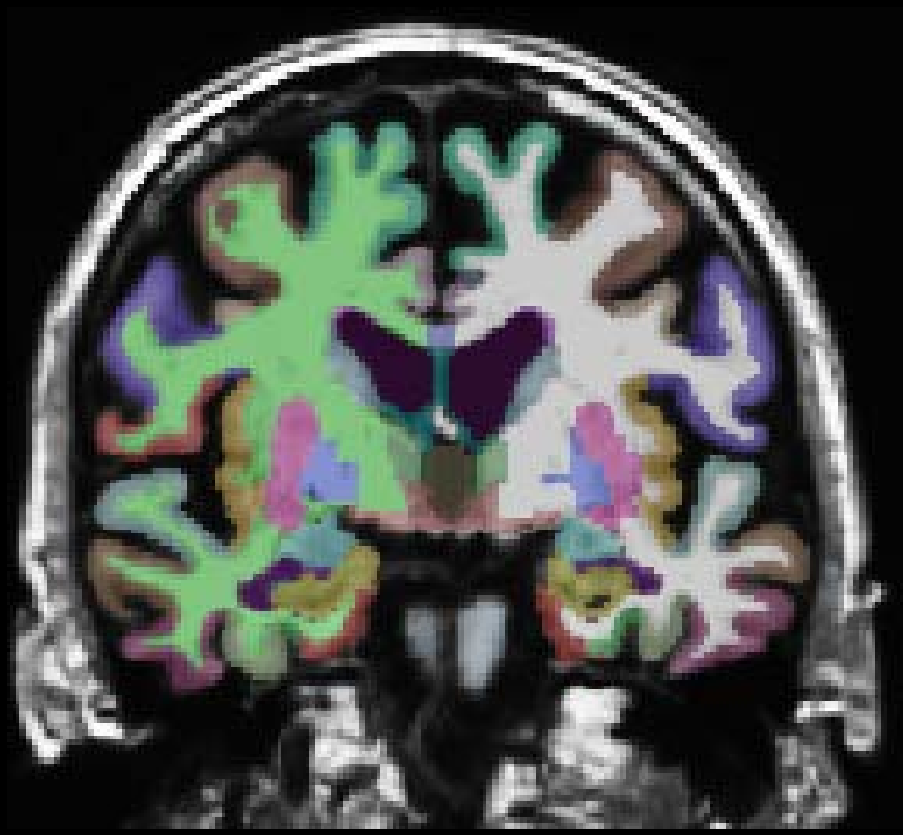
Neurodegenerative Disease



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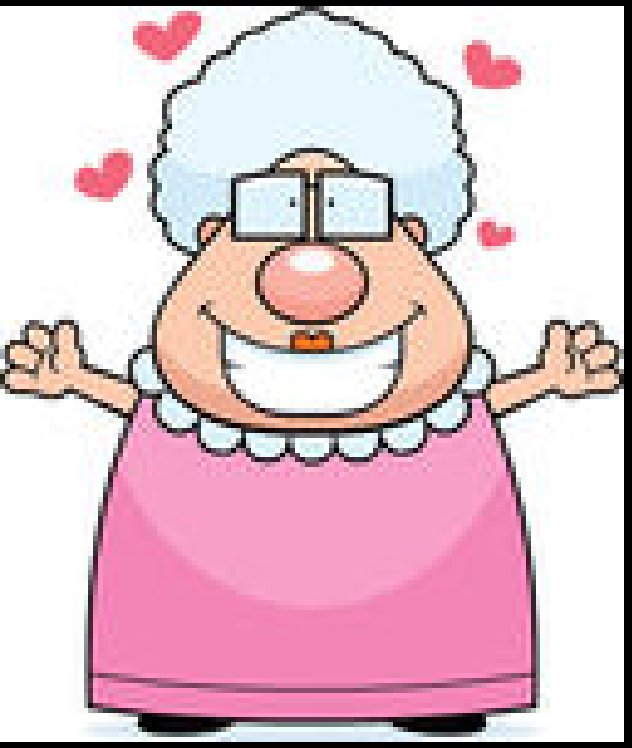
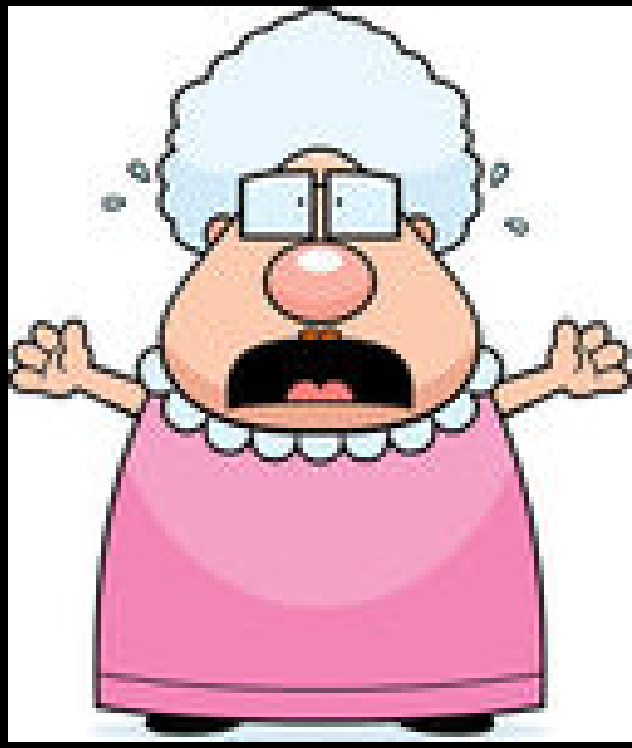
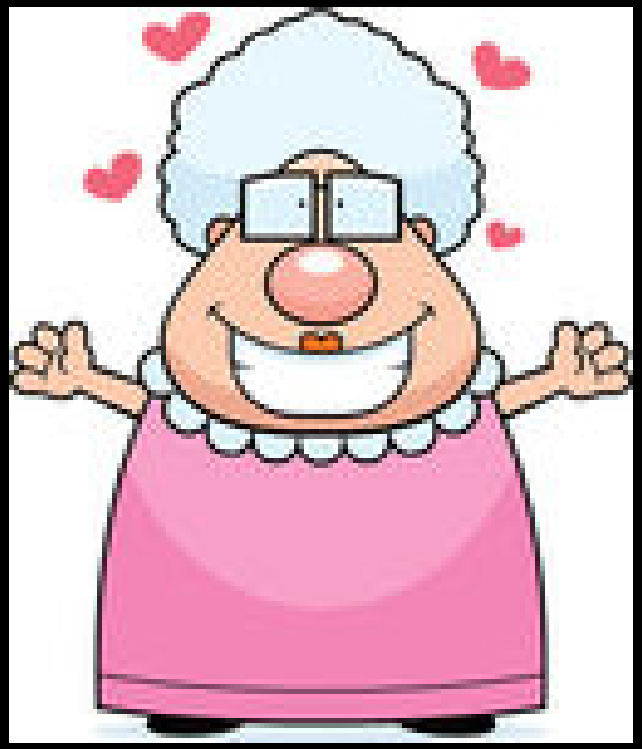
gcc9004@med.cornell.edu

GRANDMA’s been acting funny







Visit to Primary Care Physician:

Family:

"Forgetting things around the house"

"Dressing inappropriately"

"Crying spells"

Is this just old age

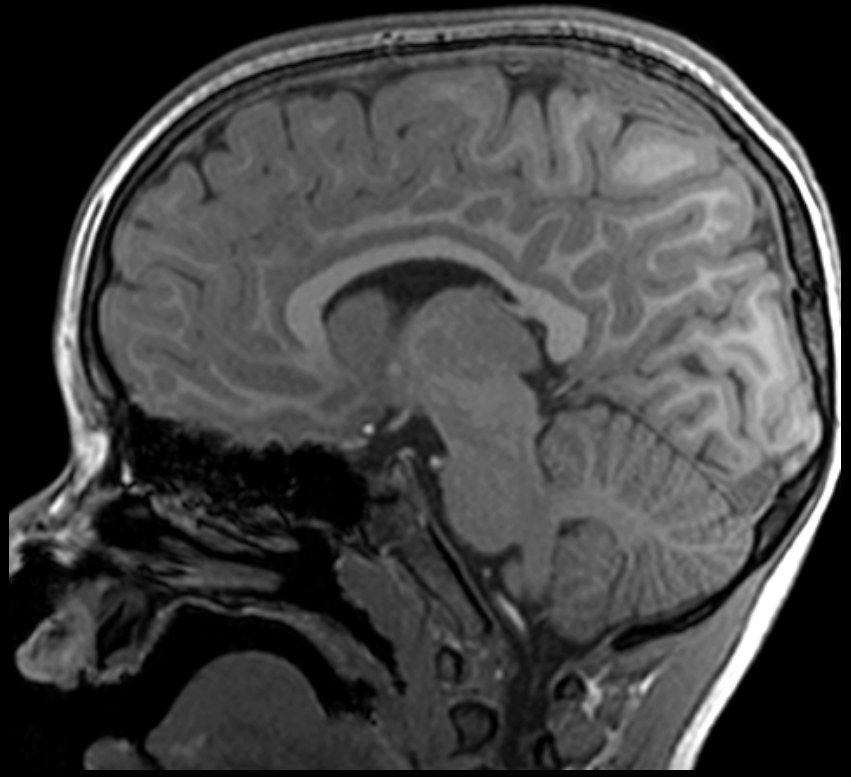
… or something else?

