Alzheimer's and Related Dementias:

The Prevention of Disease, Morbidity and Suffering

Alzheimer's Disease

- Today there seemed to be a general agreement that it is a disease of the brain in which there is a deterioration of brain function because of the deposit of amyloid plaque.
- This is a classificatory definition of the disease not an algorithmic one

Natural history of AD

- Pre-symptomatic stage
  - Amyloid plaque is there without symptoms
- Very early symptoms
  - Very mild symptoms can indicate that the plaque is there, but can also be confused with other bases of dementia
- Mild, moderate, severe stages
  - AD diagnosed and progresses over 8 years
    - Cognitive symptoms
    - Loss of functional independence
    - Behavioral problems
    - Nursing home placement
    - Death

Population Health and AD

- Demographics of aging
  - Over 85 year olds are fastest growing segment of population
- Alzheimer's is a disease of old age
  - A very high proportion of over 85 year olds suffer it.
- What policies should we adopt for this scenario given the natural history of AD?

Normal and at Risk Aging & AD

- Angela Troyer:
  - Develop Neuronal Reserve
    - Activities that require complex thinking
    - Mental Fitness Clubs as the boomer response
      - Physical exercise does not prevent Alzheimer's (and according to my inexpert reading of the graph, puts one at slightly higher risk)
- Serge Gauthier: Good diet, watch BP, Anti-oxidants
- Rob van Reekum: Be happy
- Mary Tierney: 17Beta Estradiol
- Patrick McGeer: Anti-inflammatory drugs

Pre-Symptomatic Predictors of AD

- Paul Verhoeff
  - Many efforts to detect plaque early through improved imaging techniques
- Rob van Reekum and Mary Tierney
  - Other pre-symptomatic predictors
    - Single factors such as Late Onset Depression
    - Multiple factors
      - Education
      - Levels of activity
      - Genetic makeup
      - Sense of smell
    - Weighted factors as they contribute to an empirically refined algorithm may increase our non-imaging predictive capacity

Pre-symptomatic Interventions

- Paul Verhoeff: pharmacological interventions to stop, reduce or reverse formation of plaque,
- Serge Gauther: Amyloid deposition modifying treatment
- Angela Troyer: Delaying the disease
  - Activities that require complex thought
  - Developing alterative memory skills
- Rob van Reekum: Be happy
- Mary Tierney: 17Beta Estradiol
- Patrick McGeer: Anti-inflammatory drugs

Paul Verhoeff: Amyloid Imaging in Vivo

- Discussed Chemical Basis for Alzheimer's
- We may be able to identify chemical build up before symptoms through imaging
- May be possible to intervene to reduce chemical build up before symptoms by using other chemical agents
- Described world wide search for agents to identify existence of amyloid plaques or to reduce their effects.

Amyloid Imaging in Vivo

- The many stream of research include
  - 6-OH-BTA-1 a promising agent in rats
  - BTA-1 analogues seemed to work in baboons
  - 6-OH-BTA-1 Human PET study in Sweden
  - SB 13 for Dog Study in Toronto
  - BF-126 Study in Japan
  - Finally changes in MRI allow for in vivo imaging in mice but it cannot yet be used for humans
- Conclusion: There is promise that it will soon be possible to identify AD before its has become symptomatic

Rob van Reekum: Late Life Depression as a Predictor of AD

- Disease advances before cognitive impairment
- Clinical factors might allow one to direct interventions at those who are at high risk
- Late life depression is such a risk factor

Historical Studies

- Reversible dementia occurred with depression
- It emerged that people with such pseudo-dementia were at higher risk of dementia
- Retrospective studies showed that patients with AD
  - had more depression
  - had more late life depression
- 176 twins at least one with probable AD
  - Factors indicated increased risk were
    - Depression 2
    - LOD Depression 4.6
    - LOD + Genetic Marker 8.5

Work at Baycrest

- LOD + Mild Cognitive Impairment
- Trying to Increase prediction of Alzheimer's
  - by identifying other factors
  - E.g. discriminating different smells
- This will allow us to target particular populations for intervention
  - Either of imaging
  - Or drug intervention
  - Or of other interventions

