



UNIVERSITY OF TORONTO
FACULTY OF MEDICINE

Differences between FTD and Alzheimer's: Opportunity for a New Approach to the Science?

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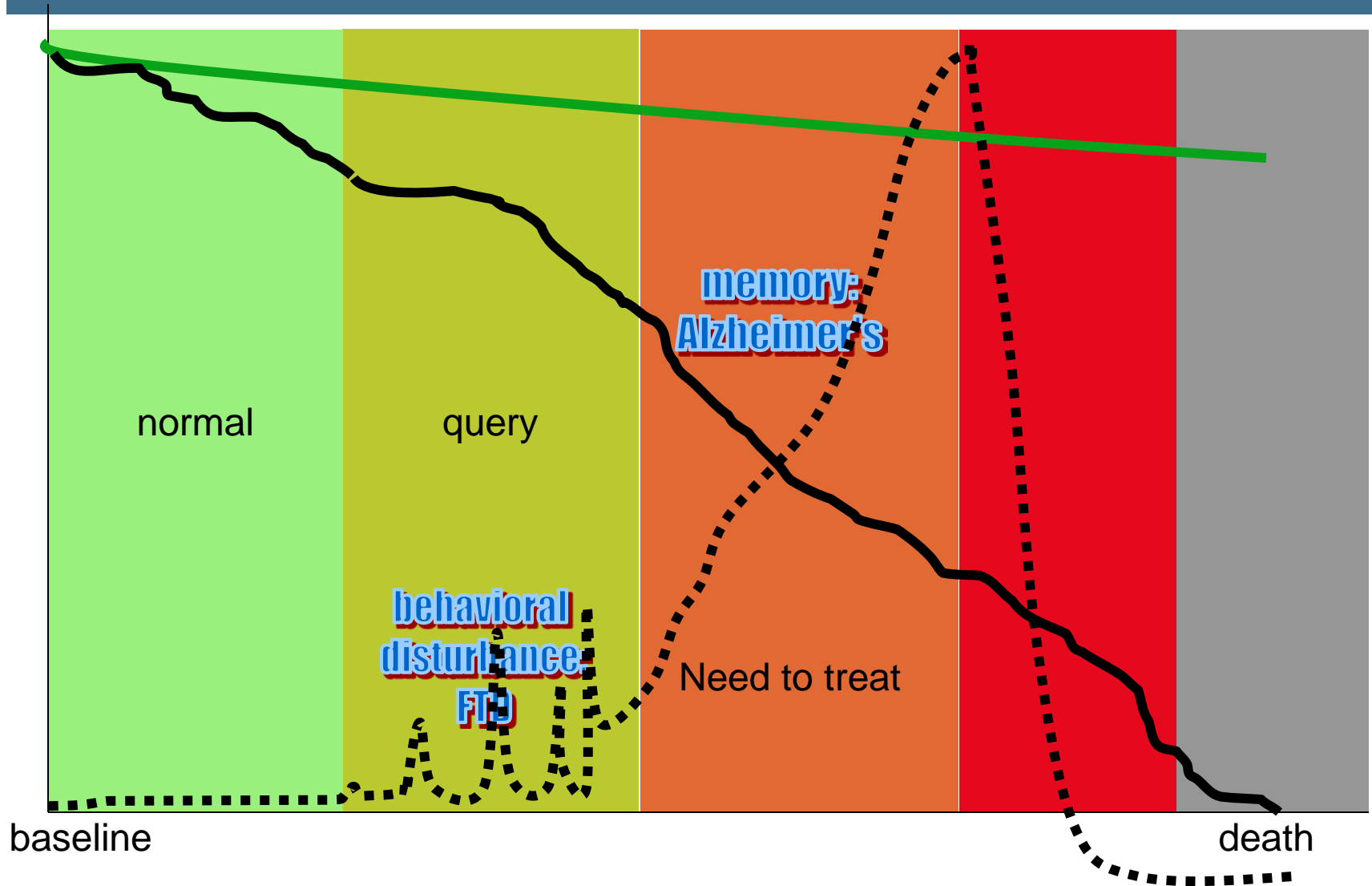
Assistant Professor of Psychiatry, University of Toronto

