Anatomical Correlates of Longevity in 905 Elderly Subjects

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Introduction:

Understanding factors that promote longevity is critical for the growing elderly population. Regional brain volumes decline with age, are associated with greater risk for dementias such as Alzheimer's disease and can predict longevity (Good, 2001; Kuller 2007; Sluimer, 2009). Here we used tensor based morphometry (TBM) to localize where differences in brain tissue volumes are associated with longevity and which health factors are significantly associated with survival. Our sample of 905 elderly subjects ranged from cognitively healthy to Alzheimer's dementia. We expected to see greater regional brain volumes in elderly individuals who survived longer, in women versus men (as women tend to live longer), and in individuals with greater mobility, as slower gait has been linked to decline in gray matter and information processing in the elderly (Rosano, 2012).

Methods and Results:

Subjects

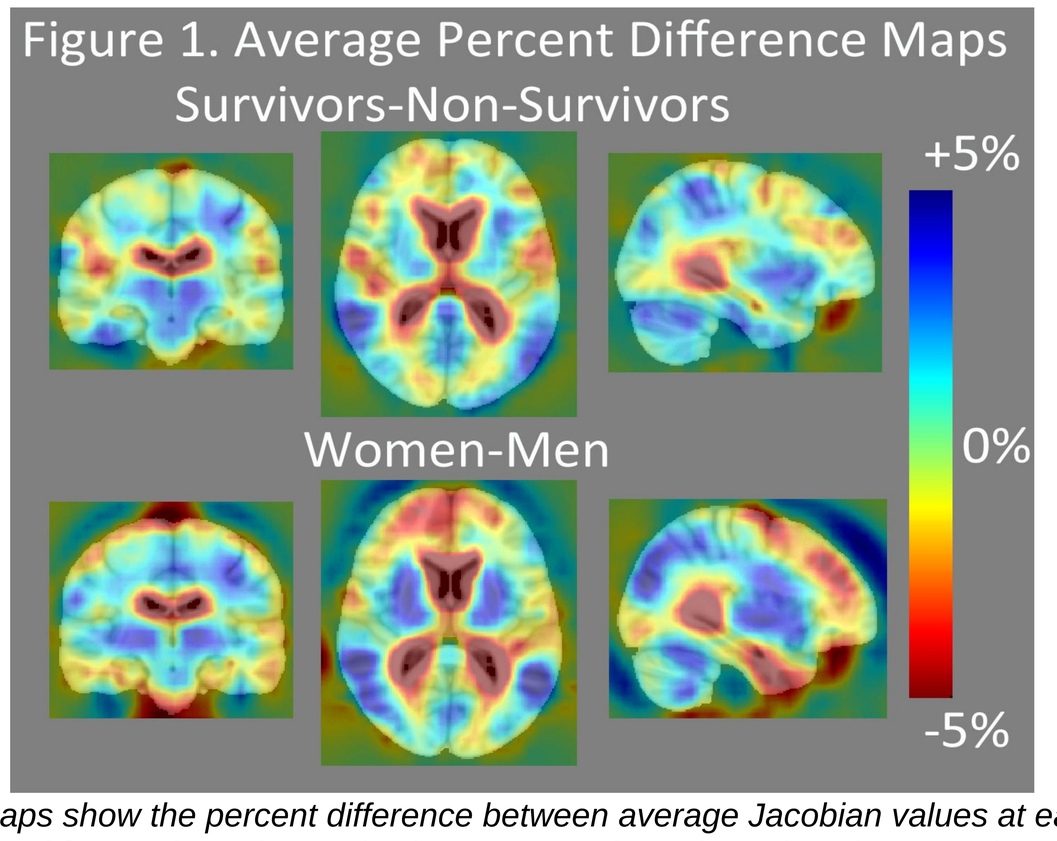
- N=905 subjects scanned by the Cardiovascular Health Study (3D T1-weighted MRI)
- Age: 72.9±4.2 years; Sex: 377 males, 528 Females
- Diagnosis: 693 Controls, 114 Mild Cognitive Impairment, 97 Alzheimer's Dementia

Clinical Measures:

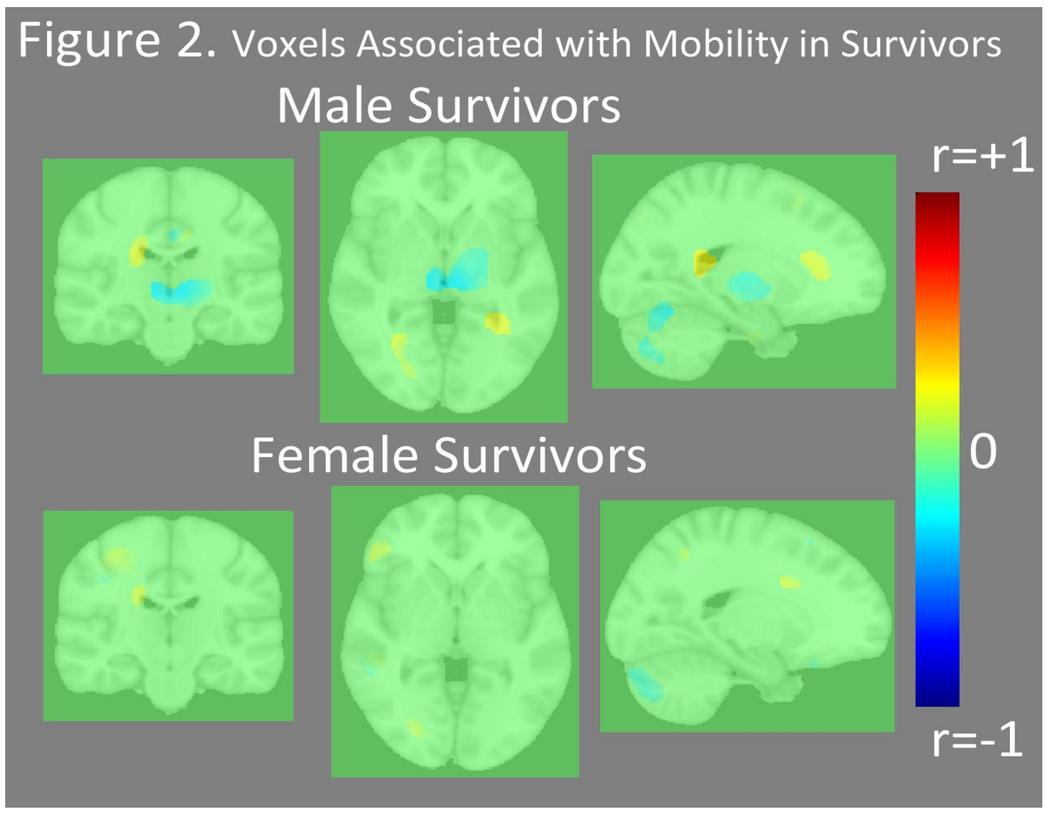
- Longevity: days surviving after date of MRI acquisition (data available up to 8 yrs after scan, subjects alive at this time are considered 'survivors')
- Mobility: seconds taken to walk 15 feet (measured 10 years after MRI acquisition)

Tensor Based Morphometry (TBM)

- Linear registration to study-specific mean template (40 controls in standard MNI space)
- Jacobian values showing expansion or contraction calculated at each voxel
- Multiple regression calculated association between regional brain volumes and longevity at each voxel in all non-survivors, controlling for age, sex, education, diagnosis, and total intracranial volume.
- After separating by sex and survival status, another voxel-wise regression associated mobility with regional brain volumes, controlling for age, education, and diagnosis.
- False Discovery Rate (FDR) corrected for multiple comparisons.



