

Early adolescent development is impacted by heavy alcohol use: Preliminary evidence of grey matter changes using VBM.



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INTRODUCTION

- Heavy alcohol use in adolescents has been associated with changes in brain structure, function and cognition. While a number of studies in heavy alcohol using adults have shown an impact on brain structure¹, the extent to which (1) these findings can be translated into the developing brain of adolescents, and (2) the reliability with which the finding can be isolated to being the specific effect of alcohol remains unclear. A number of studies are now underway in adolescents in which these questions are being addressed. Few if any have been able to exclude the co-existing use of other drugs of abuse². As such, the ability to disentangle the effects of alcohol from other substance remain limited.
- Adolescence is a period of rapid brain development. Synaptic growth and pruning in widespread brain regions including the prefrontal and temporal cortices as well as sub-cortical areas including the thalamus¹.
- In the Cape Town region of South Africa, a relatively unique opportunity exists to examine the effects of alcohol use on the developing brain of adolescents who have recently begun drinking heavily and who do not use other substances.
- The aim of this ongoing study is to examine differences in regional grey matter (GM) volumes and white matter (WM) parameters such as fractional anisotropy (FA) and mean diffusivity (MD) in adolescents aged 13-15yrs who are heavy alcohol users without any history of co-morbid psychiatric disorders or other substance use.
- Previous research have shown decreases in prefrontal GM volumes and decreased fractional anisotropy (FA) in frontal association fibers as well as the splenium of the corpus callosum².

METHODS

- Heavy alcohol using (DSM IV Alcohol Abuse/Dependence) adolescents aged between 13-15yrs and of mixed racial origin (Coloured) were recruited from elementary schools in Cape Town, South Africa.
- Psychiatric, developmental and other substance abuse disorders were exclusion criteria with informed consent obtained from parents and written assent from the subjects.
- MRI was conducted on a Siemens Magnetom 3T Allegra located at the Cape Universities Brain Imaging Centre, Stellenbosch University.
- Three DWI sequences with 30 diffusion directions and $b_0=1000\text{m/s}^2$ were acquired with the following parameters: TR=8800, TE=88, 960x960x60 mosaic matrix and slice thickness of 2.2 mm.
- A high-resolution T1 image was acquired as follows: TR=2080, TE=4.88, 256x192x176 matrix and slice thickness of 1mm.
- Grey matter volumes were measured using a voxel-based morphometry (VBM) approach with FSL³. The T1 images were brain-extracted using BET, GM segmentation was performed using FAST, the partial GM volume images were affine and non-linearly registered to MNI152 space. These images were then used as the study-specific template to which all subjects' T1 data were aligned. Voxelwise statistics were performed at $p<0.05$ corrected.
- The sample in this interim VBM analysis includes 43 heavy drinkers (24 males and 19 females), and 41 (20 males and 21 females) age, education, and socio-economic status matched controls. For the WM analysis the cohort sizes were 22 controls (13 males and 9 females) and 22 heavy drinkers (11 males and 11 females). FA and MD maps were extracted from the DWI tensors using tools from FSL.
- Final analysis was carried out in TBSS (a toolbox of FSL).⁴ The MD and FA maps were projected onto a study-specific mean FA tract skeleton and voxelwise statistics were carried out at a $p<0.05$ corrected.