Primary Care Physician:

1. History / Physical
   - other medical problems
2. Medications
3. Labs
4. Depression screen

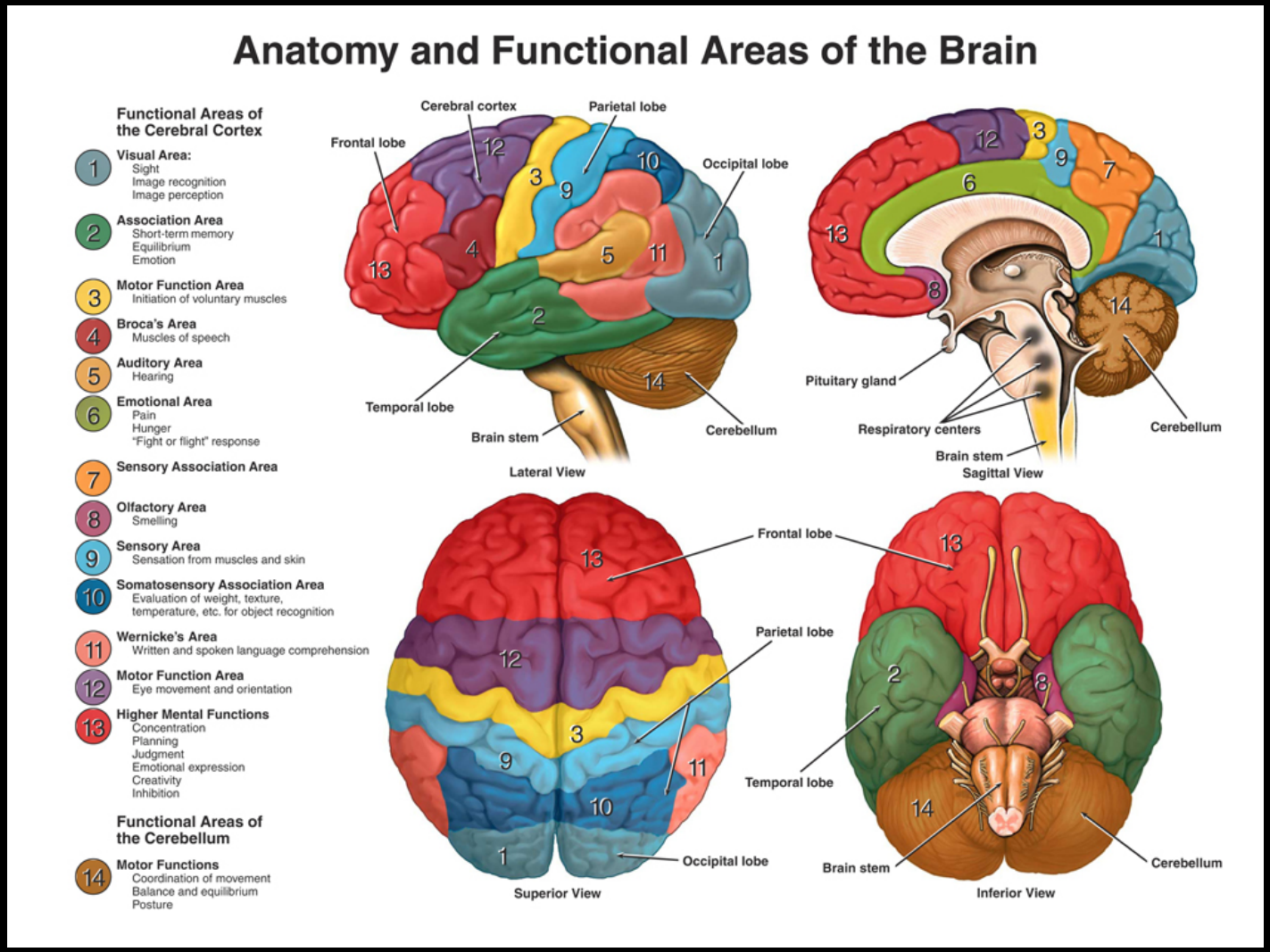
Primary Care Physician:

5. Imaging of the brain (MRI)
   - referral to neuroradiology



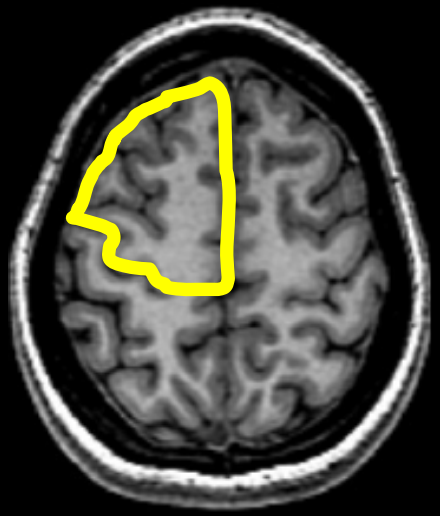
Neuroanatomy 101

Neuroanatomy:



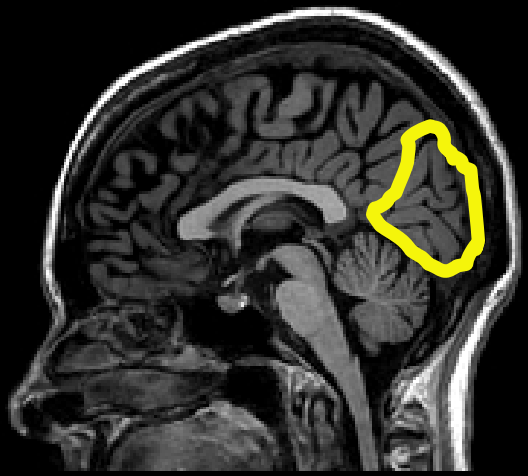
http://farrahsharpe.com/2012/08/23/developments-in-neuroanatomy/

Neuroanatomy:

