

Introduction

Long-term alcohol dependence (AD) is known to be associated with cognitive impairments and brain atrophy, but there is evidence that both phenomena may be at least partially reversible with long-term abstinence. Many recent studies have found a relationship between short-term abstinence and neurocognitive recovery, with some longitudinal studies finding brain volume recovery within the first few weeks of abstinence from alcohol. We have previously demonstrated normal cognitive functioning in a group of middle-aged long-term abstinent alcoholics (LTAA), with the exception of some persistent deficits in the spatial processing domain, suggesting abstinence-related recovery in many brain regions normally affected by AD. In the current study, we examined regional gray matter volumes in the cerebral cortex of these LTAA vs. age- and gender-comparable non-alcoholic controls (NAC), specifically looking for persistent atrophy within the parietal lobe, which is involved in spatial processing.

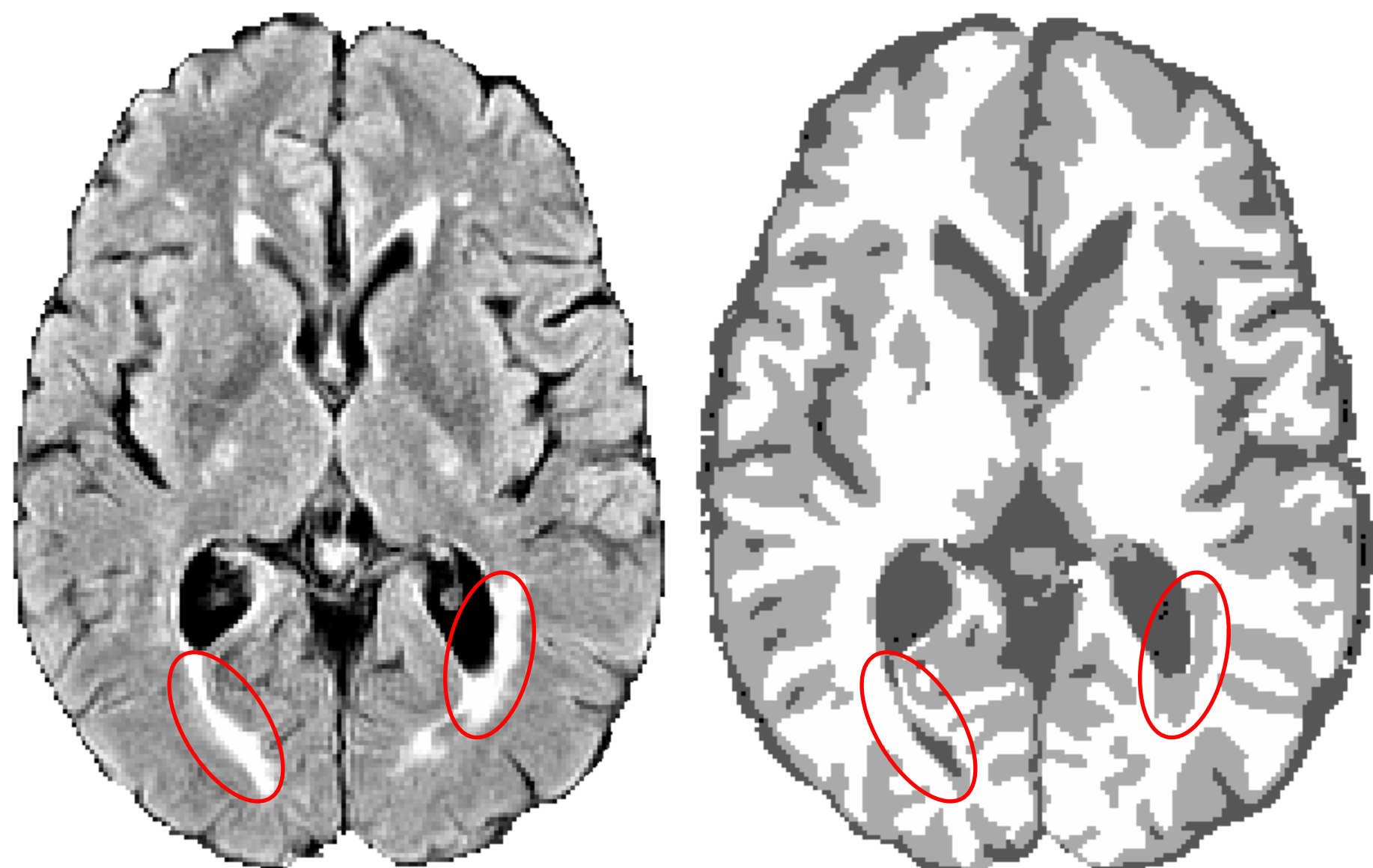
Methods

Data

- 52 LTAA (at least six months abstinent) and 48 NAC. Both groups ranged from 34 to 60 years old.
- Subjects underwent three sessions of psychological and cognitive testing.
- Structural brain MRIs: T1-weighted and FLAIR images.

