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The interactive effects of peers and alcohol on functional brain connectivity in young adults

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ABSTRACT

Alcohol and peer influence are known to have independent effects on risky decision making. We investigated combined influences of peers and alcohol on functional brain connectivity and behavior. Young adults underwent fMRI while completing response inhibition (Go/No-Go) and risky driving (Stoplight) tasks. Intoxicated participants made more mistakes on Go/No-Go, and showed diminished connectivity between the anterior insular cortex (AIC) and regions implicated in executive function (e.g., dorsal anterior cingulate). During the Stoplight game, peer observation was associated with increased connectivity between the AIC and regions implicated in social cognition (e.g., ventromedial prefrontal cortex). Alcohol and peers also exerted interactive influences, such that some connectivity changes only occurred when participants were observed by peers and under the influence of alcohol. These findings suggest that brain systems underlying decision making function differently under the combined influence of alcohol and peers, and highlight mechanisms through which this combination of factors is particularly risky for youth.

Compared to childhood and later adulthood, the adolescent and early adult years are characterized by a heightened tendency to engage in risky decision making. While some degree of risk taking is normative and even adaptive, these behaviors can also lead to a variety of adverse outcomes that represent a significant threat to public health. The leading cause of death among 10–24 year olds in the United States, for example, is preventable accidents (Heron, 2016; Mulye et al., 2009).

Theoretical models based on a developmental cognitive neuroscience approach offer a useful perspective on the neurobiological basis for the intensification of risk-taking behavior during adolescence and young adulthood (Dahl, 2016). One prominent class of models, referred to broadly as dual-systems (also maturational imbalance) accounts, posits that the asynchronous maturational development of brain networks involved in executive function and emotion processing predispose youth to engage in behaviors that are rewarding but that also carry risk for dangerous outcomes (Dahl, 2016; Casey et al., 2016; Shulman et al., 2016; Steinberg, 2008).

Of course, the underlying causes of risk-taking are diverse, including not only neurobiological predilection but also social and contextual factors that may be compounding influences on behavior. Imagine, for instance, a young driver about to get behind the wheel of his car after a night out. Actuarial data collected by the insurance industry indicate that his gender and relative youth predict an increased potential for a reckless drive ahead, but also show that the threat rises markedly with the presence of friends in the car and with recent alcohol consumption (Williams, 2003). Indeed, both peer context and alcohol intoxication are known to escalate a range of youth risk behaviors including unsafe driving (Simons-Morton et al., 2005; Keall et al., 2004), criminal activity (Zimring, 1998) and illicit substance use (e.g. Barnes et al., 2002). These influences on risk behavior are also reproduced in laboratory studies manipulating the presence of peers (e.g. Gardner and Steinberg, 2005; O'Brien et al., 2011; Silva et al., 2016; Weigard et al., 2014) and alcohol intoxication (Casbon et al., 2003; Gilman et al., 2012; Lane et al., 2004).

Neurodevelopmental models of risky decision-making must

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accordingly address how these compounding factors specifically impact decision processes in the brain. Neuroimaging studies exploring these phenomena independently provide a useful foundation. For example, experimental brain-imaging studies suggest that peer observation during decision making can lead to activation changes in brain regions implicated in reward (e.g., the ventral striatum and ventromedial prefrontal cortex/orbitofrontal cortex Chein et al., 2011; Izuma et al., 2010; Smith et al., 2015), and in those implicated in social cognition (e.g., precuneus and temporoparietal junction Hoorn et al., 2016). Some of these same areas (e.g., medial prefrontal and striatal regions) have also been found to exhibit greater positive coupling (i.e. greater functional connectivity) among adolescents and young adults relative to younger children (Somerville et al., 2013), suggesting that increased connectivity within these circuits may underlie increased sensitivity to social influences during this later developmental period. Adolescents reporting a stronger inclination to resist social influences have also been found to display increased co-activation across multiple brain networks while viewing emotion-laden videos (Grosbras et al., 2007), a finding that is further suggestive of a link between peer influence and the functional coupling of interconnected brain regions.

Meanwhile, there is evidence that alcohol has wide-ranging effects on both cognition and emotion (e.g. (Gilman et al., 2012; Boileau et al., 2003),). The impacts appear to be especially disruptive to executive and self-regulatory mechanisms, including inhibition, attentional control, and working memory (Casbon et al., 2003), and concomitantly alter neural activation patterns in regions implicated in executive function, including the dorsal anterior cingulate cortex (dACC), dorsolateral prefrontal cortex (dlPFC), and basal ganglia (for a review, see Bjork and Gilman, 2014). Acute alcohol intoxication is also associated with disruption of functional connectivity between brain regions engaged during self-regulatory control, such as the anterior insula cortex (AIC) and dACC (Gorka et al., 2018).

Taken together, the findings from separate investigations of peer influence and alcohol intoxication suggest the possibility that these factors impact partially dissociable processes engaged during decision making. In light of the fact that youth typically consume alcohol in social settings, and cite social facilitation or improvement of social gatherings as a primary motivation for drinking alcohol (Kuntsche et al., 2005), an understanding of the combined and interacting impacts of peer context and alcohol is of particular importance. However, despite the typical confluence of these two influences on behavior in adolescence and early adulthood, previous research investigating alcohol's effects on the processes that undergird risk taking has typically been performed when participants have been alone. Likewise, studies of peer influence have been conducted without consideration of how intoxication might alter its effects.

In the present study, we directly pursue the possibility of interactivity between the two phenomena by exploring peer and alcohol effects within the same paradigms, administered within a single cohort. Specifically, we investigate the combined effects of peer presence and alcohol intoxication on two essential components of risky behavior: response inhibition and incentivized decision making.

