

ADHD Meets "Aging":
ADHD and Cognitive
Decline

2024 Annual International Conference
on ADHD
Anaheim, CA- Nov. 2024
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- No financial COI
- Am a member of the National BOD For CHADD
- Am a nursing professor at Concordia College
- Am here as a content expert on ADHD- views and information I present do not represent either organization
- Information is evidence-based but not meant to replace any provider directed treatment- nor any professional scope of practice

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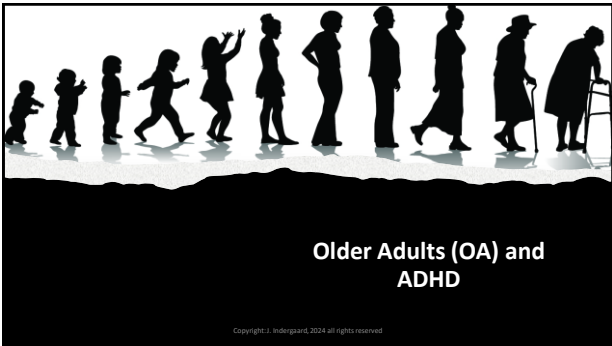
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New Frontiers in ADHD -
We've come a long way!

- 1902: Abnormal defect of moral control (Still)
- 1952: First DSM -ADHD not listed
- 1968: DSM -Hyperkinetic Reaction of Childhood
- 1980: DSM III- ADD (Attention Deficit Disorder)
- 1987 - DSM - ADHD but Childhood Only
- 1990s- early 2000s - Adult ADHD!
- 2010-2020 - Unique Needs of Women w/ ADHD

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Outline - this presentation...

- Explore complexities of diagnosing OA ADHD
- Highlight challenges in differentiation of ADHD and MCI/NCD
- Is ADHD linked to early cognitive decline or mild cognitive impairment (MCI)?
- Is ADHD linked to any form of neurocognitive disorder (NCD)?
- What are the proposed mechanisms of possible association?
- Implications for provision of clinical services for older adults, diagnostic screening, and future research?

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A collage of medical brain scans, including axial and sagittal views, with some areas highlighted in red and blue.

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Background/Impetus

- Aging population worldwide
- Global prevalence of neurodegenerative diseases & dementia
- An increasing public health concern
- *Lancet Commission - 12 modifiable risk factors to delay/prevent NCD*
- Ability to identify those at risk for future NCD vital to improve lives and decrease global, social, economic burden of dementia

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A row of colorful, stylized human figures in various colors (blue, green, red, yellow, brown) standing on a light surface.

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At the Same Time...

- ADHD in adults increasingly recognized (though has diagnostic challenges)
- Demonstrates continued impact even for OA
- 3% of adults aged 50 and older

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It's a Fact...

ADHD will be one of many psychiatric contributors to morbidity in the aging population.

(Goodman et al. 2015)

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A man with a beard and mustache, wearing a bright yellow sweater over a white collared shirt, is shown from the chest up. He has a thoughtful expression, with his hand resting on his chin and looking upwards and to the left.

So, what happens when ADHD meets aging...

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A composite image featuring two women. On the left, a younger woman with dark hair is smiling. On the right, an older woman with white hair is also smiling. They are both wearing light-colored tops.

Climacteric (Menopause)

Exacerbation of symptoms

Onset of new symptoms

Increased inattention

More vulnerable to mood disorders

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A woman with blonde hair and glasses, wearing a bright yellow sweater, is shown from the waist up. She has her hands raised in the air, palms facing forward, and a glowing yellow aura surrounds her head and shoulders.

Menopause ADHD Symptom Exacerbation...