Clinician-Scientist, The Rotman Research Institute, Baycrest

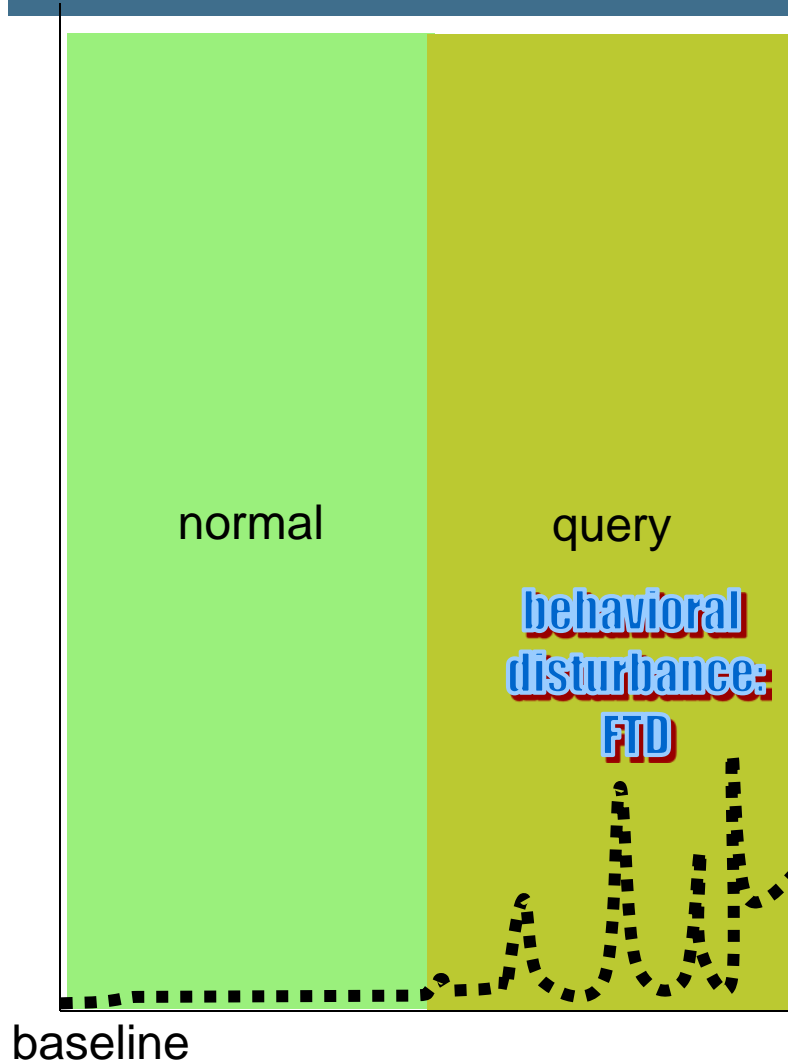


Toronto Dementia Research Alliance

Rolling back time may not be desirable



Clinical characterization

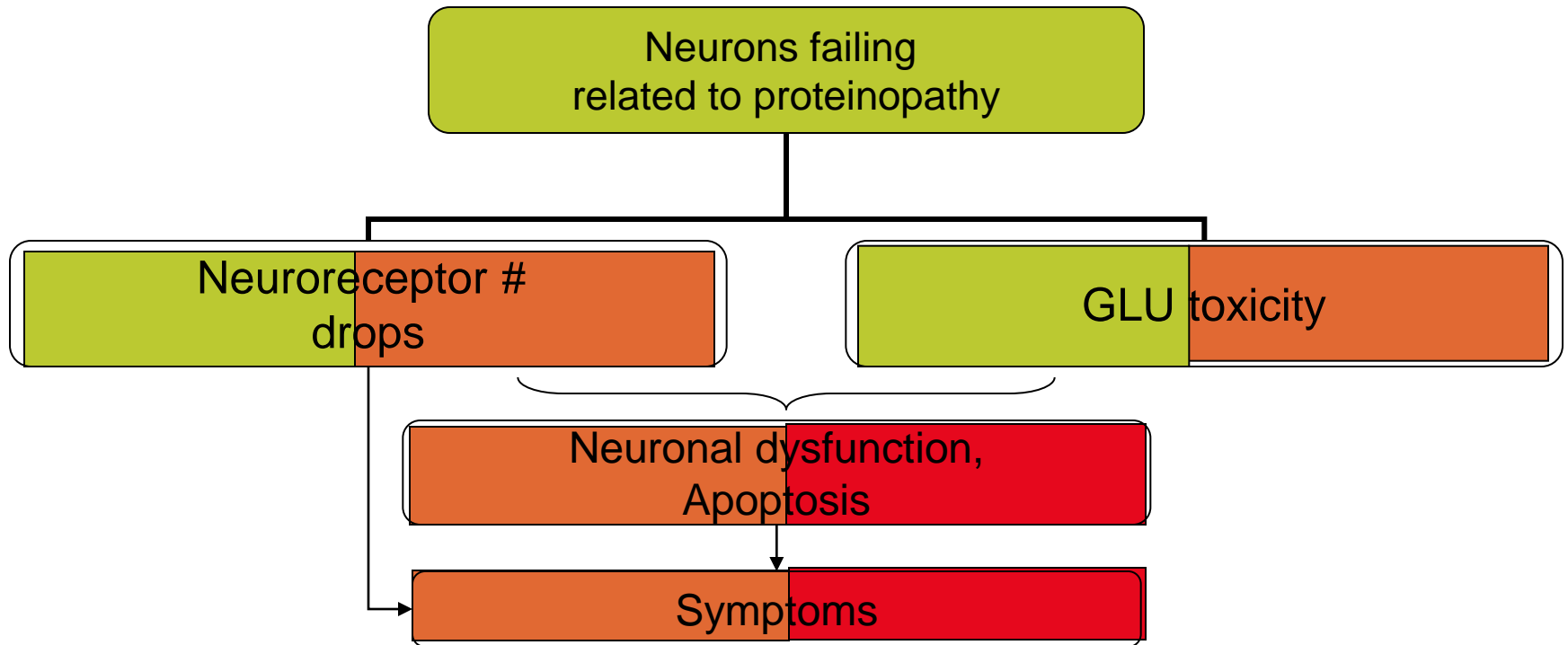


THE U of T FTD WORKGROUP

- Theory of Mind (OMHF)
- Primitive Reflexes?
- Emotional Valence and Non-verbal Memory
- Alexithymia
- Citalopram Challenge
- SLP interventions for semantic dementia and other PPAs



What's happening?

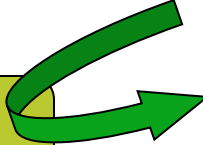


Could use a radioligand for TDP-43...



