Vascular Cognitive Impairment: From Prevention to Treatment

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Presentation Overview and Objectives

• Cognition and Aging
• Risk Factors
• Strokes and TIAs
• Types of Cognitive Impairment
• Diagnosis
• Intervention
• Prevention
Age-Related Memory Cognitive Changes

- Few changes
  - Crystallized Intelligence
  - Procedural Memory
  - Long-term Memory
  - Auditory Attention
  - Verbal Fluency
  - Working Memory?

- Declines in:
  - Sensory Memory
  - Short-term Memory
  - Visual and Verbal
  - Complex/Selective Attention
  - Executive Skills
  - Processing Speed
  - Motor Tasks
  - Working Memory?
Abnormal Memory Loss

Cognitive Functioning

Early Life  Late Life

Age

MCI
Dementia
Dementia

• Clinical Presentation: A syndrome of acquired impairment of two or more cognitive domains sufficient to affect daily life.

• Etiology: Any disorder causing progressive dysfunction to brain systems involved in cognition.
Playing the Odds

Alzheimer’s Disease

Vascular Dementia

Dementia with Lewy Bodies

Frontotemporal Dementia

Mixed Dementia
Mixed Dementia
(Langa et al. JAMA, 2004)

• Mixed AD and VaD
  ▪ Most frequent form of mixed dementia
  ▪ 28% in dementia clinics
  ▪ >50% in community samples
  ▪ Periventricular lesions in 90% of AD cases

• Other Mixed Dementias
  ▪ 31% with Lewy Body and VaD
Atlas of Brain Perfusion SPECT Multi-infarct (Vascular) Dementia
Harvard Medical
www.dementiatoday.com
Lacunar Infarcts

Selnes OA and Vinters HV (2006) Vascular cognitive impairment
*Nat Clin Pract Neurol* 2: 538–547 10.1038/ncpneuro0294
Neuropathological Findings in 233 Cases

- AD: 14%
- AD/DLB: 23%
- AD+Vasc: 12%
- AD/DLB+Vasc: 13%
- HS+AD/DLB: 2%
- HS+AD+Vasc: 0%
- HS+DLB: 1%
- HS+Vasc: 2%
- DLB: 6%
- DLB+Vasc: 7%
- Vasc: 10%
- Other: 3%
- Normal: 1%
- PSP: 2%
- Other: 3%
- Normal: 1%
Neuropathological Findings in 233 Cases

- AD: 14%
- AD/DLB + Vasc: 13%
- DLB + Vasc: 7%
- HS + AD + Vasc: 0%
- Vasc: 10%
- AD + Vasc: 12%
- HS + Vasc: 2%
- HS + AD/DLB: 2%
- HS + DLB: 1%
- AD/DLB: 23%
- HS: 4%
- DLB: 6%
- PSP: 2%
- Other: 3%
- Normal: 1%
Vascular Dementia

Classes

- Multi-Infarct (MID)
- Eloquent Infarction
- Subcortical Ischemic
- Hypoperfusion
- Hemorrhage
- Miscellaneous vascular insult
TIAs

Transient Ischemic Attacks (TIAs)

• Similar symptoms to a stroke
  ▪ Slurred speech, dizziness, difficulty walking, weakness in limbs

• Resolve quickly
  ▪ Hours to day(s)

• Return to near-baseline

• Cumulative effects

• Importance of immediate intervention!
TIAs and Strokes

Coronal section of the brain showing middle cerebral artery

Atherosclerotic clot

Blood clot
TIAs and Strokes
Vascular Dementia

• Related Health Conditions
  • Type 2 Diabetes
  • High blood pressure
  • High cholesterol
  • Heart disease
  • Coronary artery disease
  • Smoking
  • Alcohol

• Synergistic effects?
Vascular Dementia

• Genetic Forms

  » Cerebral autosomal dominant arteriopathy with subcortical infarctions and leukoencephalopathy (CADASIL)