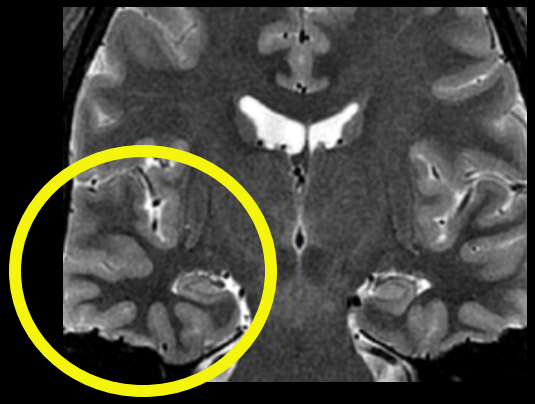


FRONTAL

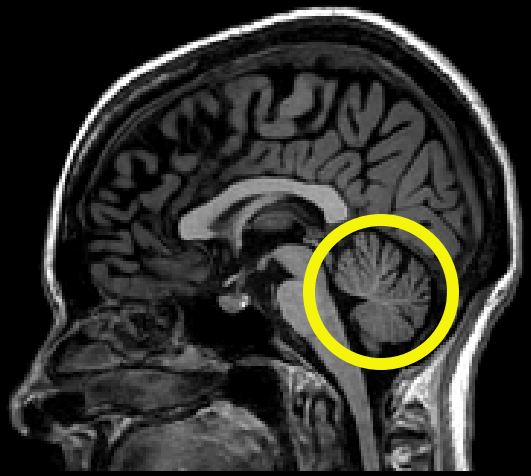
PARIETAL



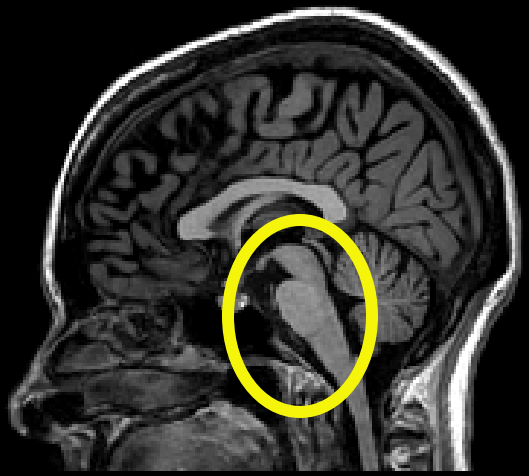
OCCIPITAL



TEMPORAL

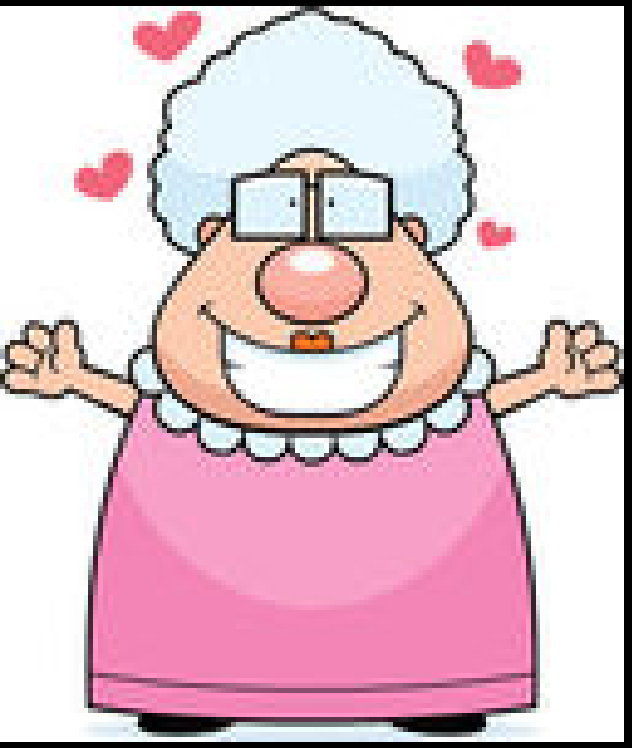


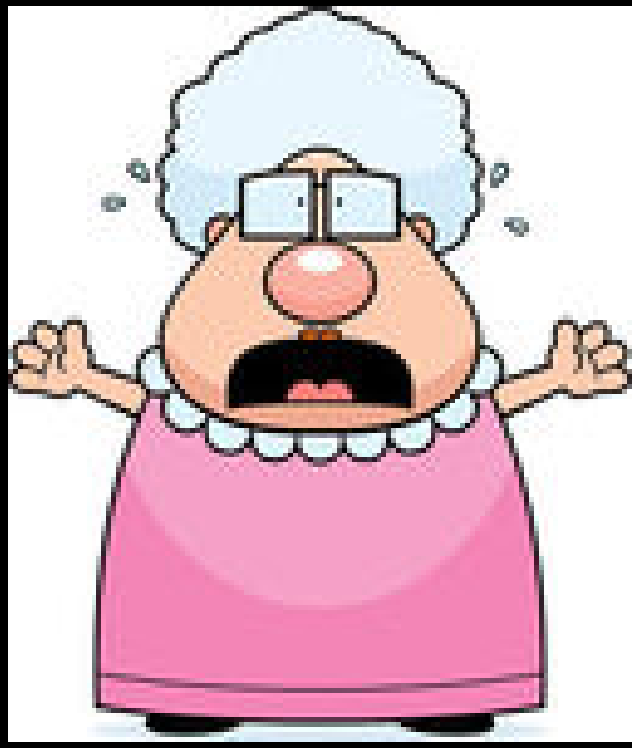
CEREBELLUM



BRAINSTEM

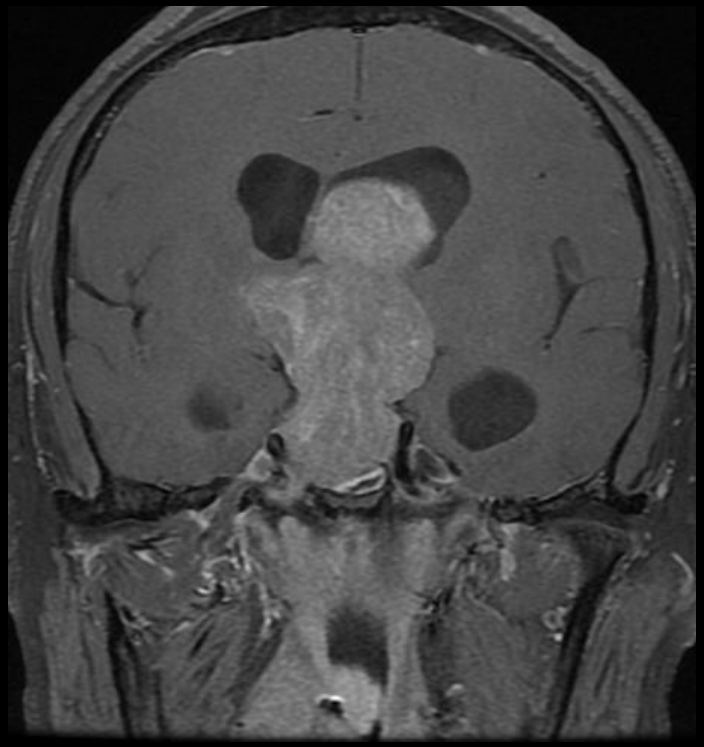
GRANDMA's been acting funny



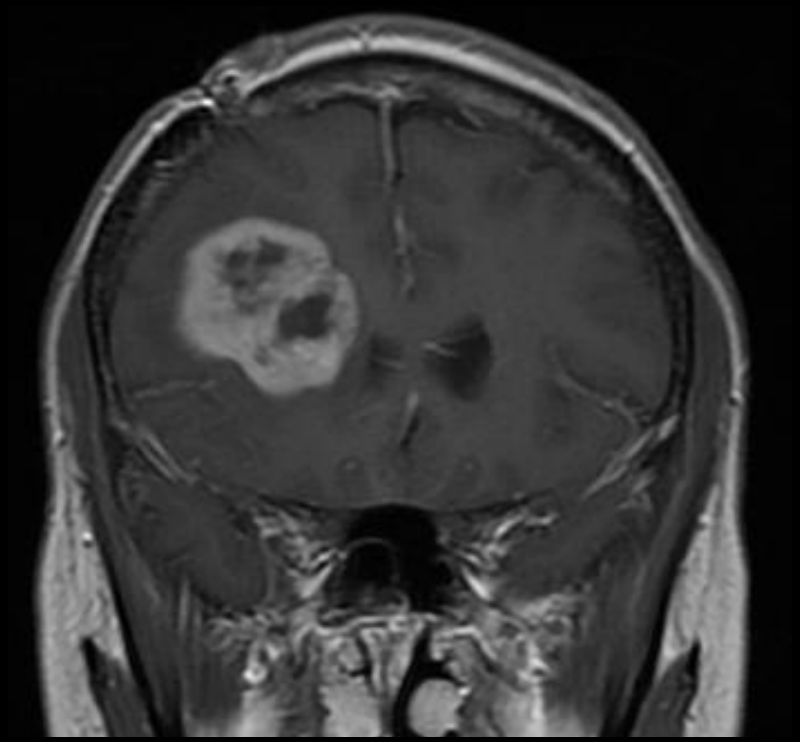


What could the Neuroradiologist see in the brain?

Tumors = abnormal mass/growth = benign/malignant

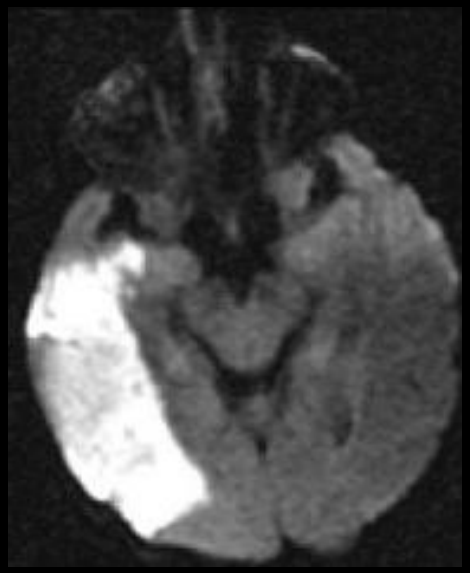
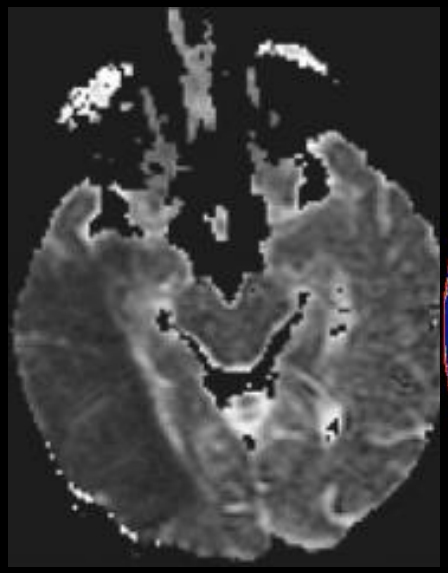
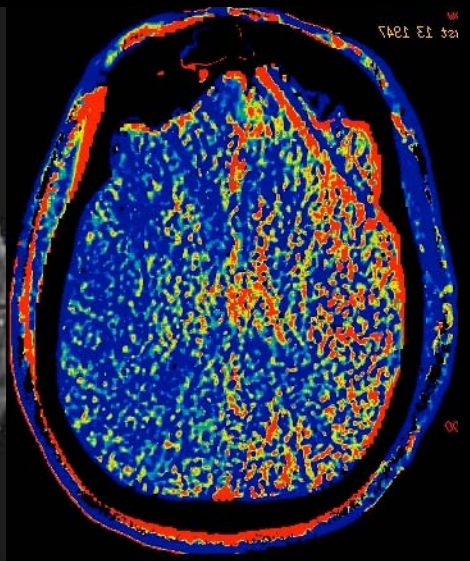
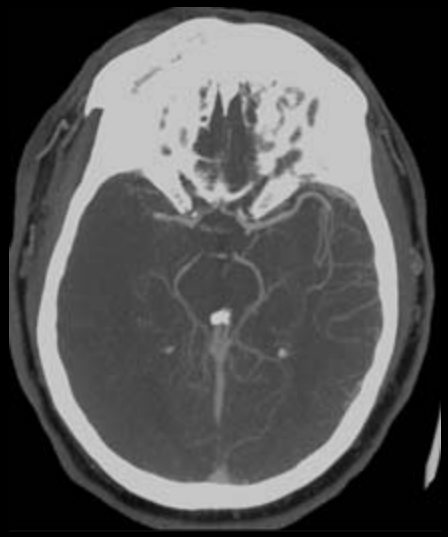


Primary brain



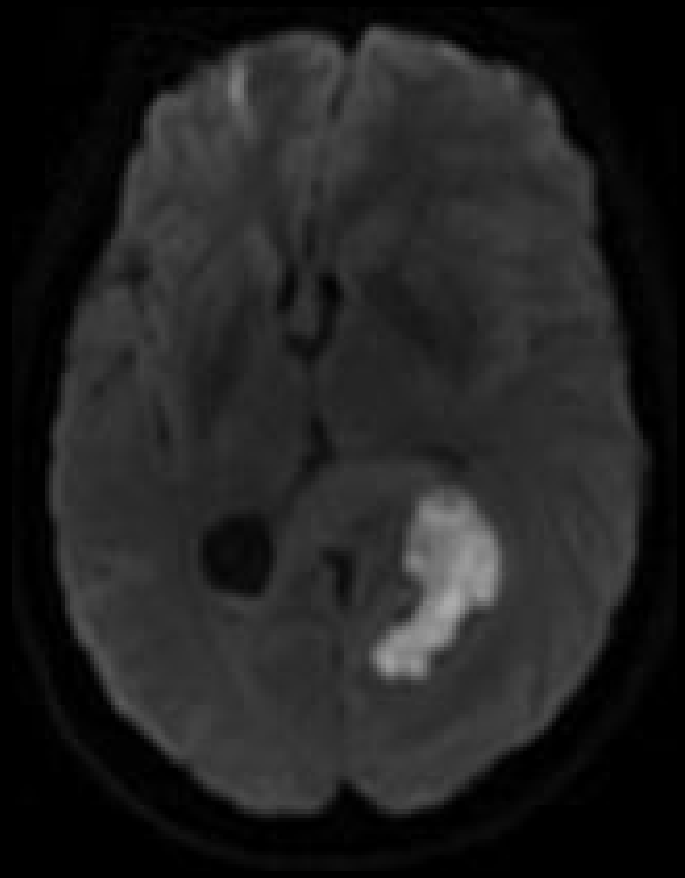
Metastases

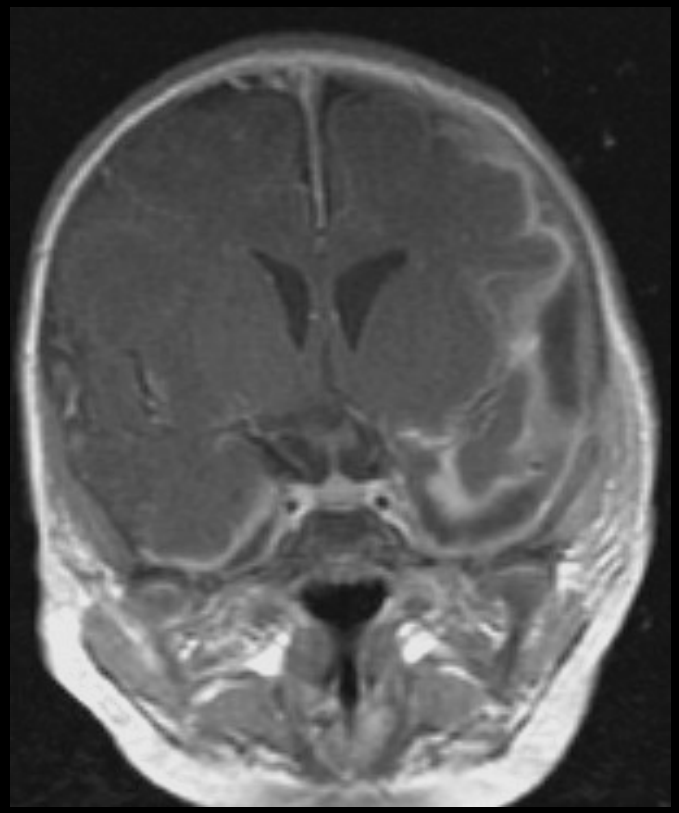
Stroke = infarct = blood supply to brain cut off

