Regional Optical Measures of Cerebrovascular Status Associated with Cortical Volume Outcome within Healthy Aging

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Introduction

Aging is accompanied by anatomical and cerebrovascular deterioration. However, the relationship between regional cortical volume and cerebrovascular status is less clear, as only gross estimates of cerebrovascular health have been available. Recently, we developed a novel tomographic optical method [1] allowing local estimates of cortical vascular status through the measure of arterial compliance. Here, we extracted MRI volumetric and arterial compliance estimates within multiple cortical regions and compared the two measurements. These regions were defined by the cortical boundaries derived using FreeSurfer [2].

Methods

Recordings:

Participants: 47 healthy participants (18-75 years old),

Structural MRI: Structural magnetic resonance images (sMRI) were collected for each participant using a 3T Siemens Trio full body scanner. A high resolution, 3D MPRAGE protocol was used.

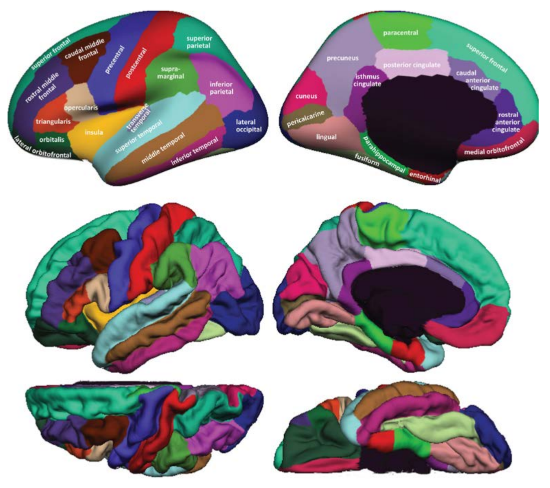
EKG : Lead I of the electrocardiogram (EKG, left wrist referenced to right wrist) was recorded using a Grass Model 12 amplifier with a sampling rate of 200 Hz and a band-pass filter of 0.1 Hz to 100 Hz.

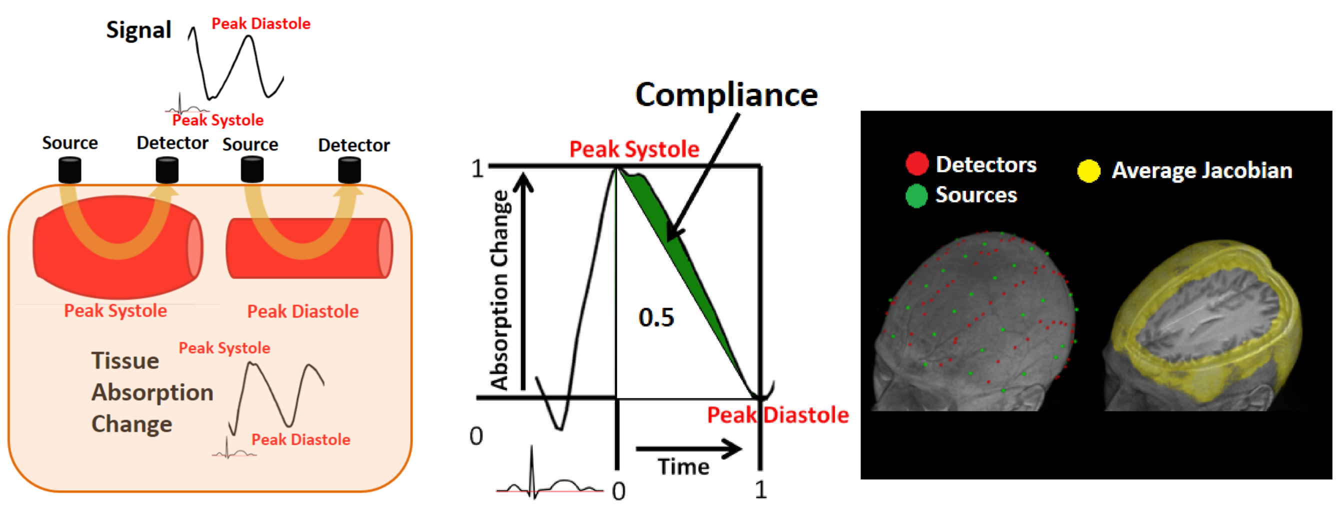
The EKG lead was recorded in order to synchronize the optical pulse data to the R wave (to ensure that the same pulse was examined regardless of location).