Additional proteinopathy?
PIB PET in early- vs late-onset FTD

Neurons failing related to proteinopathy

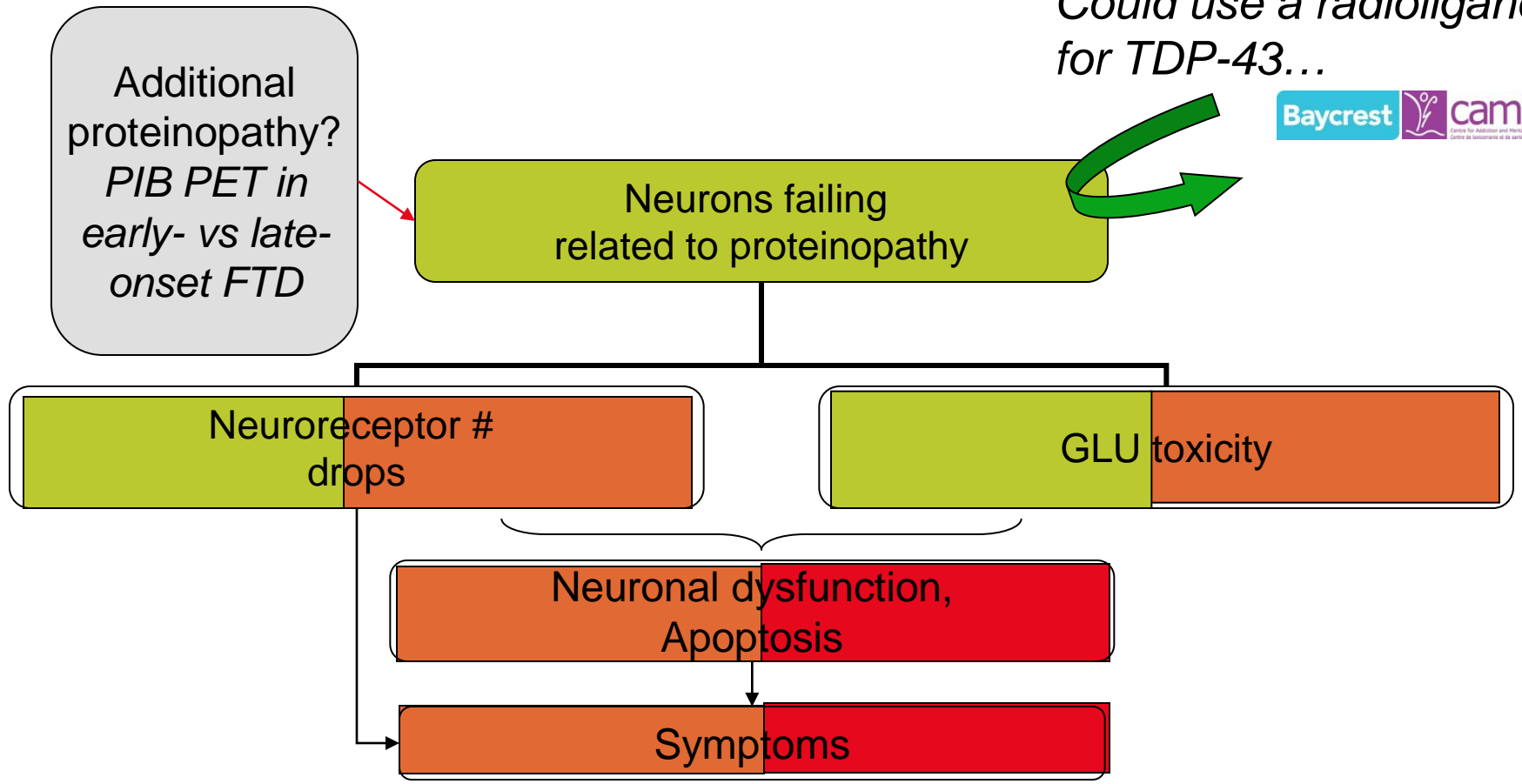


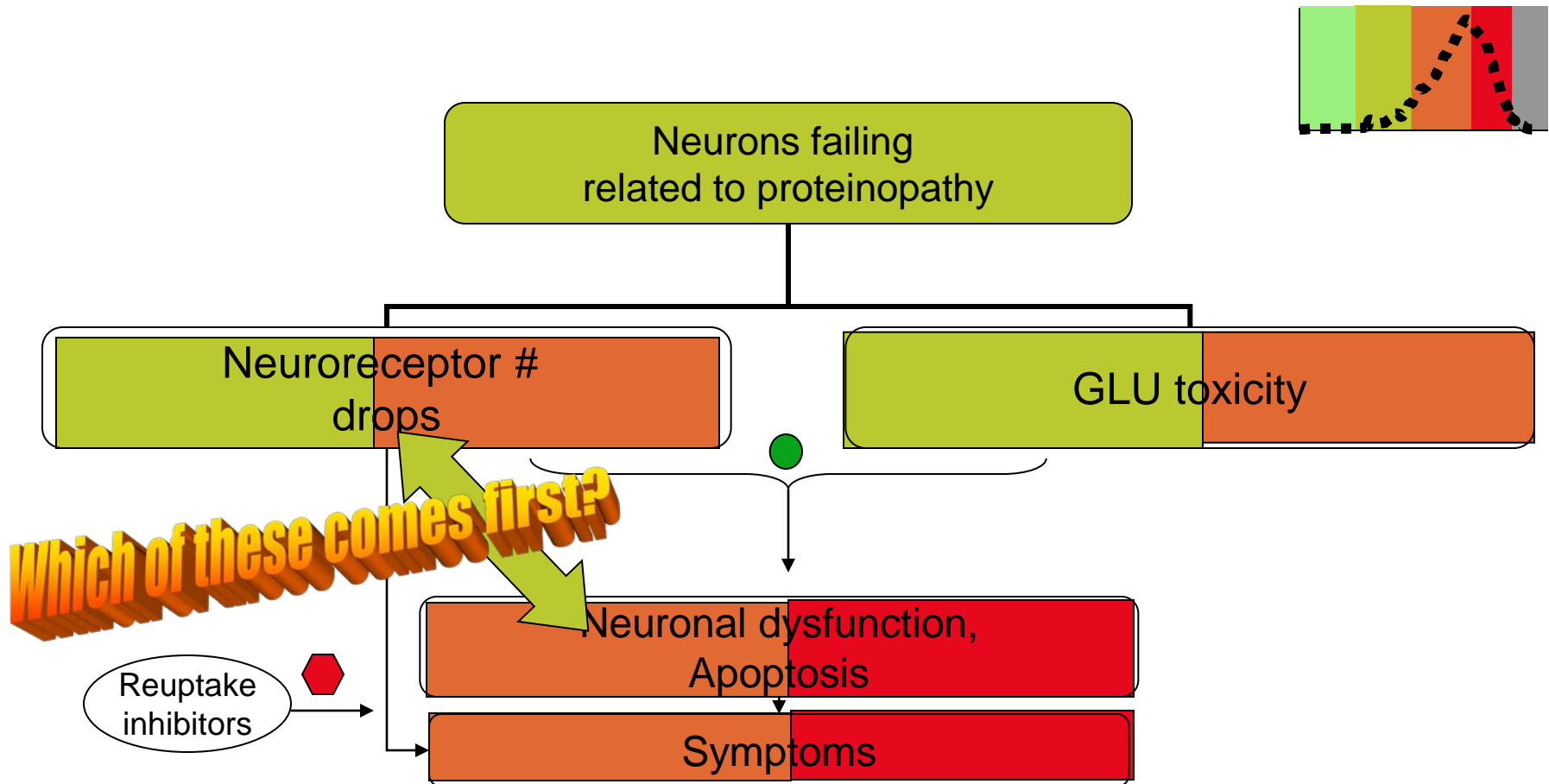
Neuroreceptor # drops