College-aged youth underwent functional Magnetic Resonance Imaging (fMRI) while completing a response-inhibition task (Go/No-Go, “GNG”) and a risky-driving task (The Stoplight Game, “Stoplight”). Participants completed both tasks while alone and while in the supposed presence of a peer, and were randomly assigned to complete the protocol after drinking alcohol or a placebo beverage. After carrying out traditional activation analyses to confirm expected task activation patterns, we focused on an analytic approach allowing us to index fluctuations in brain activity throughout the entire run of a task, rather than contrasting certain trials or behaviors. Specifically, we adopted a functional connectivity approach to investigate whether correlated activity throughout each run was influenced by alcohol and/or peers. This approach aligned with our expectation that alcohol and peer influences would be most evident in state-based effects on the brain, independent from activity changes associated with specific task events (e.g. Gorka et al., 2018). This approach also aligns with recent assertions that a circuit-based, rather than region-based, accounting of adolescent brain development is likely to prove most fruitful and explanatory (e.g. Casey et al., 2016).

To further constrain the search space of analyses, we examined how intoxication and peer presence influenced whole-brain co-activation with a theoretically-motivated region-of-interest, the anterior insula cortex (AIC). The AIC, and particularly the right AIC, is thought to serve as a cognitive-emotional hub. In this capacity, the right AIC is instrumental in orchestrating responses in brain regions implicated in both executive control and affective processing (Menon and Uddin, 2010; Sridharan et al., 2008), as well as in salience detection (Menon and Uddin, 2010) and the perception of emotional states (for reviews, see Craig, 2009; Singer et al., 2009). Because of its role in the interplay of cognitive and emotional processes, we have previously argued that the immaturity of the AIC during adolescence may also contribute to heightened risk-taking behavior (Smith et al., 2014). The right AIC is engaged during response-inhibition, reward-processing and decision-making tasks (Smith et al., 2014, 2018; Paulus et al., 2003), and emerging evidence suggests that both peer presence and alcohol use can separately influence activation of, or connectivity with, the right AIC (Gorka et al., 2018; Smith et al., 2018).

Based on the theoretical and empirical foundations outlined above, we hypothesized that alcohol intoxication would most evidently impact connectivity between the insula and brain regions implicated in executive function (especially lateral prefrontal and anterior cingulate regions), with the weight of prior evidence suggesting that disruption of regional coupling (i.e. decreased connectivity) would be the predominating pattern. Meanwhile, we anticipated that peer presence would primarily impact co-activation of the insula with brain regions implicated in social cognition and reward, such as the striatum, ventromedial prefrontal cortex, amygdala, temporoparietal junction, and posterior cingulate/precuneus. We did not have strong hypotheses regarding the directionality of peer influences on connectivity, since increased connectivity has been found in association with both greater social sensitivity (e.g., in age groups known to be more sensitive to social inputs Somerville et al., 2013) and reduced social sensitivity (e.g., within those who are relatively more resistant to social influence Grosbras et al., 2007). Importantly, we also expected a significant interaction between alcohol and peer context, such that alcohol would exaggerate peer effects on functional connectivity. With respect to behavior, we hypothesized that participants in the alcohol condition would perform less accurately on GNG, but in light of studies demonstrating the lack of a peer effect on cognitive control (e.g. Smith et al., 2018; Breiner et al., 2018), we expected that peer presence would not influence performance on the GNG task. We did, however, expect that peer presence might encourage greater risk-taking during Stoplight – an effect we have previously observed in younger cohorts, with alcohol potentially enhancing this peer effect.

1. Methods

1.1. Experimental model and subject details

Young adults were recruited from the Philadelphia area to participate in a study investigating the effects of alcohol on decision making. Participants completed a prescreening to determine eligibility. In addition to typical fMRI contraindications (e.g., left-handedness, implanted metal, history of neurological disorders, etc.), individuals with conditions for which alcohol constitutes a specific health risk (e.g., diabetes, hypertension), individuals with an alcohol use disorder (including binge drinkers), and alcohol naive individuals were excluded. Of the 52 participants scanned, one was excluded for head motion in excess of 2.5 mm (mean displacement = 5.9 mm), one was excluded for having a low quality structural scan, and one was excluded for falling asleep during the scan and neglecting to provide behavioral responses. The final sample

consisted of 49 individuals, ages 21–24 ($M_{age} = 21.9$, 23 female). Mean relative head motion ranged from 0.03 to 0.23 mm, and did not differ as a function of our experimental manipulations.

1.2. Method details

Pre-scan procedure and alcohol administration. Participants were randomly assigned to one of two alcohol administration conditions (alcohol or placebo). All participants were instructed to not eat any heavy meals 6 h prior to the study, and to not eat any food 3 h prior to the session. After arriving at the laboratory, participants completed consent procedures, were administered a drug test, and filled out a series of self-report questionnaires. Participants were instructed that another same-age peer was also participating in the study, and that this peer would be watching their performance during some of the scans. Participants in both conditions were instructed that they would be drinking two beverages that may or may not contain alcohol. Participants then consumed the alcoholic beverages designed to achieve a BAC of 0.10, or placebo beverages with only a trace amount of alcohol sprayed onto the surface of the drink (intended to mask condition status). BAC assessments were conducted prior to task performance, subsequent to task performance, and prior to final release from the study site. Approximately 30 min ($M = 32 \pm 1$ min) after the consumption of the alcoholic beverage or placebo, participants completed the task protocol in the MRI scanner. Following the scan, participants were debriefed, and individuals in the alcohol condition were required to remain at the laboratory until their BAC reached 0.03. For participants in the alcohol condition, average BAC immediately prior to the scan was 0.08 ± 0.02, and BAC immediately following the scan was 0.06 ± 0.02. The final sample consisted of 23 participants in the alcohol condition and 26 participants in the placebo condition.

fMRI procedure and peer manipulation. Neuroimaging data were collected on a Siemens Verio 3 T MRI scanner. The fMRI paradigms were presented during functional scans lasting approximately 10 min for Stoplight and 8 min for GNG (T2*-weighted echoplanar imaging sequence, TR = 2000 ms, TE = 30 ms, flip = 90°, 4-mm slice thickness with no gap, 220 × 220 field of view, 3.4 × 3.4 mm in-plane resolution). A T1-weighted magnetization-prepared rapid-acquisition gradient echo (MPRAGE) was also collected for the co-registration of functional images. Participants completed two runs of each of two tasks in the MRI scanner, including Stoplight and GNG.

