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Sexually dimorphic brain volume interaction in college-aged binge drinkers

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ABSTRACT

Background: Binge consumption of alcohol is a major societal problem associated with important cognitive, physiological and neurotoxic consequences. Converging evidence highlights the need to assess binge drinking (BD) and its effects on the developing brain while taking into account gender differences. Here, we compared the brain volumetric differences between genders in college-aged binge drinkers and healthy volunteers.
Method: T1-weighted magnetic resonance imaging (MRI) images of 30 binge drinkers (18 males) and 46 matched healthy volunteers (23 males) were examined using voxel-based morphometry. The anatomical scans were covaried with Alcohol Use Disorders Identification Test (AUDIT) scores. Whole brain voxel-wise group comparisons were performed using a cluster extent threshold correction.
Results: Several large clusters qualified with group-by-gender interactions were observed in prefrontal, striatal and medial temporal areas, whereby BD females had more volume than non-BD females, while males showed the inverse pattern of decreased volume in BD males and increased volume in non-BD males. AUDIT scores negatively correlated with volume in the right superior frontal cortex and precentral gyrus.
Conclusions: These findings dovetail with previous studies reporting that a state effect of BD in college-aged drinkers and the severity of alcohol use are associated with volumetric alterations in the cortical and subcortical areas of the brain. Our study indicates that these widespread volumetric changes vary differentially by gender, suggesting either sexual dimorphic endophenotypic risk factors, or differential neurotoxic sensitivities for males and females.

1. Introduction

Across the United Kingdom and the United States, binge drinking (BD) or episodic excessive rapid intake of alcohol is common in young adults (Fuller and Hawkins, 2014; Guttormsson et al., 2012; Johnston et al., 2014). BD is associated with serious health-related, societal and economic consequences (Miller et al., 2007) and has been linked to risky behavior, such as drink driving, sexually transmitted diseases and premature death (Anderson, 2007). In the adolescent and young adult age group, BD serves as a heightened risk factor for later alcohol-use disorders (AUDs) (Chassin et al., 2002; Crabbe et al., 2011; Feldstein Ewing et al., 2014).

Relatively few studies have addressed the neuroanatomical differences associated with binge drinking in the developing brain. Using structural magnetic resonance imaging (MRI), we have previously reported that college-aged binge drinkers have increased ventral striatal volume compared to controls (Howell et al., 2013). There are also studies showing that college-aged binge drinkers have increased mid-dorsolateral prefrontal gray matter volume (Doallo et al., 2014), while other studies suggested a thinning of the mid-anterior cingulate cortex in binge drinkers compared to light drinkers (Mashhoon et al., 2014),

Abbreviations: BD, binge drinking; MRI, magnetic resonance imaging; AUDIT, Alcohol Use Disorders Identification Test; AUDs, alcohol-use disorders; PFC, prefrontal cortex; IFG, inferior frontal gyrus; HV, healthy volunteer; NIAAA, National Institute of Alcoholism and Alcohol Abuse; BDI, Beck Depression Inventory; STAI, Spielberger Trait Anxiety Inventory; UPPS-P, UPPS-P Impulsive Behavior; SPM, Statistical Parametric Mapping; MNI, Montreal Neurological Institute; ICBM, International Consortium for Brain Mapping; WBIC, Wolfson Brain Imaging Center; GLM, general linear model; SVCs, small volume corrections; FWE, familywise error; AAL, Automatic Anatomical Labeling.

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which has also been characterized by altered neurochemistry (Silveri et al., 2014).

A recent study on adolescents which applied machine learning techniques in order to establish predictors of current and future binge drinking (defined as a minimum of three lifetime binge drinking episodes leading to drunkenness by age 14) found that current binge drinkers had smaller ventromedial prefrontal cortex (PFC) and left inferior frontal gyrus (IFG) volumes (Whelan et al., 2014). In contrast, future binge drinking was predicted by reduced bilateral superior frontal gyrus and greater volume of the right middle frontal gyrus and premotor strip. A recent longitudinal study found that adolescents who initiated heavy alcohol use showed thinning of the right middle frontal gyrus in conjunction with decreased white matter (Luciana et al., 2013). Similarly, another longitudinal study on initiators of heavy alcohol use in adolescents showed reduced left ventral diencephalon, left inferior and middle temporal gyri, and left caudate and brain stem structures compared to continuous non-users (Squeglia et al., 2014).

Volumetric alterations have also been observed in adolescents with alcohol use disorders (AUDs) which is a more chronic and severe condition compared to BD. Volume reductions in temporal lobe structures and the ventral striatum have also been reported in adolescent AUD. For example, it was shown that dual marijuana users and AUD have decreased left hippocampal volume (Medina et al., 2007). Similarly, other studies reported decreased left (Nagel et al., 2005) and bilateral hippocampal volumes (De Bellis et al., 2000) in AUD. This is convergent with our findings in binge drinkers showing an inverse correlation with alcohol severity and hippocampal, amygdalae and ventral striatal volumes (Howell et al., 2013). Studies on adolescent AUD have also found decreased volumes in the prefrontal cortices compared to controls (De Bellis et al., 2005; Fein et al., 2013; Medina et al., 2008).

