#CHAIR2019

11TH ANNUAL

CHAIR SUMMIT

CME Outfitters

Master Class for Neuroscience Professional Development

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CME Outfitters

Why Are So Many Clinical Trials in AD Failing?

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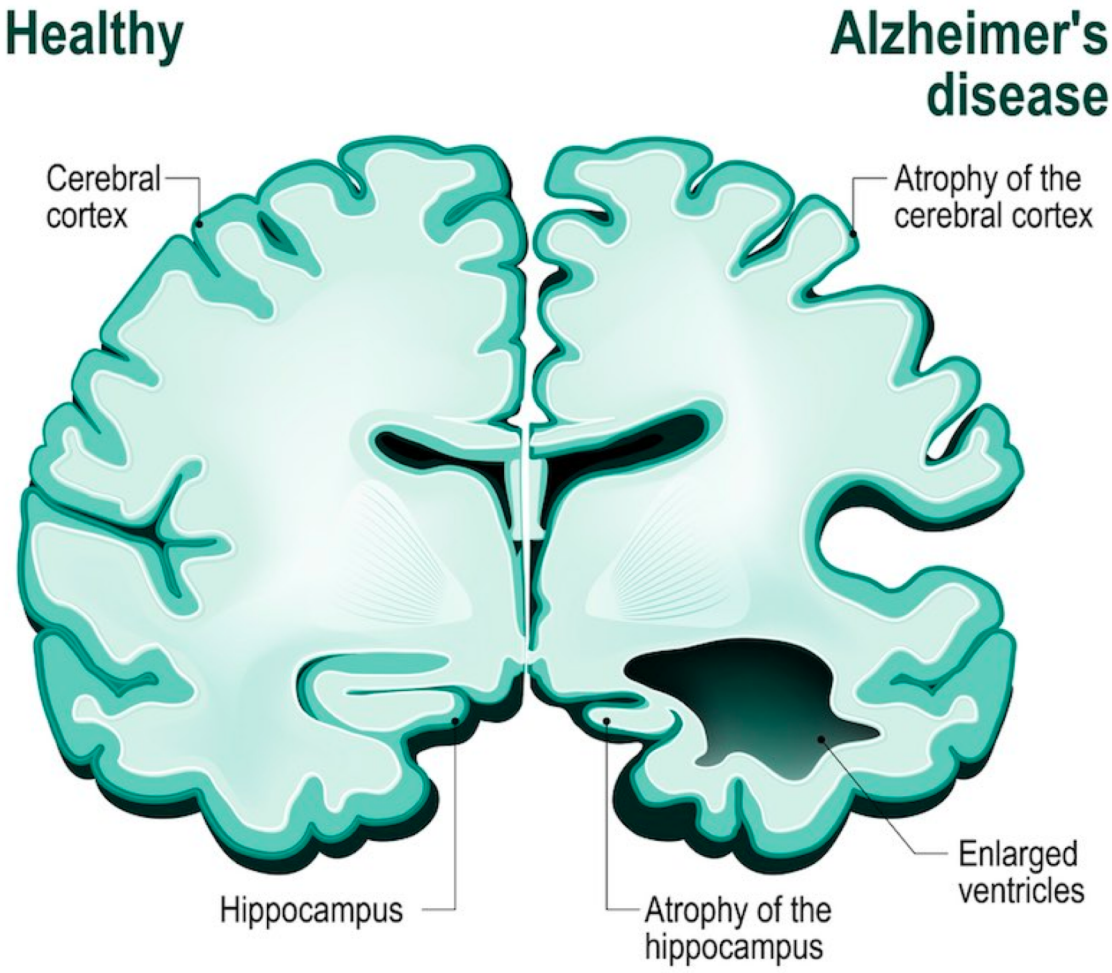
Learning Objective 1

Integrate a thorough family history in assessment of all patients at risk for Alzheimer's disease.

Background

- Alzheimer's disease (AD) pathology begins in the hippocampus and spreads through neural networks associated with memory
- Over 400 clinical trials were run between 2002 and 2012 with only one drug approval
- The pathophysiological process of AD is thought to begin decades before the diagnosis
- Clinical trial patients with advanced AD or early AD are often not adequately selected with biological markers such as amyloid deposition detectable by positron-emission tomography (PET)


Healthy
Alzheimer's disease
Cerebral cortex
Atrophy of the cerebral cortex
Hippocampus
Atrophy of the hippocampus
Enlarged ventricles

The Role of APOE

- Apolipoprotein E (APOE) is the most well-known risk factor gene
- APOE is involved in cholesterol transport in CSF and in binding and clearance of beta-amyloid (Aβ) in the brain
- APOE ε4 allele confers the greatest risk for developing late-onset familial and sporadic AD
  - LOAD = Late-onset Alzheimer's disease

Raskin J, et al. *Curr Alzheimer Res*. 2015;12(8):712-22.

LOAD: Familial Risk

- There is evidence of early limbic alterations in middle-aged, cognitively asymptomatic individuals with a family history of LOAD
- Offspring of late onset AD patients may already display cognitive deficits

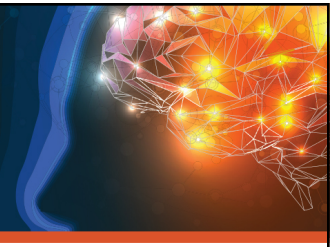
Sanchez SM, Nemeroff CB, et al. *J Alzheimers Dis*. 2017;60(3):1183-1193.

Why Are Clinical Trials Failing?

- Is the treatment of symptomatic dementia too late?
- Are the therapeutic targets incorrect?
- Are the clinical methodologies imprecise, misleading, or inaccurate?

SMART Goals

Specific, Measurable, Attainable, Relevant, Timely



- Recognize that previous clinical trials in Alzheimer's disease may have had wrong targets and patient characteristics leading to failed outcomes
- Family history or genetics may play a role in early recognition
- It remains critical that we screen for Alzheimer's disease early

Call to Action

- Integrate a thorough family history in assessment of all patients at risk for Alzheimer's disease

Questions & Answers

Don’t forget to fill out your evaluations to collect your credit.