- Brain Fog
- Poor Working Memory (remembering things)
- Poor Sleep
- Mood changes (depression, anxiety)
- Emotional Dysregulation
- Easily overwhelmed
- Word retrieval difficulties
- Concentration – staying on task

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Current Adult ADHD DSM Criteria:

5 of 9 symptoms of inattention and/or impulsivity hyperactivity

- Difficulty paying attention to details/careless mistakes
- Difficulty sustaining attention
- Not listening when spoken to directly around/climbing
- Difficulty following instructions leisure quietly
- Difficulty organizing tasks and activities
- Avoiding tasks that require sustained mental effort
- Losing Things
- Being easily distracted
- Being forgetful in daily activities

- Fidgeting/squirming
- Leaving seat
- Running
- Difficulty playing or
- Driven by a motor
- Talking excessively
- Blurting
- Interrupting
- Unable to wait turn

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Beyond DSM criteria in OA (Nadeau, 2024)

Unreliable (swiss cheese) memory

Working memory issues (thrown off)

Brain "blanks"- forgetting words

Hyperactivity "Remnants"

Misplacing items

Not getting things done

Emotional Dysregulation

Trouble Following Conversations

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In other words...

- Time-blind
- Inability to resist goal-irrelevant distractions
- Difficulty re-engaging in a task
- Not getting things done
- Social Challenges

- Cognitive Impulsivity
- Motivational Impulsivity
- Emotional Impulsivity
- Verbal Impulsivity
- Unable to Relax

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Older Adult
ADHD-
Obstacles to
Diagnosis

- Typically, not screened for in the elderly
1 out of 5 (Goodman et al. 2015)
- Many not diagnosed in childhood b/c ADHD
poorly recognized then
- Lack of data and study of "older" adults with
ADHD
- Not been studied longitudinally
- Recall bias based on longevity
- Lack of informant history from childhood
- Controversy re: Late onset vs. Manifestation

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Other
challenges to
diagnosis of
ADHD in OA

- Comorbidity
- Adaptive Functioning
- Symptoms Change
- Validity of Assessment

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So, what can be done to
screen/assess/dx OA ADHD?

- Improve diagnostic specificity and
identification for targeted treatment

How?

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In the
absence of
proper
screening
tools for OA
ADHD...

- Clinical Interview
- History (including family and succeeding generations)
- Dig Deep into Symptoms (Nadeau, 2024)
- Assess for: (Goodman, 2024)
 - sleep disturbances, polypharmacy
 - psychiatric, physical co-morbidities
 - anxiety and depression
 - self-esteem, social inadequacy

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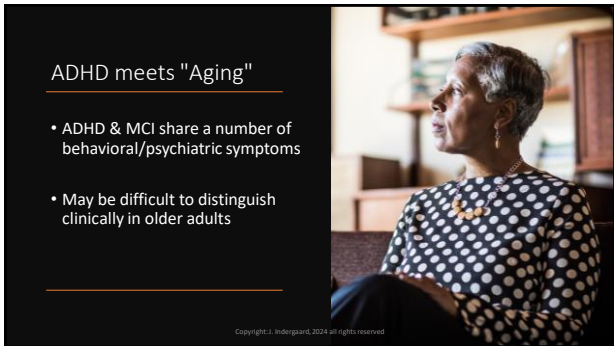
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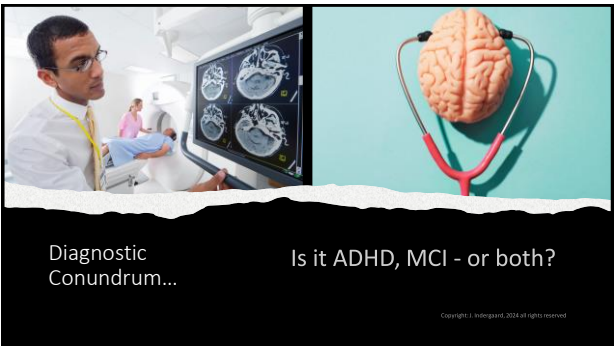
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Definitions/Comparisons

ADHD

- Neurodevelopmental Condition
- Impairing levels of difficulties regulating attention, impulses and activity levels
- Symptoms start before age 12 and persist into adulthood
- Functional impairment fluctuates across time

NCD

- Neurodegenerative Condition
- Significant decline in cognition, behavior and ability to perform everyday activities
- Aging-related progressive deterioration in cognition and ability for independent living
- Symptoms worsen over time

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In theory, the two diagnoses could be clinically differentiated by...

