Down Syndrome and Alzheimer’s Disease

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Overview

• What is Alzheimer’s disease?
• Risk factors for Alzheimer’s disease, including Down syndrome
• Symptoms of Alzheimer’s disease in Down syndrome
• Behavior in Down syndrome
• Diagnosing Alzheimer’s disease
• Other causes of confusion
• Treatments

Alzheimer’s Disease vs. Dementia

• Dementia
  – A syndrome of progressive decline in cognitive function, significant enough to interfere with daily life
Alzheimer's Disease vs. Dementia

- Causes of dementia
  - Alzheimer's disease (most common)
  - Stroke(s)
  - Frontotemporal dementia
  - Parkinson's disease
    - Dementia with Lewy bodies
  - Hydrocephalus
  - Head trauma
  - Others
What is Alzheimer’s Disease?

- Most common cause of dementia
- Marked by early memory impairment, executive dysfunction
Alzheimer’s Facts

• 5.4 million Americans have AD in 2011
• One in eight (13 percent) over 65 have AD
• Every 69 seconds someone develops AD
• $183 billion in direct and indirect costs to Medicare, Medicaid, and businesses

Alzheimer’s Association, 2011

What happens in Alzheimer's?

• The brain is composed of billions of neurons
• AD disrupts the health of neurons and communication between neurons

Brain size declines with age and Alzheimer’s Disease

39 year old man
72 year old non-demented woman
75 year old woman with mild AD
Hippocampal volume declines early in Alzheimer’s disease

19 year old male

86 year old female with AD

Risk of Alzheimer’s Disease

- Factors increasing the risk
  - Physical inactivity
    - High physical activity is associated with ~40% reduced risk of developing cognitive decline and dementia

Abbott, et al. JAMA 2004
Wilson, et al. JAMA 2002

Risk of Alzheimer’s Disease

- Factors increasing the risk
  - Mid-life (40-44 years) cardiovascular risk factors associated with increased risk of dementia later in life
    - 24% increased risk with midlife hypertension
    - 46% with midlife diabetes
    - 42% with midlife high cholesterol
    - 26% with midlife smoking
    - Additive risk when combining 2 or more risk factors

Whitmer, et al. Neurology 2005
Risk of Alzheimer’s Disease

• Factors increasing the risk
  – Family history – 4-10 times greater risk
  – Maternal family history?
    • Cognitively normal adults with a maternal family history of late-onset Alzheimer’s disease have greater amounts of atrophy in the precuneus and parahippocampus/hippocampus regions over 2 years compared to paternal- or no family history of Alzheimer’s disease
    • Perhaps a higher risk for developing Alzheimer’s disease


Risk of Alzheimer’s Disease

• Down syndrome
  – Trisomy 21
  – Amyloid Precursor Protein (APP)

• Plaques and tangles in the brain tissue
  – Present in the brains of nearly all adults with Down syndrome by the age of 40 (Malamud, 1972; Wisniewski et al. 1985)

Risk of Alzheimer’s Disease in Down Syndrome

• Obesity
  – Individuals with Down syndrome are more likely to be overweight or obese than other individuals with intellectual disability (Stancliffe 2011)
    • Intellectual disability & DS – mean BMI 30.40
    • Intellectual disability only – mean BMI 28.55
    • Intellectual disability & autism/PDD – mean BMI 27.42
    • Intellectual disability & CP – mean 24.53

<table>
<thead>
<tr>
<th></th>
<th>Obesity (BMI ≥ 30)</th>
<th>Overweight or Obese (BMI ≥ 25)</th>
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<tbody>
<tr>
<td>Down syndrome</td>
<td>44.3%</td>
<td>72.7%</td>
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<tr>
<td>U.S. population</td>
<td>33.8%</td>
<td>68.0%</td>
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(Flegal et al 2010)
Risk of Alzheimer's Disease in Down Syndrome

- Sedentary Lifestyle
  - Levels of physical activity in non-athletic adults without intellectual disability were twice as high compared to adults with an intellectual disability (Vis, et al. 2011)
  - No significant difference between Down syndrome and other causes of intellectual disability

Epidemiology

- In the general population
  - Roughly 10% of people 65 and older
  - Nearly 50% of people 85 and older
- Clinical symptoms of dementia in Down syndrome
  - <10% between 30-39 years of age
  - 10-25% between 40-49 years
  - 20%-50% between 50-59 years of age
  - 50-70% by 60-70 years of age
  - Variable, however seems to progress more quickly than in general population

