Mechanisms of Cognitive Aging

Functional Connectivity and Brain "Noise"

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What is functional connectivity?

- Even if areas in the brain appear to activate selectively for different types of stimulus features or processing, this does not mean that activity in individual areas is solely responsible for cognition

- Brain areas are heavily interconnected anatomically, so it follows that they also are interconnected functionally, i.e., they function as "networks"

- So, we are interested in exploring these network functional connections in young and older adults to see how network activity varies with age
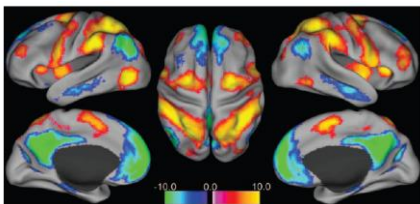

Two major brain networks

Task Network

Default Network

Fox et al, *PNAS*, 2005

Experiment details
Grady et al., Cereb Cortex (2010)

- 19 younger (20-30 yrs, m = 25 yrs); 28 older (56-84 yrs, m = 66 yrs)

- Healthy, community-dwelling, cognitively normal

- fMRI at 3T, block design

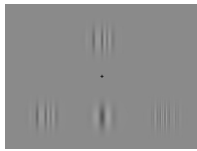- 4 tasks, with stimulus parameters set for 80% accuracy

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Tasks

Detection

Perceptual Matching

Attentional Cueing

Delayed Match to Sample

Alternated with Fixation

Task performance

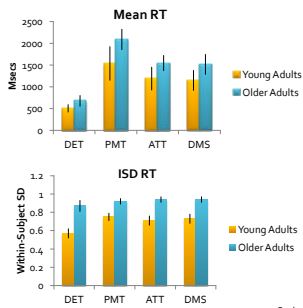Grady et al., *Cerebral Cortex,* 2010

Age differences in the DN and TN

DN, Young only TN, Young only
DN, Old only TN, Old only
DN, Both TN, Both

Grady et al., *Cerebral Cortex,* 2010

FC of the DN during fixation

p<0.002

Functional Connectivity of vmPFC

Correlation

Young   Older

Grady et al., *Cerebral Cortex,* 2010

FC of the TN during tasks

p<0.002   p<0.002

Common FC   Age-Unique FC

Correlation   Correlatioin

Young
Older

DET PMT ATT DMS   DET PMT ATT DMS

Summary

- Both young and old show DN vs TN activity in expected areas
- Young have more extensive DN activity during fixation and old have more extensive TN activity during all tasks
- Functional connectivity in the DN is more vulnerable to age than in the TN
- Older adults show unique FC pattern involving bilateral DLPFC, consistent with expanded TN and with the idea of compensatory activity in older adults
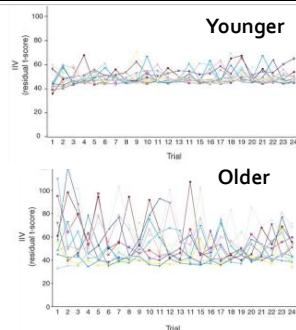

Brain "noise", and why it's important

Behavioural variability increases with age
Macdonald et al., (2006;2009); Dixon et al. (2007)

- **RT variability**
  - Neural inefficiency
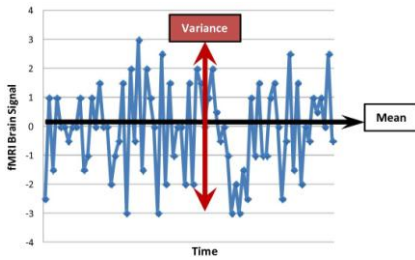 - Random lapses in attention or executive control

Might there be useful information in BOLD Variability?

The brain as a probabilistic neural system (Ma, Beck et al.)

Variability is critical for the nervous system to operate in an optimal, probabilistic manner; essentially, neural variability yields **adaptability** across levels of uncertainty in one's environment

Networks formed in the presence of noise:
- More robust to disruption
- Explore more neural states = enhancing learning and environmental adaptation

Working hypothesis
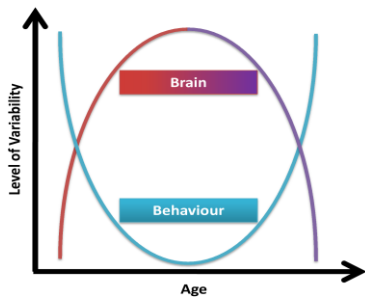
BOLD variability - Key Questions

1. How can we *calculate* a useful form of BOLD variance?

2. Can we find robust *age-related patterns* in what is typically considered "noise" in the brain?
   - Are older or younger brains more variable?

3. What is the *relative predictive utility* of mean and SD-based networks when modeling age?

4. What are the *functional/cognitive consequences* of variability?

Variability "off-task"

- Used data from previously described fMRI experiment in 19 young and 28 older adults

- We first looked at within-subject variability during fixation periods (within-subject SD at each voxel)

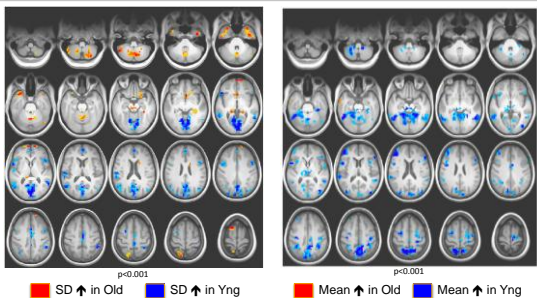- We compared spatial patterns of SD_{bold} to $Mean_{bold}$

SD and Mean brain patterns

p<0.001   p<0.001

🟥 SD ⬆ in Old 🟦 SD ⬆ in Yng   🟧 Mean ⬆ in Old 🟦 Mean ⬆ in Yng

Garrett et al, *J Neurosci*, 2010

How well can we predict age?