Stoplight (Chein et al., 2011) is a simple driving task in which participants control the progress of their vehicle along a straight track by deciding whether to brake, or not, as they approach a series of traffic signals. With variable timing before the vehicle enters into an intersection, a traffic signal turns yellow, and the participant must decide whether to chance a possible crash in the intersection, or brake (by pressing a button) and wait for the light to turn green. Importantly, both the timing of the traffic signals and the probability of a crash in the associated intersections are varied so as to be unpredictable by the participant. Successfully traveling through an intersection saves time, whereas braking and waiting for the signal to turn green wastes time (3 s). However, if the participant does not brake and a crash ensues, the loss of time is even greater (6 s) than if the participant were to brake and wait for the light. Each run of Stoplight consisted of 40 consecutive intersections, separated by a varying duration, ranging from 8 to 20 s. Unbeknownst to participants, there was a roughly 50% chance of crashing, and it was therefore similarly advantageous to stop or to run the light. Participants were told that they could earn an additional monetary bonus by completing the overall course in a timely fashion. In this way, occasional risk taking (i.e., not braking for the yellow light) was incentivized. In actuality, all participants received the same monetary bonus at the conclusion of the study, regardless of their task performance.

The Go/No-Go task is a widely-used measure of response inhibition (e.g. Durston et al., 2002). In this task, participants are presented with a sequence of simple stimuli, and are required to give a button-press response to one pre-specified (frequently occurring) stimulus class while withholding a response to a second (less frequently occurring) stimulus class. In the present version of the task, stimuli consisted of neutral and angry faces; participants were instructed to inhibit responses to angry faces only and respond to neutral faces (Hare et al., 2008; Somerville et al., 2012). Each run had 80 trials (60 Go, 20 No-Go) presented in pseudo-randomized order.

All participants completed two runs of Stoplight and Go/No-Go. For one run of each task, participants completed the task alone. During the other run, participants were instructed that a same-age, same-sex peer was watching and making predictions about their performance. To heighten the believability of the manipulation, a confederate introduced herself or himself to the participant over the MRI loudspeaker before the scan; this clip was pre-recorded but presented as if it were live. Order of the runs (peer vs. alone) was counterbalanced across participants. In the final sample, 23 participants completed the peer condition first and 26 completed the alone condition first, so task order was included as a covariate in all analyses. The experimental procedure thus yielded a mixed factorial design, with alcohol condition manipulated between-subjects and peer condition manipulated within-subjects.

In order to prevent word-of-mouth from undermining the peer deception, subjects were not debriefed until the full conclusion of the study data collection phase. Accordingly, we did not have the opportunity to ask subjects if they believed the manipulation. However, we have used the anonymous peer manipulation in several prior studies (e.g. Weigard et al., 2014; Smith et al., 2018) and affirmed that the manipulation is believed by the vast majority of subjects. Moreover, the robustness of the behavioral peer effect observed across studies provides further evidence that the manipulation is effective.

1.3. Quantification and statistical analysis

fMRI analysis. To confirm expected task-based activation patterns we first conducted activation analysis using a classic subtraction methods. This analysis was succeeded by primary analysis of alcohol- and peer-induced changes in functional connectivity with a relevant region of interest, the right AIC. This approach allowed us to index state-based changes in brain responses. The connectivity analyses were conducted using tools from the fMRI Software Library (FSL) and Analysis of Functional Neuroimages (AFNI). We used a seed-based connectivity approach to investigate changes in connectivity with the AIC as a function of our variables of interest (peer presence, alcohol). We selected this AIC region of interest based on our hypothesis (Smith et al., 2014, 2018) that the AIC, and particularly the right AIC (Sridharan et al., 2008), plays a role in adolescent risky decision-making through the integration of signals from brain networks implicated in reward responsivity and cognitive control. The location of the region of interest was drawn from the Harvard-Oxford atlas so as not to bias the connectivity results with respect to circuits or tasks. However, we confirmed that the selected right AIC region of interest was significantly activated in the present sample for contrasts of interest conducted with both the Stoplight and GNG tasks.

Functional connectivity pipeline. The analytic pipeline was identical for Stoplight and Go-No/Go. Structural images were skull-stripped and bias-corrected using FSL's Anatomical Processing Script (fsl_anat). Functional image preprocessing was based on the pipeline outlined in Prium and colleagues (Pruim et al., 2015), and consisted of motion correction in FSL'S MCFLIRT, mean-intensity normalization, 6-mm spatial smoothing, data denoising in FSL's ICA AROMA, nuisance regression of white matter and cerebrospinal fluid, application of a high-pass filter, and registration of participants' structural images and the Montreal Neurological Institute (MNI) standard brain. A time-series of mean activation for the region of interest was then extracted from each subject's brain in standard space. The region of interest consisted of a 5-mm sphere located in the right anterior insula (MNI coordinates: $x = 40$, $y = 14$, $z = -8$; from the peak coordinates in the Harvard-Oxford atlas). For each scan, the timeseries was then normalized and entered as a regressor of interest in a

whole-brain analysis in FSL's FEAT (FLAME 1). Next, for each participant, a second-level fixed-effects analysis was conducted in FEAT comparing connectivity for the peer condition vs. the alone condition. Finally, second-level contrasts were fed into a group analysis which compared connectivity using a 2 (Placebo vs. Alcohol) x 2 (Peer vs. Alone) design, with order of peer condition included as a covariate. Images were thresholded at $Z > 2.3$, $p < .05$, the default settings in FSL. A second version of the analysis was performed, which was identical except for the inclusion of task covariates, which were included simultaneously with nuisance regression of white matter and CSF. For Go/No-Go, four task covariates were modeled (Hit, Correct Rejection, Miss, False Alarms), and for Stoplight, two task covariates were modeled (yellow lights in which participants made a risky choice, yellow light in which a participant made a safe choice). Results from the two versions of the analysis (with and without task covariates) were virtually identical; all brain regions considered in the results and discussion were significantly correlated with the AIC in both models. The findings presented here resulted from the pipeline that did not include task covariates (i.e., the model with greater degrees of freedom and therefore greater power), but both sets of findings are available in our NeuroVault repositories.[1]