  » Migraine HA, neuropsychiatric symptoms, seizures

  » Rare – 400 families worldwide

  » Autosomal dominant

    ♦ NOTCH3 gene mutation on Ch. 19

  » Most do not have other risk factors

  ♦ Hypertension

  ♦ Diabetes
Vascular Dementia

• Onset can be sudden (large stroke)
  ▪ Often insidious (microvascular)

• Course can be stepwise
  ▪ More often gradual, slowly progressive in early stages

• Often confused with AD in early stages
Vascular Dementia

- Prevalence increases with age
  - Rates double every 5.3 years
- Males > Females
- Highest in those post-stroke
  - 20-30% three months
  - 45-55% three years
Vascular Cognitive Impairment

- Symptoms
  - Greater executive dysfunction
  - Motor impairment/slowing
  - Mild episodic memory impairment
    - Absence of intrusions
    - Intact cued recall
  - Weakness in limbs
  - Language problems
  - Depression, apathy, irritability, disinhibition
Vascular Cognitive Impairment

- Symptoms
  - Gait disturbance
  - Unsteadiness
  - Frequent, unprovoked falls
  - Urinary frequency, urgency, and other symptoms
  - Problems with chewing, swallowing, speech
  - Inappropriate emotional outbursts
  - Personality and mood changes
Model of Vascular Cognitive Impairment

- Heart Disease
- Diabetes

- Difficulty managing medications and following treatment plans
- Problems with planning, sequencing and problem solving

- Missing medications
- Difficulty adopting health behaviors

- Poor illness control

- White matter changes
- Disrupted frontal lobe function
Assessment of Dementia

- Interview/History
- Laboratory
- Neurological exam
- Neuroimaging
- MMSE or other screening measure
- Neuropsychological evaluation

- Repeat if unclear
  - 6-12 months
Screening: MMSE

- 30 items, 5 domains, 5-10 minutes
- Standard cutoff of 23-24
  - Sensitivity = 66-73%
  - Specificity = 87-92%
- Positive Predictive Value = 58-67%
- Misclassification rate = 15%
- Age and education effects/norms
  - Sensitivity = 92%
  - Specificity = 96%
Screening: MMSE

- Improved validity in combination
  - Clock drawing
    - Depends on scoring system
    - Sensitivity = .92 (MCI = .75)

- Several other measures as good, if not better
  - Short Blessed Memory Test & Animals (Kilada et al., 2005)
    - 5-item recall and animal naming
  - Mini-Cog (Borsen et al., 2000)
    - 3-item recall and clock

Especially true for MCI
Functional Assessment – FAQ

Tests functional limitations/changes rather than cognitive
• Sensitivity and specificity comparable to the MMSE
• Rating functional abilities over past 4 weeks
  – Not applicable
  – Normal
  – Some difficulty but does by self
  – Needs assistance
  – Dependent

Screening: MoCA
Screening: MoCA

• Better sensitivity (cutoff = 26, slightly lower in community setting)
  
  ▪ MCI
    • MMSE = 18%
    • MoCA = 90%
  
  ▪ AD
    • MMSE = 78%
    • MoCA = 100%.

• Specificity
  – MMSE = 100%
  – MoCA = 87%
Neuropsychological Assessment: Procedure

What’s involved?

- Review of records
- Clarification of referral question
- Clinical interview
  - Patient
  - Collateral
- Screening
- Battery of standardized measures
- Interpretation and integration
- Feedback
- Return to referring provider for follow-up
Domains of Assessment

- Intelligence/Premorbid Functioning
- Memory (Verbal and Visual)
- Executive Functioning
- Attention/Concentration
- Reasoning/Judgment
- Language
- Visuospatial/constructional
- Perceptual
- Motor
- Personality
- Academic
- Psychological/Affective
Detection and Differential Diagnosis

- Normal
- Early AD
- Vascular
- FTD
- DLB
- Delirium

MMSE
Verbal Memory
Visual Memory
Attention
Language
Visuospatial skills
Executive functions
Motor symptoms
Onset and Progression

