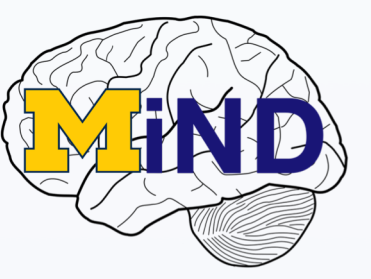




Age-related decline in brain signal variability: Cause and Consequence

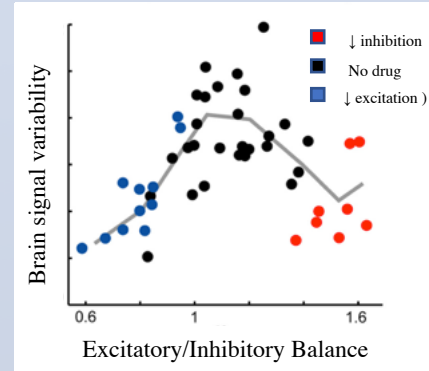


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Background

- Greater brain signal variability is thought to reflect higher flexibility, greater dynamic range and greater multi-stability in cortical neural networks.¹
- Modelling research suggests that inhibitory neurotransmitter levels play a critical role in maintaining brain signal variability.^{3,4}



Aims

- Investigate the effect of age on brain signal variability
- Investigate the association between variability and fluid processing in older adults.
- Investigate the causal link between GABA levels and brain signal variability.

Method

Participants:

- 50 older adults (65+), 50 younger adults
- Healthy native English speakers, MOCA score > 23
- Subset of 24 older and 20 young adults had an fMRI scan on/off Lorazepam (a benzodiazepine that enhances GABA activity).
- Order of scanning between drug and placebo was counterbalanced.

Behavioral Tasks (NIH toolbox)

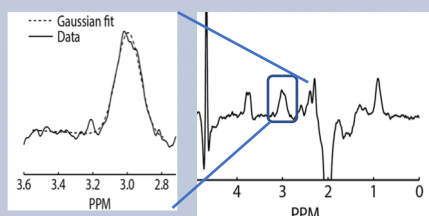
- Flanker Inhibitory task, List Sorting Working Memory, Dimensional Card Sorting, Picture Sequence Memory, Pattern Comparison Processing Speed.

Resting state fMRI (240 volumes, TR = 2sec)

- Pre-processing: Normalization, smoothing, segmentation, slice time correction, motion correction, detrending, bandpass filter, removal of noisy ICA components, registration to MNI template
- Compute SD at each voxel during resting state
- Compute average SD across all voxels in grey matter cortical mask

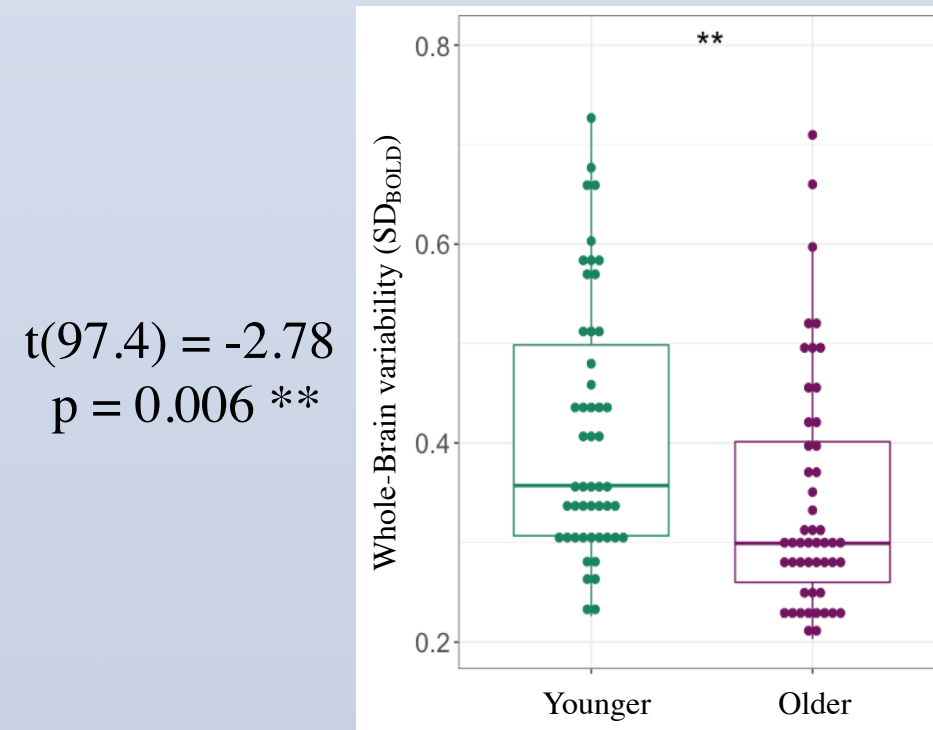
MR Spectroscopy

- MEGA-PRESS Sequence (Frequency selective editing pulses applied at 1.9ppm & 7.46 ppm (OFF))
- Using Gannet 3.0 toolbox a Gaussian curve is fit to the 3.0ppm difference-peak and GABA levels are estimated with reference to water.
- 3*3*3 cm bilateral voxels in the auditory, sensorimotor and ventrovisual cortex.