Task behavior analysis. To investigate the effects of peers and alcohol on risk-taking and response inhibition, a series of factorial ANOVAs were conducted, with a 2 (alcohol vs. placebo) by 2 (peer condition vs. alone condition) by 2 (peer condition first vs. alone condition first) design. Risk taking was defined as the proportion of trials for which participants chose to run the yellow light during Stoplight. Ability to inhibit responses during Go/No-Go was measured in two ways: we examined effects of peers and alcohol on the proportion of incorrect No-Go trials (False Alarms), as well as on loglinear d-prime (Hautus, 1995). In both cases, we excluded from analysis any trials for which reaction time was longer than 2.5x the standard deviation of that individual's mean.

2. Results

Task-based effects. Task-based activation patterns based on traditional subtraction analysis for the Go/No-Go and Stoplight tasks were consistent with prior neuroimaging work. During Go/No-Go, correct rejections ("No-Go") were associated with significantly greater activity in the bilateral insula, putamen, intraparietal sulcus, superior temporal gyrus, lateral occipital cortex, cerebellum, right dorsolateral prefrontal cortex (dlPFC), and right amygdala, compared to hit ("Go") trials. The reverse contrast (Hit > CR) yielded activation in the vmPFC, subcallosal cortex, thalamus, precuneus, and left motor cortex and parietal operculum. We observed no group differences in GNG activation patterns as a function of either alcohol or peer presence.

During trials of the Stoplight Game for which participants ran the yellow light ("Risk"), compared to trials in which they did not ("Safe"), we found greater activation in the bilateral anterior insula, dmPFC (dACC and paracingulate gyri), right dlPFC, thalamus, caudate, accumbens, bilateral occipital cortex, and precuneus. The reverse contrast (Safe > Risk) yielded activation in the sensorimotor strip, vmPFC, bilateral posterior insula and central opercular cortex, and putamen. For our contrasts of interest (Risky trials > Safe trials; Safe trials > Risky trials), we observed no effects of peer presence. For risky trials, compared to safe trials, participants in the placebo condition demonstrated greater activation than those in the alcohol group for a single cluster encompassing part of the precuneus and lateral parietal cortex (Figure S2). Thresholded and unthresholded images are available in the NeuroVault repository (https://neurovault.org/collections/3538/).

Functional connectivity of the anterior insular cortex during Go/No-Go and Stoplight. After confirming an expected pattern of task-based activation in association with each task, and noting the limited impact of our experimental manipulations on general task activation, we proceeded with a functional connectivity approach that could provide sensitivity to state-based changes. This approach investigated effects of peers and alcohol on functional connectivity throughout the entire run, rather than focus on the contrast of specific events or trials as in the subtraction analysis discussed above. Findings were highly similar whether or not we included covariates modeling individual task events, which confirms that alcohol and peers exerted wholesale influences on cognitive state, rather than changing brain activity only in association with specific trial events or trial-dependent conditions (e.g. when participants decided to run a yellow light vs. waiting).

Fig. 1 presents the results of the functional connectivity analysis for the entire sample. Brain regions significantly correlated with the AIC seed region throughout the run were highly similar during the Stoplight and GNG, thus providing a within-study confirmation of the robustness of the basic connectivity approach. Regions exhibiting connectivity with the AIC included the dmPFC (anterior cingulate and paracingulate gyri, supplemental motor area), left and right lateral prefrontal cortices, bilateral orbitofrontal cortices, sensorimotor strip, bilateral supramarginal gyri, thalamus, caudate, putamen, and cerebellum.

Main effects of alcohol on functional connectivity with the anterior insula. Functional connectivity with our AIC seed region differed significantly between individuals in the alcohol group and the placebo group (Fig. 1C and D). For both Stoplight and GNG, participants under the influence of alcohol displayed significantly *less* connectivity between the AIC seed and the dACC than those in the placebo group. We also observed decreased connectivity between the insula and other brain regions implicated in executive control in the alcohol group: during GNG, connectivity between the AIC and the dlPFC was diminished (Fig. 1C), and during Stoplight, connectivity between the AIC and the ventrolateral prefrontal cortex (vlPFC) was diminished (Fig. 1D).

Main effects of peers on functional connectivity with the anterior insula. The presence of peers was also related to significant differences in AIC connectivity. During Stoplight, connectivity between the AIC and the ventromedial prefrontal cortex (vmPFC), hippocampus, amygdala, temporal poles, and left sensorimotor cortex was greater when participants believed they were being observed by a peer, compared to when they completed the task alone (Fig. 1F). In contrast, during GNG we did not find evidence supporting a main effect of peer presence on AIC connectivity (Fig. 1E).

Interactive effects of peers and alcohol on anterior insula connectivity. Finally, for Stoplight and GNG, we observed interactive effects of alcohol and peer presence on AIC connectivity. During the Stoplight Game, only participants in the alcohol group showed significantly greater connectivity between the AIC and the posterior cingulate cortex (PCC)/precuneus in the peer condition, compared to the alone condition (Fig. 2). Furthermore, several main effects of peer context on connectivity discussed earlier appeared to be driven by effects unique to each group, though these were not significant interactions. For example, peer effects on connectivity with the vmPFC, amygdala, and hippocampus were only significant in the alcohol group.