Mary Tierney Neuropsychological Prediction of AD

Different approaches to early id of D
algorithm or classification
Scale of Ad is growing

Mary Tierney Neuropsychological Prediction of AD

- Different approaches to early id of D algorithm or classification

Argued for the use of an empirical algorithmic approach to the prediction of AD

Classification systems

- Need mem impairment + other deficits
- Different ranges
  - A series of definitions and measures
    - Focus on Mild Cognitive impairment
      - Transition state between normal aging and early AD
      - Memory focused
    - A variety of definitions
    - A variety of patient results including ones at
      - Who gets AD
      - Who does not get it

Sunnybrook and Women's

- Yet different from other two
  - Intermediate result
- Picking up problems
- Developed Alzheimer Predictive Index
  - Based on test scores + regression weights
  - Allows for reasonably accurate calculation of probabilities

Algorithm

- For patients referred by FPs
- Two tests
  - RAVLT Delayed Recall Test
  - WMS mental control test
- Scores on test + age + education
- Gave useful results

Briefer Tests

- Use Mini Mental State Examination (MMSE) questionnaire as a basis for predicting Alzheimer's
- Plus Informant CAMDEX
- Increases accuracy rate
- Takes less time
- Requires less expertise

Estrogen

- Thesis: Levels of plasma estradiol can be inversely correlated with levels of amyloid plaques
- As treatment
  - Many questions about results so far
- Will reduce risk of AD for women at high risk of AD according to API algorithm

Serge Gauthier: Pharmacological prevention strategies

- Natural history of AD
- Therapeutic Objectives
- Trial Designs to demonstrate efficacy
- Options for disease modifying strategies
- Impact on health care system

Hypothetical Treatment

- Distinction between three possible approaches
  - Control of existing symptoms (symptomatic)
    - Does not delay disease
  - Delay progression (stabilization)
    - Does delay disease
  - Delay emergence of symptoms (prevention)
    - Prevents onset of AD

- Depending on level of risk there will be different strategies for intervening in the disease.

Assessment measures

- Self-screening
  - On the web
  - On paper
- Screening with informant
- Formal professional assessment

Impact on HC

- Consequences of advances
  - Possible impacts
  - Plan for costs

Angela Troyer: Activity based interventions

- Delaying the disease
  - By engaging in activates that require complex thought
  - By memory rehabilitation

Cognitive engagement

- Demands ogn Cog skills
- Expose to complex envi
- Studied y looking at activities
- More activities - higher bilitt
- Complexity of work duties - higher cog abilities

Engagement and Dementia

- Education reduces risk of AD
- Engaging leisure activates
  - Prospective longitudinal studies
    - High leisure activity delays for 2 years
    - Adjusted for age and ed
  - Retrospective case control studies
    - Intellectual activities made a difference
- Correlation studies only so far
  - It could go either way

Experimental Design

- On animals
  - Rats in a complex environment vs. rats in a cage had more developed brains
  - Neuronal reserve hypothesis
  - More muscular brains can lose more before you dement

Memory Rehabilitation

- Not just because of increased stimulation
- For people with TBI
- Not with AD
  - No reversal of cog prob
  - Skill to reduce effects of impairment
  -

Interventions

- Memory training
  - Spaced retrieval
  - Face-name association
  - Vanishing cues

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- Outcomes
- Personal facts
- New Names
- New Skills

Spaced Retrieval

- Retrieve information at expanding intervals
  - 0,20,40 60,90,120,150, 180 sec
  - Learning new name
  - Calendar training
  - Anomia
  - Reduce repetitive questioning

Memory rehabilitation in aging

Memory rehabilitation in aging

- Interventions
- Memory training
  - SEMANTINC ACSSOCIAIO
  - External aids
- Attention training
- Relaxation

- Outcomes
- Improve
- Fewer faileis
- More relaxed

Early intervention

- Mild Cognitive Impairments, Mild mem changes no functional impairments
- Provide practical interventions to delay functional impairments
- Dementia is defined by functional impairments, so it delays dementia