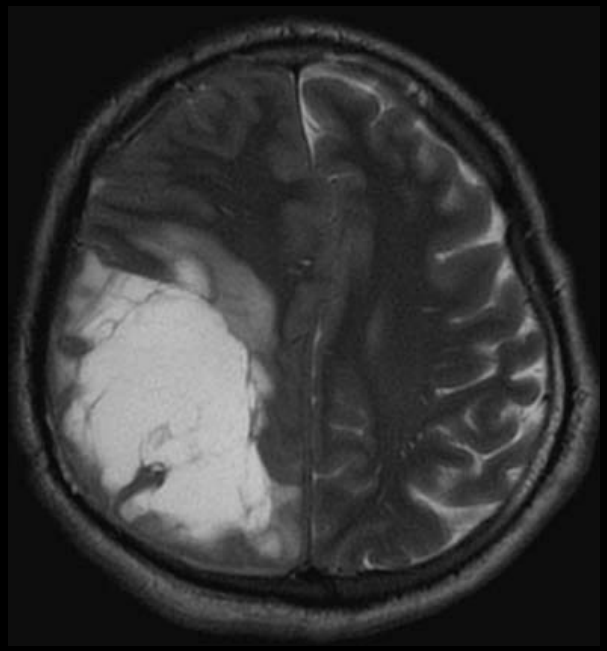
Trauma = hemorrhage = subdural, contusion

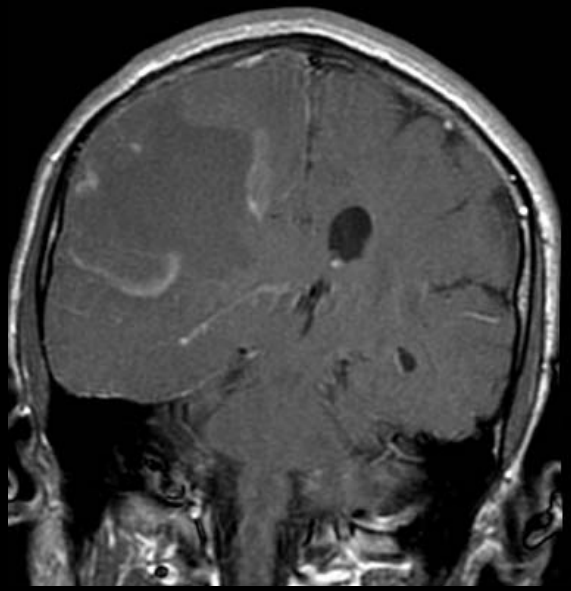
Infection = abscess, meningitis



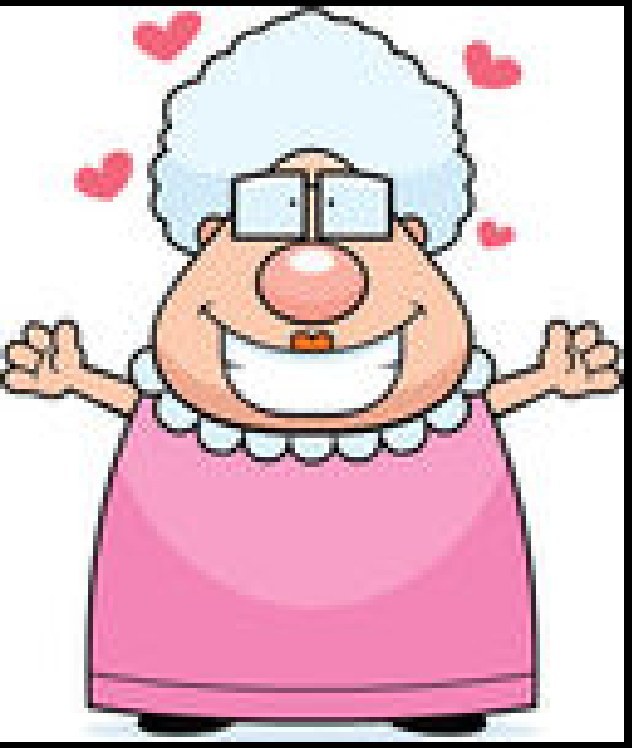


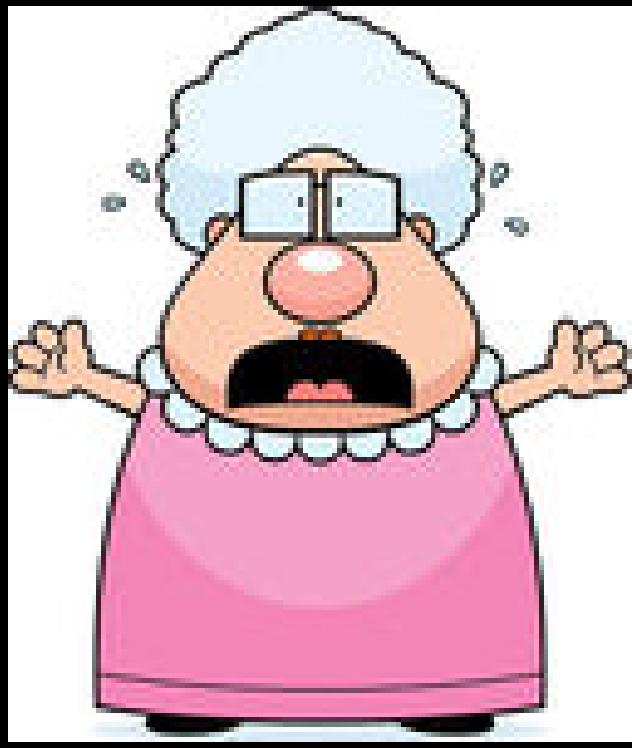
Inflammation = demyelinating disease, multiple sclerosis



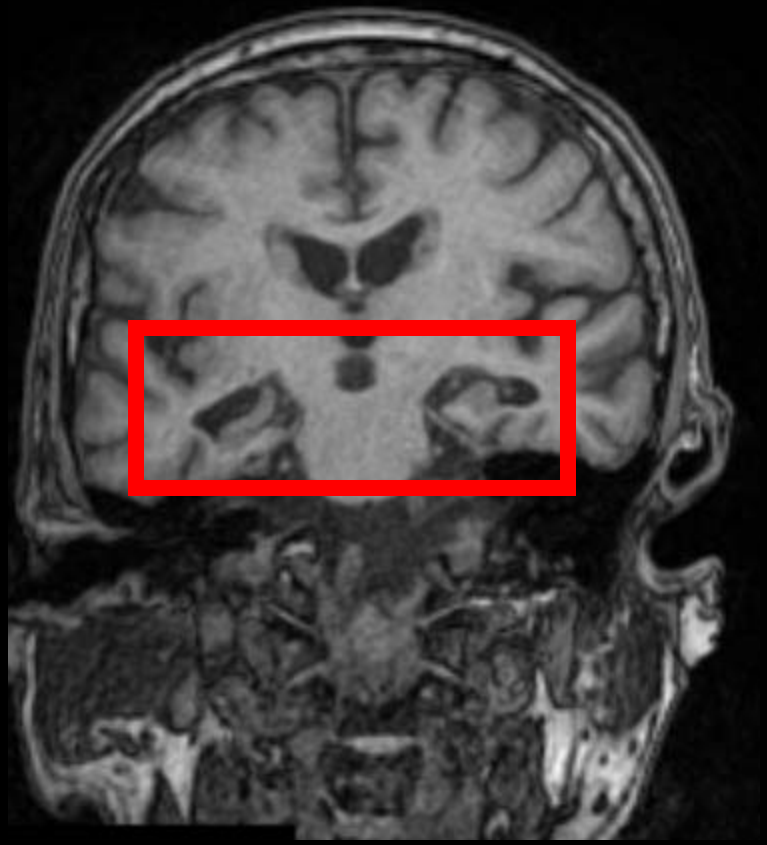


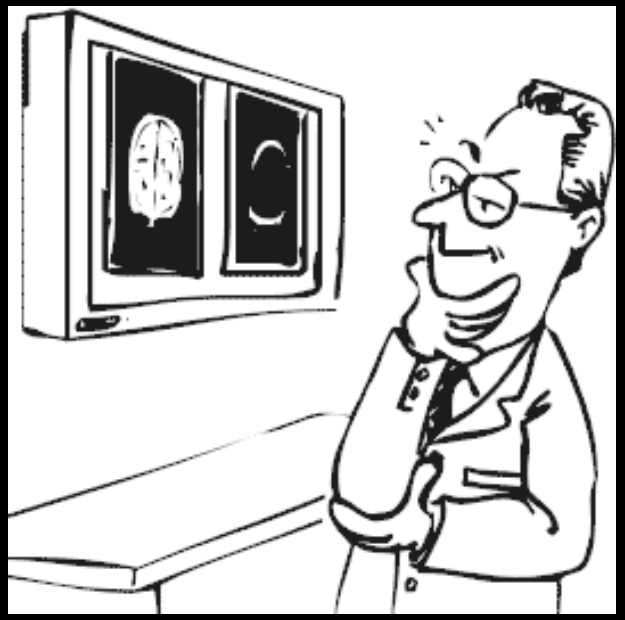
GRANDMA’s been acting funny





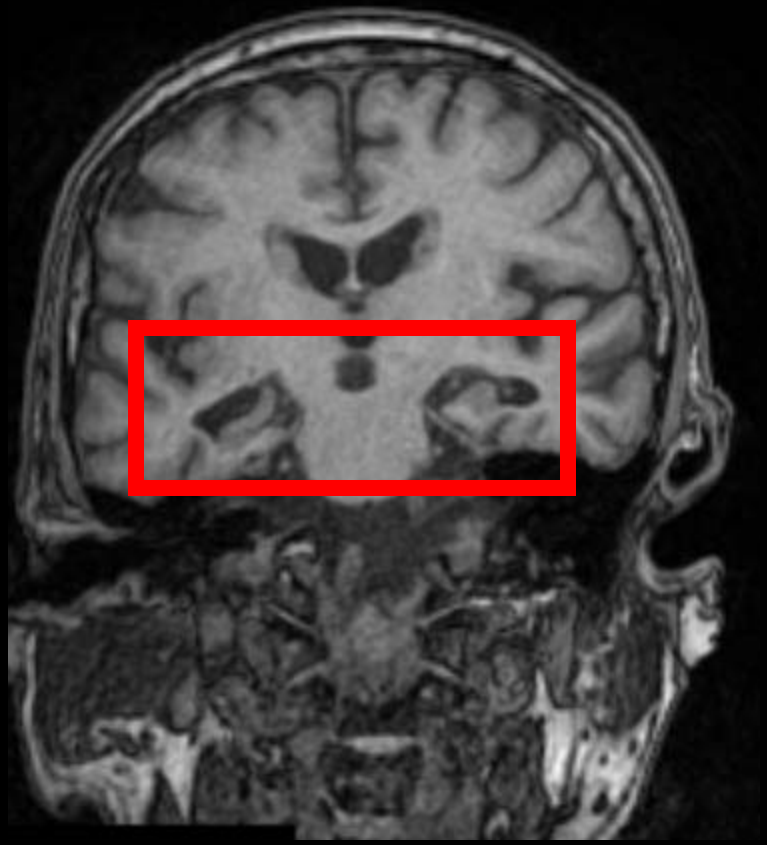
What did Grandma’s brain MRI show?