During Go/No-Go, a significant interaction was observed for connectivity with the cerebellum. Peer presence was related to significantly greater AIC-cerebellum connectivity, but only for participants in the placebo group (Fig. 3).

Behavioral effects of alcohol and peers on response inhibition and risk-taking. During GNG, participants under the influence of alcohol had a significantly higher proportion of false alarms on No-Go trials than those in the placebo group ($M_{alc} = 0.42$, $M_{plac} = 0.31$, $F(1, 45) = 6.88$, $p = .01$), with no significant effect of peer presence ($M_{peer} = 0.37$, $M_{alone} = 0.36$, $F(1, 45) = 0.11$, $p = .74$), condition order ($M_{peerfirst} = 0.34$, $M_{alone\text{-}first} = 0.38$, $F(1, 45) = 0.79$, $p = .38$) and no significant interactions (all $ps > .05$). A non-significant trend for alcohol on d-prime was found, with participants in the alcohol group ($M = 1.75$) performing less accurately

[1] Full thresholded and unthresholded brain maps are available on NeuroVault. Main findings are available at the following link: https://neurovault.org/collections/3515/All supplemental findings are available at the following link: https://neurovault.org/collections/3538/.

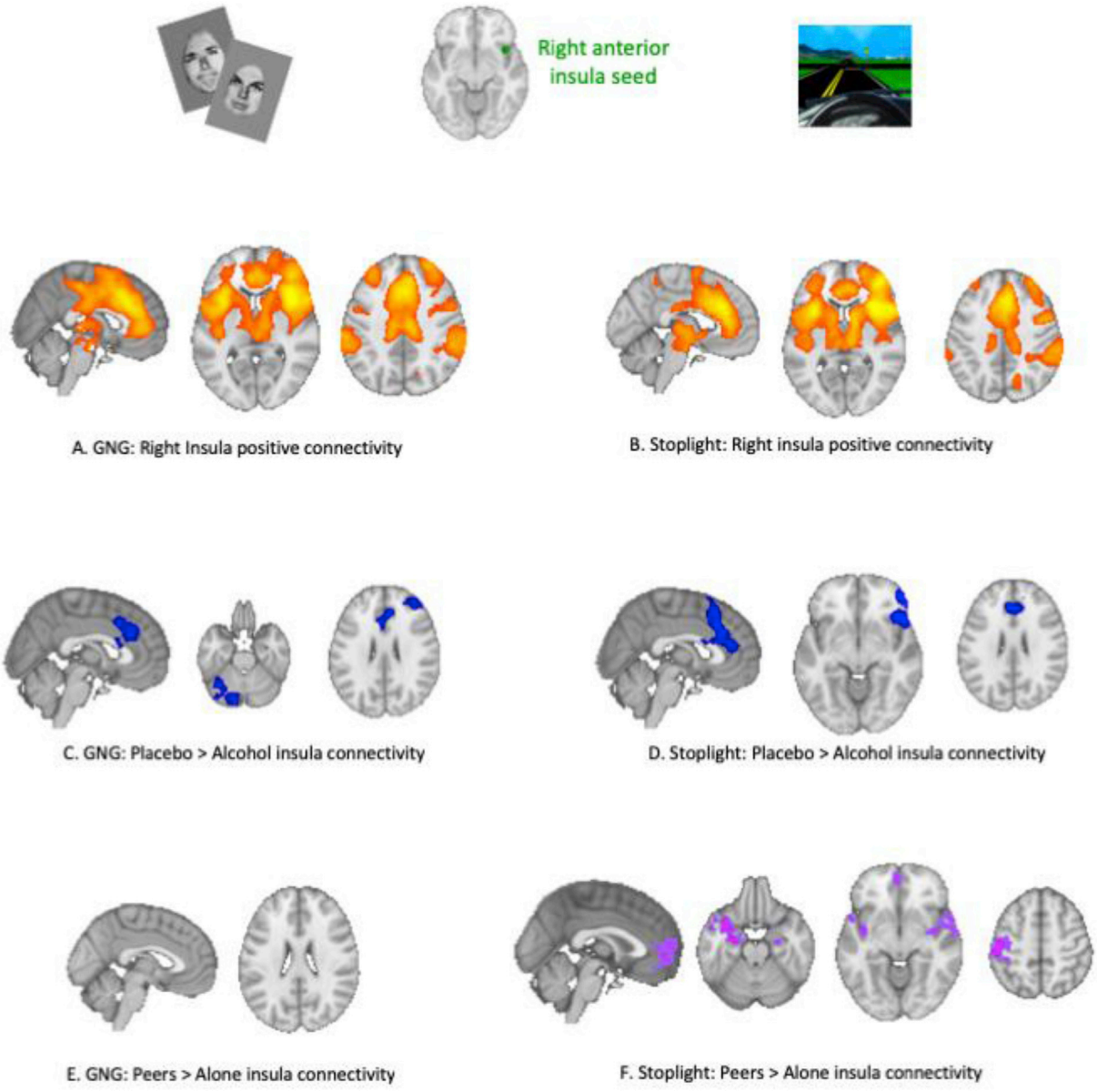

Fig. 1. Functional brain connectivity with the anterior insula during Go/No-Go (GNG) and The Stoplight Game (Stoplight). Panels A and B depict brain regions for which activation was positively correlated with the anterior insula seed. Panels C and D depict effects of alcohol intoxication on anterior insula connectivity; brain regions depicted in navy were less correlated with the anterior insula for those in the alcohol group than those in the placebo group. Panels E and F depict effects of peer observation. During Go/No-Go, no brain regions were significantly more correlated to the anterior insula during peer observation (E). Brain regions in violet showed greater co-activation with the anterior insula when participants believed they were being observed by a peer (vs. alone) during the Stoplight Game (F). All brain images thresholded at $Z > 2.3$, cluster corrected at $p < .05$.

than the participants in the placebo group ($M = 2.03$, $F(1, 45) = 3.46$, $p = .07$). D-prime did not differ significantly as a function of peer presence ($M_{peer} = 1.90$, $M_{alone} = 1.88$, $F(1, 45) = 0.09$, $p = .77$) or condition order ($F(1, 45) = 1.80$, $p = .19$), and no significant interactions were found (all $ps > .05$).