GLU toxicity

Neuronal dysfunction, Apoptosis

Symptoms

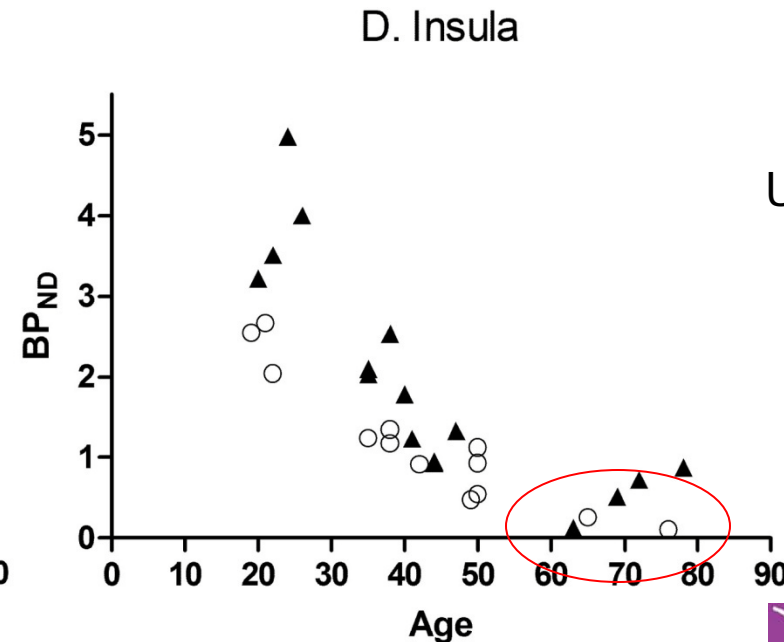
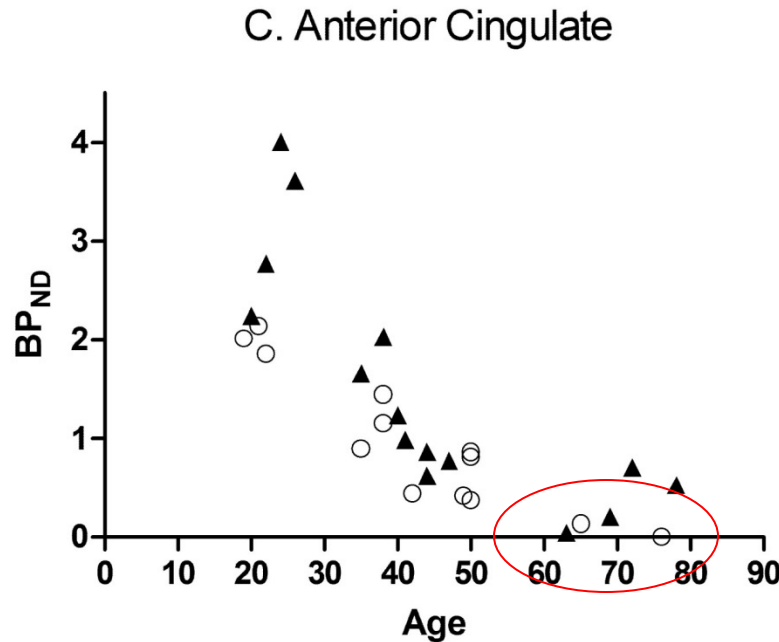
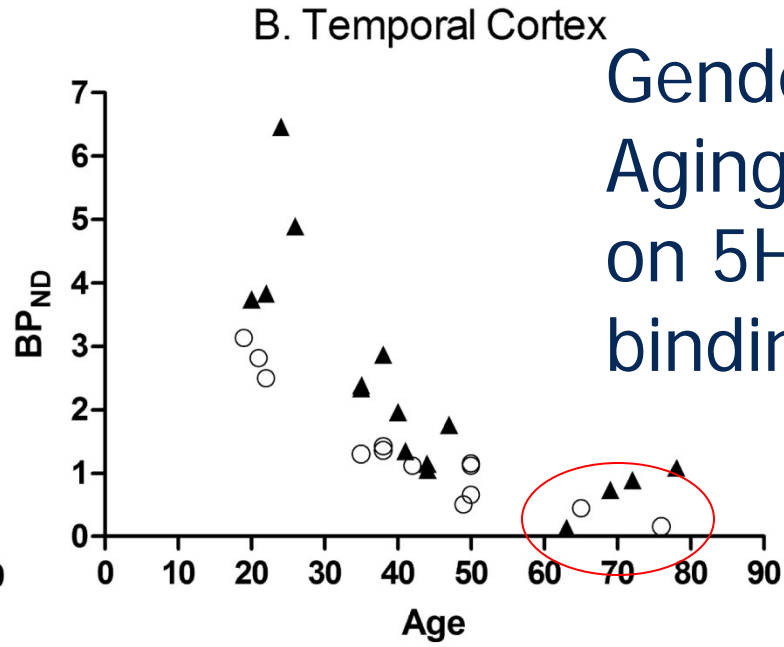
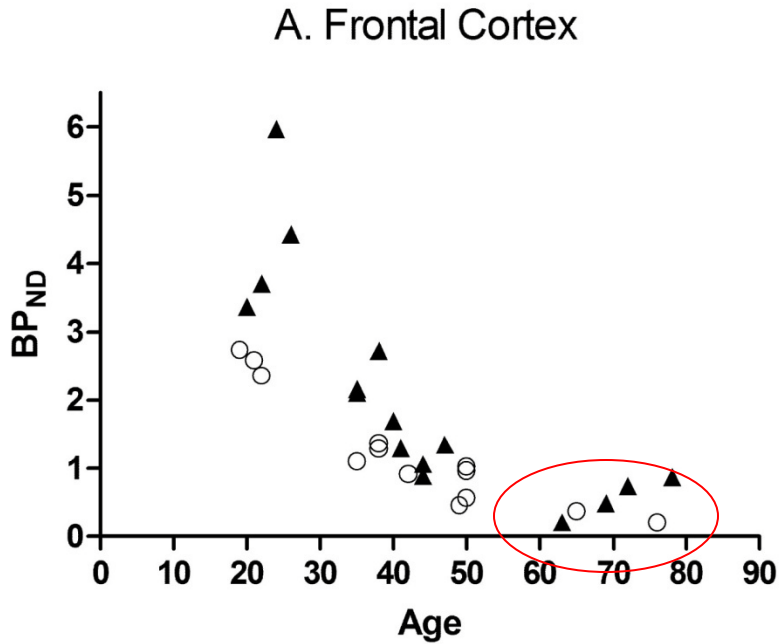




