Alcohol Cues Elicit Different Abnormalities in Brain Networks of Abstinent Men and Women with Alcohol Use Disorders

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Running Title: Gender, brain responses, and alcohol
Highlights: Brain reward regions activate highly when individuals with a history of alcohol use disorders view alcoholic beverages.
The brain regions identified subserve vision, memory, and judgement.
Opposite abnormalities in activation patterns appeared for alcoholic men and women.

Abstract

We employed fMRI in 84 men and women with and without a history of alcohol use disorders (ALC and NC, respectively), to explore how gender interacts with alcoholism as reflected in brain activity elicited by alcohol cues. Brain activation was measured in a working memory task (delayed matching-to-sample) with emotional faces as the sample and match cues. During the delay period, intervening distractors were either reward-salient cues (alcoholic beverages) or neutral cues (nonalcoholic beverages or scrambled pictures). ALC women (ALCw) had higher accuracy than ALC men (ALCm). Analyses of scans during the viewing of distractor images revealed significant group-by-gender interactions. Compared to NC men, ALCm evidenced lower activation contrast between reward-salient cues and neutral cues in *default mode network* regions (including superior prefrontal and precuneus areas), while ALCw had more activation than NC women. Similar interactions were observed for *task-regions* (including superior parietal, lateral occipital, and prefrontal areas). Region of interest analyses showed that the ALC group had significantly higher levels of activation throughout reward-related circuitry during alcohol distractor interference than during scrambled picture interference. These results suggest that abstinent ALCm and ALCw differ in processing reward-salient cues, which can impact treatment and recovery.

1. Introduction

Alcohol use disorders (AUD) have been associated with deficits in cognitive and emotional functions (Oscar-Berman *et al.*, 2014). Because of their reward salience, alcohol cues such as pictures of alcoholic beverages elicit attentional bias and brain activation in individuals with AUD (Carter & Tiffany, 1999; Goldstein & Volkow, 2002; Schacht *et al.*, 2013). Alcohol cues induce a hyperattentive state with attention drawn to the rewarding stimuli (Townshend & Duka, 2001; Franken, 2003; Field & Cox, 2008; Vollstädt-Klein *et al.*, 2011). Therefore, the cues selectively interfere with other cognitive abilities such as memory. Importantly, attentional bias toward alcohol-related stimuli also has been associated with level of craving, consumption, dependence, and physiological arousal (Sharma *et al.*, 2001; Ryan, 2002; Field *et al.*, 2004; Field & Eastwood, 2005; Bordnick *et al.*, 2008; Sinha *et al.*, 2009; Wiers *et al.*, 2014; Sawyer *et al.*, 2015).

Functional magnetic resonance imaging (fMRI) studies of attentional biasing, and specifically cue sensitivity, have often included either only men with and without a history of AUD (ALC and NC groups), or groups of men and women with sample sizes too small to examine gender effects (Fryer *et al.*, 2013; Schacht *et al.*, 2013). However, gender impacts the ways in which alcohol affects the brain and behavior (Becker *et al.*, 2017; Sawyer *et al.*, 2017, 2018, 2019; Seitz *et al.*, 2017; Rivas-Grajales *et al.*, 2018; Hoffman *et al.*, 2019; Kaag *et al.*, 2019; Fama *et al.*, 2020; Verplaetse *et al.*, 2021), due to interactions with physiological and social factors (Ruiz & Oscar-Berman, 2015; Mosher Ruiz *et al.*, 2017). In the present study, we examined gender differences using a delayed matching-to-sample (DMTS) task (Dolcos & McCarthy, 2006) with alcohol cues serving as distractor stimuli, in a cohort of ALC and NC men and women (AUDm, AUDw, NCm, and NCw). The DMTS task requires an attention-demanding

kind of memory called "working memory." In this study, the participants were required to remember photographs of emotional faces while distracting pictures of alcoholic beverages, nonalcoholic beverages, or scrambled images intervened during the delay period. We chose faces as the sample stimuli for two primary reasons. First, in a previous study (Marinkovic *et al.*, 2009) we found that men with AUD had abnormally low brain activity in temporal limbic regions when viewing faces, and second, we used the same dataset that we had acquired for a prior report (Oscar-Berman *et al.*, 2019) in which we described the brain's responses to the initial to-be-encoded emotional faces phase (the sample) of the DMTS task. For the present study, the data derived from the delay and match portions of the task allowed us to test the attentional biasing effect, wherein we expected alcohol cues, more than other cue types, to impair performance on memory for face identity.

Functional MRI tasks activate multiple brain networks, and abnormalities in the default mode network (DMN) have been implicated in AUD and in psychiatric disorders (Menon, 2011; Zhang & Volkow, 2019). The DMN has been observed to be more active during story telling, reading and memory tasks, imagining future scenarios, self-reference, rumination, and when the mind wanders while staring at a fixation cross during fMRI scanning (Tops *et al.*, 2014; Beaty *et al.*, 2016; Buckner & DiNicola, 2019). We refer to the DMN regions as *fixation-regions* because they are more active during the idle delay intervals when the fixation stimulus is presented between DMTS trials than during stimulus presentations. Vertex-wise analyses have revealed that cortical fixation-regions include: (1) an "anterior hub," consisting of portions of the rostral anterior cingulate cortex (ACC), ventromedial prefrontal cortex, and medial superior frontal cortex; (2) a "posterior hub," which includes portions of the posterior cingulate and precuneus, (3) the temporoparietal junction, which covers parts of the angular gyrus and inferior parietal

lobule; and (4) the superior and middle temporal gyrus region (Margulies *et al.*, 2016; Buckner & DiNicola, 2019; Uddin *et al.*, 2019).

In addition to the DMN regions, we used vertex-wise analyses to examine *task-regions*, which are more engaged during the DMTS task than while looking at unengaging fixation crosses. Literature on distractor interference during working memory has suggested that task-regions involve a distributed network including prefrontal cortex, along with dorsal and ventral visual association cortex, which are necessary for attentional functioning (Loeber *et al.*, 2009) and for inhibiting distracting visual stimuli (Jha *et al.*, 2004; Clapp *et al.*, 2010). Additional task-regions involved in attention, working memory, and emotional processing, include the dorsal ACC and lateral prefrontal areas. The dorsal ACC in particular has been implicated in craving and attentional biasing (Goldstein & Volkow, 2011).

In advance of any analyses, we used prior literature to select ten *a priori* anatomically-defined regions of interest (ROI) involved in alcohol cue exposure, distractor interference, craving, reward processing and salience, or working memory for emotional faces. The first nine ROI are the dorsolateral prefrontal cortex (DLPFC), ventrolateral prefrontal cortex (VLPFC), orbitofrontal cortex (OFC), insular cortex, parahippocampal gyrus, hippocampus, amygdala, fusiform, and ACC. Previous studies provide support for each of those nine a priori ROI (George *et al.*, 2001; Wrase *et al.*, 2002; Tapert *et al.*, 2003; Myrick *et al.*, 2004; Heinz *et al.*, 2007; Ray *et al.*, 2010; Goldstein & Volkow, 2011; Schacht *et al.*, 2013; Field *et al.*, 2014; Alba-Ferrara *et al.*, 2016; Sawyer *et al.*, 2020). The tenth ROI is the "extended reward and oversight system" (EROS) as described and named in our previous papers (Makris *et al.*, 2008; Sawyer *et al.*, 2017). The EROS ROI is a single large but discontinuous composite ROI that had been created by combining 11 regions (seven of the ROI noted above, all but the VLPFC and fusiform), plus

an additional four: nucleus accumbens, ventral diencephalon, subcallosal cortex, and temporal pole. For each of the ten ROI, we intended to confirm findings from each of the aforementioned studies that had identified abnormal activation by alcohol cues in AUD, and additionally to investigate differences between men and women. We expected lower brain activation in the ALC group in regions involved in facial identity and inhibition of distractor interference, but higher in regions responsible for reward salience.

In summary, we investigated brain activation for ten ROI, and for vertex-wise cortical analyses of fixation-regions and task-regions. We examined the accuracy of the participants' memory for the face identities after exposure to attentionally salient pictures to test our hypothesis that alcohol cues would distract the ALC group more than the NC group. We determined how brain regions were activated by the distractor contrasts, how the contrasts differed for ALC and NC groups, and how those abnormalities varied by gender. We hypothesized that attentional biasing would be evident for the ALC group in the form of stronger brain activity contrasts (alcoholic beverage cues compared to nonalcoholic and scrambled stimuli). Regarding gender differences, we made predictions based upon previous work in our laboratory wherein we found that brain regions of ALCw (compared to NCw) were overactive in response to highly charged emotional stimuli (Sawyer *et al.*, 2019). We hypothesized that the ALCw would evidence hyperactivation to emotionally valent stimuli, whereas the activation contrasts for ALCm would be weaker. We also expected to replicate prior results (Marinkovic *et al.*, 2009; Sawyer *et al.*, 2019) showing lower responses in ALCm than NCm.

2. Materials and Methods

2.1 Participants

Participants in this study included 42 abstinent long-term ALC individuals (21 ALCw) and 42 NC controls (21 NCw), with comparable age, education, and IQ (see Table 1 in the Results). Participants were recruited through flyers placed in treatment and after-care facilities, the Boston VA Healthcare System facility, Massachusetts General Hospital, the Boston University School of Medicine, and in public places (*e.g.*, churches, stores), as well as through newspaper and internet advertisements. This study was reviewed and approved by human studies Institutional Review Boards at the affiliated institutions. All participants gave written informed consent prior to participation, and they were compensated for their time.

Selection procedures included a telephone interview to determine age, education, health and alcohol and drug use history, including prescription drugs. Participants were right-handed, had normal or corrected-to-normal vision, and spoke English as their first language (or had acquired English as a second language by age five). Current drug use excepting nicotine was cause for exclusion, as were history of alcohol-related liver disease, epilepsy, head trauma resulting in loss of consciousness for 15 minutes or more, HIV, schizophrenia, or metal implants.

2.2 Neuropsychological Assessment

Neuropsychological testing was conducted at the Department of Veterans Affairs (VA) Boston Healthcare System facility prior to scanning. Participants completed a medical history interview, vision test, handedness questionnaire (Briggs & Nebes, 1975), and a battery of tests as described below. All subjects were screened using the Hamilton Rating Scale for Depression (Hamilton, 1960) and the Diagnostic Interview Schedule for the DSM-IV (Robins *et al.*, 2000).

The majority of participants also were administered the Wechsler Adult Intelligence Scale (WAIS-III) and the Wechsler Memory Scale (WMS-III) (Wechsler, 1997). Four participants (two ALCw and two ALCm) received the WAIS-IV and WMS-IV (Holdnack & Drozdick, 2010), and WMS-III scores were not obtained from one ALCm. The scores for these participants were adjusted to account for differences in scoring outcomes relative to the earlier versions of the scales. Because craving for the rewarding effects of alcohol is known to serve as a trigger for relapse in those recovering from AUD (Schneider *et al.*, 2001), and alcohol cue exposure in particular is known to be related to relapse (Lubman, 2007), all participants were administered the Penn Alcohol Craving Scale (Flannery *et al.*, 1999) immediately before and approximately two weeks following the scan to assess any changes in alcohol craving patterns.

2.3 Alcohol Screening

The ALC participants met criteria for alcohol abuse or dependence, and consumed 21 or more alcoholic drinks per week for five or more years. Extent of alcohol use was assessed by calculating Quantity Frequency Index (QFI) scores (Cahalan *et al.*, 1969). QFI scores approximate the number of drinks consumed per day, and take into consideration the amount, type, and frequency of alcohol consumption either over the last six months (NC participants), or over the six months preceding cessation of drinking (ALC participants), and yields an estimate of ounces of ethanol per day. To remove the influence of current alcohol abuse, ALC participants must have been abstinent for at least four weeks before the scan date to be included. The ALC participants did not display symptoms of Korsakoff's Syndrome nor dementia (Oscar-Berman & Maleki, 2019). Potential NC participants who had consumed 15-20 drinks per week for any length of time or who engaged in binge drinking were disqualified.

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189 ## *2.4 Functional Imaging Task*

190 All participants were given a delayed matching-to-sample memory task (Dolcos &
191 McCarthy, 2006) in a magnetic resonance imaging (MRI) scanner, whereby they were asked to
192 encode two faces that both had one of three emotional valences: positive, neutral, or negative
193 (Figure 1). The face stimuli were shown in grayscale and were taken from a set of faces used in a
194 previous study (Marinkovic *et al.*, 2009). These faces were displayed simultaneously for three
195 seconds, followed by an asterisk (*) for one second. Subjects were asked to maintain these faces
196 in memory while a colored distractor stimulus was shown. On different trials, the distractor
197 stimulus was either a picture of an alcoholic beverage (*alcbev*; beer, wine, liquor, or mixed
198 drink), a picture of a nonalcoholic beverage (*nonalcbev*; water, juice, milk, soda, coffee, tea,
199 etc.), or a scrambled nonsense picture (*scrambled*). Alcoholic and nonalcoholic beverage pictures
200 were a combination of images used with permission from the Normative Appetitive Picture
201 System (NAPS) (Stritzke *et al.*, 2004), and other previously published works on alcohol cues
202 (Grüsser *et al.*, 2000; Wrase *et al.*, 2002; Myrick *et al.*, 2004). Additional distractor images were
203 modified from digital photographs taken at bars, liquor stores, and convenience stores. The
204 scrambled images were created by inverting half the alcoholic and half the nonalcoholic
205 beverage images and distorting them until they were not recognizable as any particular object,
206 while preserving a match of primary visual characteristics. Each distractor picture was shown for
207 three seconds, followed by an asterisk (*) for one second. Following the distractor picture, a
208 single probe face was shown for two seconds, and the participants were instructed to report
209 whether this face was one of the two faces they had just seen.

Each trial was 10 seconds in length, and was followed by a variable delay period (with a mean duration of 10 seconds, ranging from 2-22 seconds) during which the subject saw a set of crosshairs (+++) serving as a visual fixation. The task was divided into nine runs, each of which contained 18 trials. There were nine trial types made up of each combination of face valence and distractor type (*e.g.*, positive faces followed by alcohol distractor). Each emotion-distractor combination appeared twice per run. The stimulus order and variable inter-trial intervals were determined using *optseq2* (http://surfer.nmr.mgh.harvard.edu/optseq), which optimizes statistical efficiency and hemodynamic response estimate accuracy for event-related experimental designs (Dale, 1999). In total, there were 54 trials for each distractor type (combined across facial expressions) and each face valence (combined across distractor types), for a total of 162 trials across the entire scan. The stimulus faces were balanced to contain 50% male and 50% female faces. Within a trial, the two encoded faces and probe face were matched on emotional expression and gender. This way, on match trials the probe facial image was identical to one of the encoded images, and on mismatch trials the facial identity changed but the emotional expression and gender did not.

The probe face matched one of the encoded faces on 50% of the trials, and match/mismatch trials appeared in a randomized order within each run. Responses were made by pressing one of two buttons with the index finger (match) or middle finger (mismatch) of the right hand. Participants were instructed to respond as quickly as possible without sacrificing accuracy. Additionally, participants could immediately correct a response by pressing the opposite button. To ensure the distractor images were viewed by all participants, they were told that it was necessary to pay attention to the pictures shown in between the faces on each trial, as they would be questioned about those images following the scan.

2.5 Behavioral Task Analyses

Responses to the face memory task were analyzed on the first level (individual subjects) using custom Excel templates. Trials were organized by Distractor type, facial Emotion, and Face Gender. Each trial was scored as correct, incorrect, or miss (*i.e.*, no response). When more than one response was made to a trial, the last response type (*i.e.*, yes/match or no/nonmatch) was accepted as the final answer, provided that the final response was at least 200 ms after the preceding response and no more than 10 s following the preceding response. When a single response was recorded and the reaction time was less than 200 ms, the trial was scored as a miss. For each participant, a mean overall reaction time (regardless of trial type) was calculated. Reaction times that exceeded three standard deviations from this mean were excluded from reaction time calculations by trial type. Participants' patterns of responses were analyzed for consecutive misses to assure that they remained awake throughout the task. Three separate runs were identified, each in a different participant, wherein greater than five consecutive trials were missed; these runs were excluded from behavioral analyses.