Symptoms – General Public

- Forgetfulness (conversations; appointments; medicines; names)
- Repetition of questions, statements
- Misplacing items
- Difficulty planning activities
- Getting lost
Symptoms – Down Syndrome

• 1st symptom is usually behavioral changes
  – Disorientation to time/place
  – Personality or productivity changes
  – Increased apathy or inactivity
  – Inability to perform activities of daily living
• Memory loss may not be first symptom noticed

Behavioral Changes

• Disorientation to time/place
  – Missing family birthdays
  – Difficulty with time changes
  – Difficulty with transportation to/from work, etc.
  – Difficulty remembering work schedule
  – Getting lost in familiar areas
  – Later on – difficulty with weekend vs. week day

Behavioral Changes

• Personality changes
  – Aggression/spitting/hitting/kicking
  – Irritability
  – Anxiety
  – Depression
  – Forgetting to take something with them to work, etc.
Behavioral Changes

• Productivity changes
  – Difficulty staying focused/easily distracted
  – Needing reminders to perform tasks
  – Anticipating breaks at work

• Increased apathy or inactivity
  – Need to rule-out depression or sleep disorder
  – Not interested in previously enjoyed activities
  – Less interested in going places and doing things

Behavioral Changes

• Inability to perform activities of daily living
  – Difficulty dressing
  – Difficulty bathing
  – Difficulty toileting
  – Later on – Difficulty eating

Diagnosing Alzheimer’s Disease

• No brain scan or blood test can make the diagnosis
• Detailed History
  – Characteristics and pattern of changes
  – Importance of informant / caregiver
Cognitive Assessment

- Can’t use the MMSE
- Down Syndrome Dementia Questionnaire
  - Scores out of 100
  - Lower score indicates stronger independence and cognitive function
- Brief Praxis Test
  - Scores out of 80
  - Higher score indicates stronger ability to comprehend and follow simple commands

Examination

- Physical Examination
  - Heart
  - Lung
  - Examine any painful areas
- Neurological Examination

Laboratory Tests

- Thyroid hormone
  - High proportion of Down Syndrome patients have abnormally low thyroid hormone
- Vitamin B12
- Lab tests to consider
  - Vitamin D
  - RPR
Imaging

• MRI or CT of the brain
  – Rule out stroke, abscess, tumor, other structural problems
  – Length of study
    • CT takes just a couple of minutes
    • MRI takes 30+ minutes
    • May need sedation for the imaging

Summary:
Diagnosis of Alzheimer's disease

• Key: History and physical
• Rule out other potential causes
  – Physical examination
  – MRI or CT scan
  – Labs: Vitamin B12, Thyroid
  – Depression
• PET scans, psychometric tests
  – Not essential to diagnosis
  – Limited sensitivity compared to history from informant

Other Causes of Confusion

• Psychiatric symptoms/conditions
  – Depression
    • Death or loss of a loved one
  – Anxiety
  – Obsessive compulsive disorder
• Stress
Other Causes of Confusion

• Changes in home or work environment
  – Roommates
  – Staff
  – Personal/quiet space
  – Disruptions in daily schedule
  – Bullying/disruptive behavior
  – Influence

Other Causes of Confusion

• Medications
  – Pain medications
    • Lortab, Percocet, morphine, codeine, etc.
  – Anxiety medications
    • Ativan (lorazepam), Xanax (alprazolam), etc.
  – Sleep aids
    • Ambien (zolpidem), Sonata ( zaleplon), Lunesta (eszopiclone)
  – Anticholinergic medications
    • Elavil (amitriptyline), Pamelor (nortriptyline)
    • Benadryl (diphenhydramine)
    • Bladder medications, particularly Ditropan

Other Causes of Confusion

• Medications, cont.
  – New or discontinued medications
  – Changes in dosage or timing

• Pain
  – Headaches
  – Neck pain
  – Back pain
Other Causes of Confusion

• Sleep apnea
  – Up to 100% of adults with DS have abnormal sleep studies
  – 83% of these showed sleep apnea

• Other factors affecting sleep
  – Depression
  – Anxiety
  – Pain
  – Environmental factors