Symptom Onset (Age)

Progression

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Mild Cognitive Impairment (MCI)

- Defined by the presence of impairment in 1 or more cognitive domains
- Does not affect functional independence
- Does not fulfill diagnostic criteria for dementia

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	ADHD- neurodevelopmental 3-4% prevalence among older people	NCD- neurodegenerative- 7.1% MCI = 5-20%
Symptom Profile/Dx	• ≥5 sx hyperactivity, impulsivity, inattention • Sx present before age 12 • Male Predominance	• Decline in cognition affecting multiple domains of intellectual fn • Onset sx for AD typically mid-60s • AD higher in females
Cognitive Impairment	• Difficulty engaging/sustaining attention • Difficulty switching tasks • Episodic Working Memory Deficits • Slow Processing Speed • EFD	• Problems w/communication • Inability to perform ADLs • Memory Loss • Flattening of the Learning Curve • EFD
Behavioral Disturbances	• Anxiety (35%)/Depression (44%) • Sleep Disturbances (70%)	• Anxiety (14%)/ Depression (29%) • Sleep Disturbances (59%) • In MCI sleep disturbance (17%)

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Shared Symptoms

- Inability to provide sustained attention
- Challenges with mental effort
- Difficulty organizing & planning
- Forgetfulness
- Impaired Memory
- Sleep disturbances
- Depression & Anxiety

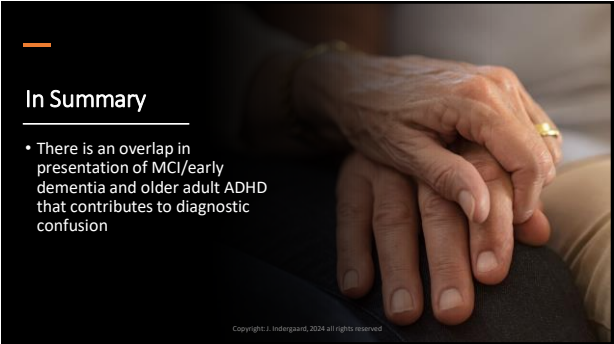


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In Summary

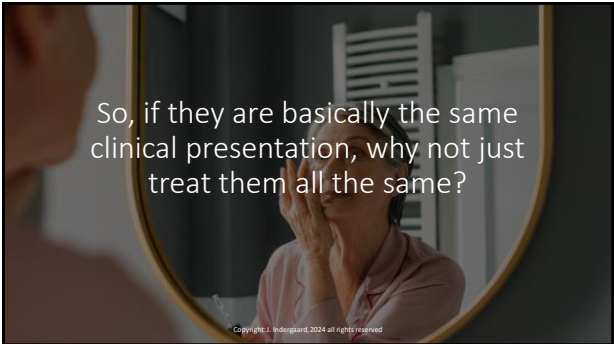
- There is an overlap in presentation of MCI/early dementia and older adult ADHD that contributes to diagnostic confusion



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So, if they are basically the same clinical presentation, why not just treat them all the same?

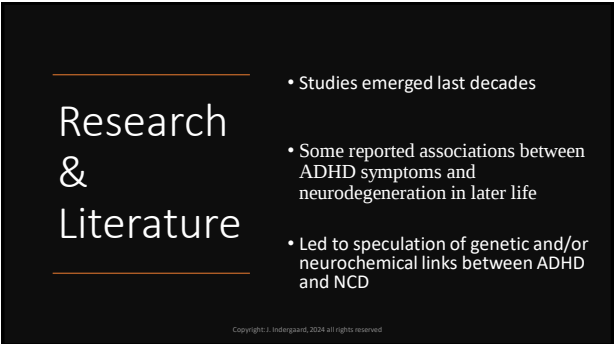


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Research & Literature

- Studies emerged last decades
- Some reported associations between ADHD symptoms and neurodegeneration in later life
- Led to speculation of genetic and/or neurochemical links between ADHD and NCD



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Thus, the questions...