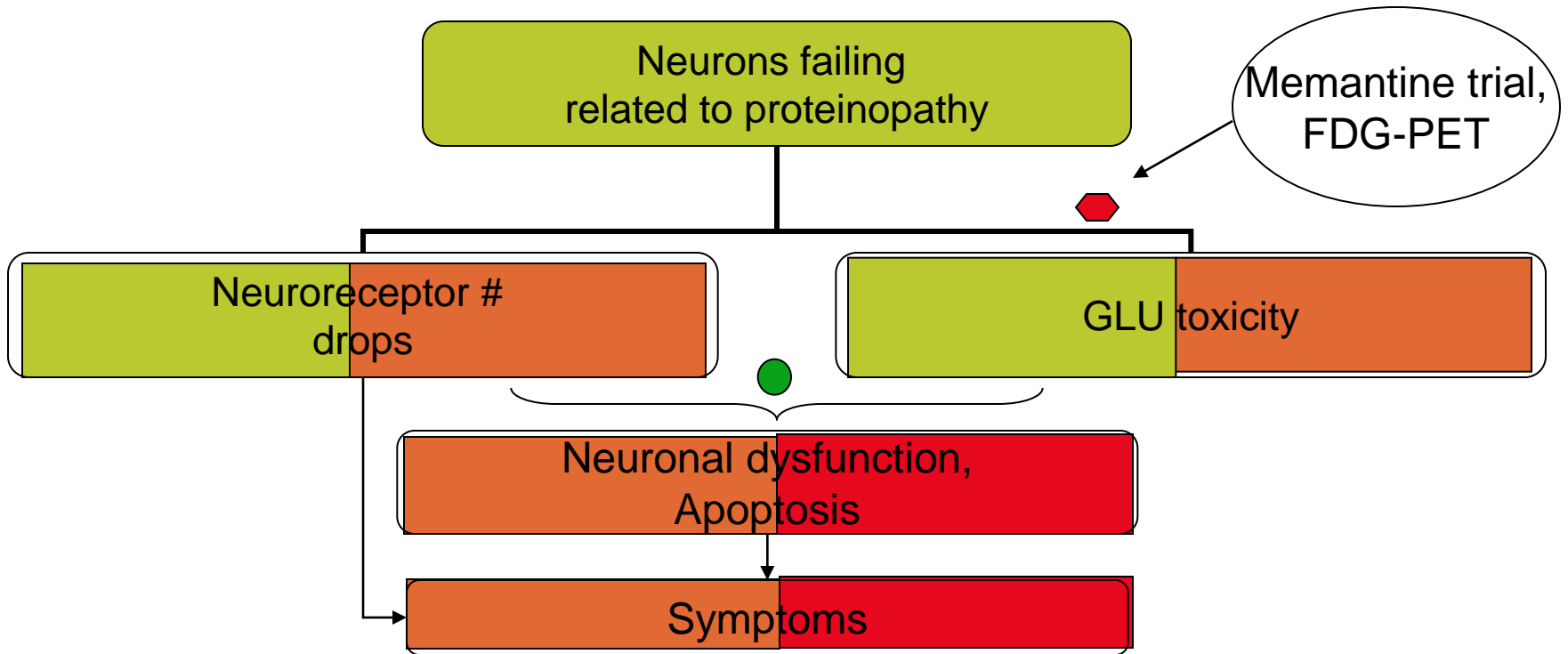
If reuptake inhibitors are helpful, does that indicate overcompensation by survivor-neurons or that neuroreceptor changes predate neuronal death?

