Older adults from a Cognitive Neurology clinic (40 ADHD, 29 MCI, 37 controls) underwent neuropsychological assessment.
- Both groups (ADHD, MCI) displayed normal executive functioning.

- A subsample (n = 80) underwent structural neuroimaging.

- **Results:** Memory was impaired in both patient groups
  - a storage deficit in MCI (supported by relatively smaller hippocampi)
  - an encoding deficit in ADHD (supported by frontal lobe thinning).

- Semantic retrieval was uniquely impaired in MCI.

Brandy L. Callahan, et al. Journal of Atten Disorders 2022; 1118-1129

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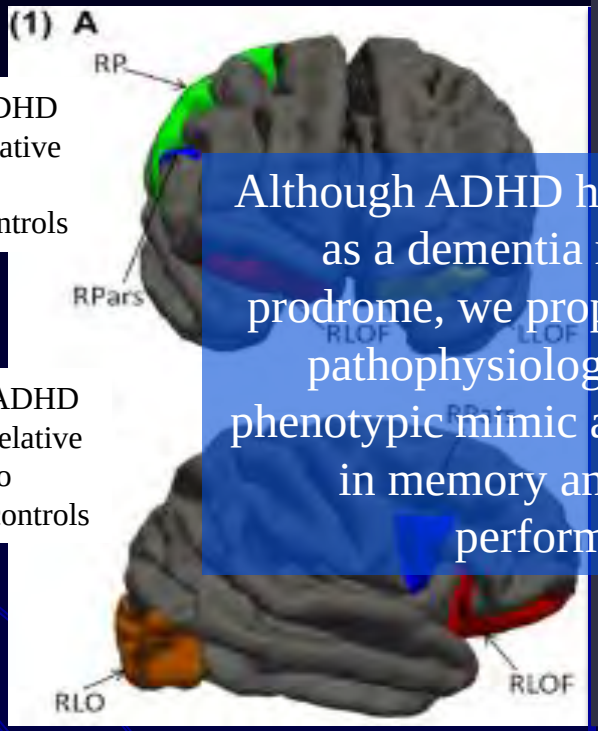
Neuroimaging Cortical Thickness: Older Adult ADHD vs MCI



ADHD relative to controls

ADHD relative to controls

Although ADHD has been proposed as a dementia risk factor or prodrome, we propose it is rather a pathophysiologically-unique phenotypic mimic acting via overlap in memory and executive performance.

Frontal-lobe (1) and whole-brain (2) cortical thickness analysis showing frontal regions with decreased cortical thickness in(A) ADHD relative to controls and (B) ADHD relative to MCI.

Callahan BL, et al. Journal of Atten Disorders 2022; 1118-1129.

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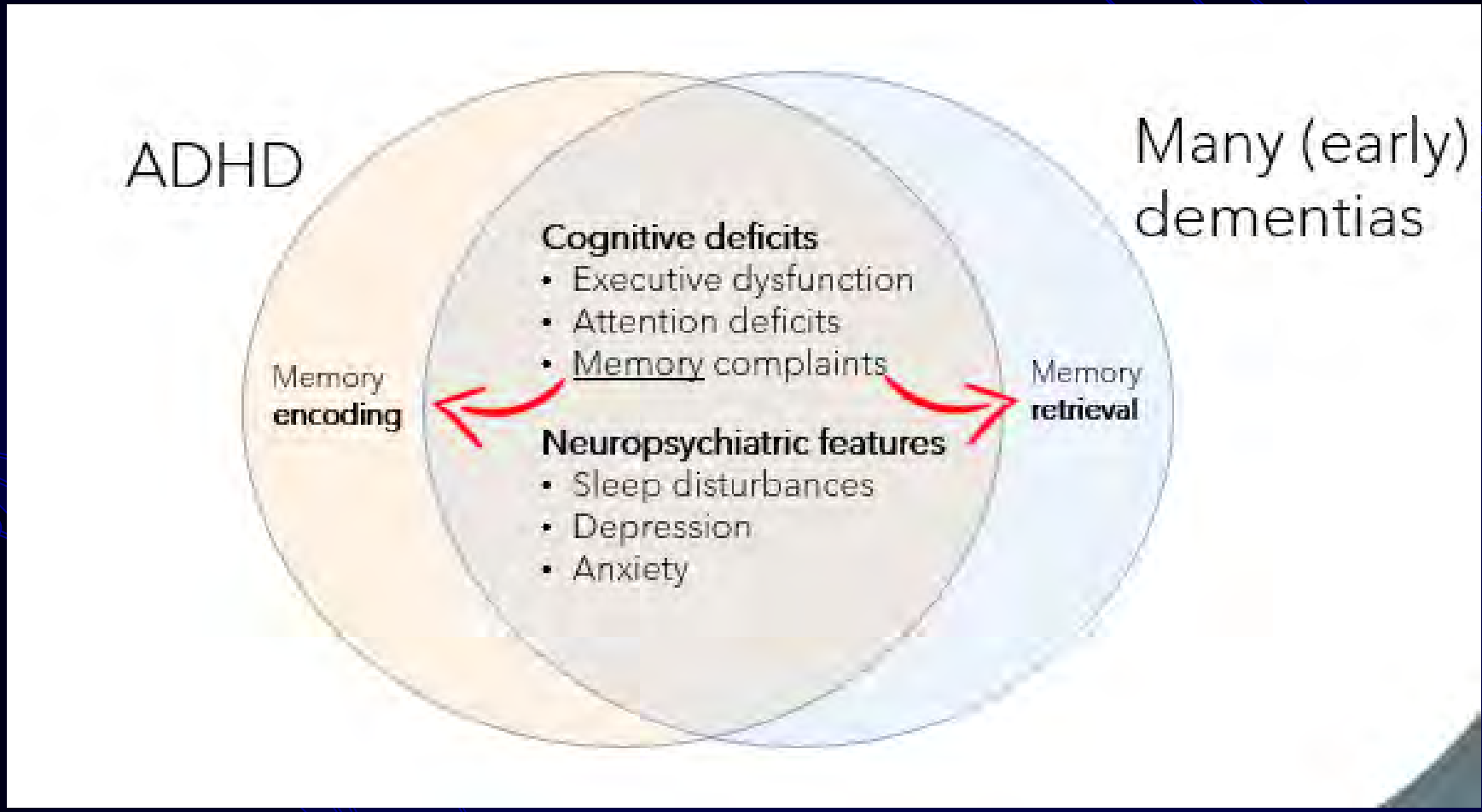
Cognitive Processing: ADHD vs MCI