Is ADHD a risk factor for NCD (dementia)?

Is ADHD linked to later NCD (dementia)?

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Research & Literature

- Some studies reported an association b/t ADHD & NCD (especially AD or LBD)
- Some studies suggest ADHD represents an early point on neurogenerative continuum
- Some studies suggest ADHD could be a modifiable risk factor for NCD
- Some studies suggest it is merely a phenotypic "mimic"

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Examples-Studies that "found" links

Multi-generational cohort study
Antecedent ADHD significantly predicted AD, stronger for early onset, associated with any dementia across generations (Zhang et al., 2023)

Population-based register study
ADHD increased risk for NCD & MCI; MCI>Dem (Dobrosavljevic et al., 2021)

Critical appraisal 8 studies, ADHD increases risk for LBD (and later life NCD) up to 5- fold (Becker et al., 2022)

Prospective national cohort study
ADHD diagnosis associated with 2.77 fold increase in dementia risk (Levine et al., 2023)

Population-based cohort study (Taiwan)
Adults with ADHD have 3.4-fold risk of developing dementia (Tseng et al., 2019)

Prospective observational cohort study
ADHD is independently associated w/increased risk for developing LBD & dementia, and no MCI (Golimstok et al., 2024)

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Examples Findings of Studies- that found no links

Case Control Study =
Prior ADHD not associated with AD (Golimstok et al., 2011)

Quasi-experimental Cohort Study =
No correlation b/t childhood ADHD and MCI or dementia (hanchak et al. 2011)

Cohort Study =
No association ADHD, MCI, NCD (Das et al., 2014)

Clinical Study
Found ADHD/MCI each have unique cognitive & neuroimaging profiles (Callahan et al., 2022)

Cross Sectional Study
Based on clinical, cognitive, and behavioral assessments, MCI and ADHD are dissociated clinical entities with overlapping cognitive profiles (Mendonca, et al., 2021).

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Limitations and
Confounding
issues r/t
studies/literature

- Data are from registries - methodological issues
- Clinical samples may not be representative
- ADHD may be undetected in comparison samples
- Timing: 63 years old - may not capture dementia of later years
- Methodological limitations of the research

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Clearly....more research needed.

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Mechanisms
- how might
there be a
link?

- ADHD/NCD highly heritable:
Pleiotropic genetic variants – two
points on a continuum
- ADHD increases risk through health,
familial, environmental factors
associated with ADHD
- ADHD is a "phenotypic mimic"

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What does Biology Show?

	ADHD	NCD
Genetics	Common Genetic Factors - 6- SORCS2 Common neurochemical disturbances (Alemany et al., 2015)	Common Genetic Factors - 6- SORCS2 Common neurochemical disturbances (Alemany et al., 2015)
Neuroimaging	Memory deficit – encoding issue/ frontal lobe thinning Subtle Global reduction in brain volume Smaller prefrontal volumes Reduced activation frontostriatal networks Reduced activation in parietal networks (Callahan et al. 2021)	Memory deficit – storage deficit/ smaller hippocampus Hippocampal atrophy (AD) Parietal hypometabolism (AD) Significant Vascular Disease (VaD) Occipital Hypoperfusion focused atrophy midbrain (LBD) (Callahan et al. 2021)

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What do Socio/Environ/Familial Factors Show?

ADHD can be associated with increased:	Risk factors for NCD are:
Smoking Alcohol & Substance use DM, Obesity Lower Educational Attainment Lower SES Psychiatric Comorbidity Diminished quality relationships (Beehuspoteea & Badrakalimuthu, 2023)	Low educational attainment 12 Metabolic Syndrome Sleep disorders Head injuries Psychiatric Disorders Substance Use Disorder

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Risk factors of Dementia which are similar to commonly associated ADHD outcomes

- Lower Educational level
- Increased prevalence TBI
- Obesity
- Smoking
- Alcohol related disorders
- Depression
- Social isolation from peer rejection
- Physical inactivity
- Oxidative Stress Neuroinflammation

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What does mimic theory say?