Second level (group) effects on percent correct and reaction time (correct trials) were investigated using SPSS Version 17.0 (IBM, Chicago, IL, USA). Repeated-measures analyses of variance (ANOVA) were carried out with between-subjects factors of Group (ALC or NC) and Gender (female participant or male participant) and within-subjects factors of Distractor (alcbev, nonalcbev, or scrambled), Emotion (positive, negative, or neutral), and Face Gender (female face or male face).

2.6 Image Acquisition

Imaging was conducted at the Massachusetts General Hospital's Athinoula A. Martinos Center for Biomedical Imaging in Charlestown, MA. Data were acquired on a 3 Tesla Siemens (Erlangen, Germany) MAGNETOM Trio Tim MRI scanner with a 12-channel head coil. Sagittal T1-weighted MP-RAGE scans (TR = 2530 ms, TE = 3.39 ms, flip angle = 7˚, FOV = 256 mm, slice thickness = 1.33 mm, slices = 128, matrix = 256 x 192) were collected for all subjects. For most participants, two such volumes were collected and averaged to aid in motion correction. An auto-align localizer was employed to adjust the acquired slices such that they ran parallel to an imaginary plane between the anterior and posterior commissures. Echo planar functional MRI blood oxygen level dependent (BOLD) scans were collected axially with 5 mm slice thickness and 3.125 x 3.125 mm in-plane resolution (64 x 64 matrix), allowing for whole brain coverage (32 interleaved slices, TR = 2 s, TE = 30 ms, flip angle = 90°). The event-related design included 18 trials per run with a total of nine runs. Within each six-minute run, 180 T_2*-weighted volumes were collected. Functional volumes were auto-aligned to the anterior/posterior commissure line to ensure a similar slice prescription was employed across participants. Prospective Acquisition Correction (3D-PACE) was applied during collection of the functional volumes to minimize the influence of participants' body motion (Thesen *et al.*, 2000). An IBM ThinkPad (Windows XP) running Presentation version 11.2 (NeuroBehavioral Systems, Albany, CA) software was used for visual presentation of the experimental stimuli and collection of participants' responses. Stimuli were back-projected onto a screen at the back of the scanner bore and were viewed by the participants through a mirror mounted to the head coil. All participants wore earplugs to attenuate scanner noise.

2.7 Structural Image Processing

Structural MPRAGE image analyses were performed for all participant data using the FreeSurfer (version 4.5.0) image analysis suite (http://surfer.nmr.mgh.harvard.edu). A multi-stage cortical surface reconstruction process was run on the two collected T1-weighted MP-RAGE scans (Dale *et al.*, 1999), starting with motion correction, intensity normalization (Sled *et al.*, 1998), Talairach registration (Talairach & Tournoux, 1988), skull stripping (Ségonne *et al.*, 2004), and segmentation (Fischl *et al.*, 2002) of white matter, gray matter, and ventricles. Subsequently, boundaries were calculated delineating where gray and white matter meet, and where gray matter adjoins cerebrospinal fluid ("pial surfaces") based on maximal shifts in image intensity between tissue types. These boundaries, as well as the subcortical segmentations, were visually inspected on each coronal slice for every subject, and manual interventions (*e.g.*, white matter volume corrections) were made when needed. The surface boundaries were used to generate computationally inflated two-dimensional cortical surface models, which allowed individual subjects to be registered to a spherical atlas by utilizing each subject's cortical folding patterns. This registration was used to align the cortical geometry of all subjects within a group. Creation of these cortical surface models allowed improved data visualization as well as improved accuracy of within-group co-registration relative to an affine morph procedure (Fischl *et al.*, 1999). The cortical surface models were employed in an automated parcellation procedure that divides the surface into subregions based on gyral and sulcal anatomy. The Destrieux atlas parcellation for FreeSurfer (Destrieux *et al.*, 2010) was used to define anatomical ROI in the functional analyses.

2.8 Functional Image Processing and Statistical Analyses

Effects of Group, Gender, Distractor, and Emotion on the BOLD signal were evaluated using both a whole-brain cluster analysis as well as ROI analyses. Processing of the functional data was performed using the FreeSurfer Functional Analysis Stream (FS-FAST) version 5.3, SPSS Version 17.0, and Matlab 7.4.0.

2.8.1 First-Level Functional Analyses

Preprocessing of the functional images for first-level (individual subject) FS-FAST analysis included motion correction, intensity normalization (Sled *et al.*, 1998), and spatial smoothing with a 5-mm Gaussian convolution kernel at full-width half-maximum. Trials were first combined across runs by distractor-emotional face valence pairs (i.e., alcbev-positive, alcbev-negative, alcbev-neutral, nonalcbev-positive, nonalcbev-negative, nonalcbev-neutral, scrambled-positive, scrambled-negative, scrambled-neutral) and then collapsed across emotional valence. The BOLD response was estimated using a Finite Impulse Response (FIR) model, which allows for estimation of the time course of activity (percent signal change for a given condition) within a vertex or ROI for the entire trial period. For each condition, estimates of signal intensity were calculated for 2 pre-trial and 10 post-trial onset TRs, for a total analysis window of 24 seconds. Motion correction parameters calculated during alignment of the functional images were entered into the analysis as external regressors. Alignment of the T2*-weighted functional images with T1-weighted structural volumes was accomplished through an automated boundary-based registration procedure (Greve & Fischl, 2009). These automated alignments were manually inspected to ensure accuracy.

Statistical maps were generated for each of the 84 individual subjects for contrasts between experimental conditions. Three contrasts were used to identify DMN regions (as described below); they were made between distractor types and fixation: (1) alcbev vs. fixation, (2) nonalcbev vs. fixation, and (3) scrambled vs. fixation. Another three contrasts were used to assess cue responsivity: (1) alcbev vs. nonalcbev, (2) alcbev vs. scrambled, (3) nonalcbev vs. scrambled. Analyses of each of these contrasts included removal of prestimulus differences between the contrasted conditions by averaging the first three time points (two pre-trial onset and one post-trial onset) for each condition and subtracting this mean from each time point for that condition. Time points summed for inclusion in each contrast were chosen to reflect peak stimulus-related activity: FIR estimates of hemodynamic responses to the distractors were analyzed using a mean of the five TRs collected during the time period of 2-12 seconds post distractor onset. Since the distractor is shown 4 seconds after the trial onset, the analysis window is 6-16 seconds following trial onset (time points 3 through 8).

2.8.2 Cortical Surface Cluster Analyses

We investigated cue-related brain activation in two separate cortical brain networks: (1) cue reactivity in DMN regions, and (2) cue reactivity in task-regions. The brain network that was more active during presentation of the fixation cue than during the distractor images was used as our measure of DMN regions (fixation-regions). The network that was more active during the presentation of distractor images than during presentation of the fixation stimulus was used as our measure of the task-regions. In what follows, we first describe masking procedures and analyses we used to separate the networks.

The *t*-statistic maps for each condition vs. fixation were thresholded at $p < 0.05$ vertex-wise and were used to generate binary masks (Figure 2) separating fixation-regions and task-regions, thereby forming the six masks: alcbev greater than (or less than) fixation, nonalcbev greater than (or less than) fixation, scrambled greater than (or less than) fixation. These masks were used to separate the between-distractor analyses (described below).

Second-level (group) analyses on cortical regions were accomplished using FS-FAST, a surface-based morphing procedure for intersubject alignment and statistics (Fischl *et al.*, 1999). Group-averaged signal intensities during each experimental condition (alcbev, nonalcbev, scrambled) relative to fixation were calculated using the general linear model in spherical space for cortical regions, and were mapped onto the canonical cortical surface *fsaverage*, generating group-level weighted random-effects *t*-statistic maps masked to include only the cortex. Weighted random effects models were employed to reduce noise by taking into account individual subject variance. A 5 mm smoothing kernel (full-width half-maximum) was employed for all group and intergroup maps. Cluster correction on maps showing activity for each distractor condition vs. fixation was applied using FS-FAST Monte Carlo simulation with a clusterwise threshold of $p < 0.05$ corrected for three spaces (left hemisphere cortical, right hemisphere cortical, and subcortical). Cortical surface cluster regions were identified by the location of each cluster's peak vertex on the cortical surface according to the Desikan-Killiany atlas (Desikan *et al.*, 2006).

When we examined brain activation differences between the distractor types, we used three contrasts: alcbev vs. nonalcbev, alcbev vs. scrambled, and nonalcbev vs. scrambled. We investigated each direction of these contrasts separately. For example, brain regions with higher

366 activation for alcbev than nonalcbev would be analyzed separately from those regions with
367 higher activation for nonalcbev than alcbev.

368 Intergroup comparison *t*-statistic maps were generated using FS-FAST by comparing
369 activation levels of all of the ALC participants with levels of all of the NC participants.
370 Additionally, Group-by-Gender interaction maps for each contrast were calculated.

371

372 **2.8.3 Region of Interest Analyses**

373 The anatomically-defined ROI for the distractor analyses included areas hypothesized *a*
374 *priori* to be implicated in alcohol craving, distractor interference, and working memory for
375 emotional faces, as described in the Introduction. These were DLPFC, VLPFC, OFC, insular
376 cortex, parahippocampal gyrus, hippocampus, amygdala, fusiform, ACC, and the multi-regional
377 EROS (Makris *et al.*, 2008; Sawyer *et al.*, 2017). Left and right hemisphere regions were
378 analyzed as separate ROI.

379 Statistical preprocessing and time course visualization of ROI data were performed using
380 scripts written for Matlab version 7.4.0. Signal intensity for each region was averaged across all
381 vertices (for surface-based ROI) or voxels (for volume-based ROI) included in the region for
382 each condition on the individual participant level. To compute percent signal change for each
383 participant within an ROI, signal estimate per condition and time point was divided by the
384 average baseline activity for that participant. Time courses were normalized at the individual
385 subject level for each condition by taking the mean of the first three time points (two pre-trial
386 and one post-trial onset) and subtracting this mean from each time point. Group and Group-by-
387 Gender averages of the normalized time courses were computed for each condition, and were

388 visualized by plotting the percent signal change for each condition at each time point (*i.e.*, TR) of
389 the trial.

390 For the distractor ROI analyses, percent signal changes of the BOLD signal within each
391 ROI for the time window from 2 to 12 sec after distractor onset were entered as dependent
392 variables into repeated-measures ANOVA models with between-group factors of Group (ALC or
393 NC) and Gender (men or women) and within-subjects factor of Distractor type (alcbev,
394 nonalcbev, or scrambled).

395

396 ## 3. Results

397 ### *3.1 Research Participant Characteristics*

398 Table 1 summarizes means, standard deviations, and ranges of participant demographics,
399 drinking variables, and IQ and memory test scores.

400

	ALCOHOLICS			CONTROLS		
	ALC	ALCw	ALCm	NC	NCw	NCm
	n = 42	*n* = 21	*n* = 21	*n* = 42	*n* = 21	*n* = 21
Age[a] (years)						
mean	53.9	53.4	54.4	53.9	57.7	50.2
standard deviation	11.0	11.4	10.8	12.4	13.6	10.1
range	26.5 - 76.7	26.5 -73.0	26.6 - 76.7	25.8 - 76.9	25.8 - 76.9	29.0 - 69.6
Education[b] (years)						
mean	14.7	15.3	14.1	15.5	15.6	15.4
standard deviation	2.0	2.0	1.9	2.0	2.3	1.6
range	12 - 19	12 - 19	12 - 18	12 - 19	12 - 20	12 - 18
WAIS-III Full Scale IQ						
mean	110.3	110.1	110.5	111.6	111.2	112.0
standard deviation	15.0	14.2	16.0	16.3	19.3	13.1
range	72 - 140	72 - 137	81 - 140	79 - 152	79 - 142	90 - 152
WMS-III IMI						
mean	109.7	114.4	104.7	111.9	114.8	109.0
standard deviation	16.6	18.3	13.4	16.9	16.4	17.4
range	63 - 144	63 - 144	82 - 130	80 - 146	84 - 138	80 - 146
WMS-III DMI						
mean	112.6	116.7	108.3	111.8	113.5	110.1
standard deviation	17.3	20.4	12.5	16.0	14.9	17.2
range	52 - 140	52 - 140	86 - 132	83 - 150	83 - 140	84 - 150
Duration of Heavy Drinking[cdef] (years)						
mean	17.4	14.3	20.5	0.0	0.0	0.0
standard deviation	7.7	5.2	8.5	0.0	0.0	0.0
range	5.0 - 35.0	6.0 - 25.0	5.0 - 35.0	0.0 - 0.0	0.0 - 0.0	0.0 - 0.0
Quantity Frequency Index[cde] (ounces ethanol/day; ~drinks/day)						
mean	11.2	8.7	13.7	0.3	0.2	0.4
standard deviation	8.8	5.8	10.5	0.6	0.5	0.7
range	2.7 - 38.4	2.7 - 28.1	4.5 - 38.4	0.0 - 2.6	0.0 - 2.4	0.0 - 2.6
Length of Sobriety[cde] (years)						
mean	8.3	10.6	5.9	2.1	3.6	0.5
standard deviation	10.3	11.1	8.8	6.4	8.5	1.3

range	0.1 - 32.3	0.1 - 32.1	0.1 - 32.3	0.002 - 29.2	0.002 - 29.2	0.002 - 5.1
Penn Alcohol Craving Scale[cde]						
mean	3.8	3.8	3.9	1.2	1.1	1.3
standard deviation	4.4	5.1	3.8	2.0	2.2	1.8
range	0 - 19	0 - 19	0 - 12	0 - 9	0 - 9	0 - 5
Hamilton Rating Scale for Depression[g]						
mean	3.5	4.9	2.2	2.4	3.1	1.8
standard deviation	4.2	4.1	4.0	2.8	3.3	2.1
range	0 - 18	0 - 17	0 - 18	0 - 12	0 - 12	0 - 8

401 **Table 1. Participant characteristics**

402 Participants Characteristics ($p < 0.05$): [a]Control Women > Control Men; [b]Control Men > Alcoholic Men;
403 [c]Alcoholics > Controls; [d]Alcoholic Men > Control Men; [e]Alcoholic Women > Control Women; [f]Alcoholic Men >
404 Alcoholic Women; [g]Alcoholic Women > Alcoholic Men. See Results for additional details on number of
405 participants.
406 Abbreviations: WAIS = Wechsler Adult Intelligence Scale; WMS = Wechsler Memory Scale; IMI = Immediate
407 Memory Index; DMI = Delayed Memory Index. Five NCm and two NCw reported being lifetime abstainers, and
408 one NCw was unable to report an accurate length of sobriety.
409
410 The ALC and NC groups did not differ significantly by age. Although the NCw were
411 older than the NCm, controls did not differ significantly from their respective ALC counterparts
412 by age. ALCm had on average one year less education relative to NCm. Groups did not differ
413 significantly on WAIS-III Full Scale IQ scores. While ALCw had higher Hamilton Rating Scale
414 for Depression scores than AUDm, the average scores for all four subgroups (ALCm, ALCw,
415 NCm, and NCw) were low (all means below 5, whereas mild depression threshold is 8), so
416 depression likely contributed little to our observed gender differences.
417 By definition, the ALC group had longer durations of heavy drinking than the NC group.
418 The ALCm on average drank heavily for six years more than did the ALCw, and showed a trend

toward drinking larger average daily quantities (QFI, $F_{1,40} = 3.66$, $p = 0.06$). Five NCm and two NCw reported being lifetime abstainers (and as such did not have relevant length of sobriety values). The ALC group reported higher levels of craving for alcohol than the NC group on the PACS administered immediately prior to the scan; ALCm and ALCw did not differ on reported level of pre-scan alcohol craving. Eighty-one of the 84 participants were reached approximately two weeks after their scan date to be reassessed on alcohol craving level. One ALCw, one ALCm, and one NCw could not be reached for follow up assessment on PACS scores. Neither the ALC group nor the NC group displayed an increase in alcohol craving (*i.e.*, a significant change in PACS scores) from the assessment on their scan date to their follow up assessment.

