Age-related change in resting state bold variability: vascular or neuronal?

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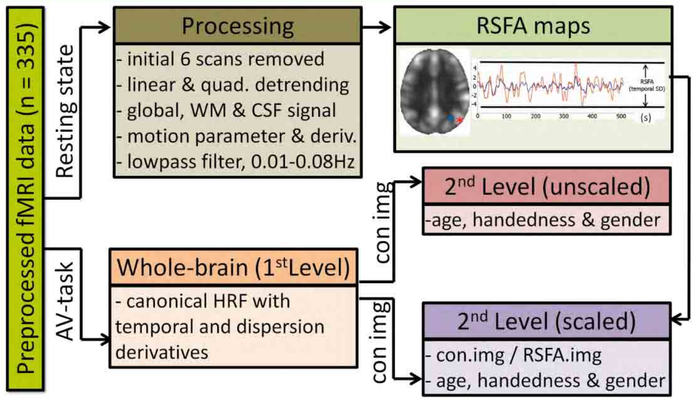
Background

The impact of ageing on the vasculature can have significant effect on the fMRI signal. Therefore, fMRI studies in ageing should include an estimate of vascular reactivity for each subject. Standard approaches that adjust for vasculature changes (e.g. breatholding and hypercapnia) may be difficult for older adults to perform and impractical to implement in large-scale cohort studies. A task-free alternative such as resting state fluctuation amplitude (RSFA) can be implemented to account for age-dependent alterations in the vasculature[1].

Using 335 population-representatitve healthy adults (aged 20-85) from the Cambridge Centre for Ageing and Neuroscience (www.cam-can.com), we applied the RSFA scaling approach to correct for age-related vascular contributions in fMRI-BOLD signal during an audio-visual cued motor task(AV-task). Furthermore, we explored whether RSFA reflects neural variance or it is induced by the vascular properties of the brain tissue.

RSFA application

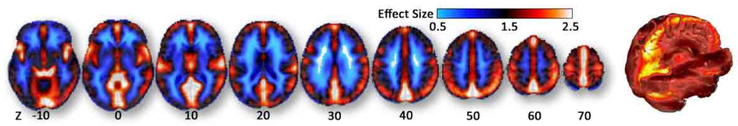
Processing



- FWE-corrected threshold (< .05) on a cluster level was applied

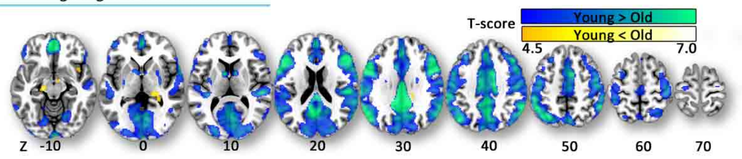
Results

Whole-group RSFA



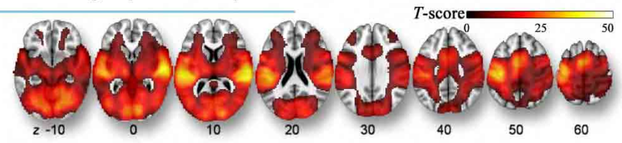
Group RSFA prevailed in the frontal orbital, inferior frontal gyrus, dorso-lateral prefrontal cortex, superior frontal vcortex, frontal cingulate, posterior cingulate and lateral parietal cortex.

Ageing effects in RSFA



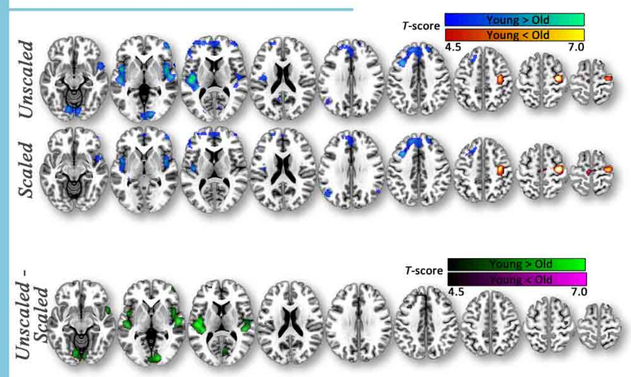
Decrease in RSFA as a funciton of age in the inferior frontal gyrus, dorso-lateral prefrontal cortex, superior frontal cortex, cuneus, precuneus and lateral parietal cortex.

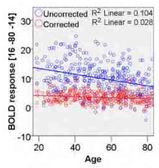
Whole-group AV-task response



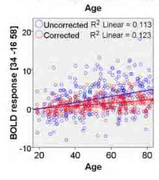
Group BOLD activations in the primary visuval, motor and auditory cortices in response to AV-task stimulation.

Ageing effects in AV-task





Decrease in BOLD response as a function of age in the occipital lobe (blue) is abolished after correcting the AV-task signal with RSFA (red).