Optical : The optical system Imagent, ISS, Champaign, Illinois, was used. It was equipped with 128 laser diodes (64 emitting light at 690 nm and 64 at 830 nm) and 24 photo-multiplier tubes (PMTs). Sampling rate was set to 40 Hz. Light was sent to the scalp by using optic fibers (0.4 mm core) and from the scalp back to the detectors by using fiber bundles (3 mm diameter). 1536 channels were acquired from all the scalp of each participant.

Analysis:

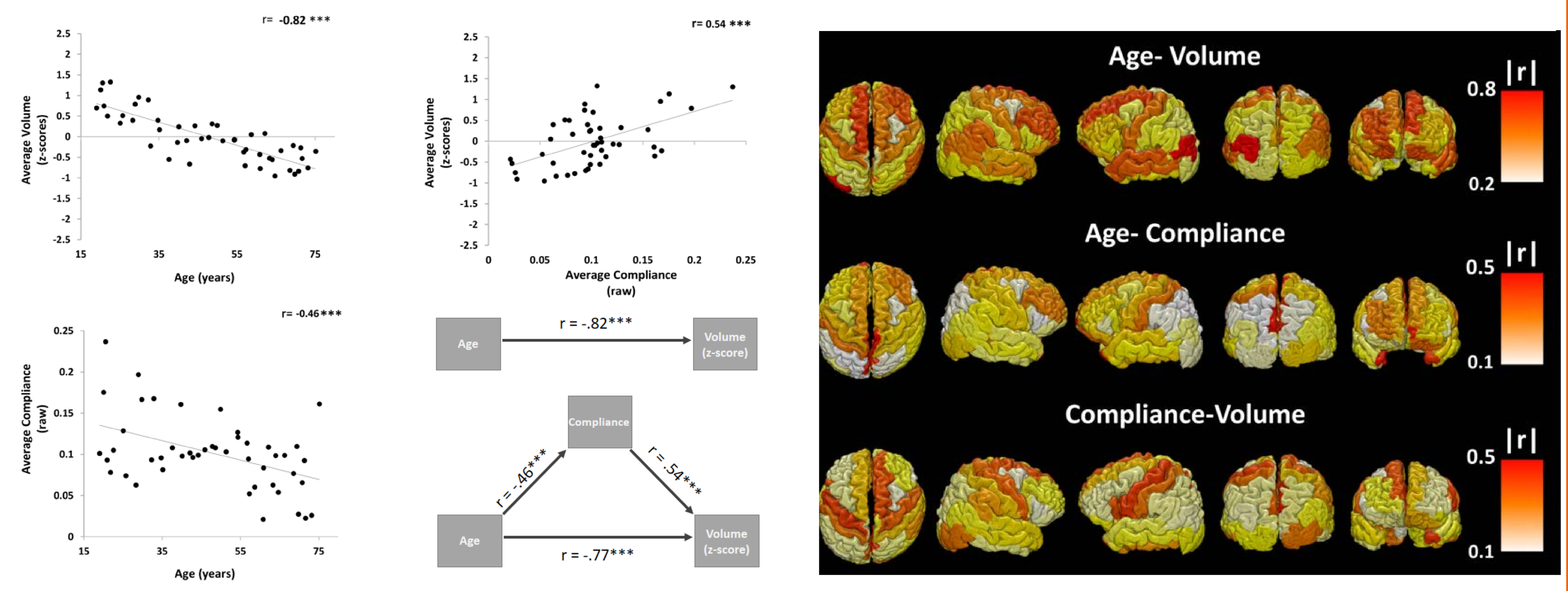
- **MRI segmentation** using Freesurfer:
  - **50** superficial **cortical regions (ROI)** identified.
- **Volume computation** and Intra-cranial volume **normalization** of each ROI .
- Optode-sMRI **co-registration.**
- Optical **signal (DC component) filtering** (0.5-5 Hz).
- **EKG** locked optical signal **averaging.**
- Diffuse Optical Tomography (**DOT**) procedure developed for fNIRS (using **FEM** [3] and **inverse** algorithms [4]) applied.
- Average arterial **Compliance** extracted from **each ROI** and **subject.**
- **Statistical analysis** of **age, Cortical Volume, Arterial Compliance** and their **correlates.**