We found no significant main effects of alcohol, peer presence, or condition order on risk-taking behavior during Stoplight ($M_{alc} = 0.17$, $M_{plac} = 0.15$, $F(1, 45) = 0.42$, $p = .52$; $M_{peer} = .17$, $M_{alone} = 0.16$, $F(1, 45) = 0.70$, $p = .41$; $M_{peerfirst} = 0.17$, $M_{alonefirst} = 0.16$, $F(1, 45) = 0.07$, $p = .79$). However, we did find a significant interaction between condition order and peer presence ($F(1, 45) = 21.63$, $p < .001$). Specifically, participants took more risks in the presence of peers when the peer condition was presented first ($M_{peer} = 0.21$, $M_{alone} = 0.13$, $t(22) = 5.58$, $p < .001$). If the alone condition was presented first, participants took more risks in the alone condition ($M_{peer} = 0.13$, $M_{alone} = 0.19$, $t(22) = 2.18$, $p < .04$). We were curious whether the interaction was the product of an order effect, or of a peer effect that was limited to participant's first experience with the game. Therefore, we ran an independent-samples *t*-test investigating the effect of peer presence during the first run of Stoplight *only*. While participants in the peer condition ($M = 0.21$) took more risks than those in alone condition ($M = 0.19$), this difference was not significant ($t(47) = 0.45$; $p = .71$). And indeed, participants generally took significantly more risks on their first round of Stoplight ($M_{firstround} = 0.20$) than their second ($M_{secondround} = 0.13$; $t(48) = 4.85$, $p < .001$). These results provide evidence for an order effect, rather than a peer effect. All other interactions were nonsignificant (all $ps > .05$).

3. Discussion

Although previous research has investigated the separate effects of

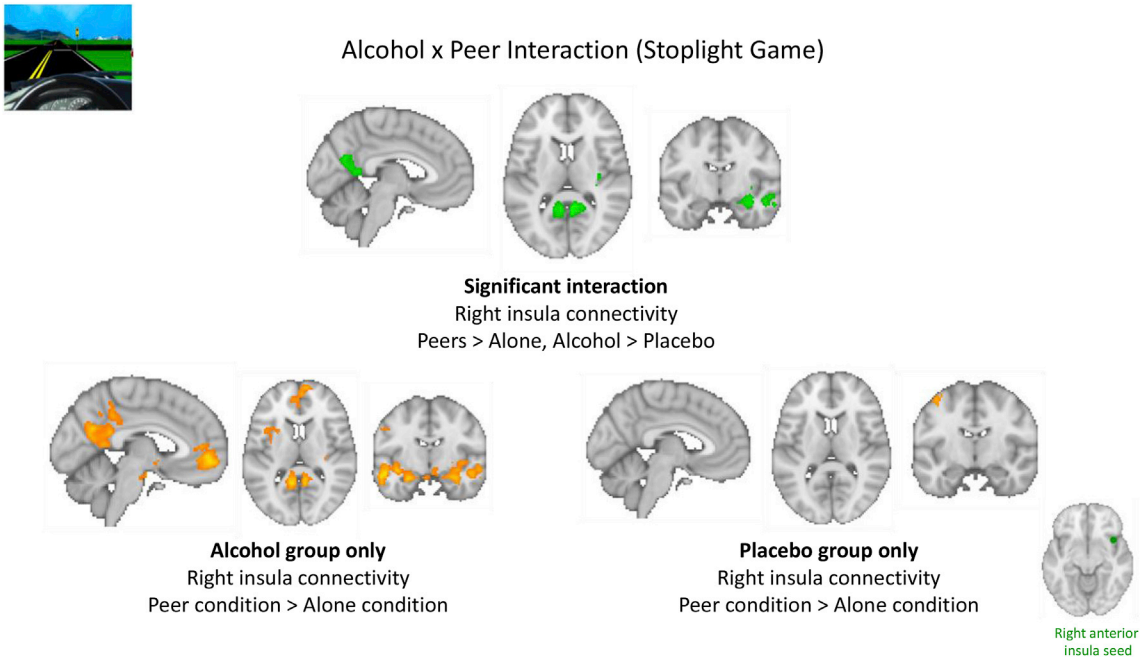

Fig. 2. Peers and alcohol exert interactive influences on anterior insula connectivity during the Stoplight Game. Images thresholded at $Z > 2.3$, cluster corrected at $p < .05$.