Treatment

• Address treatable conditions
  – Limit sedating medications
  – Treat metabolic issues
  – Treat sleep disorder

Treatment

• Treat psychiatric symptoms/conditions
  – Celexa (citalopram)
  – Lexapro (escitalopram)
  – Desyrel (trazodone)

  – If psychiatric symptoms are not easily treated, consider a referral to psychiatry
Treatment of Alzheimer's Disease

- Two classes of approved medications
  - Acetylcholinesterase inhibitors → increase acetylcholine levels
    - Aricept (donepezil)
    - Razadyne (galantamine)
    - Exelon (rivastigimine)
  - NMDA antagonist
    - Namenda (memantine)
    - Found to not be effective in Down syndrome

Treatment of Alzheimer's Disease

- Aricept (donepezil)
  - FDA approved for mild, moderate, severe AD
- Exelon capsules and patch (rivastigimine)
  - FDA approved for mild, moderate AD
- Razadyne (galantamine)
  - FDA approved for mild, moderate AD

Treatment

- Physically active
- Mentally active
- Socially active
Psychiatric Symptoms and/or Behavior

- Prevalence in adults with DS, no dementia
  - Approximately 26%
    - Most frequent = conduct disorder, aggression, stereotyped behavior, and attention deficit disorder
  - Perhaps an underestimate
    - Signs and symptoms of bad behavior are often attributed to mental retardation

Collacott, Cooper, & McGrother, 1992
Meyers & Pueschel, 1991

Depression in Adults with Down Syndrome

- Percentage of patients with depression
  - 18.4% of non-demented adults with DS
  - 44% of adults with DS and possible dementia
  - 60% of adults with DS and definite dementia

Urv, TK 2008

Behaviors in Adults with Down Syndrome and Dementia

- Compared to younger non-demented individuals with Down syndrome
  - More irritation
  - Fearful
  - Restlessness at night
  - Sadness
  - Suspiciousness
  - Loss of appetite

Haveman, et al. 1994
Adaptive Behavior in Middle-Age Adults with Down Syndrome

• No significant age-related decline in skills is seen
  – Excluded individuals with significant medical disorders (dementia, depression, hypothyroidism)
• If age-related changes are identified, it is important to assess physical and psychological factors
  
Prasher 1998

Adaptive Behavior in Middle-Age Adults with Down Syndrome

• Particular areas of decline in skills in early stages of dementia
  – Independent functioning
    • Eating
    • Toilet use
    • Cleanliness
    • Appearance
  – Numbers and time
  – Responsibility
  – Socialization
  
  • Care of clothing
  • Dressing and undressing
  • Travel

Evaluation of Behavior Changes in Adults with Down Syndrome

• Consider the individual’s underlying personality/behavior
• Change in behavior could represent
  – Depression/anxiety/stress
  – Pain
  – Physical or neurological condition such as cervical stenosis
  – Dementia
Where To Go For An Evaluation

• KU Down Syndrome Dementia Clinic
  – Call (913) 588-6820
  – New patient evaluations
    • Heather Anderson, M.D.
    • First Thursday afternoon of the month
  – Follow-up evaluations
    • Anne Arthur, ARNP

Where To Go For An Evaluation

• KU Sleep Medicine Clinic
  – Call (913) 588-6820
  – Suzanne Stevens, M.D.
    • Overnight sleep studies
    • Overnight oxygen levels
    • Sleep Medicine Clinic appointments

Where To Go For An Evaluation

• Down Syndrome Guild of Greater Kansas City
  – (913) 384-4848
• Alzheimer’s Association – Northwest Missouri Regional Office, St. Joseph, MO
  – Brenda Gregg
  – Phone: 816.364.4467
  – email: brenda.gregg@alz.org
Where To Go For An Evaluation

• Research Opportunities
  – University of California-Los Angeles (UCLA) Department of Psychiatry
  – Brain imaging project focused on detecting early signs of Alzheimer's disease in adults with Down syndrome age 40 and over with and without signs of dementia
  – For more info contact UCLA at 310-206-7392

Where To Go For An Evaluation

• Research Opportunities
  – University of California-Irvine
    • Dr. Ira Lott (714) 456-5333
  – Kennedy Krieger Institute and Johns Hopkins University
    • Wayne Silverman, PhD (443) 923-2738