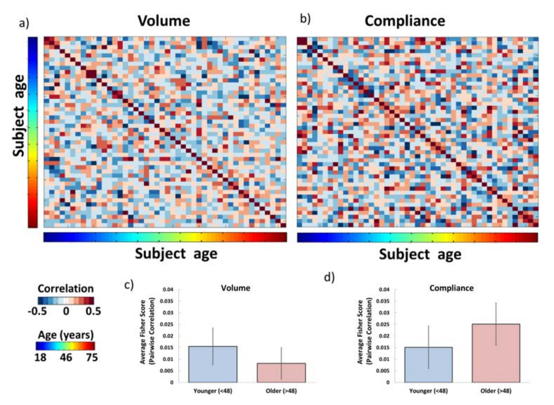
Results:

Between participants analysis:



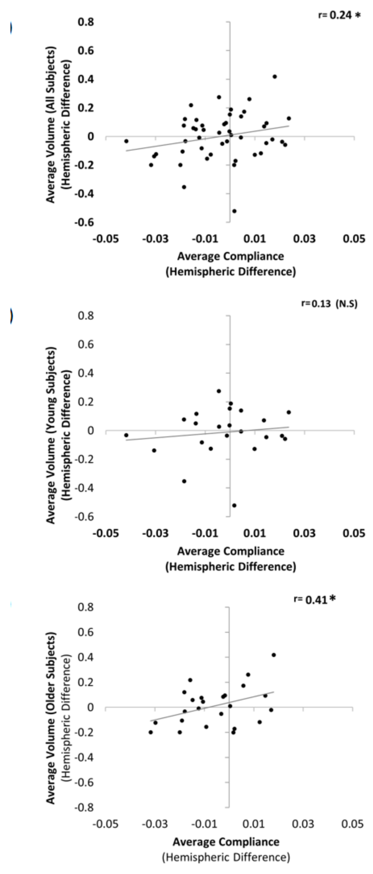
Pairwise spatial correlation analysis:

No particular structure of volume nor compliance was found across subjects, even in the older age group.



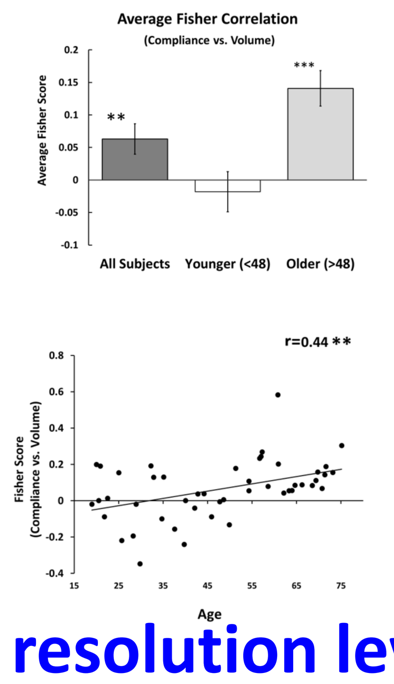
Hemispheric analysis

As a first step for determining possible spatial association between local vascular and volumetric measures within each participant, the relation between hemispheric differences in volume (total right hemisphere volume z scores – total left hemisphere volume z scores) and hemispheric differences in compliance (average right hemisphere compliance – average left hemisphere compliance) was explored. Across all participants analysis showed a significant hemispheric association (r = .24, p< .05). Interestingly, after a median split was performed, only the association of oldest participants (age>48) remained significant.