3.2 Behavioral Results

Measures of participant performance on the face memory task were calculated for overall performance and for performance by each Distractor type and facial Emotion. Means, standard deviations, and ranges are reported for percent correct responses and reaction times in Table A1 and Table A2, respectively.

A significant Group-by-Gender interaction was found for accuracy ($F_{1,80} = 6.880$, $p = 0.01$, Figure A1 and Table A1). The significant interaction indicated that the better performance for the ALCw than the ALCm was larger than the difference between NCw and NCm. Accuracy and reaction times did not vary significantly as a function of the Distractor, nor were there any significant interactions of Distractor with Group or Gender (all $p > 0.05$). The main effect of Emotion was significant for percent correct responses, wherein ALC and NC participants alike performed better on both positive and negative faces relative to neutral faces. Performance on positive and negative faces did not differ significantly. The effect of Emotion on percent correct

responses did not vary as a function of Group or Gender (all $p > 0.05$). Regarding reaction time and Emotion, participants responded more quickly to positive face trials relative to neutral face trials; this effect did not vary by Group nor by Gender. The main effect of Face Gender on percent correct responses also was significant ($F_{1,80} = 6.80$, $p = 0.01$), with the overall performance being better for male than for female faces. The effects of Group and Gender on percent correct responses and reaction times for Face Gender were not significant (all $p > 0.05$).

3.3 fMRI BOLD Effects

Effects of the distractors on the BOLD signal were assessed using group and intergroup cluster analyses for cerebral cortex, along with a-priori analyses of anatomical ROI that had been implicated by the literature. Below, we report group analyses of fixation contrasts and between-distractor conditions, followed by intergroup analyses of the same contrasts.

3.3.1 Cortical Cluster Analyses of Distractor Effects

Analyses of task contrasts revealed broadly similar activation patterns for the ALCw, ALCm, NCw, and NCm groups. During fixation, regions involved in the DMN (the anatomical network described in the Introduction) were significantly more active than during the presentation of distractor images. We refer to those more active regions as fixation-regions. As detailed in the Methods, these regions were masked and examined separately for subsequent analyses of contrasts between distractor types. Identical analyses were then performed for the task-regions. Significant clusters for between-distractor contrasts can be seen for fixation-regions first (Figure 3 and Figure A3), and then for task-regions (Figure 4 and Figure A4).

All four groups had more brain activity (Table A3) in response to alcbev than scrambled distractors in the four main fixation-regions (the anterior and posterior medial hub regions, the temporal parietal junction, and the middle temporal gyrus), while the nonalcbev vs. scrambled contrast was less consistent. The alcbev vs. nonalcbev contrast generally indicated higher activation for the alcbev than nonalcbev. For task-regions, alcbev and nonalcbev elicited higher activation than scrambled in the occipital lobe and adjoining visual areas in temporal and parietal cortex (Table A3, Figure A4).

3.3.2 Distractor Intergroup Cluster Analyses

The pattern of results indicated that ALCw and NCm had strong activation contrasts (beverages > scrambled) in visual areas and the medial DMN regions, especially the posterior hub. The ALCw had greater activation contrast than NCw, while ALCm had lower activation contrast than NCm. Table 2 summarizes the regions where significant Group-by-Gender interactions were found for the distractor contrasts, i.e., for alcbev vs. nonalcbev, alcbev vs. scrambled, and nonalcbev vs. scrambled. Table A4 provides all significant Group-by-Gender interactions, and Figure 3, Figure 4, Figure A3, Figure A4 illustrate alcbev vs. scrambled contrasts. In total, we observed 22 clusters where the Group-by-Gender interaction was statistically significant: Seven in fixation-regions and 15 in task-regions.

Fixation Masking	Distractor Contrast	Clusters	Annotation (Hemisphere: Number of Clusters)
fixation-regions	alcbev > scrambled	4	superior frontal (L: 1, R: 2), precuneus (R: 1)
fixation-regions	nonalcbev > scrambled	3	superior frontal (R: 2), caudal middle frontal (R: 1)
task-regions	alcbev > scrambled	5	superior parietal (L: 1, R: 2), fusiform (R: 1), lingual (R: 1)
task-regions	nonalcbev > scrambled	4	superior parietal (L: 1, R: 1), lateral occipital (R: 2)
task-regions	scrambled > nonalcbev	4	superior frontal (L: 2), rostral middle frontal (L: 2)
task-regions	nonalcbev > alcbev	2	superior frontal (L: 2)

Table 2. Group-by-gender cortical cluster summary

Annotations (using the Desikan-Killiany atlas) are shown for each of the 22 clusters with significant Group-by-Gender interactions in distractor contrasts. The Fixation Masking column refers to the separate analyses conducted for fixation-regions and task-regions as shown in Figure 2. The clusters reported can be understood to span multiple functional regions [71]. That is, they are not limited to a single region, as reported by the maximal vertex or voxel. Abbreviations: alcbev = alcoholic beverages; nonalcbev = nonalcoholic beverages; L = left hemisphere; R = right hemisphere. See Table A4 for detailed cluster information. Note: for the fixation-regions, superior frontal and caudal middle frontal are part of the anterior hub; and precuneus is part of the posterior hub.

For the seven clusters in fixation-regions, six were in the anterior hub and one was in the posterior hub. For alcbev > scrambled, we observed one cluster in the posterior hub and three in the anterior hub. For three of these four clusters, ALCw and NCm had the strongest contrasts; in the fourth cluster, ALCw had the strongest contrast, whereas ALCm had the weakest. The remaining three clusters were found for nonalcbev > scrambled. As with the alcbev contrasts, ALCw and NCm had the strongest contrasts. All three clusters were in the right hemisphere of the anterior hub. Thus, the overall pattern consistent among the seven clusters was as follows: NCm had stronger contrast (beverage > scrambled) than ALCm, while muted or opposite direction comparison was observed for the women.

Of the 15 task-regions clusters, two were found for nonalcbev > alcbev (left superior frontal cortex). In both clusters, NCw had higher activation to nonalcoholic beverages, while NCm had higher activation to alcoholic beverages. In the other 13 clusters, the strongest contrasts were found for NCm and ALCw. Of those, the significant interactions were found in visual regions where nonalcbev > scrambled, while significant interactions in frontal regions were found for scrambled > nonalcbev.

Setting aside gender, analyses of activation levels comparing ALC and NC groups revealed 15 cortical clusters with significantly greater contrast levels for the ALC group than for the NC group (Table A5). Two of the clusters were in the DMN: one alcbev-region (temporoparietal junction), and one nonalcbev-region (posterior hub). The other 13, all alcbev-regions, were in task-regions located throughout the cortex: 7 frontal, 3 temporal, 2 parietal, and 1 occipital.

3.3.3 Distractor Region of Interest Analyses

Results of ANOVAs examining between-subjects effects of Group and Gender and within-subjects effects of Distractor type on BOLD percent signal change within each ROI are summarized in Table 3. Reported means and standard deviations represent the percent signal change across each ROI (unmasked) for the time period of 2 to 12 seconds post-distractor stimulus onset. These anatomically-defined ROI included regions in EROS areas (Makris *et al.*, 2008; Sawyer *et al.*, 2017), as well as in regions associated with face memory maintenance and distractor interference, as described in the Introduction and Methods.

Results from the ROI analyses of distractor effects indicated strong effects of distractor type on neural activation patterns. Specifically, among all participants, significantly higher

525 responses were observed in several regions (EROS, left DLPFC, left VLPFC, right OFC,
526 bilateral parahippocampal gyrus, bilateral hippocampus, bilateral amygdala, and bilateral
527 fusiform) to both alcbev and nonalcbev relative to scrambled stimuli. The effect was
528 significantly larger for the ALC group than the NC group in the left EROS and left fusiform
529 regions, and in four prefrontal brain areas (left DLPFC, left VLPFC, left OFC, and right OFC).
530 Additionally, in the alcbev vs. nonalcbev contrast, the ALC group showed significantly higher
531 responses than the NC group in the left OFC ROI. Figure 5 shows percent signal change over
532 time for the OFC, VLPFC, fusiform, and ACC activation, to demonstrate representative activity
533 patterns. The left OFC shows the heightened activation for alcbev for the ALC group, the
534 fusiform and VLPFC show higher activation in both groups to both beverage types, and the ACC
535 demonstrates how activation is lower during distractor presentation than during fixation (for both
536 groups and for all three distractor types).

537 Applying a Bonferroni correction accounting for all 25 tests would set a critical value for
538 statistical significance of main effects and Distractor, Group, and Gender interactions at $p <$
539 0.002. Using this threshold, main effects of Distractor would remain significant in left OFC,
540 bilateral parahippocampal gyrus, bilateral hippocampus, right amygdala, and bilateral fusiform
541 gyrus. All main effects of Group and Gender, as well as all interaction effects were $p > 0.002$.
542

	ALCOHOLICS				NONALCOHOLIC CONTROLS				
	Alcoholic Beverage	Nonalcoholic Beverage	Scrambled Picture	Distractor Main Effect	Alcoholic Beverage	Nonalcoholic Beverage	Scrambled Picture	Distractor Main Effect	Distractor by Group
	Percent Signal Change: Mean ± SD			$F_{1,41}$	Percent Signal Change: Mean ± SD			$F_{1,41}$	$F_{1,80}$
EROS	.073 ± .093	.059 ± .072	.030 ± .068	**8.795*ab**	.047 ± .089	.051 ± .085	.040 ± .063	.407	3.650^{+}
EROS LH	.071 ± .097	.058 ± .079	.024 ± .071	**10.567*ab**	.049 ± .093	.055 ± .093	.040 ± .066	.580	**4.217***
EROS RH	.075 ± .093	.061 ± .071	.037 ± .069	**7.003*a**	.047 ± .089	.048 ± .081	.041 ± .067	.247	3.034^{+}
DLPFC LH	.060 ± .111	.049 ± .103	.017 ± .085	**7.529*ab**	.041 ± .098	.047 ± .096	.040 ± .073	.032	**4.481***
DLPFC RH	.069 ± .111	.060 ± .094	.039 ± .077	3.953+	.034 ± .097	.035 ± .093	.039 ± .077	.169	3.382^{+}
VLPFC LH	.198 ± .132	.181 ± .147	.145 ± .111	**11.680*ab**	.157 ± .115	.182 ± .129	.154 ± .097	.062	**5.820***
VLPFC RH	.210 ± .122	.195 ± .134	.173 ± .124	**5.387*a**	.157 ± .114	.174 ± .134	.155 ± .104	.039	2.925^{+}
OFC LH	.125 ± .130	.090 ± .135	.057 ± .107	**16.019*ac**	.071 ± .164	. 085 ± .193	.058 ± .157	.399	**6.105***
OFC RH	.256 ± .179	.234 ± .203	.178 ± .210	**10.130*ab**	.184 ± .224	.195 ± .249	.177 ± .199	.176	**5.608***
Insula LH	.104 ± .105	.096 ± .091	.069 ± .077	**5.920*a**	.067 ± .088	.082 ± .080	.066 ± .061	.001	3.275^{+}
Insula RH	.098 ± .097	.082 ± .091	.068 ± .073	**4.084*a**	.061 ± .088	.068 ± .075	.059 ± .066	.025	2.109
Parahippocampal LH	.126 ± .149	.125 ± .098	.052 ± .101	**12.216*ab**	.130 ± .136	.136 ± .141	.083 ± .100	**4.915*ab**	0.894
Parahippocampal RH	.156 ± .140	.136 ± .093	.083 ± .090	**12.220*ab**	. 160 ± .119	.167 ± .126	.109 ± .090	**9.013*ab**	0.743
Hippocampus LH	.085 ± .131	.077 ± .096	.021 ± .094	**13.908*ab**	.050 ± .108	.054 ± .105	.012 ± .090	**7.179*ab**	1.394
Hippocampus RH	.088 ± .120	.066 ± .083	.024 ± .088	**11.669*ab**	.077 ± .106	.074 ± .088	.038 ± .085	**7.955*ab**	1.134
Amygdala LH	.093 ± .188	.098 ± .154	.041 ± .154	**6.019*ab**	.094 ± .194	.095 ± .203	.064 ± .137	2.207	0.581
Amygdala RH	.105 ± .140	.089 ± .126	.027 ± .134	**14.976*ab**	.121 ± .175	.118 ± .160	.085 ± .130	**4.389*a**	2.519
ACC LH	-.059 ± .119	-.080 ± .094	-.095 ± .106	**5.019*a**	-.092 ± .109	-.088 ± .116	-.089 ± .105	.036	3.195^{+}
ACC RH	-.056 ± .119	-.068 ± .102	-.080 ± .111	2.026	-.085 ± .107	-.089 ± .100	-.085 ± .097	0.000	1.179
Fusiform LH	.758 ± .258	.743 ± .207	.553 ± .120	**65.492*ab**	.705 ± .285	.724 ± .294	.579 ± .259	**22.579*ab**	**4.803***
Fusiform RH	.855 ± .303	.851 ± .234	.669 ± .229	**49.514*ab**	.823 ± .292	.845 ± .301	.694 ± .253	**49.438*ab**	3.322^{+}

Table 3. Percent signal change for each distractor type by group, for a-priori regions

Distractor by Group F-values are reported from a full factorial ANOVA model with between-groups factors of Group and Gender and within-groups factor of Distractor type. Distractor main effect F-values within each group are reported from ANOVA model including within-subjects factor of Distractor type. Abbreviations: EROS = Extended Reward and Oversight System; DLPFC = Dorsolateral Prefrontal Cortex; VLPFC = Ventrolateral Prefrontal Cortex; OFC = Orbitofrontal Cortex; ACC = Anterior Cingulate Cortex; LH = Left Hemisphere; RH = Right Hemisphere

a. Alcoholic Beverage > Scrambled Picture, $p < .05$

b. Nonalcoholic Beverage > Scrambled Picture, $p < .05$

c. Alcoholic Beverage > Nonalcoholic Beverage, $p < .05$

*$p < .05$

+.05 <p <.10

4. Discussion

4.1 Behavioral Responses to Probe Face and Distractor Cues

In this study, ALC and NC participants alike were able to use emotional face valence information to improve face memory, as assessed by a DMTS task (LeDoux, 1996; Dolcos *et al.*, 2005; Dolcos & McCarthy, 2006). This was evidenced by better memory performance (*i.e.*, higher accuracy) on positive and negative faces, and faster reaction times to positive faces, than neutral faces. Because it has been shown that alcoholism is associated with impaired emotional perception, and specifically impaired emotional face decoding (Oscar-Berman *et al.*, 1990; Philippot *et al.*, 1999; Clark *et al.*, 2007; Marinkovic *et al.*, 2009; Hoffman *et al.*, 2019; Lewis *et al.*, 2019), we had postulated that normal enhancement of memory by emotional content (in this case, emotional facial expressions) would not be as strong in the ALC group. In those studies, the ALC groups were mostly or exclusively men. However, our results suggest that the ability to use emotional information to aid face memory implicitly may be relatively preserved in AUDw. A significant Group-by-Gender interaction was observed on recognition accuracy as shown in Figure A1 and Table A1. Although the Group-by-Gender interaction for reaction times was not significant (Figure A2 and Table A2), the pattern is congruent with the accuracy data. The higher accuracy of the ALCw (~6 percentage points better than ALCm or NCw) may reflect their greater focus and sensitivity to emotional faces and resistance to distraction or underlying differences in personality or motivation (Mosher Ruiz *et al.*, 2017).

We had postulated that the ALC group would show more recognition errors after alcohol distractors (relative to other distractor types), whereas the NC group would not. However, we found that regardless of the group, the distractor type did not substantially influence accuracy or reaction time. Although we also had expected performance by the ALC group to be impaired by

alcoholic beverage cues, a significant interaction between group and distractor type was not evident. We did not find an attentional bias effect: The alcoholic beverage distractors (relative to nonalcoholic beverage or scrambled picture distractors) did not disproportionately decrease the number of correctly recalled faces among either the ALC or the NC groups. A review by Field and Cox (2008) suggested that the strength of the bias among ALC groups depends on drinking history. Interestingly, Loeber and colleagues (2009) found that reduced attentional biasing to alcohol cues was associated with longer durations of heavy drinking, and our sample also had long durations. Combining participants with variable drinking histories might have masked the attentional biasing effect. However, measures of neural activity may be more sensitive than behavioral measures to changes associated with long-term heavy drinking.