Cognitive Functioning

Early Life
Late Life

AD
VaD
DLB
FTD
Prevention: Healthy Aging

- Cardiovascular health
  - Exercise
  - Diet
  - Alcohol
  - Smoking
- Activity levels
- Engagement
- Mood
Prevention and Interventions

• Medication
  ▪ Right things at right times

• Exercise
  ▪ Intensity versus frequency

• Diet
  ▪ Fats: Saturated vs. unsaturated
  ▪ Sugars: Simple vs. complex
  ▪ Glycemic Index: high vs. low
Prevention and Interventions: Hypertension/Diabetes

• Higher midlife BP predicts cognitive decline

• Multiple domains of cognitive impairment
  ▪ Attention
  ▪ Learning & memory
  ▪ Perceptual skills

• Decreased cerebral blood flow/metabolism

• 1.2 - 1.5 x more rapid decline vs. controls
Prevention and Interventions: Exercise and the Brain

• Sedentary community-dwelling adults (age 60 – 79)
• Intervention (6 months)
  ▪ Aerobic
  ▪ Stretching/toning
• Aerobic ex group increased gray and white matter
  ▪ Pre-frontal
  ▪ Temporal
Prevention and Interventions:
Exercise Dosage

• Meta-Analysis of 18 RCT of aerobic fitness training in ages 55 - 80
  ▪ Greatest effects:
    • Combined aerobic + strengthening
    • Longer duration (>30 min.)
    • Executive function
    • Ages 60 - 70 benefitted the most
Prevention and Interventions: Exercise and Dementia

• Dose-response relationship
  - Intensity
  - Session duration
  - Total exercise time
• Age matters (improvement in all groups)
• Multicomponent program most effective
• Protective effect differs with pathological mechanism (vascular, AD pathology)
Prevention and Interventions: Exercise Recommendations

• 30+ minutes of moderate physical activity at least 5 days per week (60-70% of max heart for age)

• 20+ minutes of vigorous physical activity at least 3 days per week (70-80% of max heart for age)

• Can be done in 10 minute bouts?

• More complex movement = more complex synaptic connections with thicker myelin
Prevention and Interventions: Diet

• Fats
  • Low saturated
    • Butter, cheese, fatty beef, lamb, pork, poultry with skin, beef fat (tallow), lard and cream
  • Higher monounsaturated and polyunsaturated
    • Olive oil, canola oil, peanut oil, sunflower oil, sesame oil, avocados, peanut butter, nuts and seeds

• Cholesterol
  • Minimize LDL, triglycerides and Lp(a)
  • Moderate levels of HDL may be protective
    • Olive, peanut and canola oils, nuts, fish/omega-3 fatty acids
Prevention and Interventions: Diet

- **Antioxidants**
  - Vitamin E
  - Vitamin C
  - Coenzyme Q10
  - Lipoic Acid
  - Flavonoids
    - Green tea, red wine, berries, cocoa
  - Resveratrol
    - Red grapes, red wine,
  - Carotenoids
    - Carrots, yams, squash
Prevention and Interventions

- Alcohol
  - 1-2 drinks a day for men; 1 for women?
  - Red wine
  - Grape seed extract
  - Pomegranate juice

- Once impairments are present:
  - Minimal if any alcohol use

- Smoking
  - Controversial, smoking unhealthy, nicotine...
Prevention and Interventions: Medications

- Antihypertensives
- Anticoagulants
  - Warfarin (Coumadin)
  - Aspirin
- Cholinesterase inhibitors
  - Donepezil, Galantamine, Rivastigmine
- NMDA receptor antagonists
  - Memantine
- Vitamins
  - Vitamin E and C
- Supplements/Nootropics
  - Ginkgo
  - Vincamine, lipoic acid, CoQ10
Summary and Conclusions

• Cognition and aging
  ▪ Some things change, some do not

• Risk Factors
  ▪ Diabetes, high blood pressure, cholesterol, smoking, alcohol, sedentary lifestyle, depression

• Strokes or TIAs
  ▪ Early intervention is key!

• Prevention & Treatment
  ▪ Never too late
  ▪ Complex, and specifically tailored to individual
Thank You for Your Attention!

Questions?