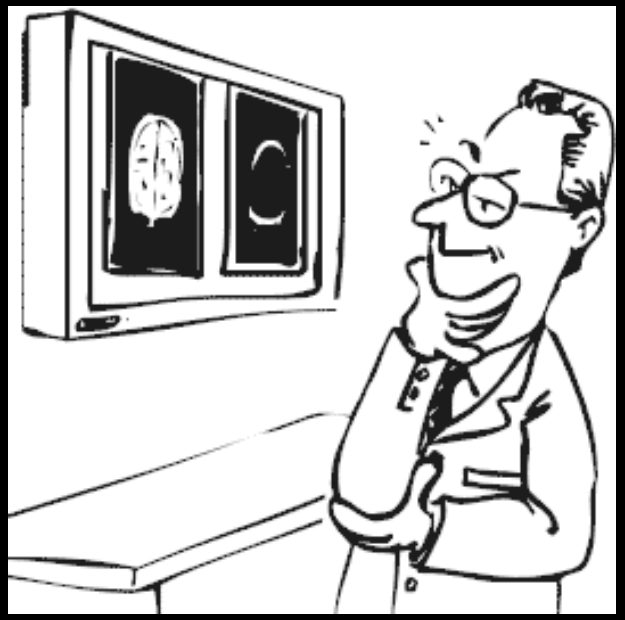




- No tumor
- No infarct (stroke)
- No hemorrhage
- No infection
- No inflammation

+ Hippocampal atrophy

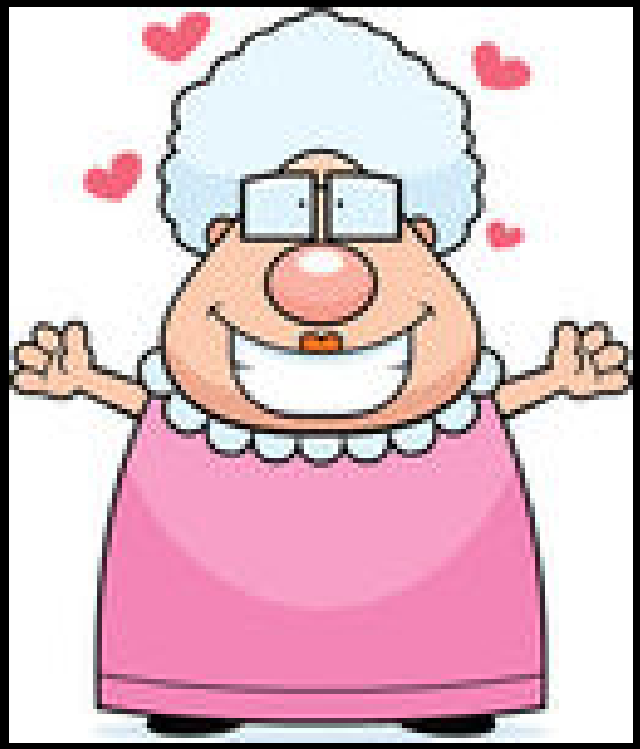




Hippocampal atrophy

* early site for Alzheimer's pathology postmortem

* important in memory

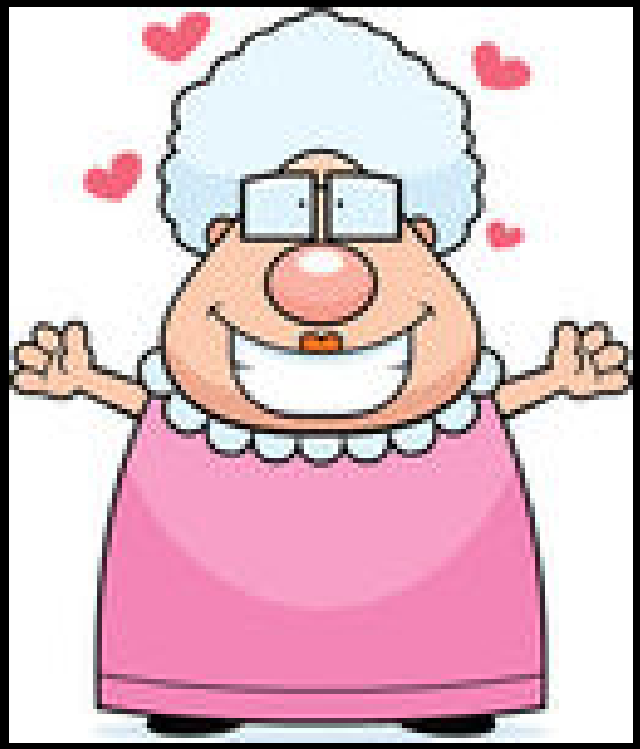


Alzheimer's disease prevalence

- 5% of people aged 70
- 20% aged 80
- 50% aged 90

Neurodegenerative disease

= progressive degeneration and death of neurons



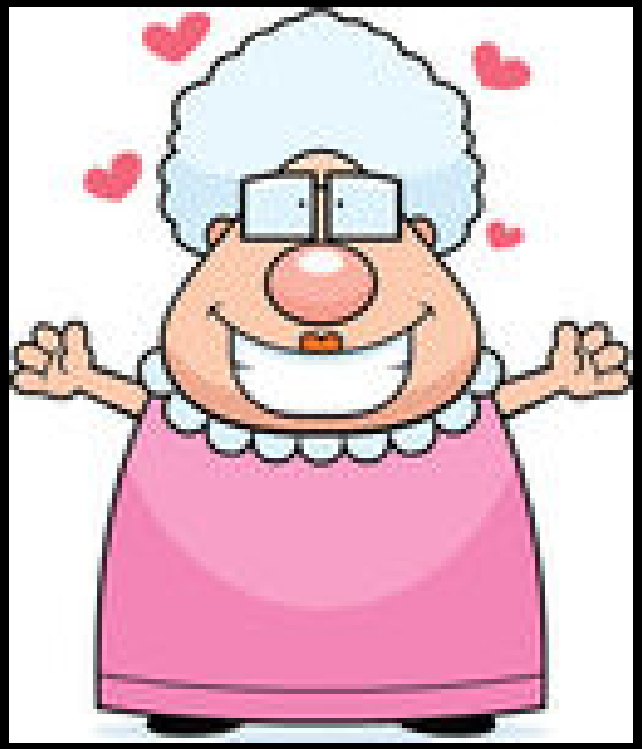
Alzheimer's disease prevalence

- 5% of people aged 70
- 20% aged 80
- 50% aged 90

Differential:

- Frontotemporal dementia
- Diffuse Lewy Body dementia
- Vascular dementia
- Parkinson's dementia
- Normal pressure hydrocephalus

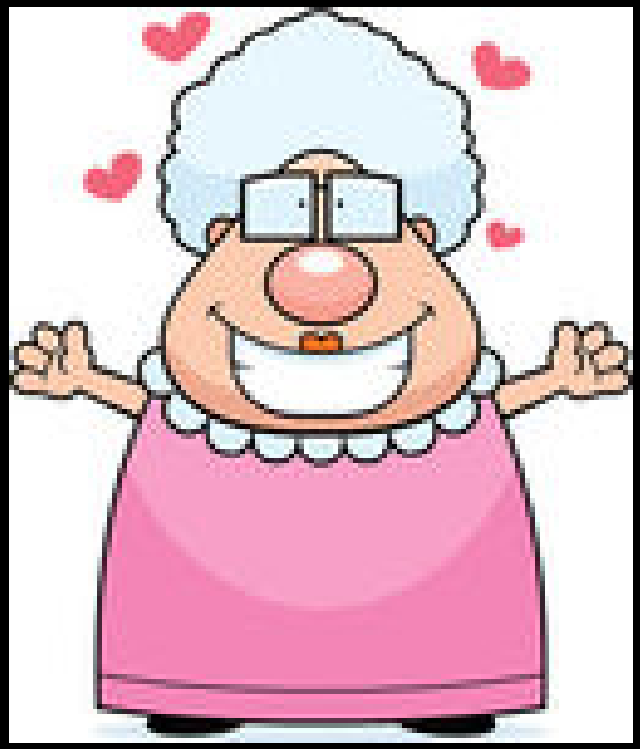
* *atrophy pattern & symptoms*



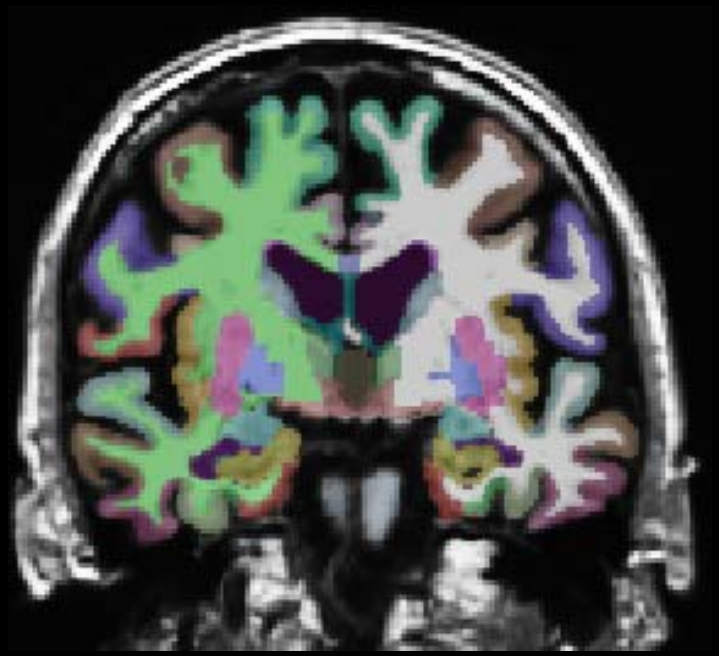
Alzheimer's disease
- quantitative methods