4.2 Distractor fMRI Contrasts

The fMRI contrasts revealed broadly similar patterns of brain activity among the four groups, for both fixation-regions and task-regions. In both brain networks, the beverages (alcbev and nonalcbev) elicited higher activation than the scrambled distractors. This amounts to internal replications of our present fMRI results, with four independent samples (ALCm, ALCw, NCm, and NCw) revealing the same fixation-regions, same task-regions, and with mostly the same direction of effects for task contrasts within those regions. The results reflect the existence, location, and extent of the DMN (Buckner & DiNicola, 2019; Uddin *et al.*, 2019), and also indicate that beverage pictures elicit higher activation than scrambled pictures in the DMN. Moreover, our results indicate that DMN regions are sensitive to the informational content of visual stimuli. In task-regions, the occipital lobe, along with adjoining visual areas in temporal and parietal cortex, were clearly more activated by beverage stimuli than by scrambled images.

601 The results further suggest that content processing is not solely performed by those visual
602 regions, because activation to beverage cues was identified in middle to posterior cingulate
603 regions, which are involved in a multitude of cognitive functions (Heilbronner & Hayden, 2016;
604 Yeo *et al.*, 2016).
605
606 ### *4.3 Gender Differences*
607 The present research provides further evidence for the importance of considering gender
608 when exploring effects of alcoholism on the brain (Mann *et al.*, 2005; Ruiz *et al.*, 2013). Many
609 factors contribute to the observed differences in function for abnormalities identified comparing
610 ALCm with NCm vs ALCw with NCw.
611 Cortical group-level cluster analyses revealed significant Group-by-Gender interaction
612 effects in 22 clusters. The general pattern of those findings indicated that ALCm had lower
613 activation contrasts than NCm, while ALCw had higher activation contrasts than NCw. This
614 pattern was observed primarily in contrasts between beverage and scrambled distractor
615 conditions, and they were found in the two core medial DMN regions, as well as in visual
616 association cortices. A similar pattern of results was found in a previous report (Sawyer *et al.*,
617 2019) in which emotional vs. neutral image contrasts were lower in ALCm than NCm, and
618 stronger in ALCw than NCw. The lower brain reactivity for ALCm, and higher for ALCw,
619 highlighted gender effects, suggesting possible differences in the underlying basis for
620 development of AUD. Of note, the results from other modalities also have indicated similar
621 directions of the fMRI effects, with ALCw having larger reward regions than NCw, and higher
622 fractional anisotropy than NCw, as compared to the smaller regions and lower fractional
623 anisotropy found for ALCm than NCm (Sawyer *et al.*, 2017, 2018).

624 The gender-divergent abnormalities in the anterior and posterior hub regions of the DMN
625 could be reflective of other gender differences observed in conjunction with AUD. The role of
626 these regions in internal monitoring could relate to differences in pre-existing risk factors (Ruiz
627 & Oscar-Berman, 2015; Brighton *et al.*, 2016; Mosher Ruiz *et al.*, 2017), or could represent
628 differential consequences of alcohol abuse (Merrill & Read, 2010). A similar pattern of group
629 differences was identified in cortical regions associated with visual processing. That is, the
630 results could represent a more fundamental impact that is not regionally-specific. In the present
631 study, effects of both increased activation in reward regions and decreased deactivation in DMN
632 regions in response to alcohol pictures were strongest among ALCw in particular. One reason
633 stronger alcohol cue-specific responses were observed among ALCw could be related to gender-
634 based differences in physiological responses to alcohol cues (Rubio *et al.*, 2013). Aligned with
635 this, larger responses to alcohol cues by female social drinkers relative to male social drinkers
636 have been reported in superior and middle frontal gyri (Seo *et al.*, 2011).
637 Another explanation for greater effects of alcohol cues among women than men could be
638 related to depression (Saraceno *et al.*, 2012). Symptoms of depression among non-treatment
639 seeking heavy drinkers were reported to be correlated with increased activation in response to
640 alcohol cue exposure in the insula, cingulate, ventral tegmentum, striatum, and thalamus
641 (Feldstein Ewing *et al.*, 2010). Because ALCw tend to experience depression and anxiety
642 symptoms (Benishek *et al.*, 1992; Schulte *et al.*, 2009), we expected to see higher responses to
643 alcohol cues among ALCw than ALCm in these regions. Indeed, in our sample, ALCw had
644 higher Hamilton Rating Scale for Depression scores than did ALCm, although the scores for men
645 and women were low.
646

4.4 Group Differences

In addition to significant gender interactions, we identified regions with differences between the ALC and NC groups. For the simple comparisons of the ALC group with the NC group, cluster analyses showed that the ALC group had higher activation in 2 fixation-regions and 13 task-regions (Table A5). Differences in the posterior hub were identified in regions with stronger activation to nonalcoholic beverages than to scrambled images, while the other clusters had stronger activation to alcoholic beverages. The higher contrasts observed for the ALC group indicate a processing bias toward beverage cues across fixation- and task-regions. Further, the fact that this cue-sensitivity is not isolated to a single region in the brain likely reflects a widespread divergence in emotional and cognitive activity.

4.5 Brain Responsivity in Fixation-Regions (Default Network)

Compared to the NC group, cluster analyses showed that the ALC group, and the ALCw in particular, had stronger contrasts in the anterior and posterior hubs, along with the temporoparietal junction. The results for ROI that include DMN regions also support the finding of contrast dampening in response to alcohol cues. Abnormal DMN functioning has been observed in other addictions and neuropsychiatric conditions (Broyd *et al.*, 2009; Bednarski *et al.*, 2011; Zhou *et al.*, 2020). In AUD, abnormal functional connectivity among DMN regions has been reported (Chanraud *et al.*, 2011). ALCw in particular had stronger contrasts for both the anterior and posterior hubs, an abnormality which could indicate a limitation in the level of detail processed, or the way in which it is integrated (Sormaz *et al.*, 2018). Lower activation of the anterior hub specifically has been associated with dynamic attention allocation during task executions (Koshino *et al.*, 2011), suggesting that reduced deactivation of this region during

viewing of alcoholic beverage pictures among alcoholics could be associated with failure to reallocate attention back to the task when the alcohol distractors were presented.

4.6 Brain Responsivity in Regions of Interest

The ROI analysis of the OFC provides evidence for reward-specific processing in the ALC group. In particular, reward-specific processing refers to their higher activation from the contrast between alcbev and nonalcbev. Several studies have reported enhanced OFC activation to alcohol cues (Wrase *et al.*, 2002; Myrick *et al.*, 2008; Ray *et al.*, 2010; Shields & Gremel, 2020), and research has established the role of the OFC in alcohol and drug addiction more generally (Goldstein & Volkow, 2002). The OFC activity may be particularly important for preoccupation and anticipation stages of the addiction cycle (Koob & Volkow, 2010). Additionally, activity in this region has been shown to correlate with subjective craving ratings of viewed alcohol cues (Myrick *et al.*, 2004), and further correlated with relapse risk (Reinhard *et al.*, 2015).

In many ROI, differences in activation levels among beverage distractor conditions (alcoholic and nonalcoholic) were larger relative to scrambled pictures in the ALC group than in the NC group. The higher responsivity of the ALC group to alcoholic beverages supports our hypothesis of greater attentional bias in the form of stronger alcbev vs. nonalcbev activity contrasts, but we did not expect the ALC group to have greater activation than the NC group to nonalcoholic beverages relative to scrambled cues. One explanation for this result is that many of the nonalcoholic beverages contain caffeine or sugar (*e.g.*, coffee, tea, soda), which, like alcoholic beverages, also stimulate reward-network activity (Garber & Lustig, 2011). As was suggested in an earlier meta-analysis (Field *et al.*, 2009), the attentional bias for caffeine-related

693 cues may correlate more strongly with subjective craving than for alcohol-related cues.
694 Moreover, craving for both caffeine and alcohol utilize similar neural circuits as are used for
695 processing alcohol reward (Kunz *et al.*, 2008), as do the effects of sugar-related reward (Avena
696 *et al.*, 2008; Volkow *et al.*, 2013).

697 The regions that responded more to beverage cues relative to the scrambled pictures were
698 the total EROS and many of its subcomponents (DLPFC, VLPFC, OFC, parahippocampal gyrus,
699 hippocampus, amygdala) and fusiform. In all of the regions where an interaction of Distractor
700 type and Group was identified, the distractor effect was found to be significant among the ALC
701 group, but not among controls. In the EROS, DLPFC, VLPFC, and OFC, the distractor effect in
702 the ALC group was driven by greater activity during both alcoholic and nonalcoholic beverage
703 pictures relative to scrambled pictures. In the OFC, however, the alcohol distractors elicited more
704 activity in the ALC group than did the nonalcoholic beverages or the scrambled pictures. Thus,
705 the strongest ROI effect specific to processing alcohol cues was observed in the OFC. Crucially,
706 this effect was observed only in the ALC group and not in the NC group (*i.e.*, for controls, no
707 ROI were identified where alcohol distractor pictures elicited more activity than did nonalcoholic
708 beverages; see Table 3). The OFC is believed to play a major role in craving and reward function
709 (Koob & Volkow, 2010).

710 Responses to alcohol and nonalcoholic beverage pictures in the fusiform gyrus were
711 strong among the ALC and NC groups (Figure 5D), as expected, given the fusiform's role in
712 visual object recognition (Pourtois *et al.*, 2009). We hypothesized further that the ALC group's
713 decreased BOLD signal in the fusiform gyrus in response to alcohol cues would provide
714 evidence for stronger distractor interference with face memory maintenance. However, our
715 results showed that any diminishment of the BOLD signal in the fusiform was far outweighed by

its initially higher responses to the alcohol cues. While reductions in fusiform response across the time window of distractor analysis are apparent in the activation time course, an alcohol-specific decrement in the ALC group was not clear. The fact that BOLD responses in the fusiform ROI were consistently lower for scrambled pictures relative to alcohol and nonalcoholic beverage pictures in both the ALC and NC groups suggests that the differences in visual processing demands between conditions may have overridden any potential reduction in the BOLD signal as a result of distractor interference.

We hypothesized that a failure to inhibit distractor interference in response to alcohol cues would be associated with lower activity in VLPFC, given this region's role in inhibition of task-irrelevant distracting stimuli (Thompson-Schill *et al.*, 2002; Aron *et al.*, 2004). However, our ROI results showed similarly increased activation of this region for both alcohol and nonalcoholic beverage cues relative to scrambled pictures. This finding suggests that rather than a failure of VLPFC to inhibit distracting stimuli, the higher activity in this region might result from the overriding demand of emotional and reward salience of the alcohol cues. Alternatively, the VLPFC could be involved in inhibition regardless of the distractor type employed during the DMTS delay.

4.7 Limitations

It is not clear to what degree the abnormalities we observed result from or predate heavy drinking. The mean abstinence period for the ALC group was 8.3 years, and since the NC group did not have an 'abstinence period,' we could not covary for sobriety. Still, our AUD cohort had drinking history values representative of the national population (World Health Organization, 2019), which thereby improves the generalizability of our results. Sobriety in our subject cohort

739 points to how persistent the processing deficits in AUD populations are, and how short- and
740 long-term abstinence may have different paths of recovery for men and women (Fama *et al.*,
741 2020). Nonetheless, our findings illustrate how critical it is to pursue research examining gender
742 differences regarding attentional bias towards reward-related stimuli and pathological alcohol
743 consumption.

744 In conjunction with the multiple-comparison cluster correction procedures employed, the
745 significance level we used ($p < .05$) has been shown to have higher false-positive rates than
746 expected (Eklund *et al.*, 2016). However, stricter thresholds would increase the chance of false-
747 negative errors, and the significance level we used allows the size of the gender effects to be
748 highlighted. Although we report cluster labels by the location of the peak voxel or vertex, the
749 clusters reported can be understood to span multiple functional regions (Woo *et al.*, 2014). That
750 is, they are not limited to a single region, as reported by the maximal vertex or voxel.

751 Finally, our analyses did not include factors such as cigarette smoking, body mass index,
752 and hormone therapy (Luhar *et al.*, 2013; Oscar-Berman *et al.*, 2014), which could possibly
753 influence alcohol cue processing, reward, and DMN activity.

754

755 ## 5. Conclusions

756 Compared to the NC group, the ALC group had stronger activation for DMN regions, and
757 overactivated reward regions during alcohol cue distraction. This suggests that attentional
758 capture is not limited to reward regions, but also includes DMN regions. If so, the DMN has a
759 role in processing salient aspects of addictive substances.

760 The present study showed that alcohol cue distractors have powerful effects on reward-
761 related regions of the brain, even in the absence of impaired performance when alcohol cues are

762 employed as distracting stimuli. We also demonstrated that the increased responses in reward
763 regions are accompanied by dampened DMN activity during the presentation of alcohol cues.
764 Our results suggest that these effects are strongest among ALCw, and provide evidence for
765 dimorphic patterns of responses to alcohol cues between ALCm and ALCw.
766

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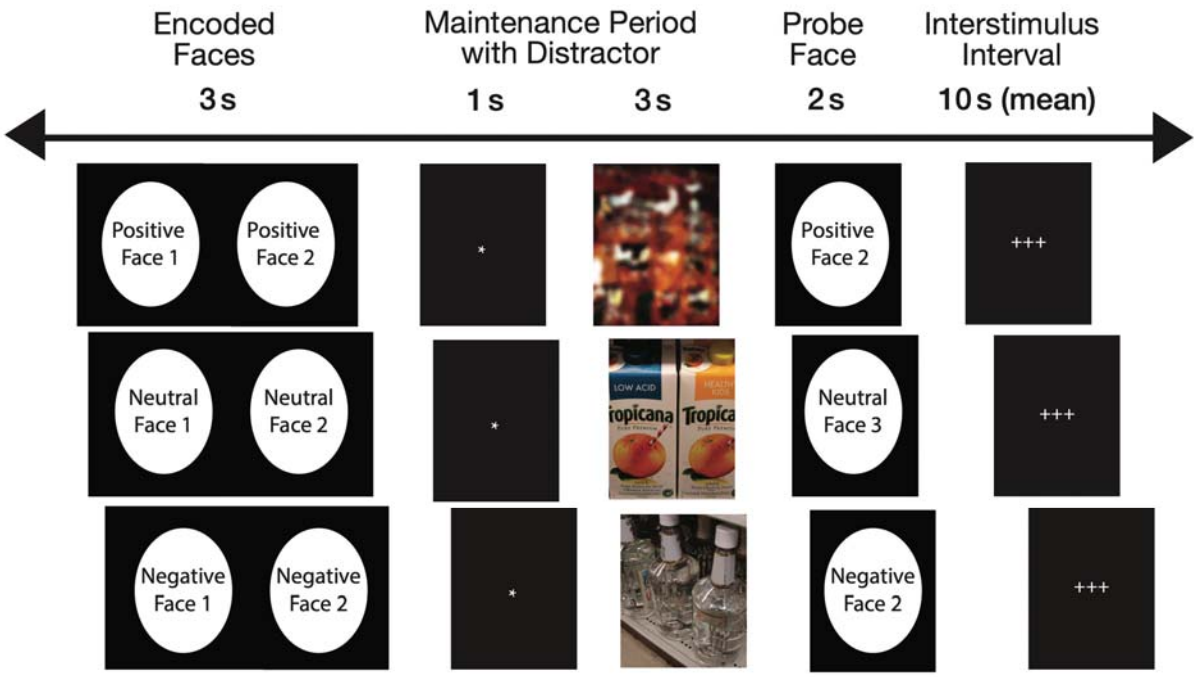
784 the official views of the National Institutes of Health, the U.S. Department of Veterans Affairs,
785 or the United States Government.