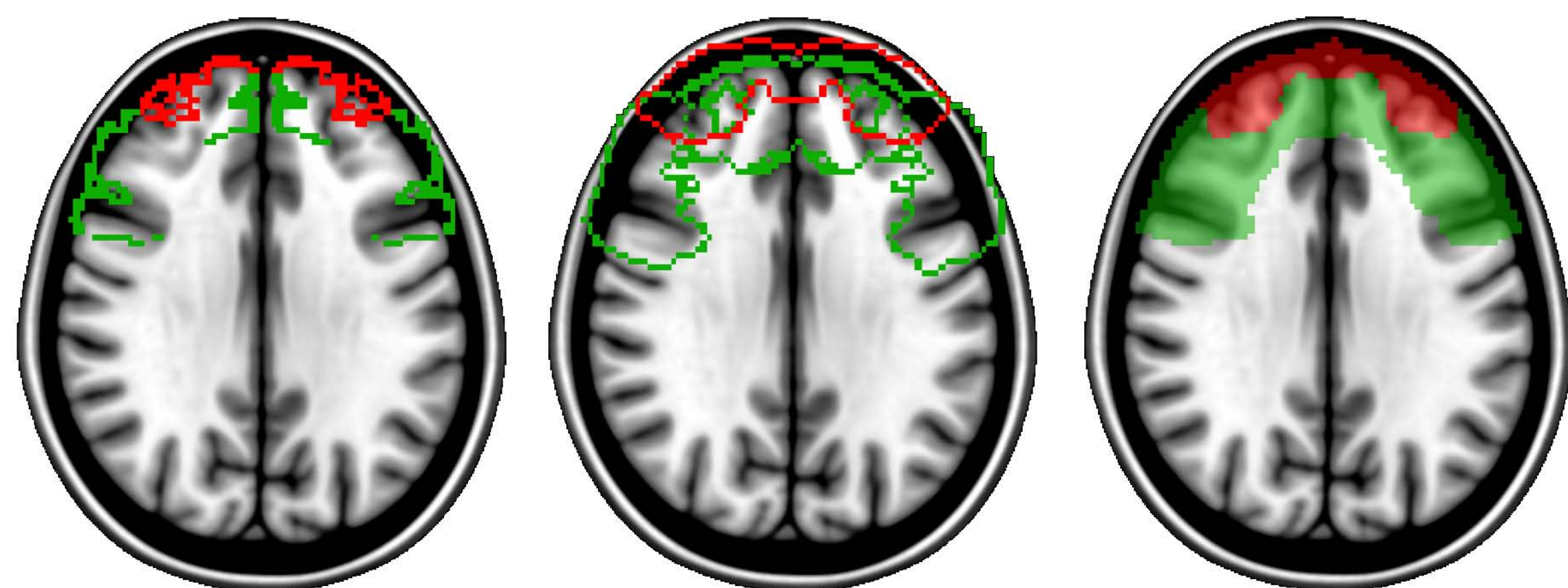
Image Processing

- T1 images were segmented into three classes (gray matter, white matter, and cerebrospinal fluid).
- The FLAIR images were used to correct areas of misclassified white matter consequent to white matter lesions.



White matter lesions, which are hyperintense in FLAIR images (left), are darker in T1-weighted images, causing segmentation algorithms to misclassify affected areas as gray matter or CSF (right).

- Regions of interest (ROIs) were created from the Talairach atlas by assigning each zero-voxel the value of its nearest non-zero neighbor.
- This provided good coverage of the cortex while overcoming the inherent problem of overlap in conventional dilation.



Left: Brodmann area-based definitions of the orbital frontal cortex (red) and the dorsolateral prefrontal cortex (green). **Middle:** Dilation of each of these areas by 6 mm does a good job of covering the gyral infoldings, but creates significant overlap between the ROIs. **Right:** Our nearest neighbor interpolation method effectively covers the cortex without the overlap caused by dilation.

- The ROI masks were transformed from standard space to T1 space to fit each individual brain.
- An automated in-house algorithm corrected for registration inaccuracies and inter-subject variation of the cortex.
- This was achieved by including small parts of the cortical sheet that were missed by the mask and excluding unconnected gyri belonging to nearby cortical regions.