Radioligands, such as 5HT2R tracer [18F]-setoperone, [11C]-WAY or [18F]-FP-TZTP.

Gender & Aging Effects on 5HT_{2a}R binding



Uchida, *Int J Geri Psych*
under review



Subject referrals:

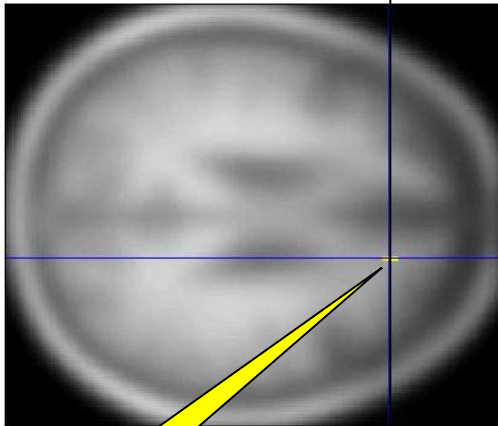
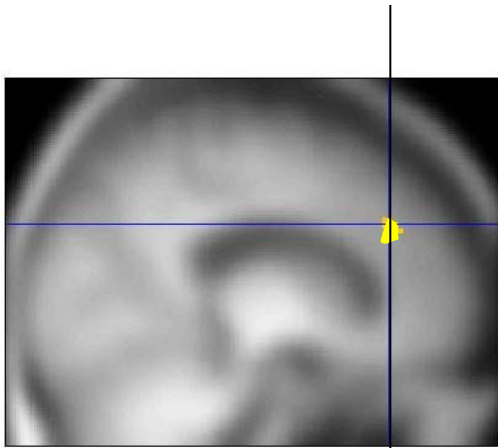


Memantine in Frontotemporal Dementia

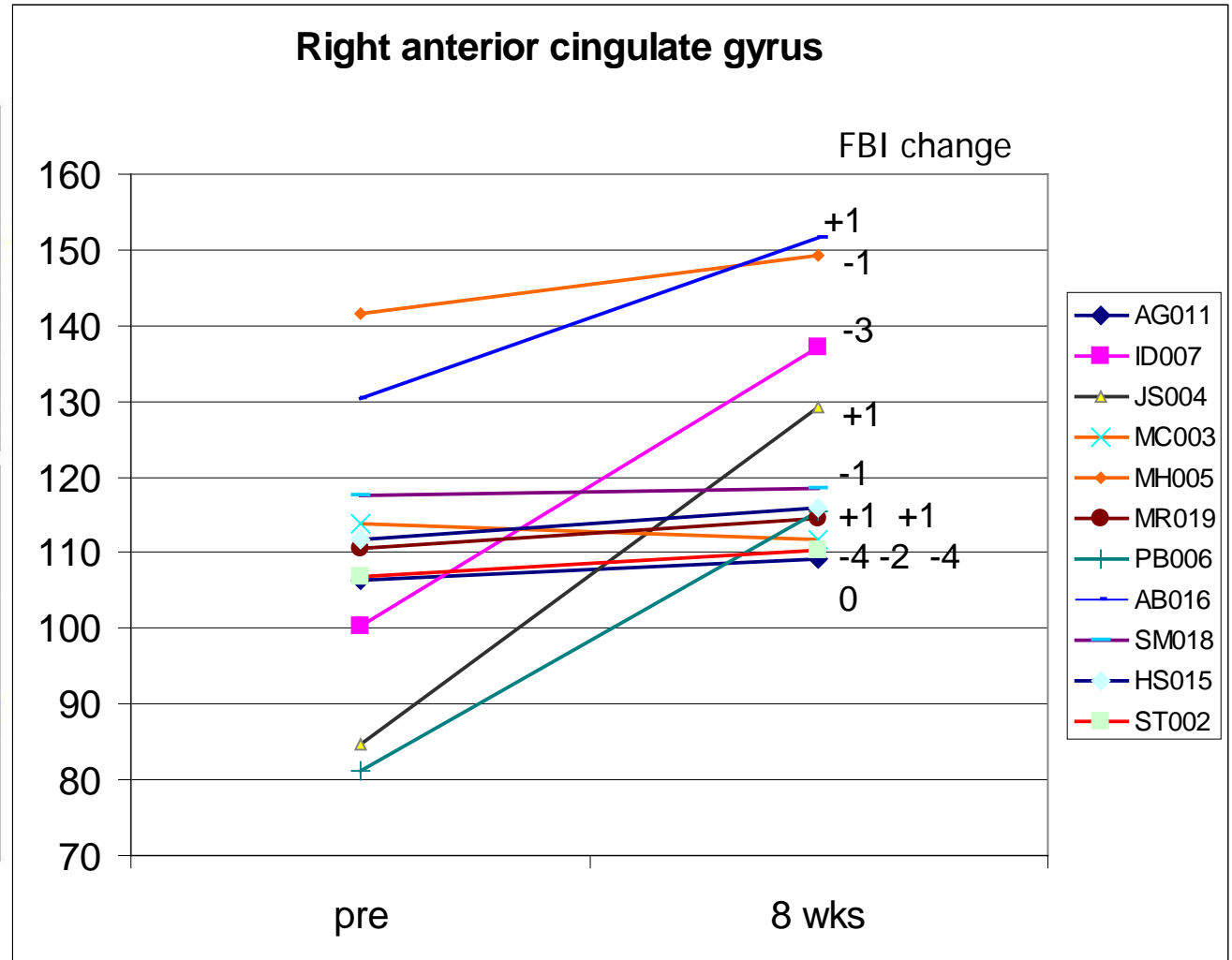
- **24-week open-label trial: N = 43, transient NPI improvement, mixed signals on other measures**
 - ▣ *Boxer Alz Dis & Assoc Dis 2009*
- **Pre- and Post-Memantine FDG-PET Imaging in Frontotemporal Dementia**
 - ▣ Co-Auths Ariel Graff-Guerrero, Morris Freedman, David Tang-Wai, Sandra Black, Bruce Pollock