786

787 ## Figures

788



789

790 **Figure 1. Task presented during functional neuroimaging**

791 Two faces were presented simultaneously for three seconds, followed by an asterisk for one second. Next, a
792 distractor was presented for three seconds. The probe face immediately followed, during which the subjects had
793 been trained to respond with a button press with either their index or middle finger to indicate whether the probe
794 face matched the encoded face. Three crosses served as the inter-trial interval, which lasted from 2 to 30 seconds
795 (mean 10 seconds). A total of 162 trials were presented. While the faces in this figure have been blurred to mask the
796 identities of the individuals, the research participants saw the original unblurred photographs.

797

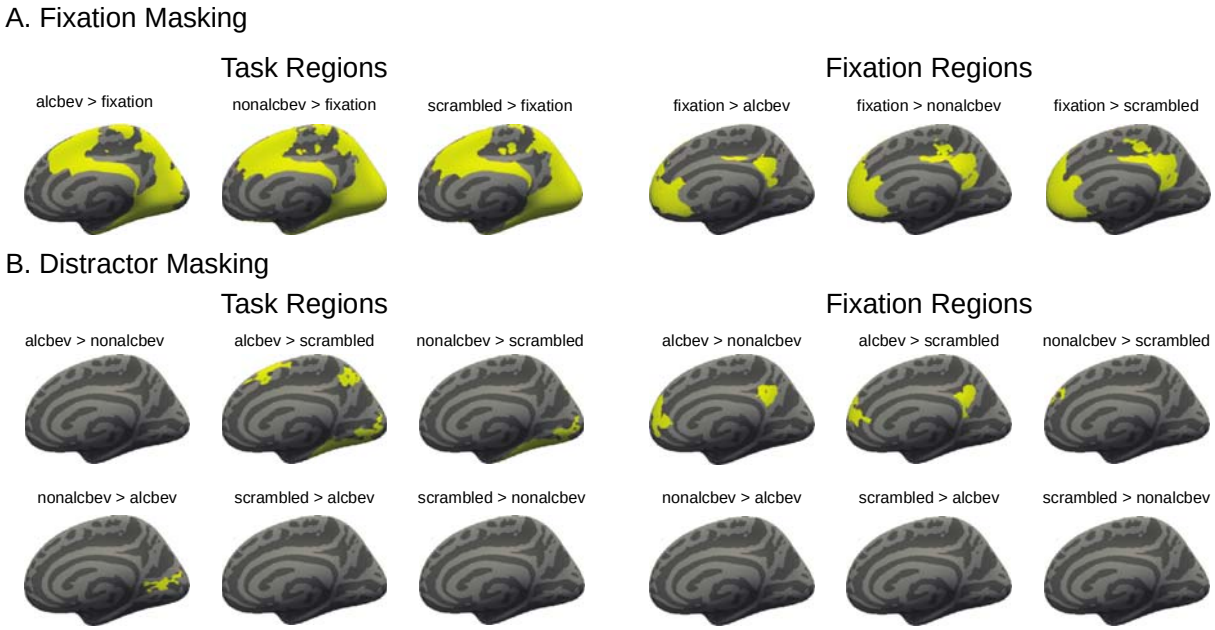


Figure 2. Analyses conducted with masked fMRI data for cortex

The top set of brains represents analyses conducted for cortical regions in which network masking (for task and fixation-regions) were performed. The bottom set of brains represents analyses conducted for cortical regions in which distractor masking (for task and fixation-regions) were performed.

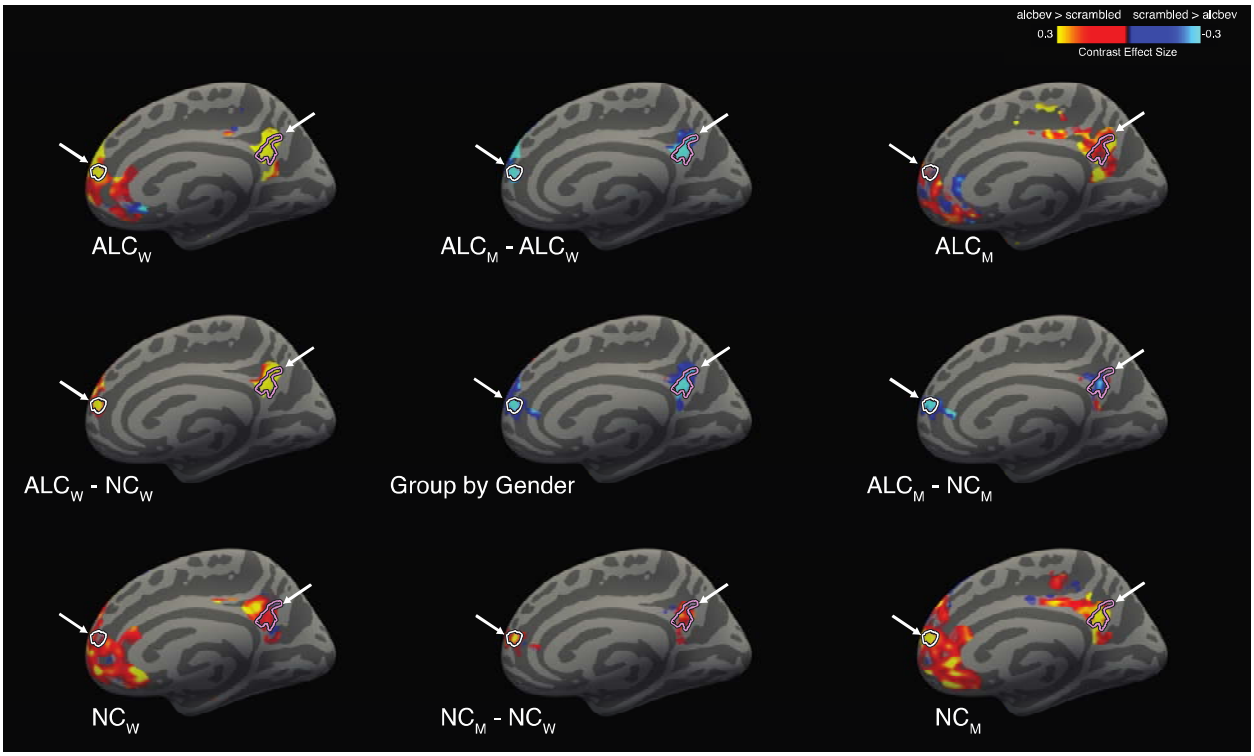


Figure 3. Cortical clusters significant for Group-by-Gender interactions for the alcbev vs. scrambled contrast within fixation-regions (right medial view)

A significant Group-by-Gender interaction revealed several clusters (see Table A4), two of which are indicated by arrows on the medial surface of the right hemisphere, with cluster outlines overlaid on contrast values between alcbev and scrambled distractors. Group mean contrast values (for alcbev vs. scrambled within fixation-regions) are displayed in the four brain images located in the corners of the figure, and group comparisons are indicated by minus signs. Abbreviations: ALCm = Alcoholic men; ALCw = Alcoholic women; NCm = Nonalcoholic men; NCw = Nonalcoholic women.

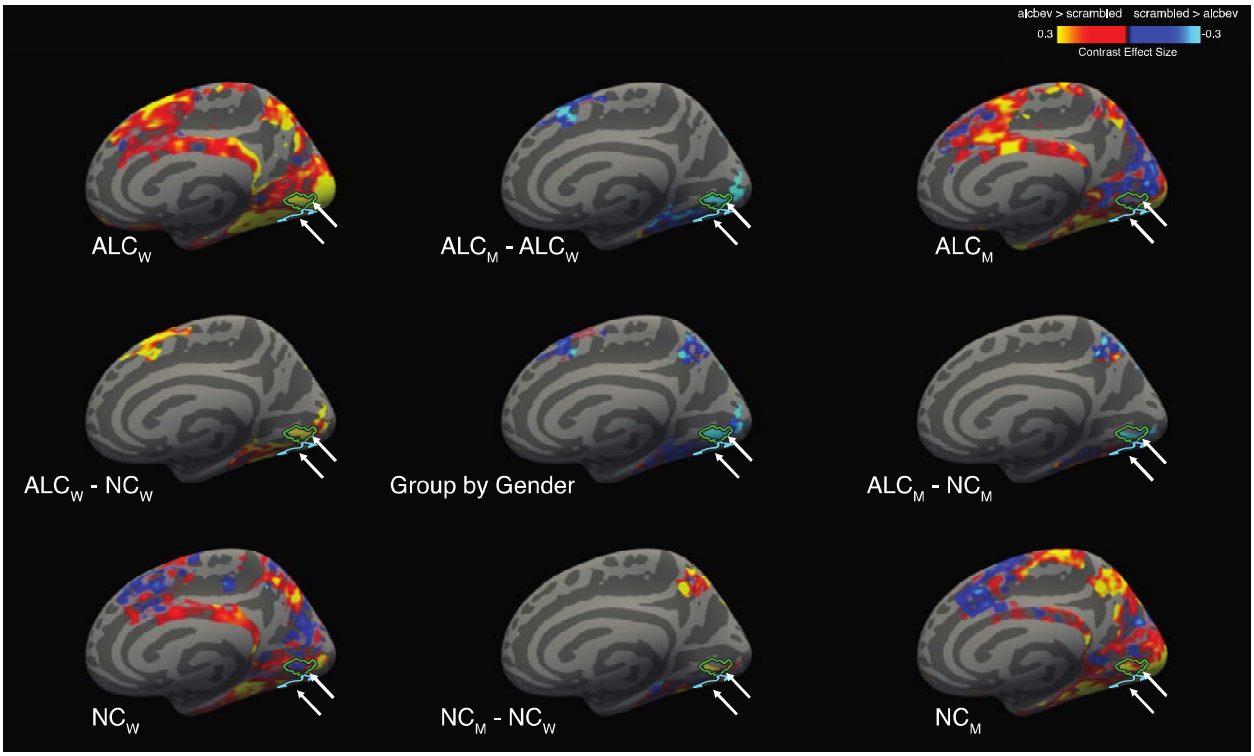


Figure 4. Cortical clusters significant for Group-by-Gender interactions, for the alcbev vs. scrambled contrast within task-regions (right medial view)

A significant Group-by-Gender interaction revealed several clusters (see Table A4), two of which are indicated by arrows on the medial surface of the right hemisphere, with cluster outlines overlaid on contrast values between alcbev and scrambled distractors. Group mean contrast values (for alcbev vs. scrambled within task-regions) are displayed in the four brain images located in the corners of the figure, and group comparisons are indicated by minus signs. Abbreviations: ALCm = Alcoholic men; ALCw = Alcoholic women; NCm = Nonalcoholic men; NCw = Nonalcoholic women.

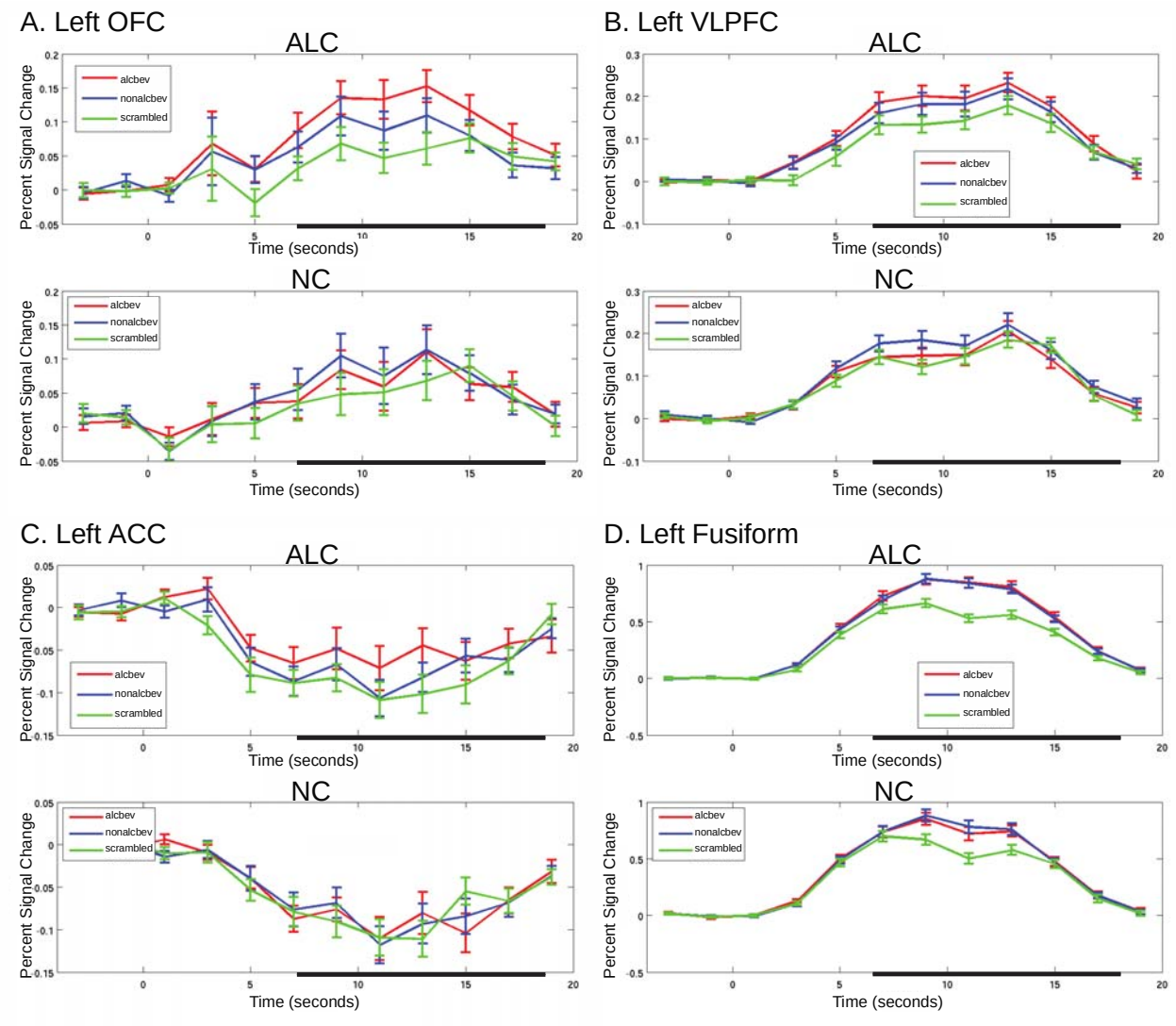


Figure 5. ROI - Percent signal changes in regions of interest for ALC and NC participants by distractor type

The percent signal change represents brain activity during presentation of fixation and the task stimuli. Error bars represent the standard error of the mean. Time zero was set to the onset of the encoded faces, and signal zero was set to the average signal for the three initial time points (two pre-trial and one post-trial onset). The analysis window used to examine the distractor was 6 to 16 seconds following trial onset (2 to 12 seconds after distractor onset), as indicated by the thick line on the x axis. Abbreviations: OFC = orbitofrontal cortex; VLPFC = ventrolateral prefrontal cortex; ACC = anterior cingulate cortex. The ACC (Panel C) is part of the anterior hub within the fixation-regions. The remaining areas are primarily task-regions.

