The Domino Effect of Diseases on Dementia

How do common diseases affect brain function?

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Pre-Test
ARE YOU AWARE THAT...

According to the CDC:

- More than one-third (34.9% or 78.6 million) of U.S. adults are obese.
- Obesity is higher among middle age adults, 40-59 years old (39.5%) than adults over 60 or above (35.4%).
- About 73.5 million adults (31.7%) in the United States have high LDL or “bad” cholesterol.
- Fewer than 1 out of every 3 adults (29.5%) with high LDL cholesterol has the condition under control.
- About 1 of 3 U.S. adults have high blood pressure.
- Only about half (52%) of these people have their high blood pressure under control.
GOALS AND OBJECTIVES

- Define dementia and describe the structural changes that occur in the brain due to dementia

- Understand how obesity, high blood pressure, and cholesterol are associated with increased risk for dementia

- Learn how to take action to reduce your risk for decline
  - Preventative measures
DEMENTIA

an umbrella term used to describe multiple diseases characterized by memory loss and structural damage to the brain

ALZHEIMERS DISEASE

- Characterized by beta amyloid plaques
  - Common in the hippocampus and the cortex
- More than 5 million Americans now have Alzheimer’s disease
- The sixth-leading cause of death across all ages in the United States
  - For those 65 and older, it is the fifth-leading cause of death
DEMENTIA

VASCULAR DEMENTIA

- Occurs after a stroke, leads to cell death
- The second most common dementia type
  - Estimated that 1-4% of people over the age of 65 develop
  - Accounts for 20-30% of cases of dementia
- Shortens lifespan
Components that cause change in the brain:

- Beta amyloid - protein pieces
- Tau - protein
- Found in Cerebrospinal fluid (CSF)
NORMAL BRAIN
VERSUS
ALZHEIMERS DISEASE

- **Beta-amyloid**: Protein that becomes toxic when it accumulates in the spaces between nerve cells in the brain.

- **Tau**: Protein that becomes toxic when it accumulates and twists inside nerve cells in the brain.
WHAT HAPPENS NEXT...

Brain Changes:

1. Memory loss that disrupts daily life
2. Challenges in planning and solving problems
3. Misplacing things and losing the ability to retrace steps
4. Decreased or poor judgement
OBESITY  a condition of excessive accumulation and storage of fat in the body

According to Whitmer et al. (2005)

- Obesity increases risk of dementia
  - Obese individuals (70%) increased risk
  - Overweight individuals (35%) increased risk
  - Women have a greater risk for dementia

- Areas in the brain related to regulation of behavior, taste, and reward are negatively affected by obesity
  - Insulin plays a major role in brain health
BMI CALCULATION

- Body mass index (BMI) is a measure of body fat based on height and weight.
  - OBESE - greater than 30
  - OVERWEIGHT - 25-30
  - LEAN - 18.5-25

Higher BMI results in greater risk of developing dementia.

<table>
<thead>
<tr>
<th>BMI FORMULA</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>USA</strong></td>
</tr>
<tr>
<td>BMI = 703 * ( \frac{\text{weight (lb)}}{\text{height}^2 \text{ (in}^2)} )</td>
</tr>
<tr>
<td><strong>METRIC</strong></td>
</tr>
<tr>
<td>BMI = ( \frac{\text{weight (kg)}}{\text{height}^2 \text{ (m}^2)} )</td>
</tr>
</tbody>
</table>
OBESITY CHART

- Normal Weight: BMI 18.5 - 24.9
- Overweight: BMI 25 - 29.9
- Obese: BMI 30 - 34.9
- Severe Obese: BMI 35 - 39.9
- Morbidly Obese: BMI 40 + +
OBESITY

a condition of excessive accumulation and storage of fat in the body

- Mice Study by Kohjima et al. (2010)

- Hyperinsulinemia - excess insulin circulating in the blood due to damaged receptors that are not absorbing insulin properly

- Amyloid Beta Peptide - precursor of beta amyloid plaques that when built up are biomarkers for AD

- Transgenic (Tg) mice vs. normal mice
  - Mice with a natural tendency for memory deterioration around six months of age (mimicking AD patients)
OBESITY a condition of excessive accumulation and storage of fat in the body

