Effects of Binge Drinking on regional gray and white matter: a preliminary MRI study

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INTRODUCTION

Binge Drinking (BD) pattern is defined as high alcohol intake (4 or more drinks for women and 5 or more for men) in a short time (about 2 hours) followed by periods of abstinence. This pattern of excessive drinking is very common among adolescents and college students (NIAAA, 2014; Courtney & Polich, 2009).

Particularly, adolescence is a phase of great physiological changes including intracellular events (e.g. loss of neurons/ increase of myelin sheaths) essential to brain's reorganization and refinement. This period of structural immaturity of cortical and subcortical regions, namely in the dorsolateral and orbital prefrontal cortex, anterior cingulate cortex and basal ganglia is related to a diminished capacity of the inhibition system during this life period, leaving adolescents more prone to take risky choices (e.g. excessive alcohol consumption) (Crews & Boettiger, 2009; Bava & Tapert, 2010; Bari & Robbins, 2013). Consequently, significant exposure to alcohol during this developmental stage may adversely affect a wide variety of neuromaturational processes. In fact, literature review suggests structural abnormalities of the prefrontal, parietal and temporal lobes, cingulate cortex, basal ganglia and cerebellum as putative neural signatures underlying BD during adolescence and early adulthood (see Hermens et al., 2013 and López-Caneda et al., 2014 for a review).

In this study, based on the neurocircuitry of addiction proposed by Crews and Boettiger (2009) we hypothesize that alterations within specific brain regions related to impulsive behaviors might be found in a BD pre clinical sample. Therefore, we performed a VBM study in a group of 20 participants with BD pattern of consumption and 16 abstinent controls.

RESULTS

Differences between BD and AC regional gray and white matter densities were found in bilateral middle frontal gyrus. Table 1 and image 1 illustrate gray matter data. Table 2 and image 2 demonstrate areas where white matter peak-level densities were higher in the BD group.

Table 1: SPM stats showing gray matter differences in inhibitory circuitry between Binge Drinkers and alcohol-abstinent subjects

Anatomical Label	Direction of difference	MNI Coordinates[a] x y z	Cluster size (K_E)	Peak *t* score	*p* value [b] (uncorrected)
Male					
Frontal_Mid_L	Increased in BD	-42 29 35	271[c]	4.91	0.000
Frontal_Mid_R	Increased in BD	33 23 33	182[c]	4.90	0.000

[a] Montreal Neurological Institute coordinates of the voxel of maximal statistical significance within each region
[b] Statistical significance set to p<0.001, uncorrected for multiple comparisons at voxel level
[c] Cluster size calculation set to minimum of 29 voxels, AlphaSim p<0.05

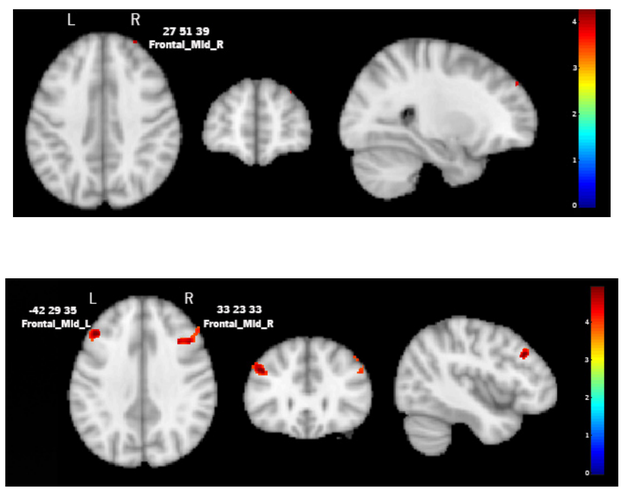


Image 1

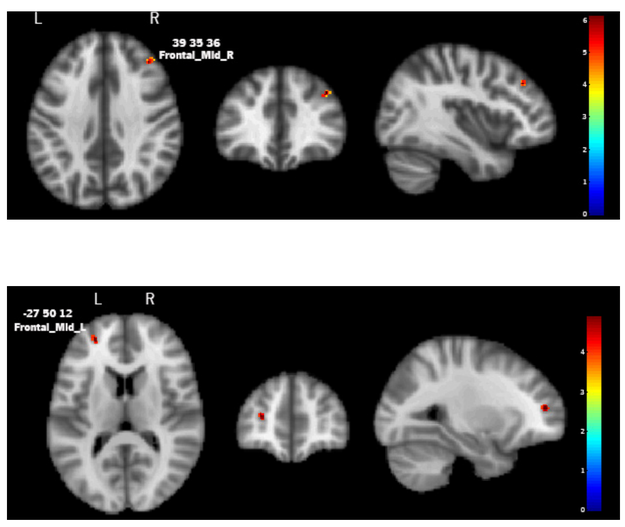


Image 2

Table 2: SPM stats showing white matter differences in inhibitory circuitry between Binge Drinkers and alcohol-abstinent subjects

Anatomical Label	Direction of difference	MNI Coordinates[a] x y z	Cluster size (K_E)	Peak *t* score	*p* value [b] (uncorrected)
Female					
Frontal_Mid_L	Increased in BD	-27 50 12	39[c]	4.88	0.000
Male					
Frontal_Mid_R	Increased in BD	39 35 36	40	6.09	0.000

