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

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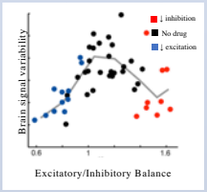
Background

- 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)

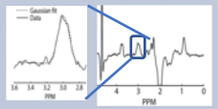
- Flanker Inhibitory task, List Sorting Working Memory, Dimensional Card Sorting, Picture Sequence Memory, Pattern Comparison Processing Speed.

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

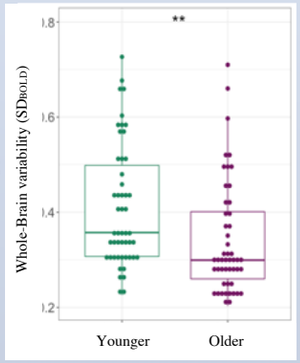
- MEGA-PRESS Sequence (Frequency selective editing pulses applied at 1.9ppm & 7.46 ppm (OFF)
- Using Gannet 3.0 toolbox a Gaussian curve is fit to the 3.0ppm difference-peak and GABA levels are estimated with reference to water.
- 3*3*3 cm bilateral voxels in the auditory, sensorimotor and ventrovisual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



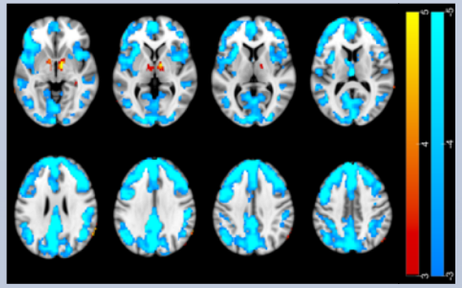
Variability declines with age

Whole-brain SD_{BOLD} declines with age

t(97.4) = -2.78
p = 0.006 **



Spatial pattern of age-effect



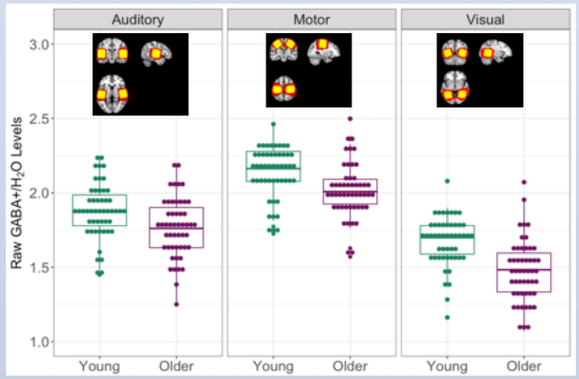
Yellow/Red show an increase with age, Blue shows a decrease with age
Bootstrap ratios are thresholded at a value of ≥3.00 (99% CI)

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

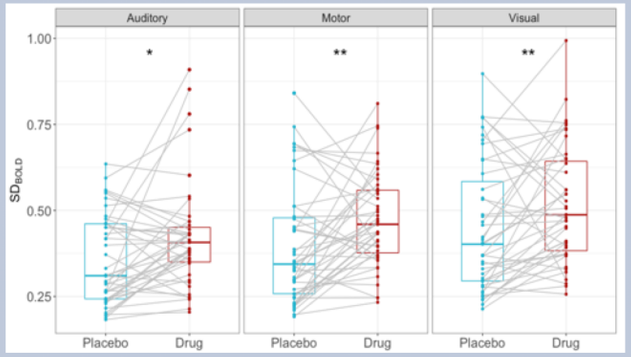
GABA levels are significantly lower in older adults



GABA levels are associated with variability in older adults

	F	p
GABA Levels	5.68	0.019*
Cortical Region	13.74	0.0001***
GABA ✕ 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

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