- Group 1-Normal diet mice
- Group 2-Normal diet Tg mice
- Group 3-High fat diet mice
- Group 4-High fat diet Tg mice
OBESITY

a condition of excessive accumulation and storage of fat in the body

- Mice Study
  - Sixteen week feeding study
  - Body weights of the mice were monitored every four weeks
  - Blood sugar measured after feeding

- Results:
  - Overeating causes high glucose levels which causes hyperinsulinemia
    - Hyperinsulinemia alters proper brain functioning leading to overeating
  - Leads to buildup of amyloid beta peptides
    - These peptides are problematic due to the brain's inability to break them down, clusters lead to beta amyloid
OBESITY a condition of excessive accumulation and storage of fat in the body

- Paired Study
  - Same test groups
- Caloric intake monitored in normal diet mice every two weeks
  - Caloric intake was matched and fed to the high fat diet mice
- Result: Caloric monitoring, regardless of group showed decrease in hyperinsulinemia
- In conclusion, monitoring caloric intake can help decrease hyperinsulinemia and sequentially decrease the risk of dementia
CHOLESTEROL

- Type of fat found in the body needed in order to help the brain, skin and other organs function properly.
- Buildup of cholesterol related amyloid in the brain leads to neurodegeneration.
- High cholesterol appears to accelerate the formation of beta amyloid.
- Two types of cholesterol:
  - High density lipoprotein (HDL)- lipids and proteins that transport cholesterol to the liver “good cholesterol”
  - Low density lipoprotein (LDL)- lipids and proteins that transport cholesterol to the liver “bad cholesterol”
In a 2010 study (Zuliani et al.), High Density Lipids (HDL, good cholesterol) levels were found to be decreased in people that had dementia.

Results:

- Keeping cholesterol healthy is proving to be just as important for brain health as it is for heart.

<table>
<thead>
<tr>
<th>Total cholesterol</th>
<th>HDL cholesterol (high is better)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Less than 200 mg/dL</td>
<td>Less than 40 mg/dL</td>
</tr>
<tr>
<td>Desirable</td>
<td>Low</td>
</tr>
<tr>
<td>200 – 239 mg/dL</td>
<td>More than 60 mg/dL</td>
</tr>
<tr>
<td>Borderline high</td>
<td>High</td>
</tr>
<tr>
<td>240 mg/dL and above</td>
<td></td>
</tr>
<tr>
<td>High</td>
<td></td>
</tr>
</tbody>
</table>
CHOLESTEROL type of fat found in the body

- Poor HDL leads to accumulation of beta-amyloid plaques in the brain
  - Consistent among dementia patients

- Plaque build up leads amyloid peptides bypassing lysosomes and attaching to “rafts”
  - Lysosomes are organelles found in cells that digest things
CHOLESTEROL type of fat found in the body

- Plaque accumulation due to the lysosomes not properly breaking them down is what leads to neural degeneration

- Mice embryo study (Simmons et. al. 2014)

- Compared the normal breakdown of beta amyloid peptide 42 accumulation to that of medically induced breakdown
CHOLESTEROL  type of fat found in the body

- Control vs. Medicine group
  - Multiple medicines tested to determine fastest rate of amyloid reduction

- Results of Experiment:
  - Medicinal treatment
    - High total cholesterol increases risk of developing plaques
    - Squalestatin reduces the accumulation of beta amyloid peptide
    - Less beta amyloid in rafts = more in lysosomes
    - This is better because more in lysosomes means beta amyloid is broken down instead of accumulating
HIGH BLOOD PRESSURE

- Force of blood pushing against the walls in the arteries
- Made up of two numbers:
  - Systolic - when the heart beats
  - Diastolic - in between beats
- Example: $\frac{117}{76} \text{ mm Hg}$
- According to the American Heart Association, about 70 million American adults have high blood pressure