Appendix

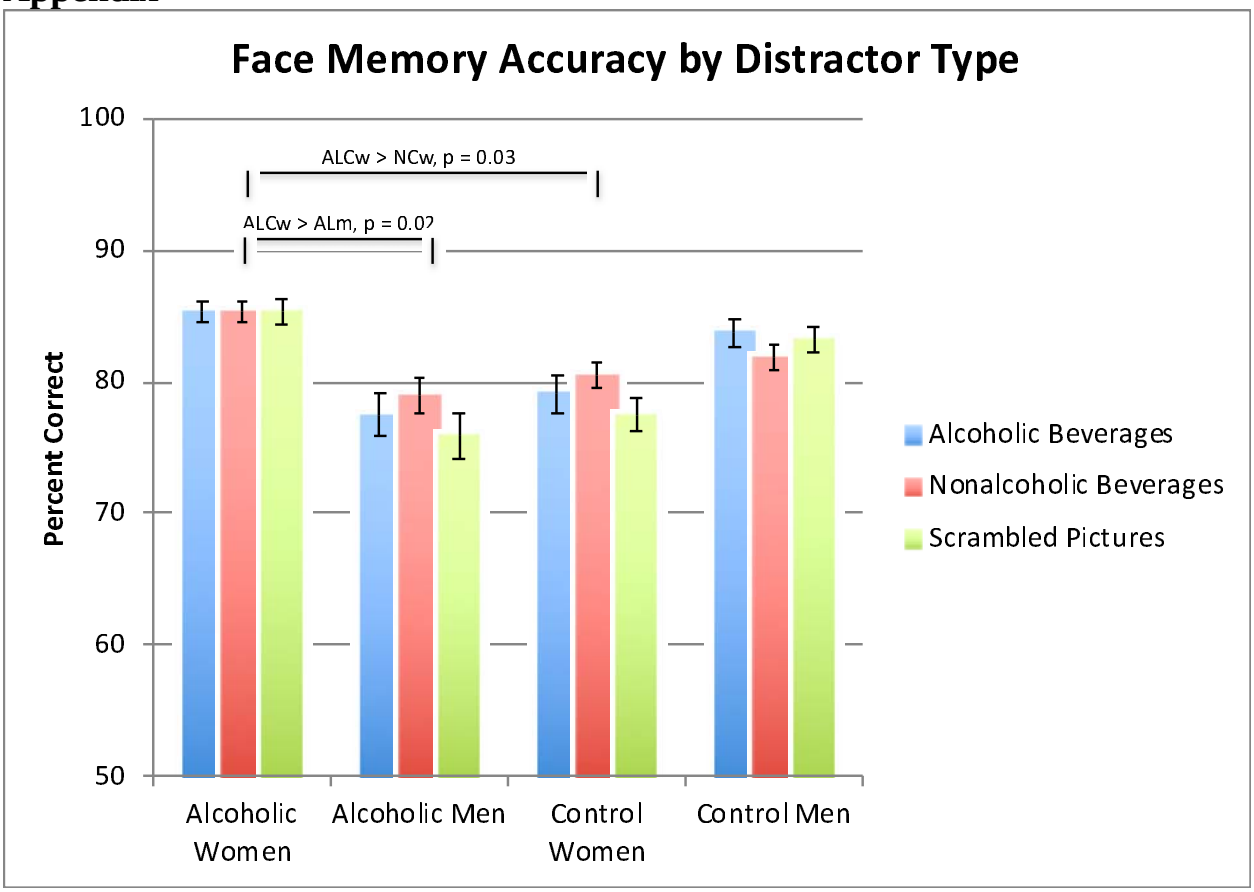


Figure A1. Group and gender comparisons in percent correct responses to the probe face

A significant Group-by-Gender interaction showed that face memory accuracy was significantly higher for the Alcoholic Women than the Alcoholic Men, a gender difference that was greater than the one observed for the NC group. Alcoholic Women also had higher accuracy than Control Women. (Also see Table A1.) There was no significant effect of Distractor type on performance accuracy. Error bars represent standard error of the mean.

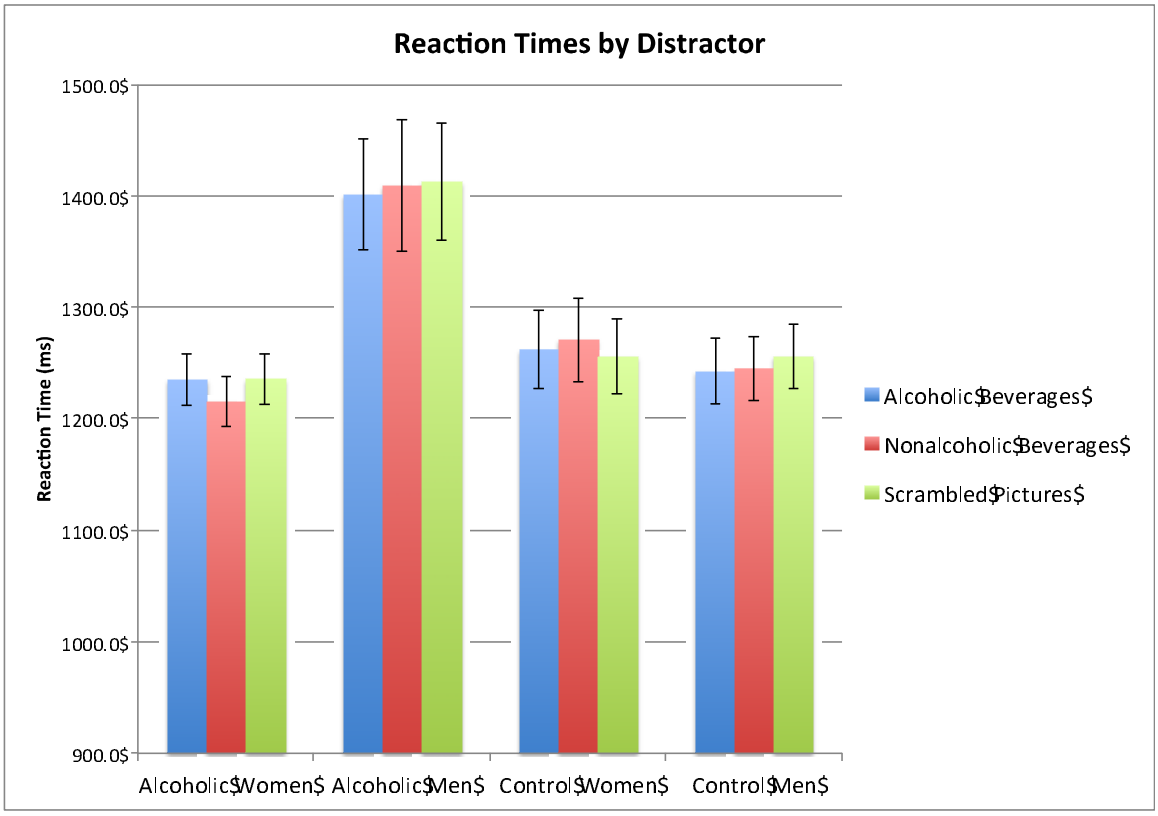


Figure A2. Face memory reaction times: group and gender comparisons in reaction times to the probe face as a function of the distractor stimuli

Reaction times (in milliseconds) are shown for correct trials sorted by conditions and groups. (Also see Table A2.) Participants did not vary significantly by Group or Gender on overall reaction times. There was no significant effect of Distractor type on reaction time, nor did reaction time performance by Distractor type significantly vary by Group or Gender. Error bars represent standard error of the mean.

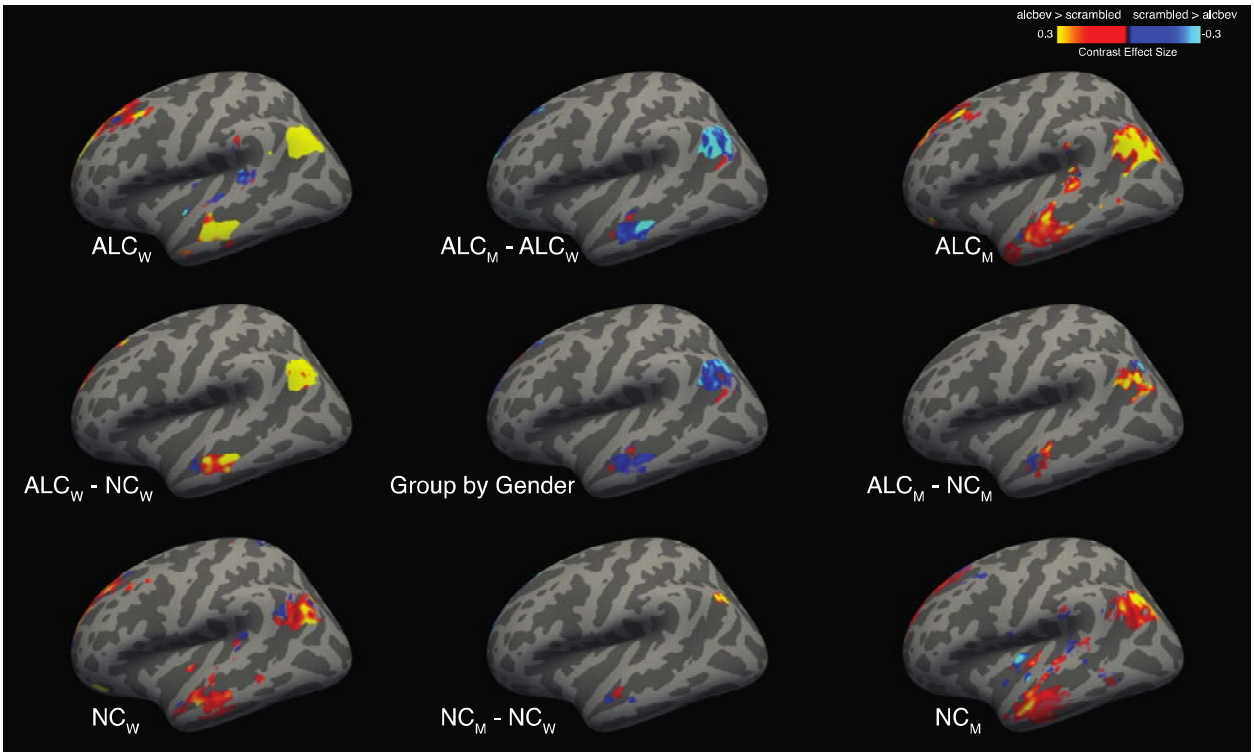


Figure A3. Cortical activation maps for the alcbev vs. scrambled contrast within fixation-regions (left lateral view)

A significant Group-by-Gender interaction revealed several clusters (see Figure 3 and Table A4), although no clusters with significant interactions were found on the left lateral surface. Group mean contrast values (for alcbev vs. scrambled within fixation-regions) are displayed in the four brain images located in the corners of the figure, and group comparisons are indicated by minus signs. Abbreviations: ALCm = Alcoholic men; ALCw = Alcoholic women; NCm = Nonalcoholic men; NCw = Nonalcoholic women.

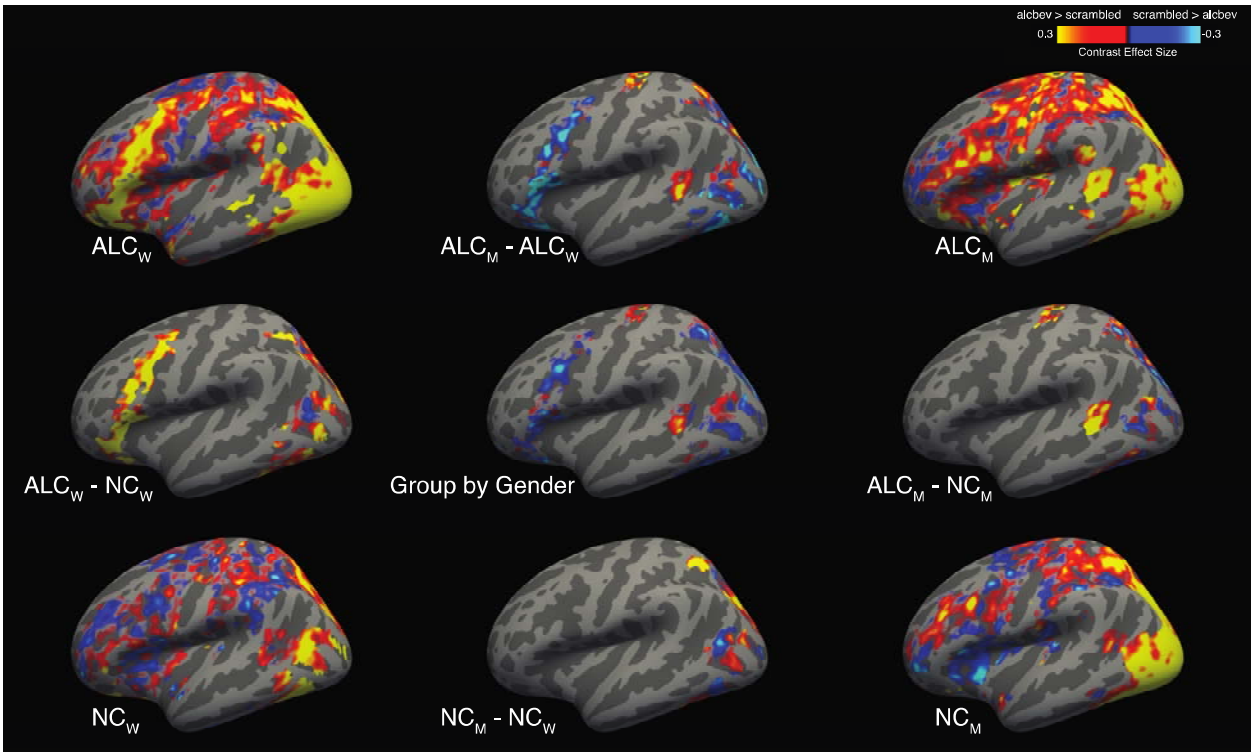


Figure A4. Cortical activation maps for the alcbev vs. scrambled contrast within task-regions (left lateral view)

A significant Group-by-Gender interaction revealed several clusters (see Figure 4 and Table A4), although none are visible on the left lateral view. Group mean contrast values (for alcbev vs. scrambled within fixation-regions) are displayed in the four brain images located in the corners of the figure, and group comparisons are indicated by minus signs. Abbreviations: ALCm = Alcoholic men; ALCw = Alcoholic women; NCm = Nonalcoholic men; NCw = Nonalcoholic women.

876

	ALC	ALCw	ALCm	NC	NCw	NCm
Percent Correct Responses Overall[abc]						
Mean	81.4	85.3	77.4	81.0	79.0	82.9
Standard Deviation	11.5	6.8	13.8	9.7	10.7	8.4
Range	50.0-97.5	66.0-96.3	50.0-97.5	54.9-96.9	54.9-92.6	71.0-96.9
Percent Correct Responses by Distractor						
	ALC	ALCw	ALCm	NC	NCw	NCm
Alcoholic Beverages						
Mean	81.4	85.3	77.5	81.4	79.1	83.7
Standard Deviation	12.4	7.4	15.0	11.4	12.9	9.5
Range	45.8-98.1	66.7-96.3	45.8-98.1	51.9-98.1	51.9-98.1	64.8-98.1
Nonalcoholic Beverages						
Mean	82.1	85.3	78.9	81.1	80.5	81.8
Standard Deviation	10.8	7.7	12.5	9.0	9.2	9.0
Range	53.7-98.1	68.8-98.1	53.7-96.3	57.4-94.4	57.4-91.7	64.8-94.4
Scrambled Pictures						
Mean	80.6	85.3	75.9	80.4	77.5	83.2
Standard Deviation	13.6	8.6	16.1	11.1	12.1	9.4
Range	44.4-98.1	62.5-98.1	44.4-98.1	51.9-98.1	51.9-91.7	61.1-98.1
Percent Correct Responses by Facial Emotion[def]						
	ALC	ALCw	ALCm	NC	NCw	NCm
Positive Faces						
Mean	82.4	86.8	78.1	80.7	79.4	82.0
Standard Deviation	12.5	9.0	14.2	10.4	11.9	8.7
Range	51.9-100.0	56.3-100.0	51.9-96.3	51.9-96.3	51.9-94.4	70.4-96.3
Negative Faces						
Mean	81.9	85.9	77.8	82.9	80.9	84.9
Standard Deviation	12.0	7.2	14.4	9.5	11.0	7.5
Range	46.3-98.1	68.8-98.1	46.3-98.1	53.7-98.1	53.7-94.4	72.2-98.1
Neutral Faces						
Mean	79.8	83.2	76.4	79.3	76.7	81.9
Standard Deviation	11.8	7.5	14.3	11.2	11.1	10.9
Range	51.9-98.1	62.5-92.6	51.9-98.1	50.0-96.3	50.0-92.6	63.0-96.3

877 **Table A1. Behavioral task percent correct responses**

878 Scores for accuracy are provided for overall performance, distractor type, and facial emotion. [a]Group x Gender;
879 [b]Alcoholic Women > Alcoholic Men; [c]Alcoholic Women > Control Women; [d]Emotion main effect; [e]Positive Faces
880 > Neutral Faces; [f]Negative Faces > Neutral Faces; all $p < 0.5$. Abbreviations: ALCw = Alcoholic Women; ALCm =
881 Alcoholic Men; NCw = Nonalcoholic Control Women; NCm = Nonalcoholic Control Men.