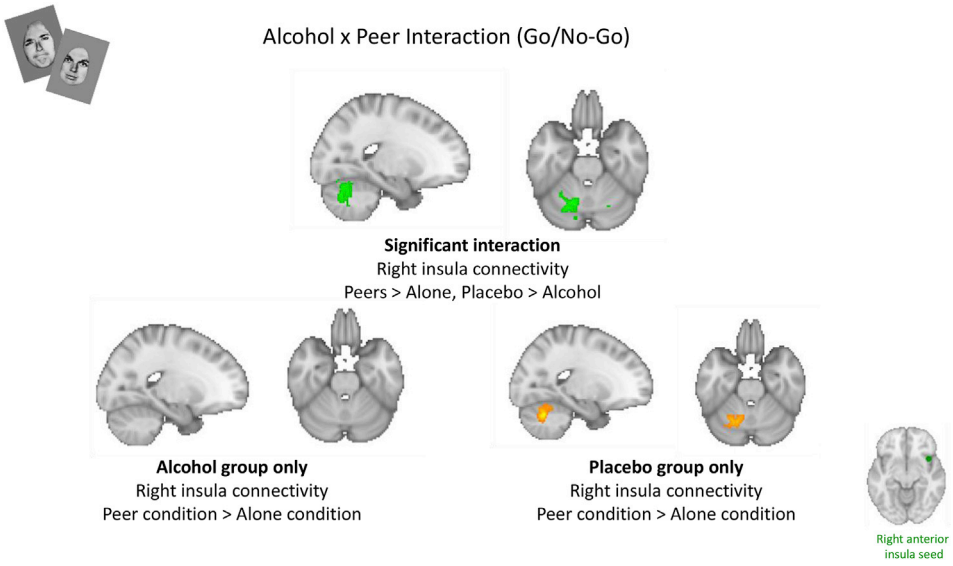

Fig. 3. Peers and alcohol exert interactive influences on anterior insula connectivity during Go/No-Go. Images thresholded at $Z > 2.3$, cluster corrected at $p < .05$.

alcohol and peer presence on neural responses during adolescence and young adulthood, the present study is the first to consider how these factors interact to influence response inhibition, risk taking, and their neural correlates. Moreover, our focus on circuit-based connectivity yielded insights that could not have been gleaned from a region-activation approach. Our findings both support previous research that examined alcohol's effects on executive function, and also yield novel insight into the interactive influences of alcohol and peers.

We found that alcohol affected response inhibition. Participants under the influence of alcohol committed more false alarms (i.e., accidently pressing a button on "No-Go" trials) than those who had consumed a placebo. The effect on d-prime, which takes into consideration both hit rate as well as false alarms, was marginal. Such findings are in line with the existing literature: Zoethout and colleagues (Zoethout et al., 2011) reported that 50% of studies investigating alcohol effects on response inhibition found a significant impairment due to alcohol. Peer presence did not affect Go/No-Go performance, in line with previous findings from our laboratory (Smith et al., 2018; Breiner et al., 2018).

Our functional connectivity findings provide important insight into the specific mechanisms that underlie the decrement in response-inhibition performance associated with alcohol use. As hypothesized, alcohol consumption was related to decreased connectivity between the AIC and brain regions involved in response inhibition and salience processing, including the dACC and the lateral PFC (see also Gorka et al., 2018), suggesting that alcohol may disrupt the typical functioning of the central executive network. The combination of peers and alcohol also had a unique influence on functional connectivity. Specifically, the AIC and cerebellum were less synchronized when participants were under the influence of alcohol, but only when they believed that a peer was watching. While the cerebellum is not frequently highlighted as a region

involved in response inhibition, cerebellar activation is actually frequently observed during successful inhibition in GNG (see Simmonds et al., 2008 for a meta-analysis), and the specific site in question was responsive during successful inhibition in our GNG task.

Peer presence did not significantly impact behavior during the Stoplight Game. However, we did observe peer effects on functional connectivity with the AIC. While alcohol primarily impacted connectivity between the AIC and brain regions implicated in response inhibition (Go/No-Go), peer presence during risky decision making (Stoplight) was related to increased connectivity between the AIC and brain regions implicated in socio-emotional processing. These regions included the vmPFC, amygdala, and hippocampus. Furthermore, the posterior cingulate cortex/precuneus, a hub of the mentalizing network, was more synchronized with the AIC during the peer condition, but only for those participants under the influence of alcohol. Thus, while young adults are less susceptible to peer pressure than younger adolescents, alcohol may impact the coordination of cognitive and emotional brain systems even during this period, heightening the salience and emotional impact of peers. Increased connectivity in these regions could also reflect increased self-referential processing during risky choice under peer observation (Andrews-Hanna et al., 2011).

The AIC is thought to play an important role in orchestrating the interplay of brain networks involved in executive control and socio-affective processing (Menon and Uddin, 2010; Sridharan et al., 2008). For this reason, we have previously asserted that the AIC should be implicated in processes underlying risky behavior across development (Smith et al., 2014). The present findings support this notion. Both Go/No-Go and the Stoplight Game involve executive control, where one must either inhibit a prepotent response or weigh the pros and cons of a risky decision, respectively. During both tasks, connectivity between the AIC and regions involved in executive functioning (e.g., dACC, dlPFC) was moderated by alcohol use. During the Stoplight Game, which has been linked to sensation-seeking behavior (Chein et al., 2011; Kim-Spoon et al., 2015; Steinberg et al., 2008), peer presence also moderated connectivity between the AIC and regions involved in reward and emotion processing (e.g., vmPFC, PCC/precuneus, amygdala).

Our findings can also be interpreted in the context of a broader literature that implicates the AIC in a variety of functions. One particularly relevant study demonstrated that alcohol disrupts salience network connectivity between AIC and ACC during rest (Gorka et al., 2018). Our study replicates and extends this prior work by demonstrating a similar effect during both Go/No-Go and Stoplight task engagement. That Go/No-Go task performance was reduced in the alcohol group demonstrates the possible functional consequences of disrupted salience-network connectivity.

Considering the AIC's involvement in the integration of perceived emotional states (Craig, 2009; Singer et al., 2009), the pattern of enhanced connectivity we observed between the AIC and affective-processing regions during the Stoplight task, particularly during peer observation, suggests that alcohol intoxication may also prime individuals for an affective, rather than controlled, decision in the presence of peers. Prior work suggests that increased AIC activation during risky decision-making signals concern about the potential consequences of taking a risk (Paulus et al., 2003). In this light, another interpretation is that intoxicated young adults may be particularly nervous about making a mistake in the presence of a peer. While both of these explanations are defensible, future studies are needed to support these speculative interpretations.