Slide courtesy of Brandy Callahan, Ph.D.

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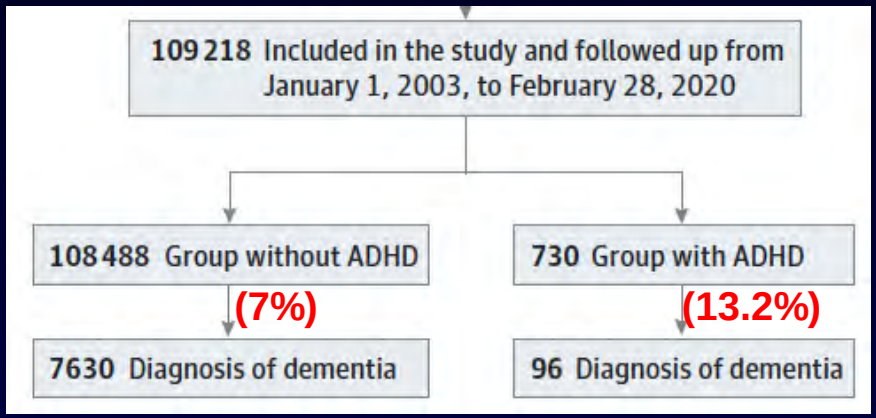
ADHD and Risk of Future Dementia

- Epidemiologic studies suggest link between ADHD and dementia
  (Levine et al. 2023; Becker 2023)
  - Levine et al. Prospective national cohort study (2003-2020)
    - 100K+ Israeli adults, ages 51-70, without baseline diagnosis of ADHD or dementia



- **Those with ADHD had greater risk of later dementia (13.2%) compared to those without ADHD (7%)**
- Of the 730 with ADHD, those taking a psychostimulant (22.3%) did not have an increased risk of developing dementia compared with those not taking medication
  -Data on neuroprotective effects of stimulants is inconclusive

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Dementia Risk Associated with ADHD

- All-cause dementia HRa 0.98–4.01
  (Dobrosavljevic et al., Eur Psychiatry 2021; Du Rietz et al., Lancet Psychiatry 2021; Levine et al., JAMA Netw Open 2023; Tzeng et al., J Atten Disord 2019)
- Lewy body diseases ORa 1.5 to HRa 2.6
  (Curtin et al., Neuropsychopharm 2019; Du Rietz et al., Lancet Psychiatry 2021)
- Vascular dementia HRa 6.3 *(Tzeng et al., J Atten Disord 2019)*
- Mild cognitive impairment HRa 1.71 *(Dobrosavljevic et al., Eur Psychiatry 2021)*

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So…

- Is the risk for dementia associated with:
  - ADHD phenotype (diagnostic criteria)
  - ADHD induced life-style choices and resultant medical illnesses (diabetes)
  - ADHD and associated medical issues (obesity)
  - ADHD genotype (polygenic risk score)

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ADHD Polygenic Risk Score (PRS) Impact in Alzheimer's Disease

High (vs low) ADHD PRS (not diagnosed with ADHD)

N=938 (MCI – 674; AD – 264) all white subjects

	MCI	Alzheimer's Dementia
Executive Function	+	+
Memory	-	-
Language	-	-
CSF Aβ	-	-
CSF P-tau	-	+
Brain glucose - hypometabolism	-	+

Leffa D., et al. Impact of the genetic risk for attention-deficit/hyperactivity disorder in Alzheimer's disease. Journal of the Alzheimer's Association. Alzheimer's Dement. 2025 Feb;21(2):e70003.

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Psychiatry: Impression and Recommendations

- Diagnostic impression:
  - **ADHD-combined presentation**
  - **Mild Cognitive Impairment ?early Alzheimer's dementia**
  - **Major Depressive Disorder, in remission**
  - **Traumatic Brain Injury over 30 years ago**

- Treatment recommendations:
  - Stop vortioxetine (no benefit on mood or cognition after 2 months)
  - Stop bupropion (no benefit on cognition, ? effect on mood)
  - Start lisdexamfetamine 20 mg for 4 days then 40 mg qAM. Within 1 month, dose was titrated to 70 mg Qam

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What happened to the patient?

- Patient was started on Vyvanse and titrated to 60 mg AM.
- Patient and wife report ~60% improvement in cognition.
- He resumed work 3 days/week, which has progressed to 5 days/week now from home.
- He resumed some of his positions that he had suspended.
- His wife is relieved that he can continue his work, leaving him in a better state of mind.
- Lifestyle choices are excellent. Exercise 6 days/week.

Yet, persistent symptoms include word-finding difficulties, word substitution, misspellings, difficulty recalling conversations, and using generic words like "stuff" and "things" in conversation.

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