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883

	ALC n = 42	NC n = 42	ALCw n = 21	ALCm n = 21	NCw n = 21	NCm n = 21
All Trials (ms)						
mean	1374.0	1302.9	1263.4	1484.6	1319.3	1286.5
standard deviation	418.2	300.0	213.0	536.1	337.2	265.0
range	896.6 - 2720.8	799.6 - 2164.9	896.6 - 1699.5	922.8 - 2720.8	931.2 - 2164.9	799.6 - 1812.7
Correct Trials (ms)						
mean	1317.6	1254.9	1229.4	1405.9	1263.1	1246.7
standard deviation	377.0	288.1	207.9	481.5	321.1	258.7
range	889.7 - 2454.1	784.2 - 2129.2	889.7 - 1649.3	912.4 - 2454.1	909.0 - 2129.2	784.2 - 1795.1
Incorrect Trials (ms)						
mean	1686.2	1564.2	1532.4	1840.0	1591.0	1537.5
standard deviation	538.2	328.2	285.2	680.3	376.8	278.1
range	1079.8 - 3883.9	1064.2 - 2480.1	1160.8 - 2374.8	1079.8 - 3883.9	1064.2 - 2480.1	1097.1 - 1939.1
	ALC	NC	ALCw	ALCm	NCw	NCm
Alcoholic Beverages (ms)						
mean	1318.3	1252.2	1235.4	1401.1	1261.7	1242.7
standard deviation	360.9	292.1	216.4	453.6	320.2	268.6
range	866.2 - 2367.9	765.7 - 2101.9	866.2 - 1578.8	926.1 - 2367.9	906.8 - 2101.9	765.7 - 1837.5
Nonalcoholic Beverages (ms)						
mean	1312.4	1257.5	1215.5	1409.3	1270.6	1244.5
standard deviation	419.1	304.9	208.2	545.0	346.9	264.4
range	886.8 - 2682.0	779.7 - 2274.0	886.8 - 1686.6	902.8 - 2682.0	910.8 - 2274.0	779.7 - 1894.5
Scrambled Pictures (ms)						
mean	1324.2	1255.9	1235.7	1412.7	1255.8	1256.0
standard deviation	378.8	281.8	213.1	482.0	306.5	262.5
range	888.7 - 2678.9	806.6 - 2004.1	914.9 - 1686.1	888.7 - 2678.9	882.4 - 2004.1	806.6 - 1825.8
	ALC	NC	ALCw	ALCm	NCw	NCm
Positive Faces (ms)						
mean	1290.5	1241.2	1227.9	1353.1	1238.4	1244.0
standard deviation	347.2	279.5	229.3	431.6	306.7	257.0
range	867.7 - 2608.6	789.2 - 2015.1	867.7 - 1617.1	894.3 - 2608.6	870.0 - 2015.1	789.2 - 1871.9
Negative Faces (ms)						
mean	1303.9	1251.2	1225.7	1382.0	1264.3	1238.0
standard deviation	322.5	294.0	186.2	407.2	323.2	269.1
range	900.0 - 2218.6	778.9 - 2128.5	900.0 - 1674.6	918.8 - 2218.6	889.4 - 2128.5	778.9 - 1803.4
Neutral Faces (ms)						
mean	1356.4	1272.4	1233.6	1479.2	1286.8	1258.0
standard deviation	492.4	307.0	235.3	640.3	346.8	269.4
range	857.7 - 3051.0	784.4 - 2226.0	857.7 - 1724.7	887.4 - 3051.0	875.3 - 2226.0	784.4 - 1706.6
	ALC	NC	ALCw	ALCm	NCw	NCm
Female Faces (ms)						
mean	1321.8	1272.3	1237.9	1405.7	1275.2	1269.4
standard deviation	369.4	288.7	206.9	471.3	311.5	271.8
range	903.8 - 2648.9	812.7 - 2089.0	903.8 - 1692.7	930.6 - 2648.9	919.7 - 2089.0	812.7 - 1830.5
Male Faces (ms)						
mean	1314.0	1237.0	1220.4	1407.6	1249.7	1224.3
standard deviation	403.4	292.6	212.4	519.7	332.7	254.0
range	872.0 - 2797.2	756.1 - 2159.7	875.7 - 1605.9	872.0 - 2797.2	880.1 - 2159.7	756.1 - 1826.1

884 **Table A2. Reaction times**

885 Group reaction times in milliseconds are provided for distractor type, facial emotion, and face gender. Footnotes
886 indicate significant differences, all $p < 0.5$: [a]Group x Gender interaction; [b]Alcoholic Women > Alcoholic Men;
887 [c]Alcoholic Women > Control Women; [d]Emotion main effect; [e]Positive Faces > Neutral Faces; [f]Negative Faces >
888 Neutral Faces. Abbreviations: ALCw = Alcoholic Women; ALCm = Alcoholic Men; NCw = Nonalcoholic Control
889 Women; NCm = Nonalcoholic Control Men.

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Group	Fixation Masking	Contrast	Annotation	Hemi	Max	VtxMax	Size (mm^2)	MNIX	MNIY	MNIZ	CWP	CWPLow	CWPHi	NVtxs
ALCw	fixation-regions	alcbev > nonalcbev	inferiorparietal	L	5.777	78109	894.36	-46.9	-56.2	24.6	0.0003	0	0.0006	1808
ALCw	fixation-regions	alcbev > nonalcbev	superiorfrontal	L	5.198	117174	2021.3	-7.3	50.7	20.6	0.0003	0	0.0006	3312
ALCw	fixation-regions	alcbev > nonalcbev	precuneus	L	4.279	104685	1114.58	-6.4	-64	36.3	0.0003	0	0.0006	2313
ALCw	fixation-regions	alcbev > nonalcbev	middletemporal	L	3.397	132409	372.86	-57.9	-28.2	-12.3	0.0006	0	0.0012	643
ALCw	fixation-regions	alcbev > nonalcbev	precuneus	R	5.031	78184	343.04	8.9	-53.5	21.9	0.0006	0	0.0012	905
ALCw	fixation-regions	alcbev > nonalcbev	superiorfrontal	R	3.007	33332	470.55	7.4	44.5	26.4	0.0003	0	0.0006	773
ALCw	fixation-regions	alcbev > nonalcbev	middletemporal	R	2.388	149193	390.07	57.3	-28.2	-12.1	0.0003	0	0.0006	583
NCm	fixation-regions	alcbev > nonalcbev	precuneus	L	2.001	28044	372.78	-5.8	-61.1	26	0.0003	0	0.0006	722
NCm	fixation-regions	alcbev > nonalcbev	inferiorparietal	R	2.093	87534	353.25	48	-63.2	30.4	0.0003	0	0.0006	646
NCw	fixation-regions	alcbev > nonalcbev	rostralanteriorcingulate	L	3.853	72938	1014.62	-5.7	40.1	-1	0.0003	0	0.0006	1732
NCw	fixation-regions	alcbev > nonalcbev	precuneus	L	3.518	88451	552.66	-6.9	-55	16.2	0.0003	0	0.0006	1155
NCw	fixation-regions	alcbev > nonalcbev	superiorfrontal	L	3.043	106164	573.38	-7.2	53.9	28.3	0.0003	0	0.0006	853
NCw	fixation-regions	alcbev > nonalcbev	superiorfrontal	L	2.719	37125	231.3	-13.6	43.2	41.7	0.01344	0.01106	0.01611	411
NCw	fixation-regions	alcbev > nonalcbev	superiorfrontal	R	3.812	154767	425.34	11.2	50.9	9.2	0.0003	0	0.0006	716
NCw	fixation-regions	alcbev > nonalcbev	superiorfrontal	R	2.997	141183	288	9.1	53.1	23.9	0.0006	0	0.0012	467
NCw	fixation-regions	alcbev > nonalcbev	precuneus	R	2.381	20851	168.89	12.5	-44.6	37.9	0.03762	0.03352	0.04171	460
ALCm	fixation-regions	alcbev > scrambled	superiortemporal	L	3.628	127514	287.34	-52.7	-19	-6	0.02056	0.0176	0.02381	534
ALCm	fixation-regions	alcbev > scrambled	inferiorparietal	L	3.532	77987	597.66	-39.4	-65.2	28.3	0.0003	0	0.0006	1239
ALCm	fixation-regions	alcbev > scrambled	precuneus	L	3.011	42213	1099.78	-4.6	-65.4	30.8	0.0003	0	0.0006	2316
ALCm	fixation-regions	alcbev > scrambled	temporalpole	R	3.202	75073	255.04	36.1	15.1	-37.4	0.00389	0.0027	0.00539	399
ALCm	fixation-regions	alcbev > scrambled	middletemporal	R	2.184	32116	246.83	55.8	-14	-19.7	0.00479	0.0033	0.00629	358
ALCw	fixation-regions	alcbev > scrambled	superiorfrontal	L	6.192	119696	1479.43	-9	45	32.5	0.0003	0	0.0006	2382
ALCw	fixation-regions	alcbev > scrambled	isthmuscingulate	L	4.52	21771	1599.1	-4.6	-46.8	28.5	0.0003	0	0.0006	3485
ALCw	fixation-regions	alcbev > scrambled	inferiorparietal	L	3.772	8342	1007.44	-46.3	-55.6	24.1	0.0003	0	0.0006	1999
ALCw	fixation-regions	alcbev > scrambled	medialorbitofrontal	L	3.625	141106	792.29	-10.2	46.2	-9.5	0.0003	0	0.0006	1321
ALCw	fixation-regions	alcbev > scrambled	middletemporal	L	3.4	132407	461.02	-57.4	-28.8	-12.1	0.0006	0	0.0012	831
ALCw	fixation-regions	alcbev > scrambled	precuneus	R	4.528	147039	407.44	6	-56.9	22.3	0.0003	0	0.0006	1063
ALCw	fixation-regions	alcbev > scrambled	rostralmiddlefrontal	R	2.928	77385	752.89	18.2	52.8	24.8	0.0003	0	0.0006	1197
ALCw	fixation-regions	alcbev > scrambled	superiorfrontal	R	2.644	116693	213.6	7.6	40.8	48.1	0.01937	0.01641	0.02233	351
NCm	fixation-regions	alcbev > scrambled	isthmuscingulate	L	4.044	159377	1127.18	-7.7	-52	21.5	0.0003	0	0.0006	2355
NCm	fixation-regions	alcbev > scrambled	middletemporal	L	3.081	46308	253.13	-57.3	-4.8	-25.2	0.02056	0.0176	0.02381	442
NCm	fixation-regions	alcbev > scrambled	medialorbitofrontal	L	2.523	119804	386.08	-7.7	57.4	-7.9	0.0006	0	0.0012	508
NCm	fixation-regions	alcbev > scrambled	superiorfrontal	L	2.157	34872	247.83	-9.7	53.4	17	0.0241	0.02085	0.02764	349
NCm	fixation-regions	alcbev > scrambled	inferiorparietal	L	2.069	117757	286.31	-34.4	-81.3	30	0.00987	0.00778	0.01195	501
NCm	fixation-regions	alcbev > scrambled	inferiorparietal	R	3.908	130241	606.24	46.4	-53.3	29.1	0.0003	0	0.0006	1136
NCm	fixation-regions	alcbev > scrambled	superiorfrontal	R	3.772	154660	398.31	9.2	56.8	18	0.0006	0	0.0012	677
NCm	fixation-regions	alcbev > scrambled	isthmuscingulate	R	2.376	85932	344.91	6.8	-49.7	13.4	0.0024	0.0015	0.0036	887
NCm	fixation-regions	alcbev > scrambled	superiorfrontal	R	2.322	18118	261.88	16.4	54.6	19.9	0.01165	0.00927	0.01403	332
NCw	fixation-regions	alcbev > scrambled	superiorfrontal	L	3.775	145688	785.15	-9.1	60.9	21	0.0003	0	0.0006	1299
NCw	fixation-regions	alcbev > scrambled	medialorbitofrontal	L	3.35	98461	869.42	-9.6	51.2	-4.8	0.0003	0	0.0006	1367
NCw	fixation-regions	alcbev > scrambled	middletemporal	L	2.379	13182	203.24	-51.4	-12.3	-20.5	0.04171	0.03733	0.04607	350
ALCm	fixation-regions	nonalcbev > scrambled	superiortemporal	L	3.138	161045	299.84	-48.8	-10.7	-17.9	0.01225	0.00987	0.01463	585
ALCw	fixation-regions	nonalcbev > scrambled	rostralmiddlefrontal	L	3.585	82490	424.57	-18.9	43.9	33.7	0.0003	0	0.0006	719
ALCw	fixation-regions	nonalcbev > scrambled	superiorfrontal	R	2.628	35019	244.79	14.4	53.7	26.1	0.00867	0.00659	0.01076	393
NCm	fixation-regions	nonalcbev > scrambled	superiorfrontal	R	3.123	149679	531.99	10.9	44.1	42.5	0.0003	0	0.0006	861
NCm	fixation-regions	nonalcbev > scrambled	caudalmiddlefrontal	R	2.592	63876	228.53	32	25.7	44.4	0.03762	0.03352	0.04171	420
ALCm	task-regions	alcbev > nonalcbev	precuneus	L	3.84	30022	820.45	-9.8	-74.1	42.2	0.0003	0	0.0006	1681
ALCm	task-regions	alcbev > nonalcbev	inferiorparietal	L	3.068	156958	724.95	-46.8	-63.5	10.3	0.0009	0.0003	0.0015	1254
ALCm	task-regions	alcbev > nonalcbev	lateraloccipital	R	2.796	46455	556.39	41.8	-68.3	-4.7	0.0176	0.01463	0.02056	770
ALCw	task-regions	alcbev > nonalcbev	fusiform	L	4.553	127987	3039.55	-41.4	-52.4	-18.5	0.0003	0	0.0006	5083
ALCw	task-regions	alcbev > nonalcbev	lateralorbitofrontal	L	3.917	9114	696	-32.3	25	-18.9	0.00509	0.0036	0.00659	1456
ALCw	task-regions	alcbev > nonalcbev	parsopercularis	L	3.709	110686	543.82	-46.6	22.6	7.6	0.03	0.02617	0.03381	1090
ALCw	task-regions	alcbev > nonalcbev	inferiorparietal	L	3.231	29327	517.43	-44.1	-69.1	20.8	0.04054	0.03616	0.04491	881
ALCw	task-regions	alcbev > nonalcbev	inferiorparietal	R	2.89	158246	972.39	42.5	-64.4	7.1	0.0003	0	0.0006	1681
NCw	task-regions	alcbev > nonalcbev	superiorparietal	L	2.749	100056	696.49	-21.3	-56.6	62.3	0.0036	0.0024	0.00509	1504
ALCm	task-regions	alcbev > scrambled	lateraloccipital	L	6.82	112623	9254.88	-23.5	-93.1	1.2	0.0003	0	0.0006	14918
ALCm	task-regions	alcbev > scrambled	precentral	L	5.097	102385	1154.47	-27.7	-22.4	62.9	0.0003	0	0.0006	2780
ALCm	task-regions	alcbev > scrambled	bankssts	L	3.981	86601	489.82	-50.3	-43.9	-0.6	0.03146	0.02764	0.03528	1124
ALCm	task-regions	alcbev > scrambled	lateraloccipital	R	5.32	129176	5250.06	25.7	-97.9	-2	0.0003	0	0.0006	7456
ALCm	task-regions	alcbev > scrambled	precentral	R	2.656	72522	782.86	42.6	-11.6	29.6	0.0009	0.0003	0.0015	1824
ALCw	task-regions	alcbev > scrambled	fusiform	L	6.095	34311	13105.37	-29.1	-78.2	-9	0.0003	0	0.0006	20562
ALCw	task-regions	alcbev > scrambled	isthmuscingulate	L	4.555	57611	563.79	-7.7	-42.1	26.1	0.02587	0.02233	0.02941	1660
ALCw	task-regions	alcbev > scrambled	parsopercularis	L	4.416	20526	2644.35	-49.9	21.3	8.8	0.0003	0	0.0006	4925
ALCw	task-regions	alcbev > scrambled	superiorfrontal	L	3.915	133846	522.69	-6.6	17.8	61.3	0.03937	0.03498	0.04375	926
ALCw	task-regions	alcbev > scrambled	lateraloccipital	R	8.832	119142	12539.17	28.1	-96.8	-1.5	0.0003	0	0.0006	19287
ALCw	task-regions	alcbev > scrambled	superiorfrontal	R	3.963	47146	785.28	7.9	18.3	50.6	0.003	0.0018	0.00419	1569
ALCw	task-regions	alcbev > scrambled	lateralorbitofrontal	R	3.159	37696	1035.15	39.4	30.1	-13	0.0003	0	0.0006	1916
ALCw	task-regions	alcbev > scrambled	rostralmiddlefrontal	R	2.655	37107	1604.06	40	25	34.3	0.0003	0	0.0006	2901
NCm	task-regions	alcbev > scrambled	lateraloccipital	L	6.805	122808	11030.59	-15.2	-95.6	-12.9	0.0003	0	0.0006	17180
NCm	task-regions	alcbev > scrambled	fusiform	R	6.25	92502	10153.11	35.9	-72.4	-12.4	0.0003	0	0.0006	15436
NCm	task-regions	alcbev > scrambled	precuneus	R	2.429	98061	571.75	10.4	-53.3	44.6	0.01017	0.00808	0.01255	1490
NCw	task-regions	alcbev > scrambled	fusiform	L	4.853	48274	2961.14	-29.9	-63.8	-13.1	0.0003	0	0.0006	4221
NCw	task-regions	alcbev > scrambled	inferiorparietal	L	3.525	45896	469.12	-43.9	-64.9	9	0.02292	0.01967	0.02617	941
NCw	task-regions	alcbev > scrambled	superiorparietal	L	2.819	157385	433.04	-24.2	-63.1	49.2	0.04083	0.03645	0.0452	920
NCw	task-regions	alcbev > scrambled	superiorparietal	L	2.682	87111	609.56	-25.6	-80.9	12.8	0.0018	0.0009	0.0027	1021
NCw	task-regions	alcbev > scrambled	lateraloccipital	R	6.04	90488	1846.73	25.4	-89.2	-9.5	0.0003	0	0.0006	3154
NCw	task-regions	alcbev > scrambled	lateraloccipital	R	3.065	114637	624.55	44.2	-71.3	-8	0.0009	0.0003	0.0015	881
NCw	task-regions	alcbev > scrambled	superiorparietal	R	2.97	157814	450.45	31.1	-73.7	17.1	0.02764	0.0241	0.03117	806
ALCm	task-regions	nonalcbev > alcbev	pericalcarine	L	-3.202	120908	591.21	-9.1	-86.2	-1	0.01225	0.00987	0.01463	837
ALCm	task-regions	nonalcbev > alcbev	pericalcarine	R	-1.915	43525	692.03	17.9	-69.6	10.6	0.003	0.0018	0.00419	1116
NCm	task-regions	nonalcbev > alcbev	lateraloccipital	L	-2.977	38531	778.52	-37.6	-85.9	-1.1	0.0006	0	0.0012	1036
NCm	task-regions	nonalcbev > alcbev	insula	L	-2.786	96569	492.26	-32.9	9.5	1.4	0.03352	0.0297	0.03762	1158
NCm	task-regions	nonalcbev > alcbev	superiorfrontal	L	-2.596	67709	754.6	-9.5	6.9	45.1	0.0006	0	0.0012	1532
ALCm	task-regions	nonalcbev > scrambled	lateraloccipital	L	6.96	148912	5460.13	-22.1	-90.6	-11.2	0.0003	0	0.0006	7794
ALCm	task-regions	nonalcbev > scrambled	lateraloccipital	R	5.663	62800	4195.98	20.1	-92.7	-8.2	0.0003	0	0.0006	5903
ALCm	task-regions	nonalcbev > scrambled	superiorfrontal	R	3.639	70680	521.47	17.4	-7.3	61.8	0.01671	0.01403	0.01967	1152
ALCw	task-regions	nonalcbev > scrambled	lateraloccipital	L	6.88	8571	8685.5	-21.4	-92.3	-11	0.0003	0	0.0006	12702
ALCw	task-regions	nonalcbev > scrambled	fusiform	R	9.645	107788	9693.99	33.9	-77	-10.9	0.0003	0	0.0006	14150
NCm	task-regions	nonalcbev > scrambled	lateraloccipital	L	9.652	49589	11945.19	-12	-96.2	-12.4	0.0003	0	0.0006	19538
NCm	task-regions	nonalcbev > scrambled	lateraloccipital	R	7.109	71808	9794.62	28.8	-95.5	-0.9	0.0003	0	0.0006	14894