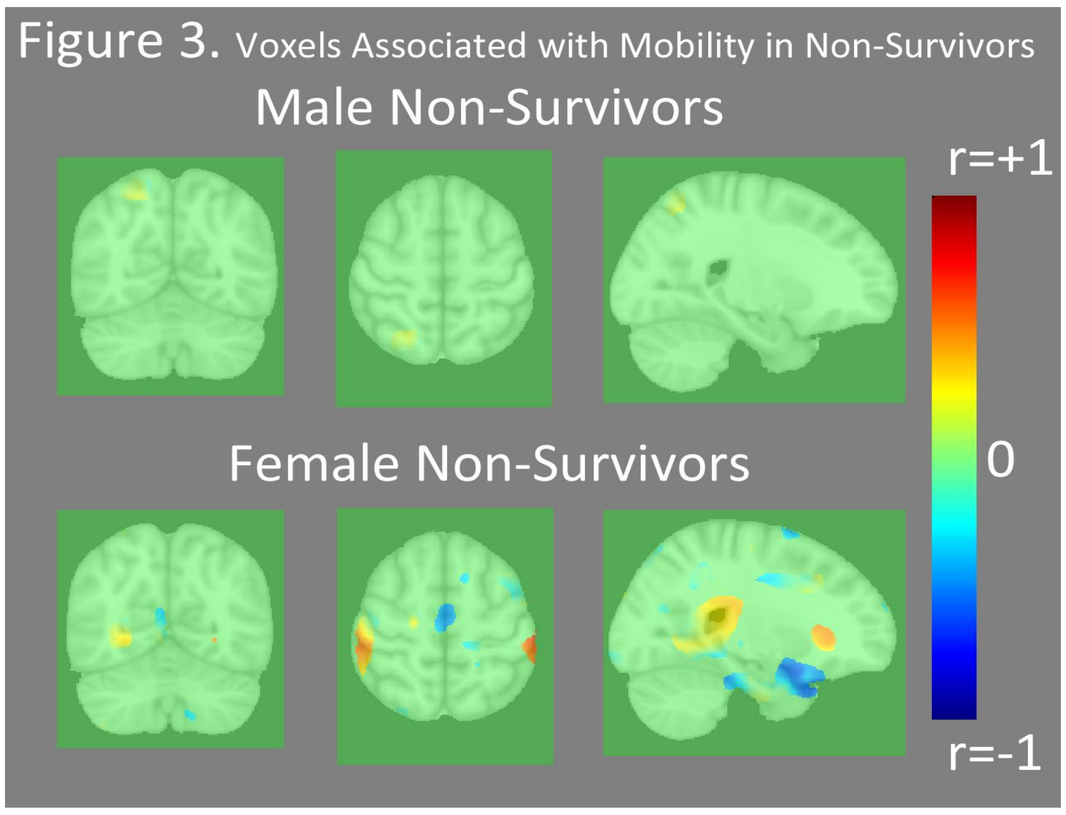
Maps show the percent difference between average Jacobian values at each voxel for survivors (N=823) minus non-survivors (N=82) and women (N=528) minus men (N=377), with the color indicating the percent difference (blue +5%, red -5% average difference) overlaid on the MNI reference brain.



Maps show significant results from the voxel-wise regression of future mobility (seconds to walk 15 feet) in male (N=325) and female (N=498) survivors, controlling for age, education, and dementia status, with color indicating r-value (red: r=+1, blue r=-1) overlaid on the MNI reference brain.

- *Men- thalamus, ventricles, cerebellum, and brainstem*
- *Women- superior parietal lobule, superior frontal gyrus, inferior and medial temporal gyri, and cerebellum.*

Only voxels that pass FDR correction are shown.



Maps show significant results from the voxel-wise regression of future mobility (seconds to walk 15 feet) in male (N=52) and female (N=30) non-survivors, controlling for age, education, and dementia status, with color indicating r-value (red: r=+1, blue r=-1) overlaid on the MNI reference brain.

- *Men- superior lateral occipital gyrus*
- *Women- paracingulate, precuneus, ventricles, temporal occipital fusiform, and inferior and medial temporal gyri*

Only voxels that pass FDR correction are shown.

Discussion:

- Tissue volumes in the inferior lateral occipital cortex were associated with longevity (i.e., survival time after the scan). Occipital lobe anatomy tends to be less variable across subjects, so a global loss of brain tissue may be more sensitively detected in this area. Gray matter and cerebral blood flow decline with age (Good 2001; Chen 2010) in the occipital lobes, and these effects may be pertinent to survival.
- We also identified multiple brain regions preserved in survivors, which were associated with future mobility in both survivors and non-survivors. Greater tissue volume may be protective and linked with longevity.
- Identifying specific protective and risk factors for cognitive decline in aging may enable targeted interventions to promote successful aging.

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