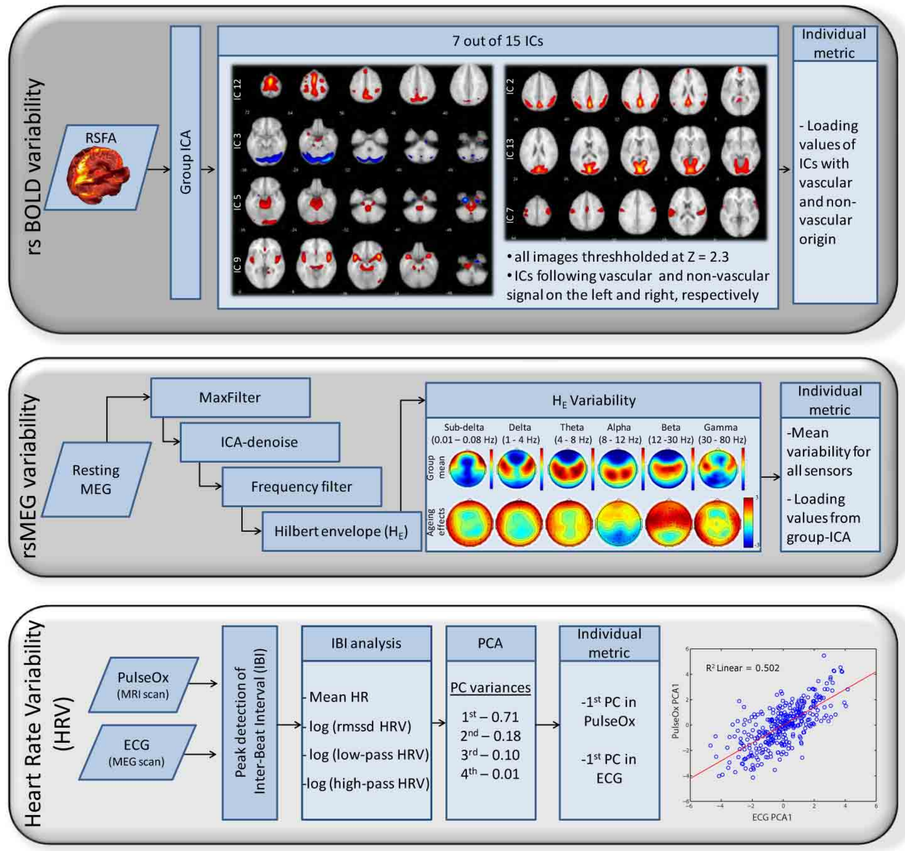


Age-related increase in BOLD response in the right motor areas remains after corrections.

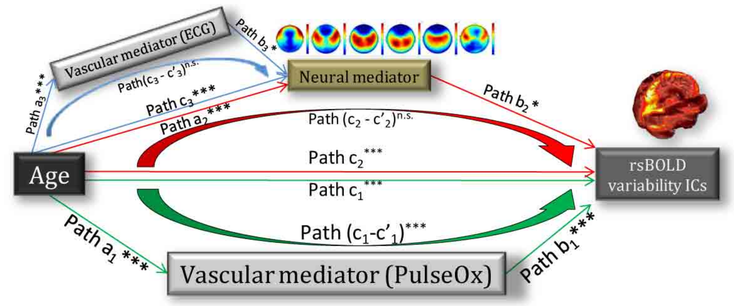
Scaling task-induced BOLD response with RSFA reduced the extend of ageing effects in primary visual, auditory and motor cortices.

RSFA validation

Processing



Mediation Analysis



Path diagram representation of three separate mediation analysis. The analysis revealed that the ageing effects on rsBOLD variability (in all 7 ICs) were significantly mediated by a summary measure of vascular health (green paths), but importantly not by rsMEG variability in any frequency bands (red paths). Also, the ageing effects on the rsMEG variability were not mediated by vascular health measures (blue paths). Asterisks indicate significance levels: * for .01, ** for .001, and *** for .0001.

Summary

- RSFA follow the spatial pattern of vascular reactivity maps from other "calibrating" approaches[1].
- Age-related decreases of RSFA were observed in the inferior frontal gyrus, dorso-lateral prefrontal cortex, superior frontal gyrus, cuneus, precuneus, lateral posterior parietal cortex.
- Age-related decreases in BOLD responses to sensory stimulation was abolished by RSFA-scaling in some, but not all, brain areas. This suggests that some effects of ageing in previous (unscaled) fMRI studies may reflect changes in vascular reactivity with age, rather than changes in neural reactivity
- rsBOLD variability, estimated by RSFA, was modulated by measures of vascular health and was not driven solely by changes in variance of neural activity, estimated by MEG.

Conclusion and Future work

- Comparison of the effects of ageing on resting MEG and fMRI responses during an audiovisual task provides evidence that in many regions, resting state fluctuations/variability are induced by the vascular properties of brain tissue and do not only reflect neural variance.
- RSFA can be used as an estimate of vascular reactivity for correction of non-neural contribution in task-specific fMRI-BOLD signal. This can be particularly useful in large-scale neuroimaging studies of ageing, where alternative measures of reactivity can be impractical.
- BOLD signal variability in task-evoked fMRI data, proposed to reflect variance in neural activity[2], is partially confounded by the vascular reactivity. Adjustment for this confound is possible where age- or group differences in vasculature are present.

References

1. Kannurpatti & Biswal (2008). *NeuroImage, 40, 1567-1574.*
2. Garett et. al. (2010). *JNeuroscience, 30(14), 4914 - 4921.A*