NCm	task-regions	nonalcbev > scrambled	caudalmiddlefrontal	R	3.904	12394	494.97	38	3.2	38.1	0.03146	0.02764	0.03528	902
NCm	task-regions	nonalcbev > scrambled	postcentral	R	3.355	133589	467.15	38.7	-31.1	47.5	0.04171	0.03733	0.04607	1096
NCm	task-regions	nonalcbev > scrambled	parsopercularis	R	2.974	124506	913.39	50.3	14.1	7.6	0.0003	0	0.0006	1651
NCw	task-regions	nonalcbev > scrambled	inferiortemporal	L	5.321	90682	2566.11	-44.4	-56.4	-7.1	0.0003	0	0.0006	3820
NCw	task-regions	nonalcbev > scrambled	superiorparietal	L	3.983	157473	694.61	-22.7	-63.1	31.1	0.0009	0.0003	0.0015	1415
NCw	task-regions	nonalcbev > scrambled	lateraloccipital	R	6.176	161836	3067.24	26.1	-88.5	-10.5	0.0003	0	0.0006	5033
NCw	task-regions	nonalcbev > scrambled	superiorparietal	R	4.612	135644	954.67	26.3	-77.1	19.7	0.0003	0	0.0006	1801
NCw	task-regions	scrambled > nonalcbev	superiorfrontal	L	-3.307	117186	558.06	-9.7	30.8	30.9	0.00479	0.0033	0.00629	1158
NCw	task-regions	scrambled > nonalcbev	rostralmiddlefrontal	L	-2.669	99318	478.08	-33.2	48.8	8.7	0.01314	0.01076	0.01582	699

Table A3. Cortical cluster characteristics for significant contrasts within each group

Annotations (from the peak voxel location in the Desikan-Killiany atlas) are shown for each of the 99 clusters with significant distractor contrasts, calculated for each group separately. The clusters reported can be understood to span multiple functional regions (Woo *et al.*, 2014). That is, they are not limited to a single region, as reported by the maximal vertex or voxel. Abbreviations: Hemi = hemisphere; Max = maximum $-\log_{10}(p\text{-value})$ for group comparison in the cluster; VtxMax = vertex number at the maximum; Size = surface area of cluster; MNIX, MNIY, and MNIZ = Montreal Neurological Institute 305-subject template coordinates X, Y, and Z for the maximum vertex; CWP = cluster-wise *p*-value further corrected for the three spaces of left cortex, right cortex, and volume; CWPLow and CWPHi = 90% confidence intervals for CWP; NVtxs = number of vertices in the cluster; alcbev = alcoholic beverages; nonalcbev = nonalcoholic beverages; L = left hemisphere; R = right hemisphere; bankssts = banks of the superior temporal sulcus.

Fixation Masking	Contrast	Annotation	Hemi	Max	VtxMax	Size (mm^2)	MNIX	MNIY	MNIZ	CWP	CWPLow	CWPHi	NVtxs
fixation-regions	alcbev > scrambled	superiorfrontal	L	-2.635	55177	313.89	-7.9	46.2	22.9	0.01136	0.00897	0.01374	461
fixation-regions	alcbev > scrambled	superiorfrontal	R	-3.304	146084	140.84	16.5	53.5	24.4	0.0021	0.0012	0.003	201
fixation-regions	alcbev > scrambled	superiorfrontal	R	-2.453	134468	116.29	12	47.4	13.5	0.01017	0.00808	0.01255	184
fixation-regions	alcbev > scrambled	precuneus	R	-1.444	122115	162.46	9.6	-54.5	24.9	0.0003	0	0.0006	418
fixation-regions	nonalcbev > scrambled	superiorfrontal	R	-3.422	59361	133.19	7.6	44.3	38.6	0.0003	0	0.0006	242
fixation-regions	nonalcbev > scrambled	superiorfrontal	R	-3.143	8241	206.58	16	53.9	24.6	0.0003	0	0.0006	313
fixation-regions	nonalcbev > scrambled	caudalmiddlefrontal	R	-2.747	29029	155.88	27.8	19.3	42.7	0.0003	0	0.0006	297
task-regions	alcbev > scrambled	superiorparietal	L	-1.996	64642	333.28	-22.2	-84.9	23.6	0.00927	0.00718	0.01136	479
task-regions	alcbev > scrambled	fusiform	R	-4.208	114347	1011.41	31.8	-74.4	-11.2	0.0003	0	0.0006	1562
task-regions	alcbev > scrambled	superiorparietal	R	-2.983	157893	409.83	21.3	-83.2	20.7	0.0012	0.0006	0.0021	627
task-regions	alcbev > scrambled	lingual	R	-2.804	79452	375.68	6.9	-68.3	2.4	0.0027	0.0015	0.00389	473
task-regions	alcbev > scrambled	superiorparietal	R	-2.679	93240	261.8	24.9	-60.1	48	0.03264	0.02882	0.03645	553
task-regions	nonalcbev > scrambled	superiorparietal	L	-2.534	120369	478.5	-17	-88.7	20.5	0.0003	0	0.0006	709
task-regions	nonalcbev > scrambled	lateraloccipital	R	-3.465	132542	658.32	29.9	-85.6	-12.5	0.0003	0	0.0006	985
task-regions	nonalcbev > scrambled	superiorparietal	R	-2.61	130192	242.3	19.9	-79.4	43	0.01908	0.01611	0.02204	404
task-regions	nonalcbev > scrambled	lateraloccipital	R	-2.437	61711	238.46	21.3	-87.7	18	0.02115	0.01789	0.0244	346
task-regions	scrambled > nonalcbev	superiorfrontal	L	-3.795	4781	140.18	-13.4	32.7	24.3	0.00718	0.00539	0.00897	238
task-regions	scrambled > nonalcbev	rostralmiddlefrontal	L	-3.026	116230	173.7	-31.1	48.1	7.1	0.0012	0.0006	0.0021	258
task-regions	scrambled > nonalcbev	superiorfrontal	L	-1.97	153483	148	-12	18.5	36.9	0.00449	0.003	0.00599	327
task-regions	scrambled > nonalcbev	rostralmiddlefrontal	L	-1.861	36306	136.94	-36.8	31.1	29.6	0.00897	0.00688	0.01106	200
task-regions	nonalcbev > alcbev	superiorfrontal	L	3.14	140803	102.82	-8.9	30.4	32	0.04287	0.0385	0.04724	180
task-regions	nonalcbev > alcbev	superiorfrontal	L	2.283	110024	120.81	-12.3	17.2	36.8	0.01403	0.01136	0.01671	290

Table A4. Cortical cluster characteristics for significant Group-by-Gender interactions

Annotations (from the peak voxel location in the Desikan-Killiany atlas) are shown separately for each of the 22 clusters with significant Group-by-Gender interactions for distractor contrasts. The clusters reported can be understood to span multiple functional regions (Woo *et al.*, 2014). That is, they are not limited to a single region, as reported by the maximal vertex or voxel. Abbreviations: Hemi = hemisphere; Max = maximum $-\log_{10}(p\text{-value})$ for group comparison in the cluster; VtxMax = vertex number at the maximum; Size = surface area of cluster; MNIX, MNIY, and MNIZ = Montreal Neurological Institute 305-subject template coordinates X, Y, and Z for the maximum vertex; CWP = cluster-wise *p*-value further corrected for the three spaces of left cortex, right cortex, and volume; CWPLow and CWPHi = 90% confidence intervals for CWP; NVtxs = number of vertices in the cluster; alcbev = alcoholic beverages; nonalcbev = nonalcoholic beverages; L = left hemisphere; R = right hemisphere. See Table 2 for a summary of the cluster information provided here.

Fixation Masking	Contrast	Annotation	Hemi	Max	VtxMax	Size (mm^2)	MNIX	MNIY	MNIZ	CWP	CWPLow	CWPHi	NVtxs
fixation-regions	alcbev > scrambled	inferiorparietal	L	4.631	58681	489.84	-50.5	-55	23.8	0.0003	0	0.0006	1036
fixation-regions	nonalcbev > scrambled	isthmuscingulate	L	1.92	93859	136.3	-14.5	-53.6	7.6	0.00748	0.00569	0.00927	325
task-regions	alcbev > nonalcbev	bankssts	L	3.748	1233	327.69	-50.5	-38.3	2.9	0.0003	0	0.0006	773
task-regions	alcbev > nonalcbev	lateralorbitofrontal	L	3.411	67740	392.95	-42.1	27.4	-14.3	0.0003	0	0.0006	737
task-regions	alcbev > nonalcbev	superiorparietal	L	2.862	123629	420.39	-30.7	-50.7	49.5	0.0003	0	0.0006	950
task-regions	alcbev > nonalcbev	superiortemporal	R	2.818	12074	230.32	46.6	-27.1	-2.4	0.0006	0	0.0012	597
task-regions	alcbev > nonalcbev	inferiorparietal	R	2.766	31474	167.47	40	-74.7	11.1	0.017	0.01403	0.01997	266
task-regions	alcbev > nonalcbev	parsorbitalis	R	2.692	27157	219.37	47.2	36.2	-10.5	0.0009	0.0003	0.0015	298
task-regions	alcbev > nonalcbev	lateraloccipital	R	2.249	56055	346.42	42.2	-72	-5.8	0.0003	0	0.0006	461
task-regions	alcbev > scrambled	superiortemporal	L	4.221	86665	439.74	-47.3	-31.5	-3.3	0.00449	0.003	0.00599	1029
task-regions	alcbev > scrambled	superiorfrontal	L	3.663	129715	522.55	-7.2	24.4	46.7	0.0015	0.0006	0.0024	919
task-regions	alcbev > scrambled	parsopercularis	L	3.155	25042	876.27	-45.5	17.6	20.3	0.0003	0	0.0006	1611
task-regions	alcbev > scrambled	parsorbitalis	L	2.208	10768	301.1	-45.3	31.4	-13.3	0.04578	0.04112	0.05043	621
task-regions	alcbev > scrambled	superiorfrontal	R	3.989	80231	427	11.6	20.7	57.1	0.0003	0	0.0006	844
task-regions	alcbev > scrambled	caudalmiddlefrontal	R	1.867	100338	259.44	38.9	7.5	55	0.03088	0.02705	0.03469	461

Table A5. Cortical cluster characteristics for significant comparisons between ALC and NC groups.

The activation levels for all contrasts were significantly greater for the ALC group than for the NC group. Annotations (from the peak voxel location in the Desikan-Killiany atlas) are shown separately for each of the 15 clusters with significant group comparisons for distractor contrasts. The clusters reported can be understood to span multiple functional regions (Woo *et al.*, 2014). That is, they are not limited to a single region, as reported by the maximal vertex or voxel. Abbreviations: Hemi = hemisphere; Max = maximum $-\log_{10}(p\text{-value})$ for group comparison in the cluster; VtxMax = vertex number at the maximum; Size = surface area of cluster; MNIX, MNIY, and MNIZ = Montreal Neurological Institute 305-subject template coordinates X, Y, and Z for the maximum vertex; CWP = cluster-wise *p*-value further corrected for the three spaces of left cortex, right cortex, and volume; CWPLow and CWPHi = 90% confidence intervals for CWP; NVtxs = number of vertices in the cluster; alcbev = alcoholic beverages; nonalcbev = nonalcoholic beverages; L = left hemisphere; R = right hemisphere; bankssts = banks of the superior temporal sulcus.

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