Results

We adjusted the gray matter ROI volumes for differences in premorbid brain size (based on the FSL cranium size estimate obtained from sienax) before performing an ANCOVA to remove the age effects between subjects. We found significantly reduced gray matter volumes within the parietal lobe and visual association and primary visual areas of the occipital lobe.

Region	Non-Alcoholic Controls		Long-Term Abstinent Alcoholics		Effect Size (%)		
	Male (n=25)	Female (n=23)	Male (n=28)	Female (n=24)	Group	Gender	Group x Gender
Cerebral Cortex	441	422	414	418	7.0**	1.8	3.7
Frontal Lobe	148	142	139	142	2.5	0.5	3.4
Posterior Prefrontal	13.0	12.1	12.2	12.4	0.6	0.7	2.5
Lateral Prefrontal	17.6	16.6	17.3	17.4	0.7	2.2	4.5*
Dorsolateral Prefrontal	24.6	23.8	23.4	23.8	1.7	0.2	1.4
Orbital Frontal	44.1	41.7	41.5	42.8	1.0	0.5	6.0*
Primary Motor	3.39	3.42	2.75	2.98	8.5**	0.5	0.4
Supplementary motor	29.0	27.7	26.5	26.9	3.7	0.3	1.0
Insula	13.4	12.9	12.8	12.7	4.4*	1.7	0.6
Limbic Lobe	57.6	55.3	55.9	56.0	0.4	2.0	2.3
Anterior Cingulate	17.7	17.2	16.7	16.8	5.7*	0.3	0.8
Occipital Lobe	51.3	48.7	45.4	46.1	12.5***	0.7	2.0
Anterior Occipital	2.63	2.60	2.52	2.54	1.0	<0.1	<0.1
Visual Association	38.5	36.4	33.5	33.8	14.8***	0.8	1.7
Primary Visual	3.51	3.17	2.90	3.11	7.3**	0.3	5.3*
Parietal Lobe	68.2	64.4	60.4	61.5	10.0**	0.6	2.2
Mesial Parietal	28.5	26.9	25.6	25.5	6.7*	1.1	0.9
Lateral Parietal	24.5	23.5	21.9	22.4	10.1**	0.1	1.8
Primary Sensory	8.70	7.93	7.30	7.68	9.1**	0.5	4.6*
Temporal Lobe	103	99.3	100	99.2	1.5	4.4*	1.4
Superior Temporal	18.7	18.6	18.2	18.3	1.5	<0.1	0.2
Mesial Temporal	38.5	36.6	37.3	36.8	1.1	4.8*	1.7
Inferior Temporal	18.8	17.8	19.8	19.0	6.9**	3.8	<0.1

All volumes are expressed in cm³.
 Effect is significant: * p ≤ 0.05, ** p ≤ 0.01, *** p ≤ 0.001.

Given the decreased spatial processing scores and lower parietal lobe volumes within the LTAA compared to the NAC, we performed correlations between these two measures and found a significant relationship between tissue loss and decreased performance on spatial processing tasks within the LTAA men, but not in the NAC group or LTAA women. We also found significant relationships between increased alcohol consumption and decreased parietal, frontal, and temporal lobe volumes in men; however, gray matter volumes of the frontal and temporal lobes did not differ between groups. Frontal lobe volumes appeared to correlate strongly with abstinence duration, but abstinence was confounded with alcohol intake and age, making it difficult to conclude a causal relationship.

Discussion

We performed ROI-based gray matter volume analyses on a group of middle-aged men and women abstinent from alcohol for an average of 6.3 years. We found that there were regional areas of persistent gray matter loss present in the LTAA compared to NAC, particularly within the spatial processing and visual association areas of the parietal and occipital lobes. The parietal lobe shrinkage was consistent with our previous report of spatial processing deficits in this sample of LTAA. More compelling, in LTAA, the magnitude of parietal gray matter loss was negatively associated with spatial processing domain performance and positively associated with average lifetime alcohol consumption.

The data suggest that region-specific recovery of alcohol-related gray matter damage occurs with very long-term abstinence. The absence of persistent atrophy in the prefrontal and temporal lobes, which are known to undergo atrophic changes due to alcohol dependence, are consistent with the intact memory and executive function in this sample.

Conclusions

- LTAA suffer from persistent gray matter volume loss in the occipital and parietal lobes.
- The severity of parietal lobe shrinkage is related to spatial processing performance and average lifetime alcohol intake in men.
- The absence of group differences within the frontal and temporal lobes, which are known to be affected by heavy alcohol consumption, indicate possible recovery with abstinence.