Sn 85%, Sp 88% for differentiating AD versus Normal aging

Laakso, Neurobiol Aging 1998



Alzheimer's disease
- quantitative methods

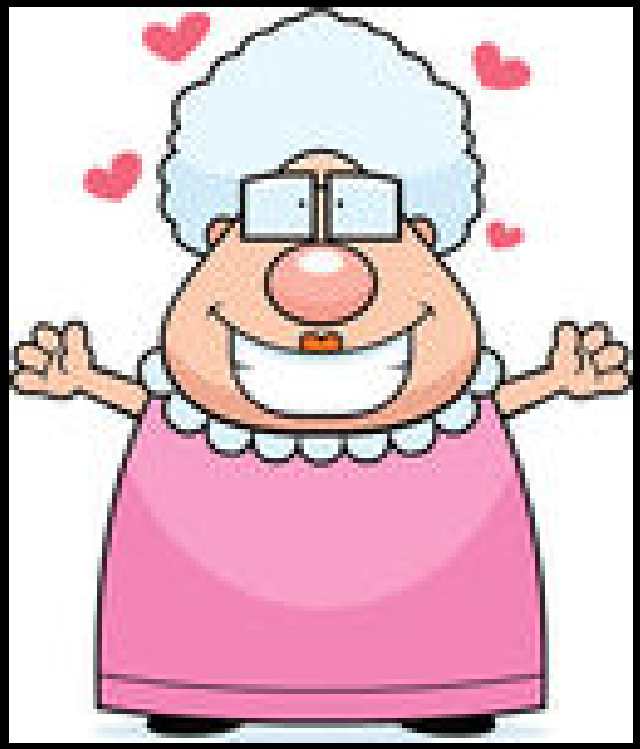


Freesurfer

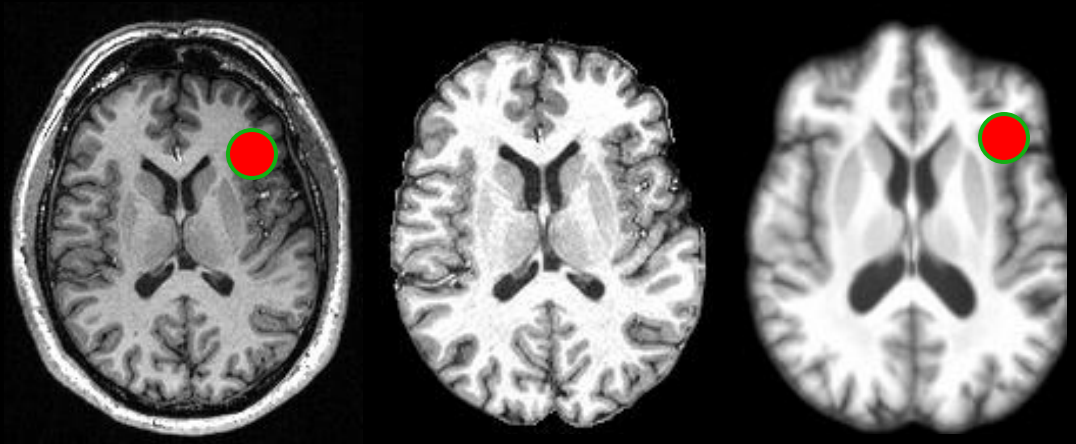
http://surfer.nmr.mgh.harvard.edu/

Registration to an atlas; Segmentation into 70 regions

- Requires computing power

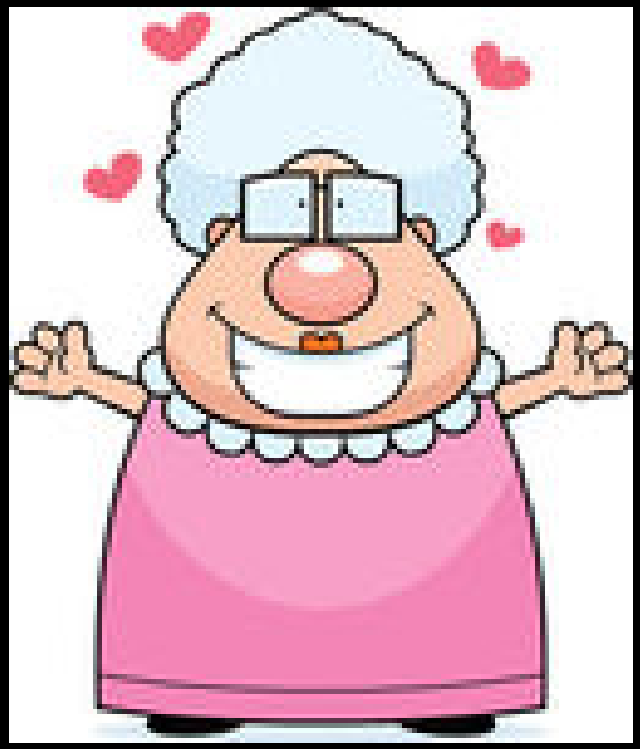


Alzheimer's disease
- quantitative methods

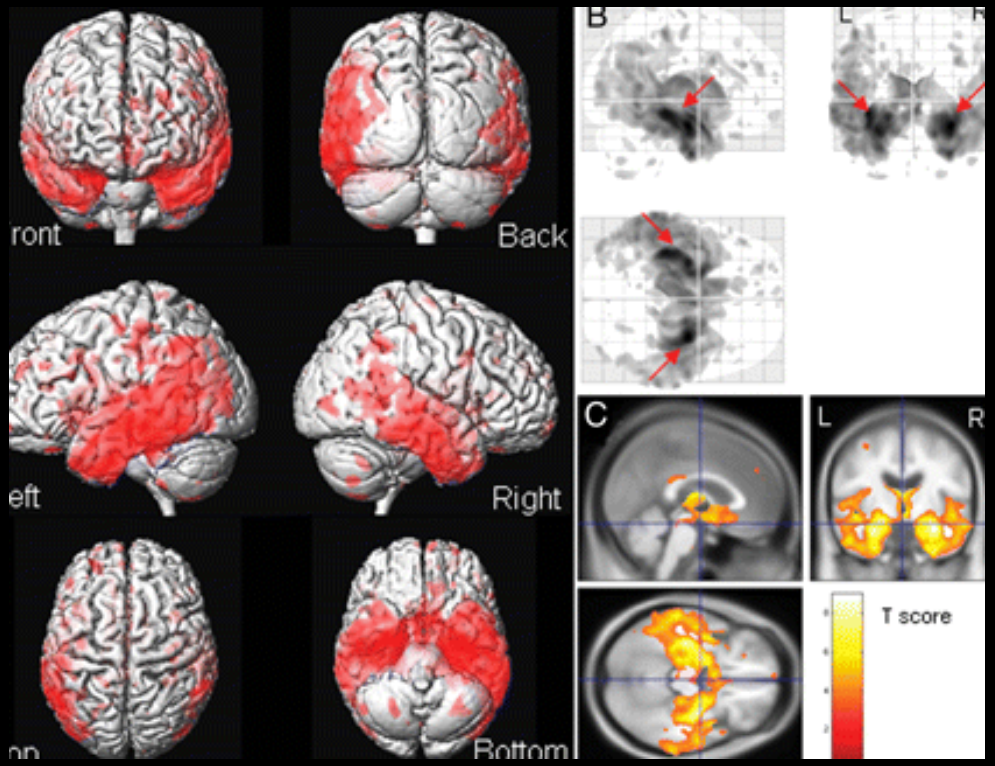


Quantitative whole-brain voxel-based morphometry

- 2000 Voxel-based Morphometry (VBM) – the methods (Ashburner, Friston)

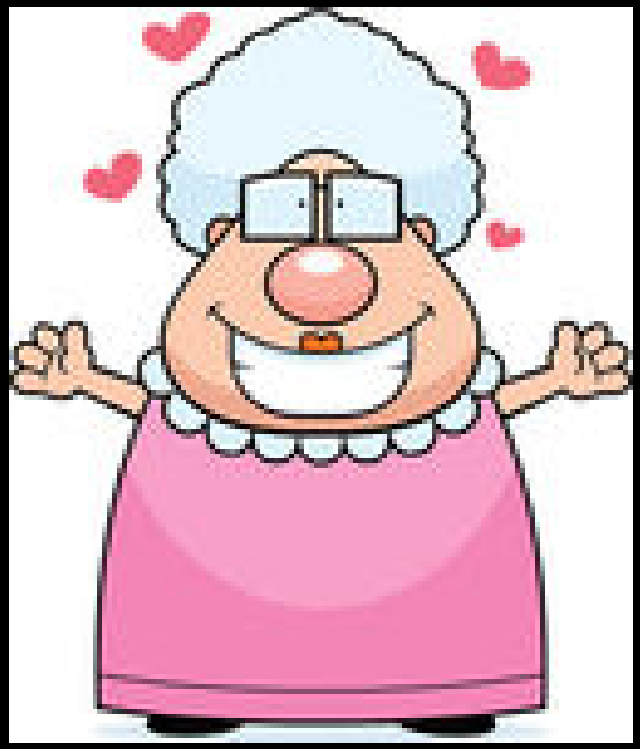


Alzheimer's disease
- quantitative methods

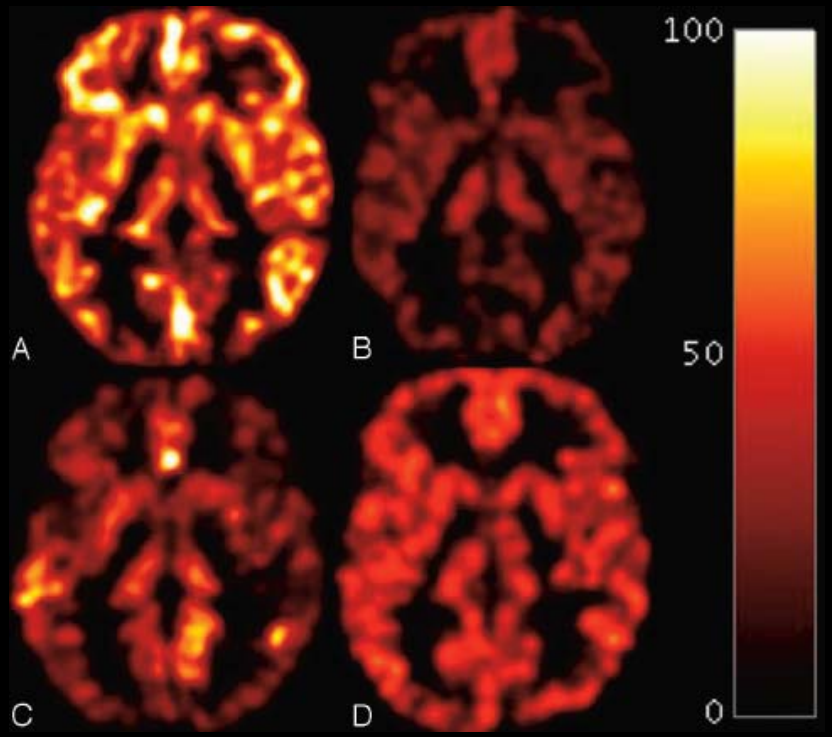


VBM: Whole-brain statistical map ($p<0.005$ FDR)

Whitwell JL. J of Neurosci 2009; 29: 9661-9664.