	ADHD	NCD
Both ↓ <u>Impaired Memory</u>	But in ADHD... Frontal lobe cortical thinning in ADHD <i>Separate storage and encoding impairments</i> (Mendonca et al., 2021) (Callahan, et al., 2022)	But in NCD... Hippocampal atrophy in MCI <i>Specific semantic weaknesses</i>

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While both display broadly overlapping features:

1. Are unique characteristics and neuroimaging markers
2. Are dissociated clinical entities that have overlapping profiles

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Implications for Practice: Treatment & Management

- Prescription of stimulant medication in menopause and OA requires individualized considerations of risk/benefit ratio and close follow-up but should not be excluded
- Role and efficacy of non-stimulant medications and non-pharmacological treatments and approaches in these populations needs to be further elucidated

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Implications for Research

- Characterize cognitive and behavioral profiles of older adults w/ ADHD & MCI
- Development of Clinical Screening Tools for OA ADHD
- More research to confirm findings & explore underlying mechanisms
- Empirically designed longitudinal studies needed
- Study oxidative stress/inflammation as possible underlying mechanisms

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Conclusion

- ADHD persists into OA and due to overlapping symptoms can be confused with MCI
- Extent that ADHD is risk for NCD is unclear
- Bulk of current evidence indicates ADHD fundamentally unrelated to MCI
- Mechanistic link b/t disorders attributed to health compromising mediators
- In the absence of clear diagnostic criteria and validated screening tools, clinicians need to be aware of converging phenotypes to avoid misdiagnosis and assure appropriate treatment

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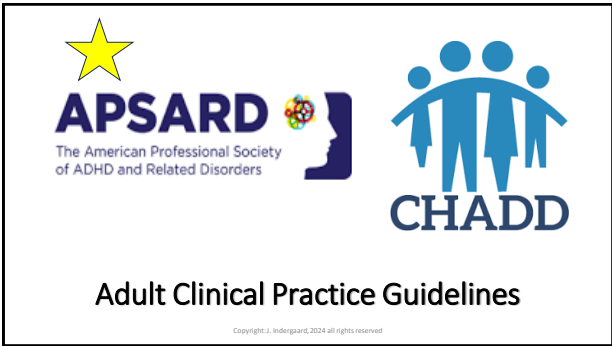
Moving Forward

If ADHD does have a neurodegenerative course or link...

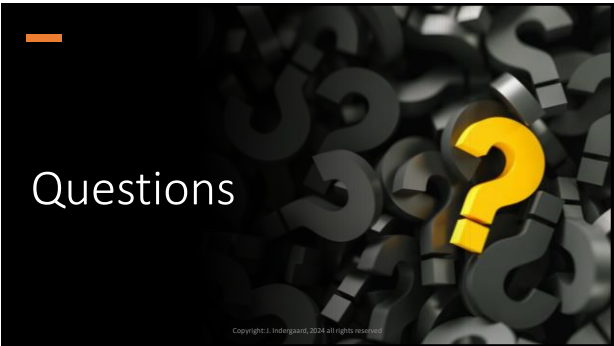
- findings must guide treatment
- if not, then must reduce dementia misdiagnosis through careful screening and identification

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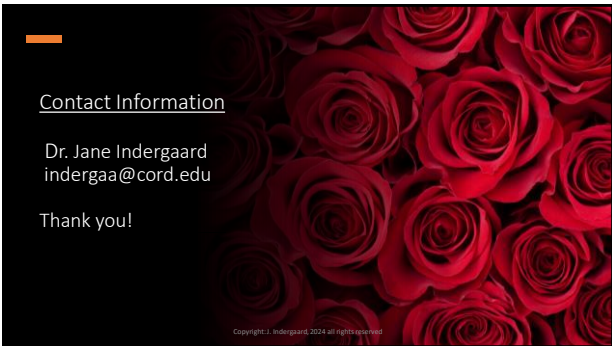
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