A gender interaction has been reported in both BD (Squeglia et al., 2012) and AUD (Fein et al., 2013; Medina et al., 2008). Thus, relative to controls, AUD males had smaller thalamus and putamen volumes while AUD-females demonstrated the opposite pattern (Fein et al., 2013). Female binge drinkers exhibited larger PFC volumes compared to controls whereas male binge drinkers showed the opposite (Squeglia et al., 2012).

A large body of evidence thus suggests that alcohol use disorder and its subtypes are marked by brain-volumetric alterations in multiple cortical and subcortical regions. Since neuromaturation carries on through adolescence and into early adulthood (Casey et al., 2005; Giedd et al., 1999; Lenroot and Giedd, 2006; Sowell et al., 2004; Tamnes et al., 2010), the effects of neurotoxic insults between different age groups may be dissociable. The consequences of alcohol intoxication may be further dispersed in older age groups as alcohol consumption increases during this transition (Hermens et al., 2013; SAMHSA, 2014). We have previously published on volume differences in binge drinkers with a 3 month duration of BD (Howell et al., 2013). Here we intend to replicate these findings using a more stringent definition of BD with a 6 month duration and focus on the effects of gender. We hypothesized structural changes in ventral striatal volume as a function of binge drinking status and a gender-specific interaction.

2. Methods

2.1. Participants

Thirty binge drinkers and 46 healthy volunteers, matched for age and gender participated in the study (Table 1). Binge-drinking subjects were recruited through local advertisements in both community- and university-based areas in the East Anglia region while the healthy volunteers (HV) were recruited from the Behavioural and Clinical Neuroscience Institute healthy volunteer list and through local advertisements. The criteria used for BD were based on the National Institute on Alcoholism and Alcohol Abuse diagnostic criteria (NIAAA, 2004): consumption of ≥5 drinks and ≥4 drinks in a 2-hour period (for males and females, respectively) at least once a week for the last six months. Participants had to report getting drunk at least once a week during these binge drinking episodes. Participants were included if they were over 18 years old, had no history of regular or current use of other substances, and were free from any major psychiatric disorders (assessed with the Mini International Neuropsychiatric Inventory, Lecrubier et al., 1997). Those who were not suitable for MRI or presented major neurological illness, or head injury were not included in the study. All participants were asked to refrain from alcohol consumption at least 24 h before the scan and underwent a urine drug screen and an alcohol breathalyzer test. Written informed consent was obtained and the study was approved by the University of Cambridge Research Ethics Committee. Participants were reimbursed for their participation and travel expenses.

2.2. Data acquisition

Participants completed the Alcohol Use Disorders Identification Test (AUDIT) (Saunders et al., 1993), Beck Depression Inventory (BDI) (Beck et al., 1988), the State Trait Anxiety Inventory (Spielberger et al., 1983) and the UPPS-P impulsivity scale (Whiteside and Lynam, 2001). The BDI score of one healthy volunteer was >30 and was removed from analysis.

Table 1
Demographic and behavioral data for healthy volunteers and binge drinkers.

	Binge drinkers (n = 30)			Healthy volunteers (n = 46)		
	Females (n = 12) Mean (SD)	Males (n = 18) Mean (SD)	Total mean (SD)	Females (n = 23) Mean (SD)	Males (n = 23) Mean (SD)	Total mean (SD)
Age[d]	21.08 (1.78)	21.38 (2.83)	21.27 (2.43)	20.26 (1.28)	22.30 (2.05)	21.28 (1.98)
AUDIT[a,b,c]	17.11 (4.59)[f]	16.25 (5.31)[g]	16.56 (4.98)	4.04 (2.57)	5.10 (4.27)[g]	4.55 (3.48)
BDI	11.44 (8.92)[f]	9.50 (6.68)[g]	10.20 (8.01)	7.70 (6.36)	5.48 (6.05)[g]	6.63 (6.24)
STAI	41.11 (9.61)[f]	39.93 (10.80)[g]	40.36 (10.20)	39.86 (10.71)	41.11 (11.0)[e]	40.41 (10.72)
UPPS-P[a,b,c]	147.67 (20.60)[f]	140.06 (16.94)[g]	142.8 (18.29)	130.09 (15.60)	126.28 (20.70)[e]	128.41 (17.88)

AUDIT: Alcohol Use Disorders Identification Test, BDI: Beck Depression Inventory, STAI: Spielberger Trait Anxiety Inventory, UPPS-P: UPPS-P Impulsive Behavior, standard deviations in brackets.
All t-tests are for 2-tailed independent samples Welch's t-tests.
[a] Female binge drinkers ≠ female controls, P < .05.
[b] Male binge drinkers ≠ male controls, P < .05.
[c] Binge drinkers ≠ controls, P < .05.
[d] Female ≠ male, P < .05.
[e] Missing values from 5 participants.
[f] Missing values from 3 participants.
[g] Missing values from 2 participants.