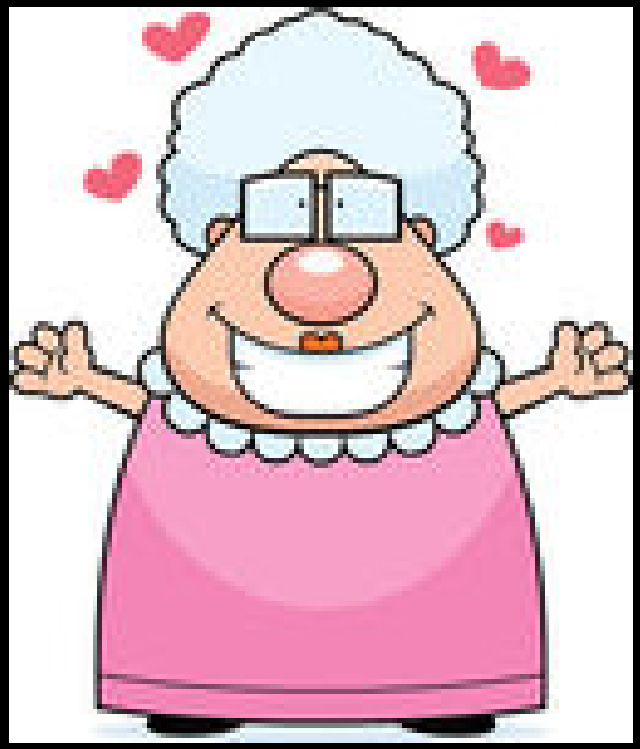


Alzheimer's disease
- quantitative methods

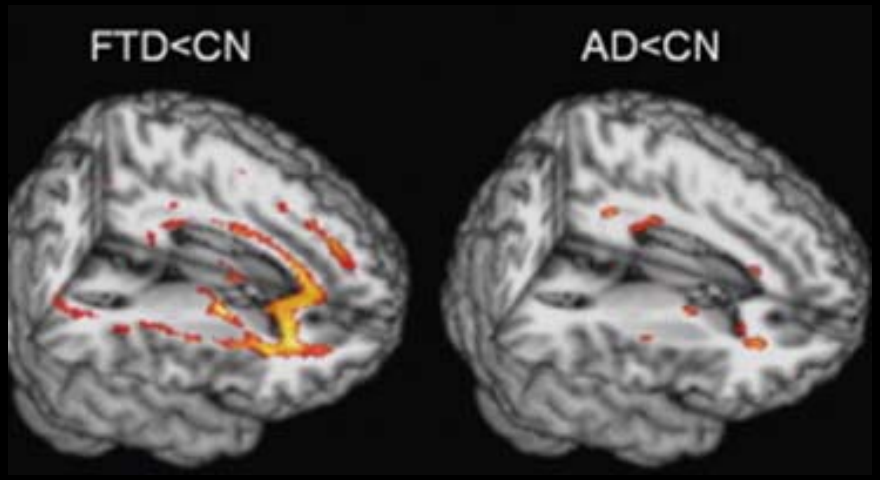


Arterial Spin Labeling (ASL) MR Perfusion:
- higher inter-rater reliability than SPGR. Sn 85%, Acc 70%

Raji CA et al. AJNR 2010; 31: 847-855. [units of ml blood/g tissue/min]



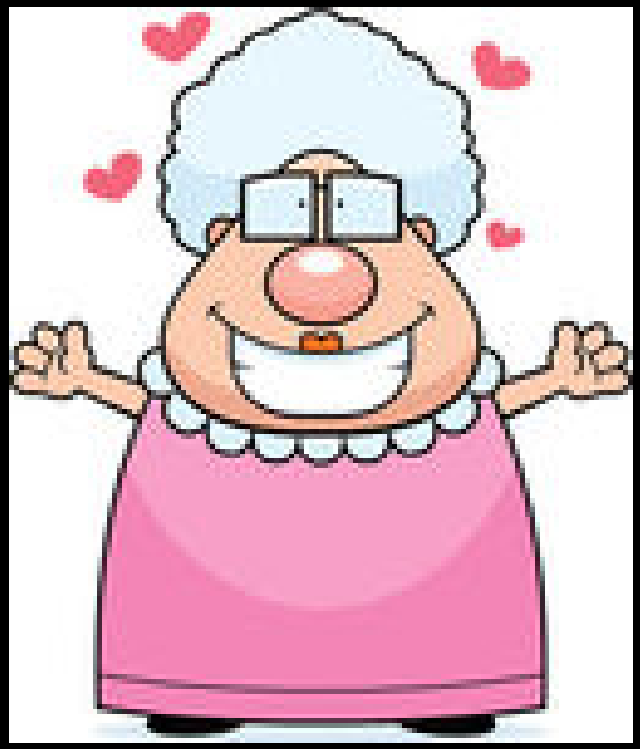
Alzheimer's disease
- quantitative methods



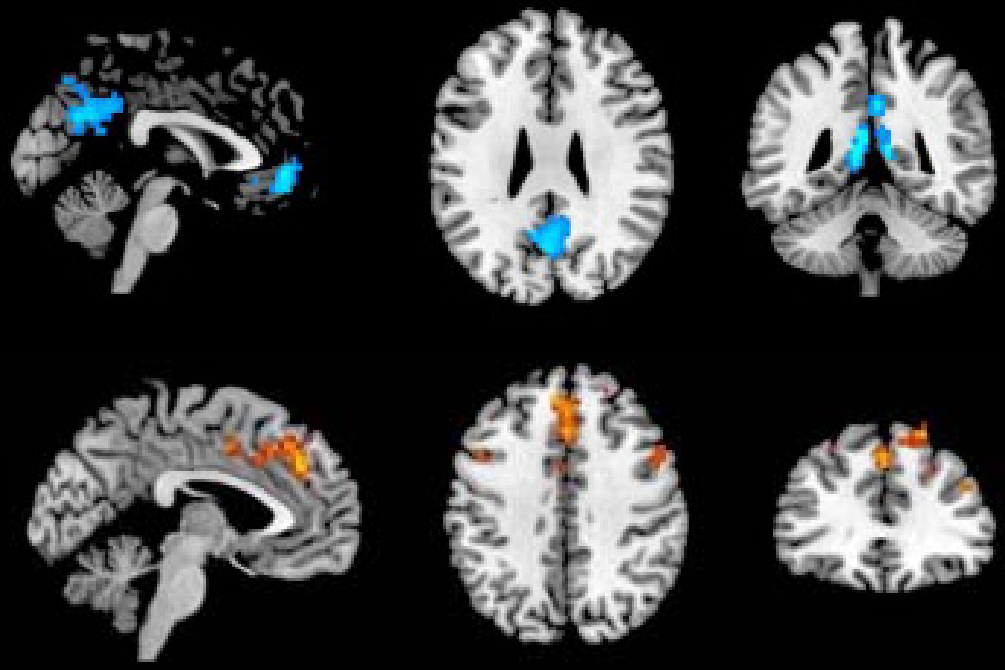
Zhang Y et al. Neurology 2007; 68: 13-19.

Diffusion Tensor Imaging (DTI) accuracy (NL vs AD): 78 → 91%

Zhang Y et al. Brain 2009; 132: 2579-2592.



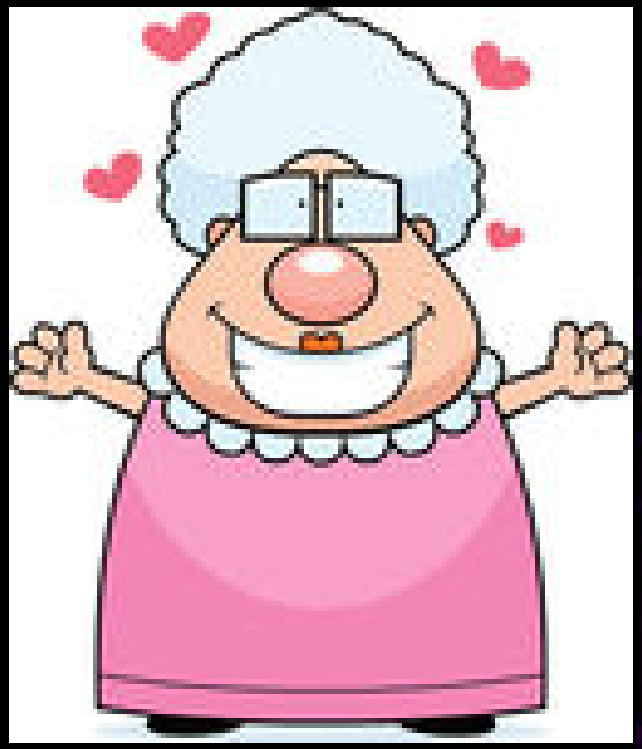
Alzheimer's disease
- quantitative methods



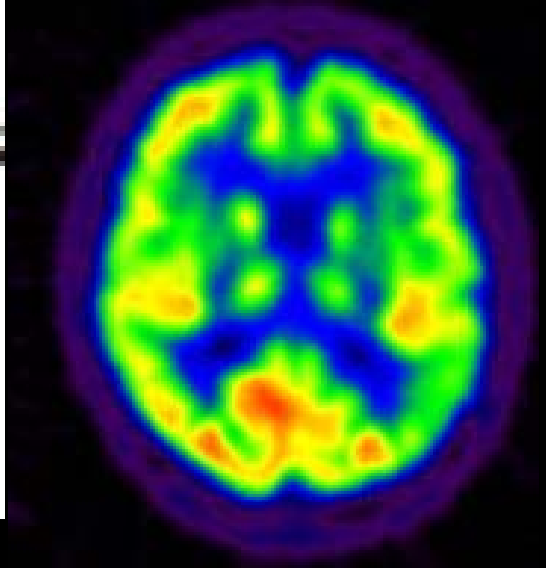
Resting State Function MRI (rsfMRI): AD vs NL

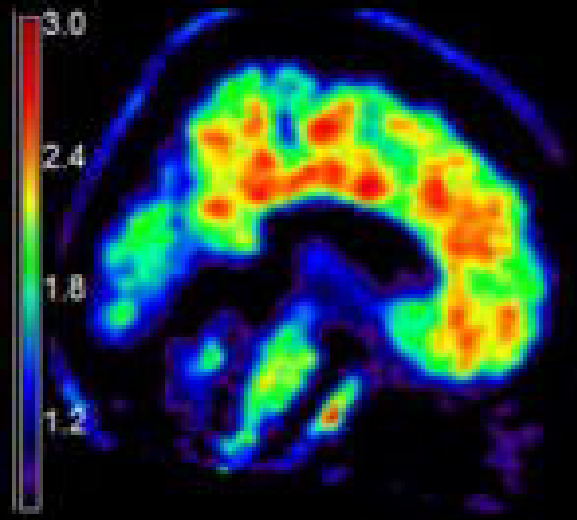
Default mode network (decreased) vs Executive network (increased)