<table>
<thead>
<tr>
<th>Blood Pressure Category</th>
<th>Systolic mm Hg (upper #)</th>
<th>Diastolic mm Hg (lower #)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>less than 120</td>
<td>and less than 80</td>
</tr>
<tr>
<td>Prehypertension</td>
<td>120 – 139</td>
<td>or 80 – 89</td>
</tr>
<tr>
<td>High Blood Pressure</td>
<td>140 – 159</td>
<td>or 90 – 99</td>
</tr>
<tr>
<td>(Hypertension) Stage 1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>High Blood Pressure</td>
<td>160 or higher</td>
<td>or 100 or higher</td>
</tr>
<tr>
<td>(Hypertension) Stage 2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertensive Crisis</td>
<td>Higher than 180</td>
<td>or Higher than 110</td>
</tr>
<tr>
<td>(Emergency care needed)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
HIGH BLOOD PRESSURE

According to Launer et. Al (2000):

- High blood pressure in middle age - high risk for dementia
- High blood pressure in middle age, but medicated - low risk for dementia
- High diastolic BP is related to Alzheimer’s Disease
  - Strong relationships between HBP, neurofibrillary tangles, and plaques
- High systolic BP is related to vascular dementia
  - Associated with arterial infarctions leading to strokes
HIGH BLOOD PRESSURE

- Blood brain barrier
  - Selective permeable membrane
  - Separates circulating blood from the brain

- Why it is important:
  - Protects the brain from foreign substances
  - Maintains a constant environment in the brain

- Damage to the barrier allows toxins access to the brain
HIGH BLOOD PRESSURE

- Study by Poulet et al. (2005)
- Conditions:
  - High blood pressure was induced in mice via surgery
    - Constricted the aorta
  - Compared to control group of mice
- Tests:
  - Injected a dye into bloodstream
  - Dye was seen in the brain MRIs of hypertensive mice, but not the normal mice

force of the blood against your artery walls
HIGH BLOOD PRESSURE

- Blood brain barrier (BBB) affected by high blood pressure
- Faulty BBB leads to susceptibility of toxins which can lead to neurodegeneration
- Hypertensive mice had damage in the hippocampus and cortex
  - Hippocampus - Memory consolidation
  - Cortex - Generates thoughts, solves problems, and makes plans
- In conclusion, high blood pressure can damage the BBB, and therefore cause damage to neurons in the brain
HIGH BLOOD PRESSURE

- White matter lesions
  - Area of tissue that has been damaged due to injury or disease in the white matter of the brain
  - White matter = Axons
- Study done by Skoog et al.
- 282 hypertensive men and women age 85
  - Normal cognition at baseline
- 3 year follow up study at the age of 88
  - 59 developed Dementia (20%)
  - 24 developed Alzheimer’s Disease (8%)
  - 28 developed Vascular Dementia (9%)
- Dementia patients had a higher ratio of WML
SUMMARY

- **Obesity:**
  - Obese and overweight individuals have an increased risk of dementia by as much as 35-70%.
  - Hyperinsulinemia increases the buildup of amyloid beta peptides, a precursor to beta amyloid plaques which is associated with dementia.

- **Cholesterol:**
  - High total cholesterol increases the risk of beta amyloid plaque build up.
  - There is a higher rate of dementia with high total cholesterol and lower HDL.

- **High Blood Pressure:**
  - Un-medicated high blood pressure in middle age is associated with an increased risk of dementia.
  - High blood pressure is directly associated with an increased risk of Alzheimer's Disease through formation of neurofibrillary tangles, beta amyloid plaques and white matter lesions.
TAKE ACTION

- These three ailments create a *domino effect* and are all preventable

- Obesity, high blood pressure, and cholesterol are all linked

- Prevention:
  - Regular physical exercise
  - Maintaining a healthy weight
  - Eating healthy
  - Not smoking
  - Drinking in moderation
  - Testing and monitoring BP, blood sugar and cholesterol levels
  - If you have high BP, talk to your doctor to see if medication is right for you

- All prevention methods are associated with a reduced risk of dementia

- Lifestyle changes are simple to make and beneficial to your health long-term!
Post Test!

Questions?

Comments...

Thank you for your time!


Zuliani, G., Cavalieri, M., Galvani, M., Volpato, S., Cherubini, A., Bandinelli, S., ... Ferrucci, L. (2010). Relationship Between Low Levels of High-Density Lipoprotein Cholesterol and Dementia in the Elderly. The InChianti Study. The Journals of Gerontology Series A: Biological Sciences and Medical Sciences, 559-564.