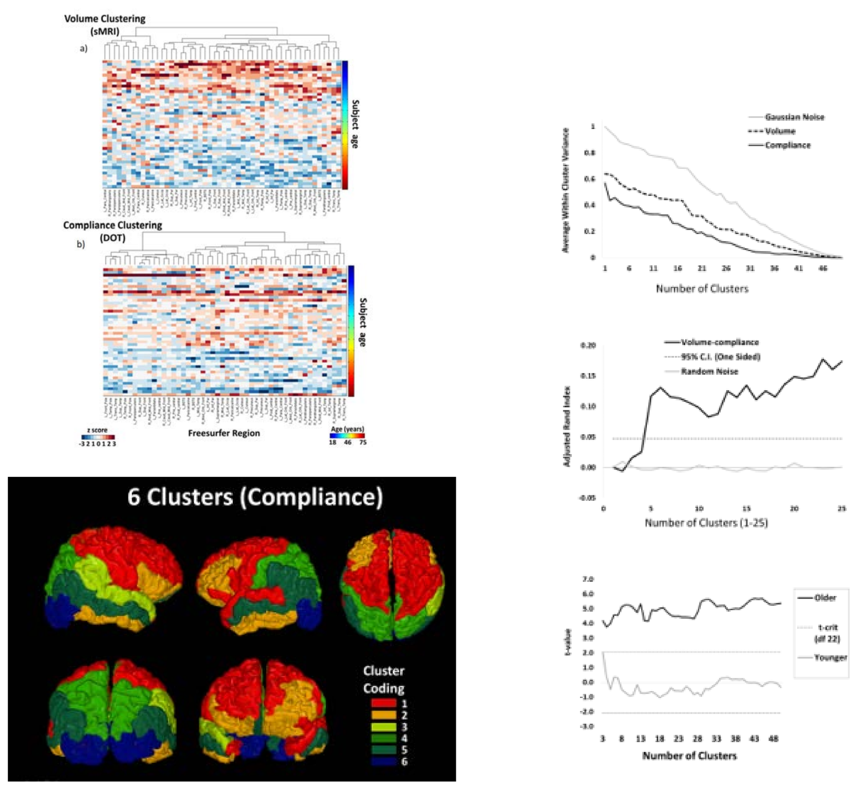
Within participants analysis

Each participant's spatial correlation was performed and Fisher Transformed. The average Fisher score obtained was M=.0632, SEM=.0234 A one-sided t-test revealed that the spatial relationship was significantly different from zero when considering all participants, t(46) = 2.70, p<.01) Median split of age separation revealed that the spatial relationship mainly exists within the older half of participants (age > 48, t=5.17, p<.001), with no significant difference from 0 seen. A positive relationship was found between age and the strength of the spatial relationship r =.44, p<.01.



Within participants analysis at multiple resolution levels: Hierarchical Clustering

We examined the reliability of the spatial correlations found using 50 ROI's as a function of different levels of spatial resolution using hierarchical cluster analysis. The results found on 50 ROIs were replicated at many levels of ROI clustering.



Conclusions

Correlations between age, cortical volume and optical arterial compliance were explored on 47 participants across multiple cortical regions. Between participants analyses revealed a correlation between cortical volume and arterial compliance. Compliance significantly mediated the association between age and cortical volume. Regional correlations revealed an average stronger effect of aging on particular cortical areas. However, no consistent pattern of atrophy was identified in younger nor older adults. Within participants analysis highlighted volume and compliance spatial association. This association was stronger in older participants (age>48 years) than younger participants. By means of hierarchical clustering, this relationship was found to be significant for multiple levels of spatial resolution. These results suggest that some of the variance of sub-clinical atrophy found in aging is associated with worsening of macro- and micro-vascular environments. This may help explain differential atrophy patterns observed across individuals.

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[1] M. Fabiani et. al. Psychophysiology, **51**:1072-1088 (2014); [2] R.S. Desikan et al. NeuroImage, **31**(3):968-80 (2006); [3] H. Dehghani et al. **25**(6), 711-732 (2009); [4] A.M. Chiarelli et al. Journal of biomedical optics 21(3) 036008-036008 (2016).