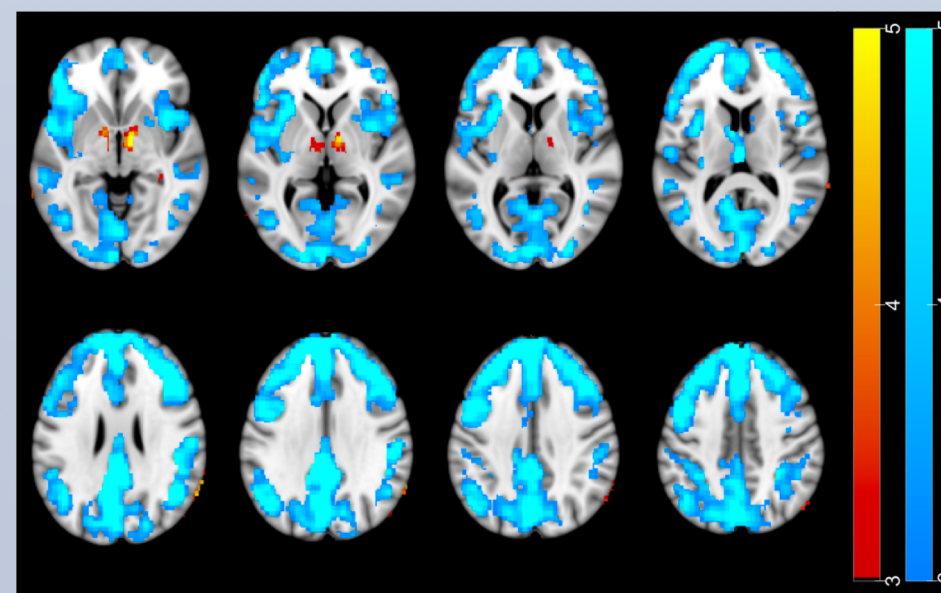


Variability declines with age

Whole-brain SD_{BOLD} declines with age



Spatial pattern of age-effect



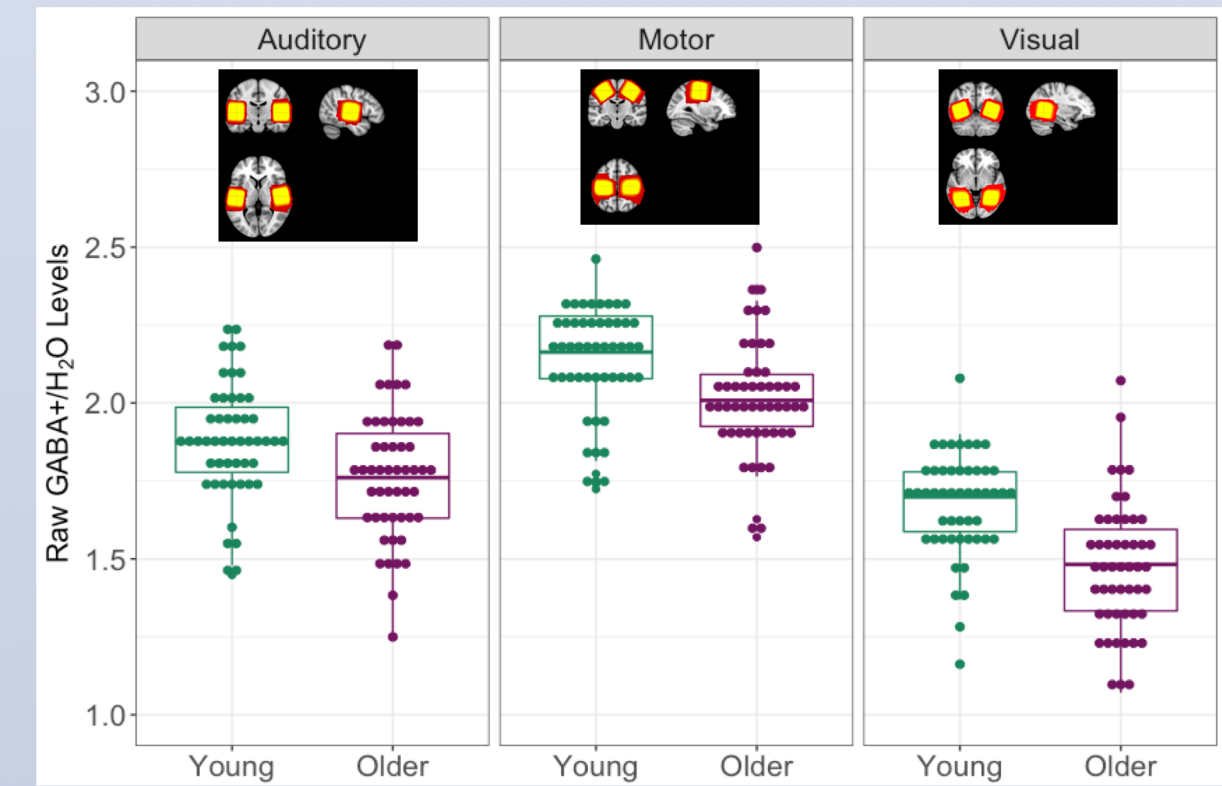
Yellow/Red show an increase with age,
Blue shows a decrease with age
Bootstrap ratios are thresholded at a
value of ≥ 3.00 (99% CI)

Variability and fluid processing ability

Brain signal variability is associated with fluid processing abilities in older adults even after controlling for age and grey matter volume ($r(55) = 0.28, p = 0.038$).