Model *R²* = 84.99%

regression
brain measures for mean and SD analyses for object
- Use both sets

Unknow 4.56%

SD: 27.28%

SD

Shared: 53.22%

Mean brain

Mean: 4.94%

Garrett et al, *J Neurosci,* 2010
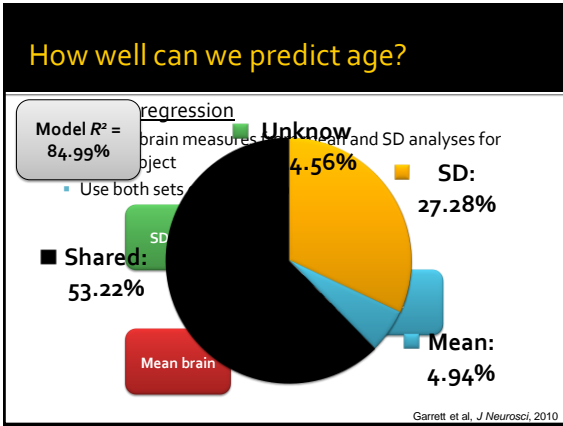
Summary

- BOLD variability during fixation was robust, more predictive of age, and largely non-overlapping with mean-based spatial maps.

- This indicates that BOLD variability is more than just "noise"

- This result suggests that older adults have less flexible brain activity or less ability to explore multiple brain states
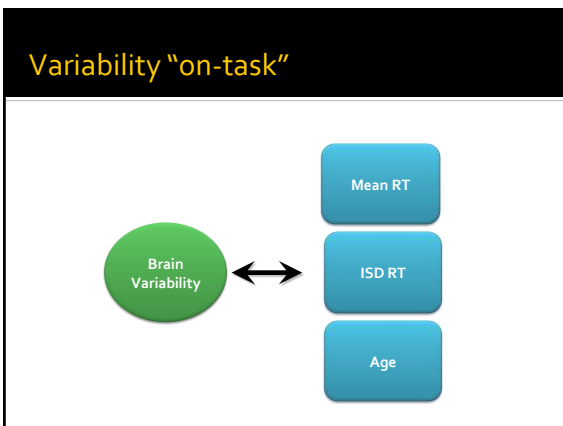
Variability "on-task"

Brain Variability ⟷ Mean RT / ISD RT / Age

BOLD variability and behaviour

Brain and RT variability

- Our results indicate that this brain is *less* variable!
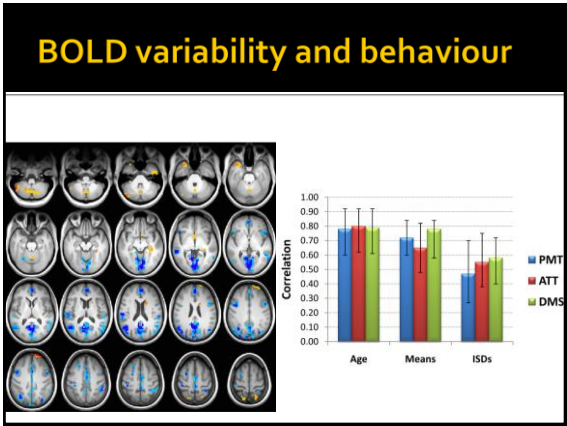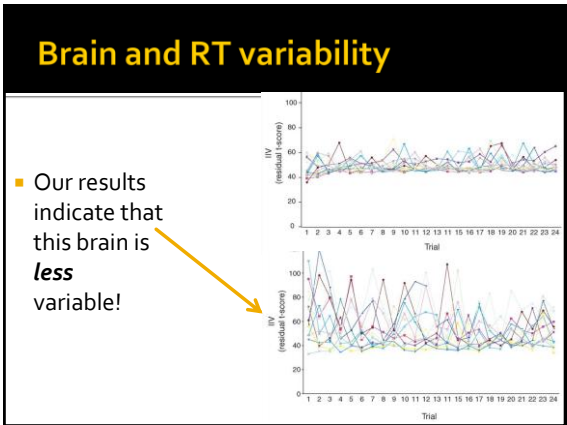
General Summary

- FC differs with age – reduced in DN but maintained, or increased, in TN

- BOLD variability is **differentiated from mean** brain signal, spatially and statistically

- BOLD variability is not just noise, but contains important information about brain function that is **linked to aging and behaviour**

Where do we go from here?

- **Meaning of age differences in FC?**
  - FC is altered with age during tasks and rest
  - How do these interact with each other and influence behaviour?

- **How do we interpret SD changes?**
  - SD and mean patterns are largely non-overlapping, but most literature based on mean activation
  - Remap brain function according to voxel variance
  - Examine changes in BOLD variability as task demands change

Thanks to ....