Agosta F et al. Neurobiol Aging 2012; 33: 1564-1578



Alzheimer's disease
- quantitative methods





GLUCOSE METABOLISM
FDG-PET

AMYLOID DEPOSITION
PET-PiB

Alzheimer's pathogenesis 1906-now

Amyloid cascade hypothesis
(Hardy, Allsop, Selkoe 1991)

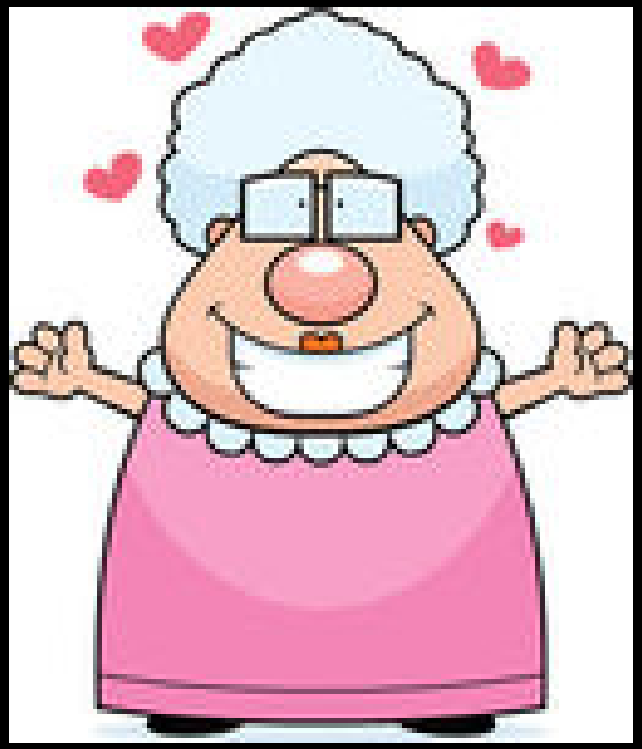
Beta-amyloid plaques

Neurofibrillary tangles (tau)

Neuronal degeneration (MRI)

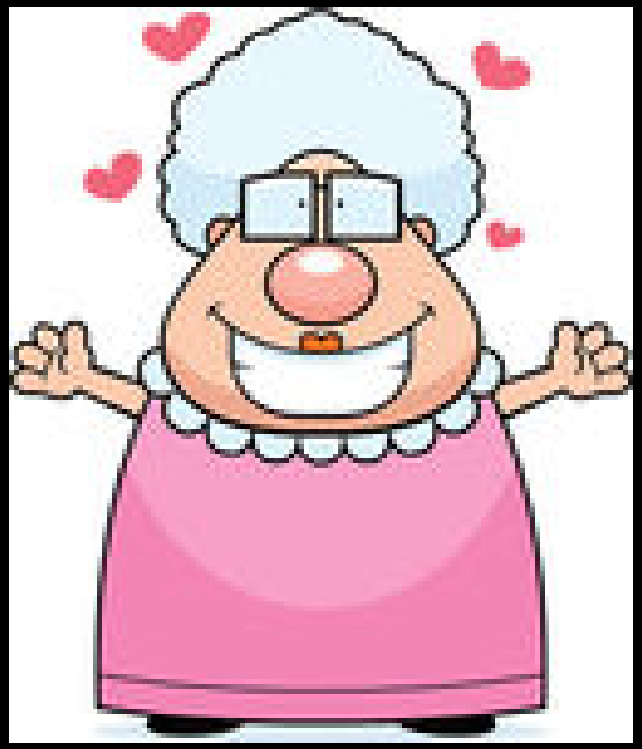
Memory dysfunction (MCI)

Clinical dysfunction (Alzheimer's Disease)



Grandma has Alzheimer's disease

- No known therapy to slow progression of disease
- Donepezil (Aricept) provides symptomatic relief (memory, behavior)

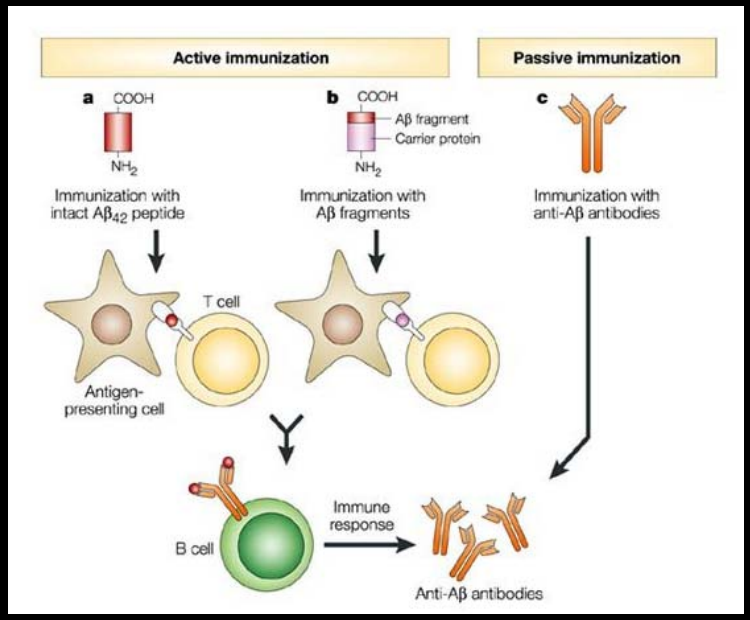


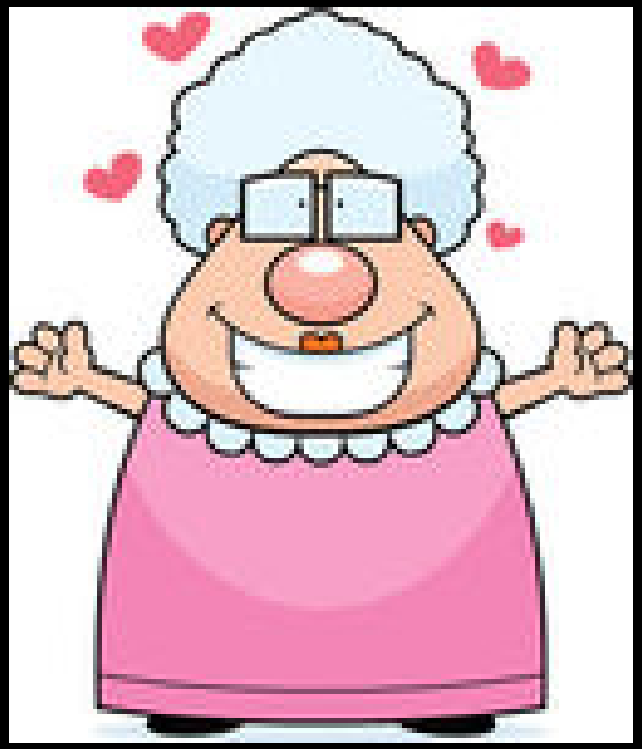
Grandma has Alzheimer's disease

- No known therapy to slow progression of disease

- Targeting amyloid?

Monoclonal antibodies against beta-amyloid





Grandma has Alzheimer's disease

- No known therapy to slow progression of disease

- Treating other risk factors?

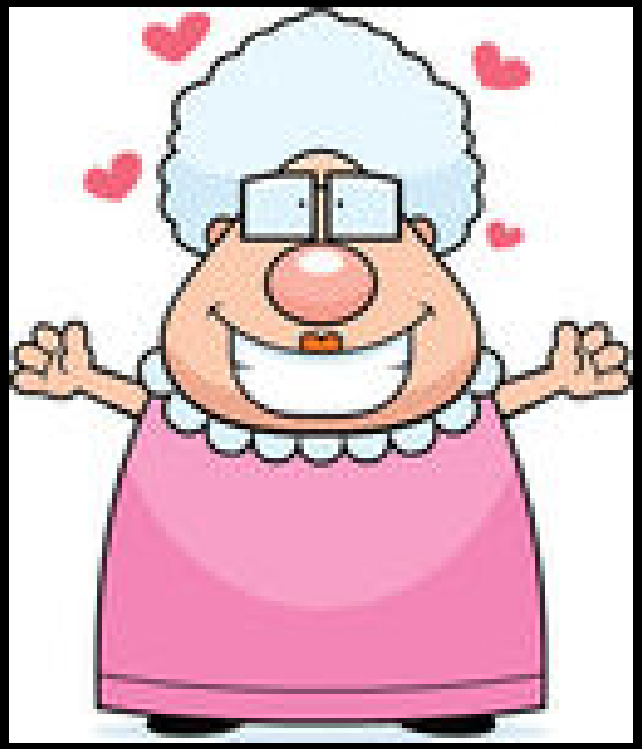
THE LANCET Neurology

Review

The projected effect of risk factor reduction on Alzheimer's disease prevalence

Dr Deborah E Barnes, PhD, Prof Kristine Yaffe, MD

Published Online: 19 July 2011



Grandma has Alzheimer's disease

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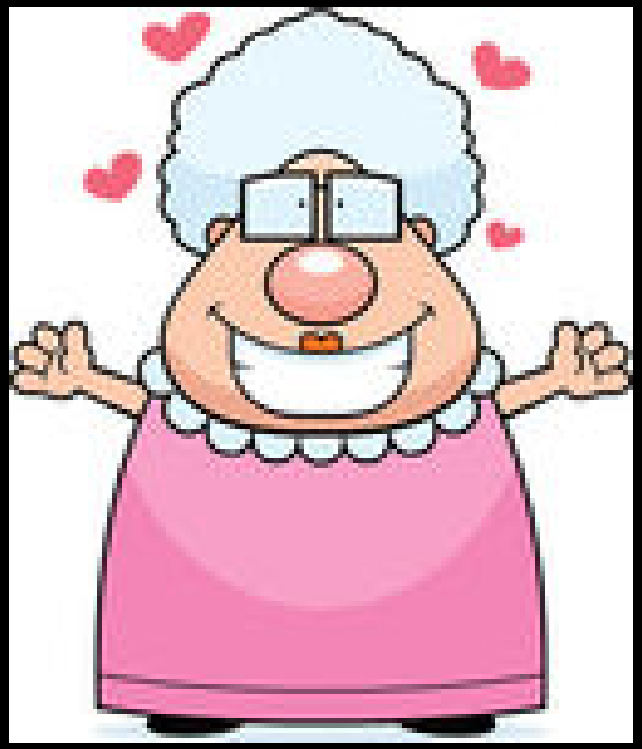
50% Alzheimer's cases attributable to modifiable risk factors:

- physical inactivity/obesity, hypertension, diabetes, smoking



Quantitative imaging
- diagnosis
- monitoring progression