Research Update From
2015
Alzheimer’s Association
International Conference

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THE PROBLEM: ALZHEIMER’S DISEASE IN US

- ~5,300,000 patients
- ~$226 billion annual cost
- ~10% of people over age 65
- 40-50% of people over age 85
Types of Alzheimer’s Disease

• Sporadic (>95%)
  • Late-onset
  • After 65
  • 50% of >85

• Pure Genetic (<5%)
  • Early-onset
  • Rare
  • Before age 65

• Down Syndrome
CURRENT ALZHEIMER DRUGS ENHANCE NEUROTRANSMITTER ACTIVITY

NERVE CELL SYNAPSE

- Aricept
- Razadyne
- Excelon
- Namenda
BRAIN PATHOLOGY IN ALZHEIMER’S DISEASE AND DOWN SYNDROME

Normal Brain             Alzheimer Brain

Plaques and tangles

George Glenner and Caine Wong 1984

DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIA

Aβ Peptide

RESEARCH TODAY: MEMORIES FOREVER
The Amyloid Precursor Protein Gene Is Encoded on Chromosome 21

The ‘Swedish’ Alzheimer’s Disease Family Inherits a Mutant APP Gene
Mice With Mutant APP Gene Accumulate Amyloid Deposits
Measuring Short-term Memory in AD Mice:

The Radial Arm Water Maze
THE AMYLOID CASCADE IN AD and DS

Amyloid Precursor Protein

N-  

Aβ  

-C

sAPPβ  

β-secretase

Aβ

sAPPα  

α-secretase

γ-secretase

soluble Aβ  

ApoE4  

Aβ protofibrils

Aβ deposition in plaques

RESEARCH TODAY: MEMORIES FOREVER
PET Imaging in Alzheimer’s Disease

Healthy Control  Alzheimer’s Disease
RESEARCH TODAY: MEMORIES FOREVER

Xu, et al. (UCSF), JNNP 2015

**RESEARCH TODAY: MEMORIES FOREVER**
Participants with low grades at age 10 were at 21% higher risk for an eventual dementia diagnosis.
Trisomy 21 In Alzheimer’s Disease

Zikovik et al.,
Alterations of the X Chromosome (Aneuploidy)
In lymphocytes of Alzheimer Disease Patients
THE AMYLOID CASCADE IN AD and DS

Amyloid Precursor Protein

\[ N- \quad A\beta \quad -C \]

- \( \beta \)-secretase
- \( \gamma \)-secretase
- soluble \( A\beta \)
- ApoE4
- \( A\beta \) protofibrils
- \( A\beta \) deposition in plaques

\[ sAPP\beta \quad sAPP\alpha \quad \alpha \]-secretase

RESEARCH TODAY: MEMORIES FOREVER
Eli Lilly: Solanezumab
(likely approval 2017)

Can cut the rate of the dementia's progression by about a third in early stage AD patients taking drug for the longest time
Biogen: Aducanumab
(recruiting for phase 3 trial)

Treatment-related dose- and time-dependent reductions in brain beta-amyloid plaque (Week 26 and further reductions at Week 54) were observed within the doses tested. There was reduced dose- and time-dependent impairment in measures of cognition.
Eli Lilly, Astra Zenica, Novartis

BACE inhibitors