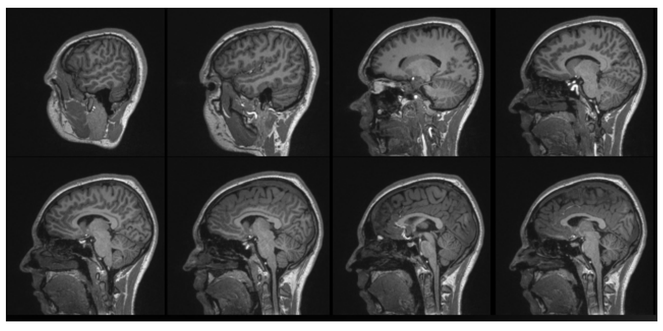
[a] Montreal Neurological Institute coordinates of the voxel of maximal statistical significance within each region
[b] Statistical significance set to p<0.001, uncorrected for multiple comparisons at voxel level
[c] Cluster size calculation set to minimum of 29 voxels, AlphaSim p<0.05

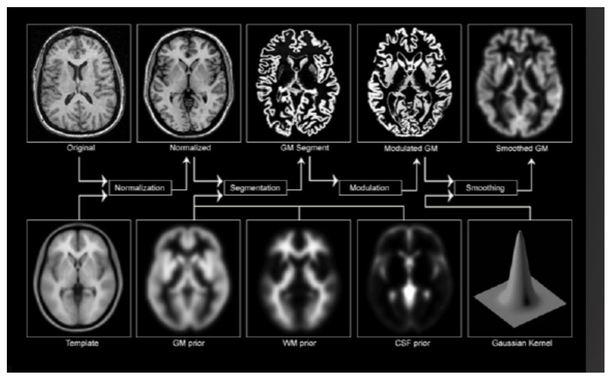
METHOD

Participants

Group	Men	Women	Total	Mean age
Binge Drinking	10	10	20	20
Abstinent Controls	6	10	16	20
Total	16	20	36	

Image Acquisition 1 wighted scans were obtained on a Siemens 3T magnet with TR = 2700ms ; TE = 2.33ms; slice thickness = 0.80mm; Voxel size-1x1x1mm; flip angle - 7º; FOV - 256x256





Data processing and Analysis: VBM data were processed using SPM12 pre-processing pipeline and statistical tools (Wellcome Trust Centre for Neuroimaging, University College London, UK; http://www.fil.ion.ucl.ac.uk/spm/). Image segmentation using an extension of the standard unified segmentation model; co-registered across participants using the DARTEL algorithm and normalized with a 8mm FWHM Gaussian filter

For the analysis, we performed a review on the cortical and subcortical areas underlying inhibitory circuitry (Koob, 2011; Koob & Volkow, 2010; Crews & Boettiger, 2009; Bava & Tapert, 2010; Bari & Robbins, 2013) and we selected the mask that included the following regions: superior and middle frontal gyrus; frontal superior orbital gyrus; anterior cingulum; nucleus caudate and accumbens. Anatomical localization and corresponding labels were obtained using MRIcron toolbox.

Statistical Analysis: Two-sample t-tests were performed to analyze regional gray matter and white matter densities differences between BD and AC split by gender. GM and WM images were assessed separately and 2 contrasts were set. SPM maps were generated for between group differences in brain areas where GM and WM densities were significantly lower/higher in BD than in AC. The threshold masking value was absolute 0.2 to exclude from the analysis tissue-related voxels. For statistical threshold criteria we accepted a p <0.001 uncorrected multi comparisons. Small volume correction for multiple comparisons was performed with a previously generated ROI mask using the WFUpickatlas toolbox version 3.0.5b (http://www.ansir.wfubmc.edu) based on the Talairach Daemon database running on MatLab R2015a (MathWorks, Natick,MA).

DISCUSSION

This study revealed increased frontal gray and white matter densities in bilateral middle frontal gyrus in BD when compared with controls. Middle frontal gryrus has been linked to executive control and attentional mechanisms playing a role in top-down attentional control (Japee et al., 2015). In particular, the left middle frontal gyrus has been related to behavioral desinhibition and the right middle frontal gyrus prospectively predicted substance use in children (Heitzeg et al., 2014; Japee et al., 2015). In accordance other studies presented similar results, namely higher left middle DLPFC gray matter density in BD compared to non-binge controls (Doallo et al., 2014) plus larger gray and white matter PFC volumes in male AUD (Medina et al., 2008). In this sense our findings suggest that abnormalities in the middle frontal region might be related to a diminished capacity to refrain the urge for high alcohol intake that characterize alcohol use disorders (Bava & Tapert, 2010; Koob, 2011; Crews & Boettiger, 2009). Of note, this pattern was more evident in males. In fact, males exhibit pruning later than females and the introduction of heavy alcohol consumption in early ages might interfere with the typical course of pruning eventually explaining the gender differences (Lenroot & Giedd, 2006).

Future studies should assess the behavioral/functional significance of these alterations and increase sample to analyze in detail this gender differences.

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