SPM2: Single Condition and Covariates

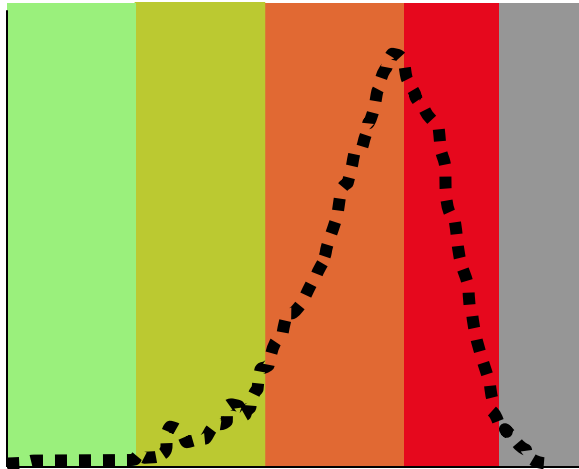
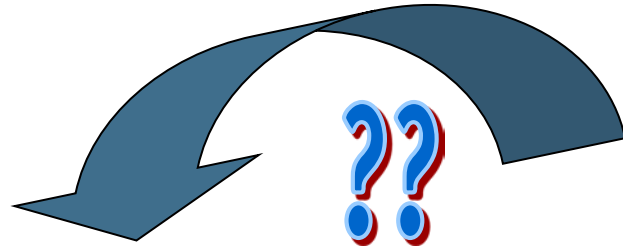
Results at $p < .05$ (N=11)



t = 2.25



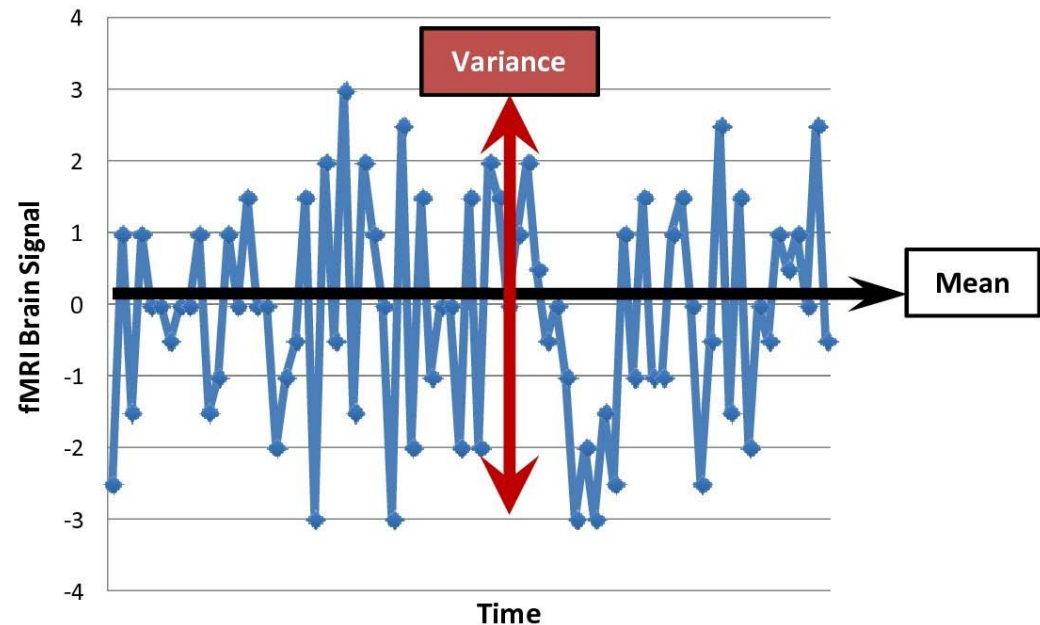
How might resting state functional connectivity relate to that peak?



Critical meltdown = ↓ salient network
+ ↓ default network?

Resting State Functional Connectivity Considerations over the Lifespan

- Individual variability on cogn testing increases with age
 - ▣ right on up to time of death!
 - ▣ C Grady tracking the changes in variability with aging.



