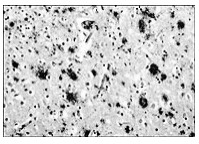
Psych 3102
Introduction to Behavioral Genetics

Lecture 18

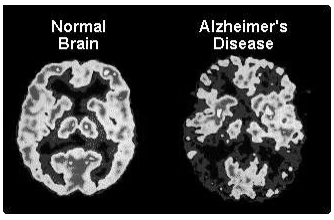
Cognitive disabilities continued: Dementia

Dementia



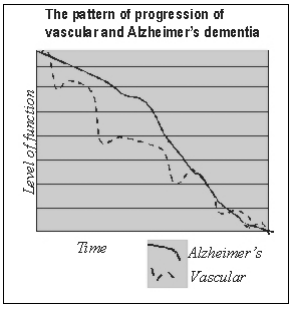
- severe cognitive decline
- age related: <1% under 65
  +13% of those aged 65
  +20% of those aged 85+

US Medicare cost/year $189 billion by 2015
not including cost to family, friends, insurance
3rd leading cause of death



<u>Alzheimer's disease (AD)</u>

- 50% of all dementia cases
- early and late-onset types
- recent memory loss
- loss of independence, death
- extensive changes in the brain: amyloid peptide buildup, tangles of fibers,plaques



<u>Multiple infarct dementia (MID)</u>(vascular dementia)

- numerous small strokes
- infarcts lead to brain damage
- more abrupt onset, focal symptoms

1/3 of all dementia cases involve both AD and MID

Alzheimer's disease

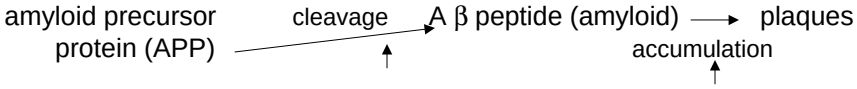
Late-onset form

- first degree relative risk = 50% (by age 85)
- twin studies indicate a moderate genetic influence:

Early-onset form

- clearly influenced by genes , runs in families in a Mendelian way, several single genes found
- only 10% of Alzheimers cases are early onset

Current treatments: 5 drugs slow progress for 6-12 months in ½ of those treated. 9 drugs in test.



Risk factors for late-onset AD

- all known genetic risk alleles only account for ~50% of genetic variation for AD
- expected than ~5 more risk alleles will be found
  candidates at 13 loci across genome (progress tracked on AlzGene database)
  small effects only – estimated sample size of +1000 needed
  alleles have relatively low penetrance but high prevalence

Apolipoprotein E gene chromosome 19
- associated with 50% of all AD cases
3 alleles : E2
E3
E4

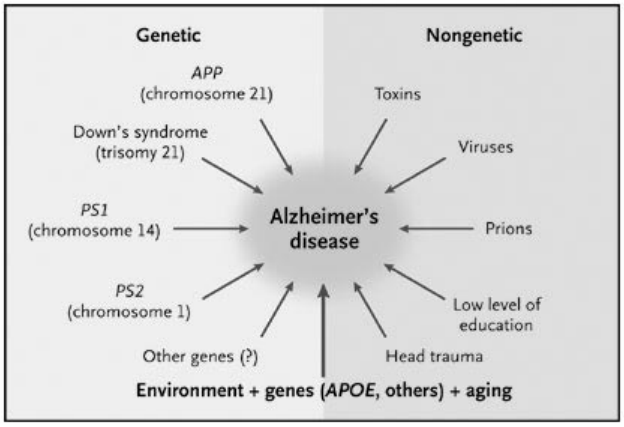
Genotype	Frequency	Mean age of onset	Risk of AD
E4/E4	2% population	68	
E4/ -	15%	75	
no E4	83%	84	

- environmental factors also play a role

Genes associated with risk for Alzheimers disease

Chromosome	Gene type	Onset	% cases familial	% cases all	Product.
19	QTL	60+		40-50%	ApoE4
14	dominant	30-60	70-80%	5-10%	Presenilin 1 (membrane protein)
1	dominant	40-70	20%	2-3%	Presenilin 2
21	dominant	45-65	2-3%	<1%	APP (amyloid precursor protein)

SORL1 gene Chr 11 lipoprotein receptor
? ApoE receptor gene
? A2M gene macroglobulin, removes toxins
no mouse model that shows all AD characteristics



PS1 = presenilin 1
PS2 = presenilin 2
Left side: genetic factors shown are KNOWN causes
Right side: nongenetic risks are speculative – none proven
Bottom: most likely pathway to AD in general population