Role of GABA in decline of brain signal variability

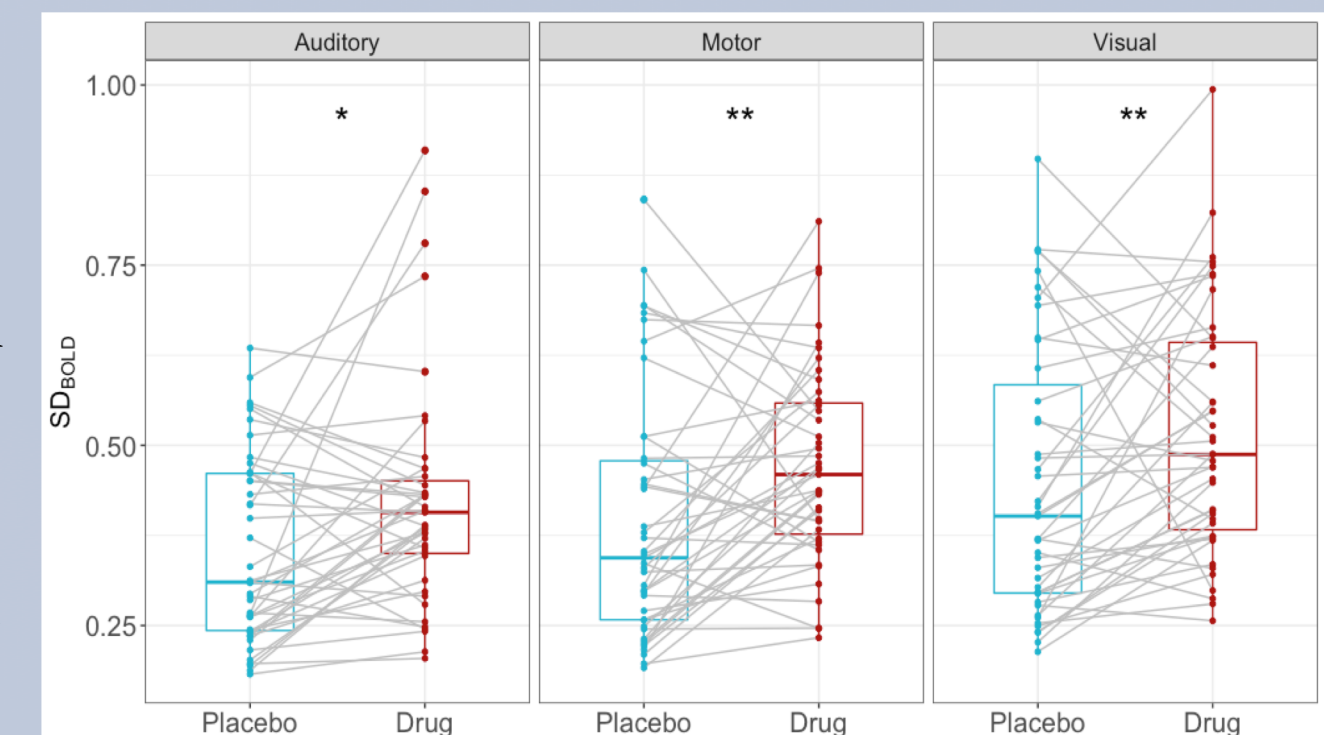
GABA levels are significantly lower in older adults



GABA levels are associated with variability in older adults

	F	p
GABA Levels	5.68	0.019*
Cortical Region	13.74	0.0001***
GABA \times Cortical Region	0.42	0.66

Brain signal variability is significantly greater on drug (increased GABA activity) in comparison to placebo in auditory, motor & visual regions.



Conclusions

- Brain signal variability declines with age
- Individual differences in variability are associated with fluid processing abilities in older adults.
- Age-related decline in GABA levels play a causal role in declines in brain signal variability

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REFERENCES

1. Garrett, Douglas D., et al. (2013) "Moment-to-moment brain signal variability: a next frontier in human brain mapping?." *Neuroscience & Biobehavioral Reviews* 37.4.
2. Grady, Cheryl L., et al. (2014) "Understanding variability in the BOLD signal and why it matters for aging." *Brain imaging and behavior* 8.2.
3. Agrawal, Vidit, et al. (2018) "Robust entropy requires strong and balanced excitatory and inhibitory synapses." *Chaos: Interdisciplinary Journal of Nonlinear Science* 28.10.
4. Shew, Woodrow L., et al. (2011) "Information capacity and transmission are maximized in balanced cortical networks with neuronal avalanches." *Journal of neuroscience* 31.1.

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