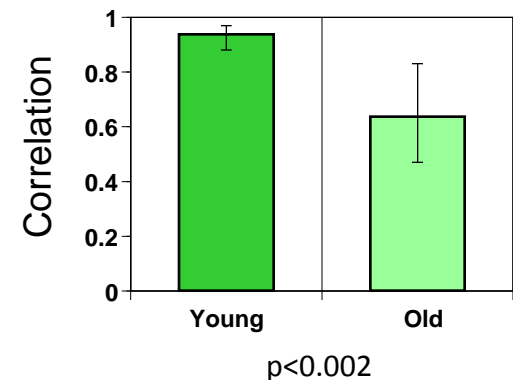
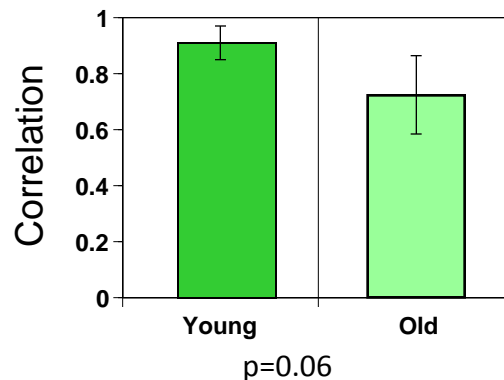
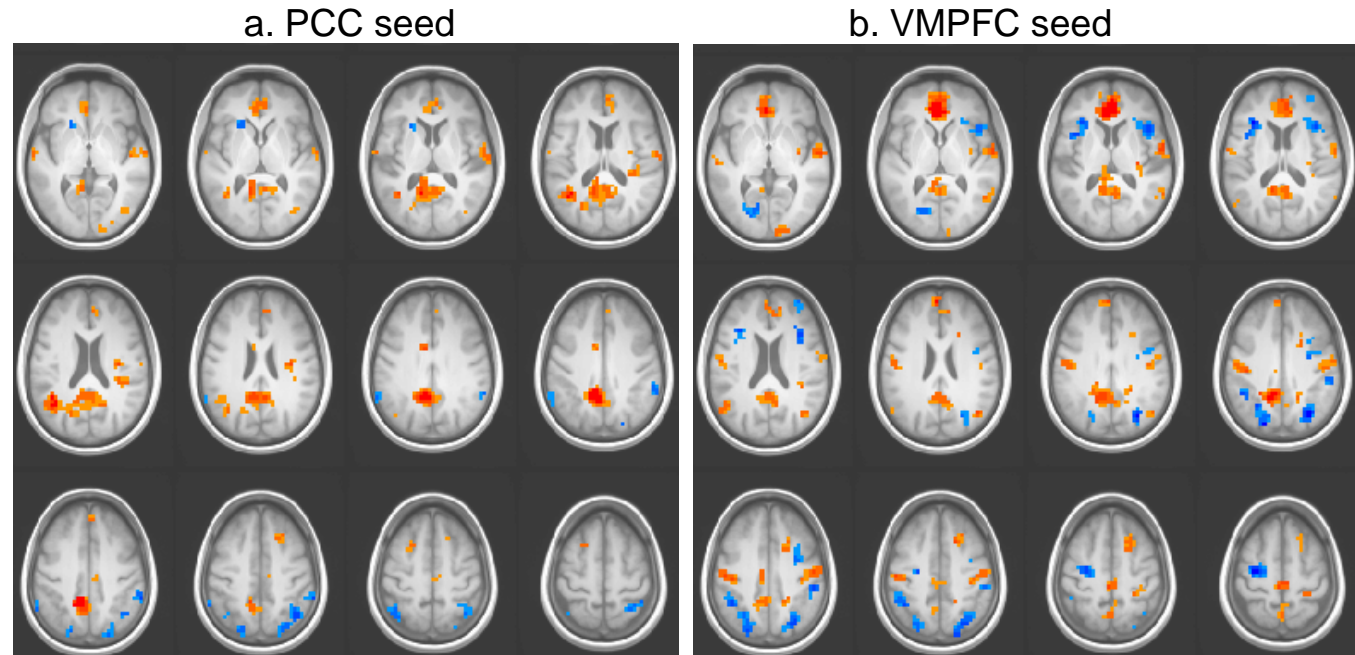
Baycrest

Enriching Care
Enhancing Knowledge
Enlightening Minds

Correlations between connected brain regions change with age, too

So watch where you're putting those seeds!

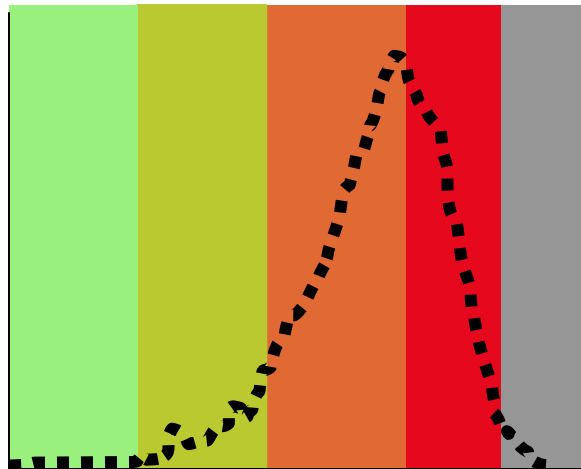
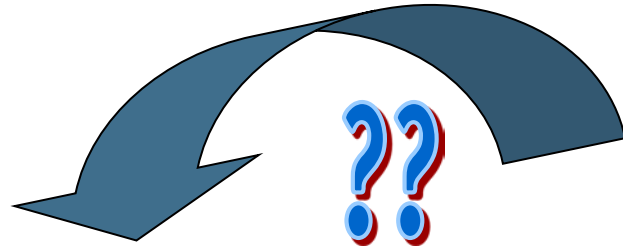
Demonstrated here in resting state, but applies to Task Processing Network as well



Functional Brain Networks and Aging

- Older adults:
 - ▣ “shrinking” of activity in the Default Network
 - ▣ reduced connectivity in the DN
 - ▣ “expanding” activity in the Task Network
 - ▣ maintained connectivity in the TN
- Default Network may be especially vulnerable to the effects of aging and Alzheimer disease

How might resting state functional connectivity relate to that peak?



Critical meltdown of salient network
vs. additional ↓ default network?

When does window of opp'y
for neuroprotection shut?

*longitudinal study
& fMRI as outcome
measure in clin drug trials*

Baycrest

Enriching Care
Enhancing Knowledge
Enlightening Minds

Also at Baycrest, Quality of Life

for Patient:

- Pain-free
- Safe
- Meaningful activities
 - +/- meaningful social interactions
- Maximal autonomy

For Cgr: *Meaningful*

interaction with patient

- Emotional connection
- “Doing for” ~feeding
- Good downtime together (rest, or even- *fun!?!)*
- Everything that can be done IS being done



NO, IT'S NOT TOO COLD HERE,
BUT YES, I DO MISS THE OCEAN!