Everything known about Alzheimer’s disease that a physicist might want to know

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The presentation will be a rapid romp along the tortuous path that took us from an obscure single case described by Alois Alzheimer in 1906 to the crescendo of interest today in what has become a baby boomer pandemic. Among all disease mechanisms from infection to cancer to auto-immunity, the neurodegenerative conditions remain the most poorly understood. The fundamental problem that underlies why specific neural cells degenerate and die remains a core puzzle that could sorely use input from innovative thinkers. During the question period the speaker will be pleased to discuss more practical issues such as diagnosis, reducing the risk of getting the disease and the state of current clinical trials.
Successful aging

Typical aging/Cognitive Aging

MCI

Dementia (AD...)

Function

Time
Alois Alzheimer 1864-1915

1907—case report of Auguste Deter
(presenile dementia)

Emil Kraepelin-named the disease in 1910

Auguste Deter
died in 1906 at age 55

Albert Einstein: 1905 Annus Mirabilis papers published in Annalen der Physik
James Joyce: 1906 1st sketch of Leopold Bloom which later became Ulysses
Neurodegeneration

Normal Brain

Alzheimer’s Brain

Brain weighed 1255 grams (2.77 lbs)
Parasagittal atrophy
Sulcal widening

Senile plaques—β-amyloid

Neurofibrillary tangle--Tau
The Association Between Quantitative Measures of Dementia and of Senile Change in the Cerebral Grey Matter of Elderly Subjects

By G. BLESSED, B. E. TOMLINSON and MARTIN ROTH
Typical PiB subjects

Paired Helical Filaments
Diseases with Tau Mutations

- Frontotemporal Dementia and Parkinsonism linked to chromosome 17 (FDP-17)
- Progressive Supranuclear Palsy (PSP)
- Pallido-Ponto-Nigral degeneration
- Pick’s disease without Pick bodies
- disinhibition-dementia-Parkinsonism-amyotrophy complex (DDPAC)
- familial progressive subcortical gliosis
- Pallido-nigro-luysian degeneration
- Cortico-basal degeneration
- Chronic Traumatic Encephalopathy (CTE) (dementia pugilistica)

but not Alzheimer’s disease
Tau Spreads Like a Prion
Why does the cell not degrade tau as it does other misfolded proteins?

What are the biophysical properties of tau that predispose it to misfolding and spread?
Why don’t we have a treatment

One reason: Absence of Model Systems

Mini-brains from hiPSCs
Brain Circuitry
Know your numbers:
- BP
- lipids
- glucose