The present results are also relevant to a discussion regarding the distinct functionality of subregions of the AIC and surrounding cortex (e.g. Bartoli et al., 2018; Cai et al., 2014; Erika-Florence et al., 2014). It has been previously argued, for instance, that the right AIC, relative to the neighboring right inferior frontal cortex, is more directly involved in the salience network and better predicts control accuracy (Cai et al., 2014). The present findings extend those results by showing that AIC connectivity with more dorsal sites is also implicated in successful control. Our AIC seed region, which falls most squarely in the ventral subdivision of the AIC (as defined in Smith et al., 2014), has previously been functionally linked to the anterior ACC and subcortical activation sites, and implicated in emotional saliency processing (Cauda et al., 2011). Here, we show that connectivity with a ventral AIC site is dependent on the experimental conditions. Thus, like other recent work suggesting that the connectivity profiles of AIC subregions can dynamically change within individuals (Nomi et al., 2016), and differ between individuals (Tian and Zalesky, 2018), we show that the AIC connectivity profile is also dynamically dependent on contextual demands. Accordingly, we think it is prudent not to over-interpret results with respect to the specific localization of AIC activations or connectivity seed regions.

The present findings also support a growing literature suggesting that the functioning of neural circuitry underlying self-control varies by emotional context (Cohen et al., 2016). Cohen and colleagues (Cohen et al., 2016; Rudolph et al., 2017) found that under emotional duress, 18-21-year-olds performed worse on Go/No-Go than 21–25 year olds, and emotional context related to differences in activation of, and connectivity between, the dACC, vmPFC, and dlPFC. Cohen and colleagues' "adult" participants overlapped in age with the participants in the present study. While our participants are considered adults by many standards, our findings suggest that alcohol may create a neural signature that more closely resembles that of an immature brain. Specifically, alcohol disrupts the integration of the salience network and creates a context in which peers exert additional influence on responses in social cognitive brain regions. Whether these alcohol effects are limited to people in their 20s or would occur throughout adulthood remains an open question. Furthermore, while United States liquor laws precluded us from examining alcohol effects in younger drinkers, it is possible, and indeed seems likely, that the combined effects of alcohol and peer presence would be even more amplified earlier in adolescence.

Our findings should be interpreted in the context of several limitations; in particular, some nonsignificant results may reflect limited ability to detect true effects. For example, in the Stoplight Game, we did not find a simple main effect of peer observation on risk taking. The lack of a straightforward peer effect may seem at odds with some previous behavioral studies in which we have found that even college-aged youth take more risks and prefer more immediate rewards in the presence of peers (e.g. Gardner and Steinberg, 2005; O'Brien et al., 2011; Silva et al., 2016; Weigard et al., 2014). However, several factors may have limited our ability to replicate this pattern in the present study. First, we manipulated peer presence within-subjects rather than between-subjects. We have manipulated peer presence using a within-subjects design in the MRI scanner in a college-aged sample in only one past study from our laboratory (Chein et al., 2011), and in that study also did not observe a significant peer effect in this age group. Notably, participants in the present study took fewer risks on their second round of play, regardless of the peer context. We suspect that in an age group that is already less susceptible to peer influence than their younger counterparts (Gardner and Steinberg, 2005) learning on the first round may have been sufficient to mitigate any peer effect during the second round. Moreover, the sample size in our study, which was constrained by the cost and complexity of conducting an fMRI study on intoxicated youth, may have been insufficient to detect an existing effect (e.g. Silva et al., 2016). Taken in aggregate, studies from our laboratory suggest that the behavioral peer effect is likely to be smaller in this age cohort, and harder to detect during the second round of a within-subjects social context manipulation.

Relatedly, when we used a traditional subtraction approach, we observed extremely limited effects of peers and alcohol on activation. If it is the case that alcohol and peer presence exert broad, state-based changes on brain function, rather than differentially affecting responses to some task events versus others, it is unsurprising that we failed to detect such effects in a subtraction analysis. Recently, Casey, Galvan, and Somerville (Casey et al., 2016) called for an increased focus on *circuit*-based rather than *region*-based approaches to understanding the

development of brain systems implicated in self-control and decision-making. The present findings are illustrative of the value of this advice. Nonetheless, it is also possible that, because of limitations discussed above (e.g., sample size, participant age), we lacked sensitivity to detect differential effects of peers and alcohol on different task events.

Although the brains of young adults are relatively more mature than those of teenagers, the present findings show that contextual factors continue to exert influence on these same brain systems in early adulthood. Accordingly, it is not only the case that young adults have more *opportunity* to drink and spend time with peers, but also that alcohol and peers separately and jointly influence the responses of brain systems that are essential to prudent decision-making. Hence, the greater financial and legal independence afforded to young adults who have yet to reach final brain maturity (as is also suggested by the late developmental asymptote of brain structural indices and resting-state connectivity (Somerville, 2016);) set the stage for especially dangerous outcomes. Thought of in this way, a peak in risky behaviors in the early 20s is in keeping with a dual systems or imbalance framework. Fortunately, young people's access to alcohol can be more readily changed than neurobiological trajectories. Our findings highlight the importance of efforts to curtail a culture of binge drinking and partying on college campuses. Even for individuals in their 20s, perhaps well on their way to closing the maturity gap, suboptimal decision processing can occur given the right – or "wrong"- circumstances.

Data availability

Full thresholded and unthresholded brain maps are available on NeuroVault. Main findings are available at the following link: https://neurovault.org/collections/3515/All supplemental findings are available at the following link: https://neurovault.org/collections/3538/

Author contributions

JMC, MM and LDS jointly developed the research concept and study design, with ARS contributing to initial study setup. AS, MB, LP, and KF collected data for the experiment under the guidance of JC. AS and GR conducted statistical analyses of behavioral data. AS, GR, and LES completed preprocessing and analysis of fMRI activation patterns, and LES conducted brain connectivity analyses. LES prepared the initial draft of the manuscript, and GR, ARS, LDS, and JC contributed further sections to the manuscript, and participated in final editing.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.neuroimage.2019.04.003.

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