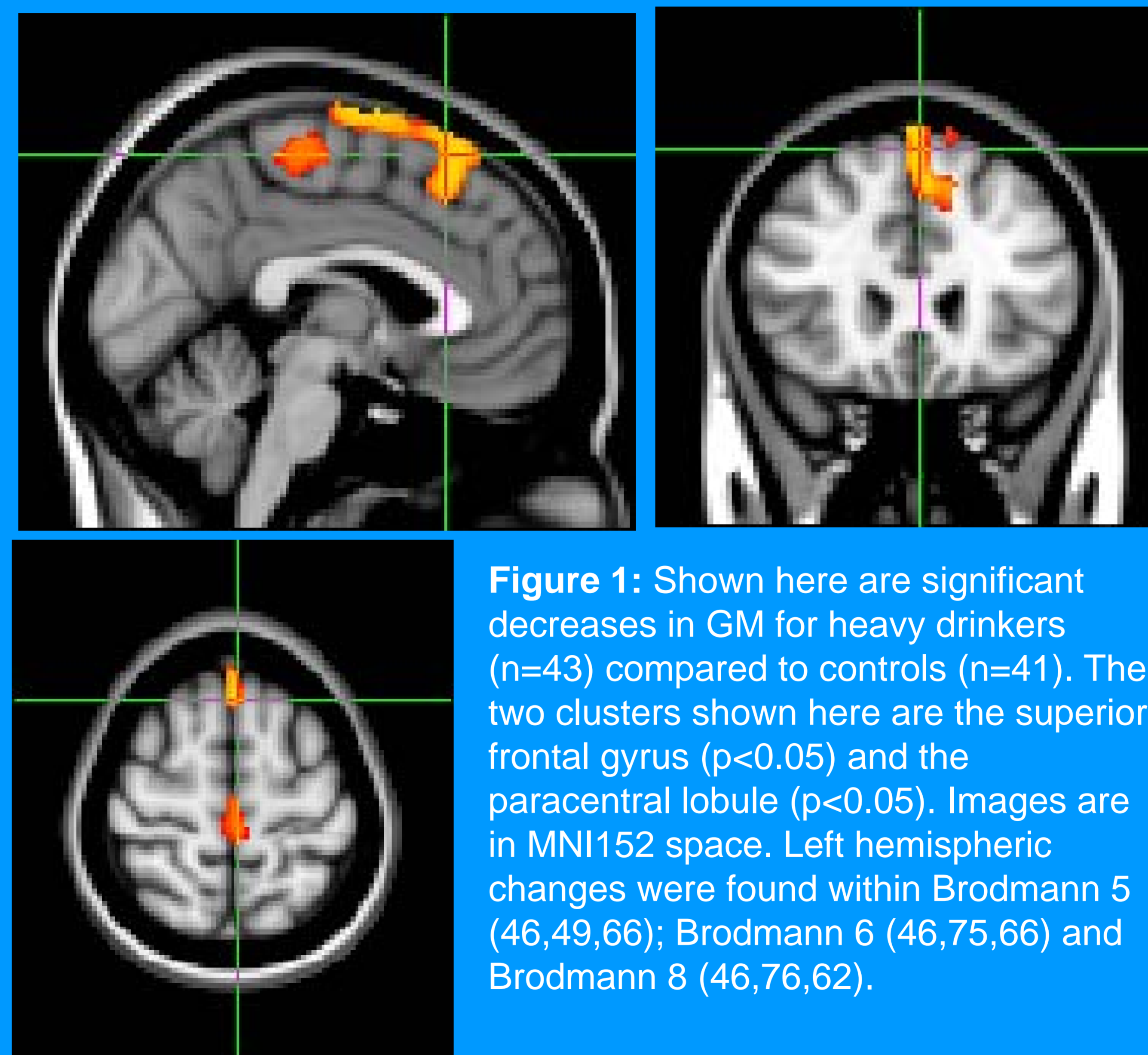


Figure 1: Shown here are significant decreases in GM for heavy drinkers (n=43) compared to controls (n=41). The two clusters shown here are the superior frontal gyrus ($p<0.05$) and the paracentral lobule ($p<0.05$). Images are in MNI152 space. Left hemispheric changes were found within Brodmann 5 (46,49,66); Brodmann 6 (46,75,66) and Brodmann 8 (46,76,62).

RESULTS

- Decreases in GM volume as determined by VBM were found for the adolescent heavy drinkers compared to healthy matched controls.
- Three were located in Brodmann 6 and 8 in the superior frontal gyrus and Brodmann 5 in the paracentral lobule.
- The clusters were thresholded at a p-value of 0.05 with no cluster threshold (as threshold-free cluster enhancement was used (TFCE)).
- The Brodmann regions correspond to the premotor cortex, the somatic sensory association cortex and the frontal eye fields.
- As expected no decreases in GM volume were found for the control cohort compared to the heavy drinkers.
- For the TBSS analysis no significant increases or decreases were noted in FA or MD.

DISCUSSION

- During adolescence, the frontal lobe, associated with planning, inhibition, emotional regulation and integration of stimuli goes through phases of maturation increasing in efficiency⁵.
- Our results demonstrate that smaller frontal brain volumes – specifically the pre-motor cortex, somatic sensory association area and frontal eye fields are evident in heavy alcohol users.
- We did not find prefrontal cortex decreases in heavy drinkers as shown by previous studies in adolescence².
- In the TBSS analysis, no differences in MD between groups were found. This contrasts with evidence from previously published work². We also found none of the hypothesized group differences in FA. In par this may be due to the smaller sample size in this cohort (n=22 for controls and heavy drinkers). It may also be possible that FA measurements, usually sensitive to microstructural changes in WM, may not be as vulnerable in 13-15 year old adolescents at this early phase of their alcohol use trajectory.

References:

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