Received: 21 March 2017 | Revised: 3 November 2017 | Accepted: 11 December 2017

DOI: 10.1002/hbm.23931

RESEARCH ARTICLE

WILEY

The role of the dorsal anterior insula in sexual risk: Evidence from an erotic Go/NoGo task and real-world risk-taking

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Funding information
NIDA, Grant/Award Number: R01DA031626; NIMH, Grant/Award Number: RMH082671A.

Abstract

The insula plays an important role in response inhibition. Most relevant here, it has been proposed that the dorsal anterior insular cortex (dAIC) plays a central role in a salience network that is responsible for switching between the default mode network and the executive control network. However, the insula's role in sexually motivated response inhibition has not yet been studied. In this study, eighty-five 18- to 30-year-old sexually active men who have sex with men (MSM) performed an erotic Go/NoGo task while in an MRI scanner. Participants' real-world sexual risk-taking (frequency of condomless anal intercourse over the past 90 days) was then correlated with their neural activity during the task. We found greater activity in bilateral anterior insular cortex (both dorsal and ventral) on contrasts with stronger motivational information (attractive naked male pictures versus pictures of clothed, middle-aged females) and on contrasts requiring greater response inhibition (NoGo versus Go). We also found that activity in the right dAIC was negatively correlated with participants' real-world sexual risk-taking. Our results confirmed the involvement of the insular cortex in motivated response inhibition. Especially, the decreased right dAIC activity may reduce the likelihood that the executive control network will come online when individuals are faced with situations requiring inhibitory control and thus lead them to make more risky choices.

KEYWORDS
fMRI, insula, MSM, motivated response inhibition, salience network

1 | INTRODUCTION

Although only 2% of the population, men who have sex with men (MSM) make up 67% of new diagnoses of HIV (CDC, 2015b) and 82% of new diagnoses of syphilis and gonorrhea, with MSM younger than 30 among the most impacted (CDC, 2015a). Despite interventions, many MSM continue to have condomless anal intercourse (CAI), a risk factor for contracting HIV and other sexually transmitted infections.

A better understanding of the neural bases of sexually risky MSM's response inhibition might facilitate the development of more effective interventions for increasing condom use. The insular cortex (IC) is one of the key contributors to response inhibition, involved in all phases of the process, including refocusing attention onto relevant stimuli, evaluating available behavioral options, implementing action, and processing outcome information (Droutman, Bechara, & Read, 2015a). The right anterior IC is considered to be the "cortical outflow hub" of the salience network (Sridharan, Levitin, & Menon, 2008). The salience network (SN), comprised of the dorsal anterior insula and ACC, is responsible for resource switching and coordinating between the executive control and default mode networks (Menon & Uddin, 2010). According to Bechara et al. (Bechara & Damasio, 2005; He et al., 2014; Noël, Brevers, & Bechara, 2013), the IC is one of the three key neural systems of decision-making that responds to homeostatic and interoceptive signals triggered by states of deprivation, or by exposure to environmental cues that elicit craving.

Mounting evidence supports the IC's critical role in different types of risk-taking. For example, IC activation was found to predict the

Ethical approval: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

selection of a safer choice in an economic task (Kuhnen & Knutson, 2005). It has been called the "island of addiction" (Naqvi & Bechara, 2009) due to its fundamental role in connecting stimuli and environmental cues with urges and in activating drug-seeking goals (Droutman, Read, & Bechara, 2015b). The IC may also play an important role in the decision to quit gambling (Campbell-Meiklejohn, Woolrich, Passingham, & Rogers, 2008). Although evidence suggests that the IC is sensitive to erotic stimuli (Gizewski et al., 2006; Safron et al., 2007), its role in sexually motivated response inhibition has not yet been examined. This article begins to fill this gap by examining the relationship between IC activity in a response inhibition task with erotic stimuli and individuals' real-world sexual risk-taking.

Using a functional parcellation meta-analysis, Chang et al. (2012) found the IC can be divided into dorsal anterior (dAIC), ventral anterior (vAIC), and posterior (PIC) portions regarding their functional specializations. We recently reviewed (Droutman et al., 2015a) the IC literature and suggested that although there is an overlap between IC components' functionality, each has a unique responsibility: (1) the dAIC in salience processing and action initiation; (2) the vAIC in tracking risk prediction errors; and (3) the PIC is responsible for signaling homeostatic imbalance. Each component has a unique role in urge processing. The dAIC and vAIC support different aspects of decision evaluation as well as error-awareness and social outcomes (Droutman et al., 2015a). Most relevant for this work, a recent meta-analysis of 21 neuroimaging studies (Swick, Ashley, & Turken, 2011) concluded that engagement of the AIC is critical for successful performance on response inhibition tasks. Response inhibition deficit was identified as a predictor of problem drinking (Noël, Bechara, Dan, Hanak, & Verbanck, 2007) in adult alcoholics and in drinking and illicit drug use in adolescents (Nigg et al., 2006). However, the extent to which behavioral and neural deficits in response inhibition relate to risky sexual behavior has not yet been examined. This article advances this line of research by examining the role of each IC subregion in a motivationally relevant (erotic) response inhibition task (Go/NoGo), and it addresses how such activity may relate to real-world sexual risk-taking.

This study used a newly developed erotic Go/NoGo task that was performed by MSM who in the past 90 days had engaged in one or more acts of condomless anal intercourse. Participants engaged with the task in a functional magnetic resonance imaging (fMRI) scanner to examine the neural mechanisms underlying risky sexual response inhibition. In this task, half of the stimuli were motivationally relevant, that is, pictures of highly attractive, naked young men, and half of the stimuli were not motivationally relevant, that is, pictures of clothed, middle-aged women. A few weeks prior to the experiment, participants reported the occurrence of condomless anal intercourse in the past 90 days (CAI90). According to Schrimshaw et al. (2006), assessing sexual behavior in the past 90 days, as we do here with CAI90, has been shown to have very high test–retest reliability. Therefore, CAI90 was used as an index of real-world risk-taking. We were interested in examining how participants' real-world sexual risk-taking is related to activity in the different subregions of the IC during the erotic Go/NoGo task. Given that weaker activation in the AIC has been predictive of higher monetary risk-taking (Kuhnen & Knutson, 2005; Xue, Lu, Levin, & Bechara, 2010), and that the AIC is a key region in the salience network, we hypothesized that neural activity in the AIC would be negatively correlated with participants' real-world sexual risk-taking.

2 | METHODS

2.1 | Participants

We recruited 177 participants using Internet advertisements in Southern California. We recruited approximately equal numbers of White/Caucasian, Latino/Hispanic, and Black/African-American men who had sex with men (MSM) as these are the three most at-risk populations of MSM for contracting HIV in the United States (CDC, 2014). Qualified participants were 18–30 years old, sexually active nonmonogamous MSM, HIV negative (tested within the last 6 months), nonbinge drinkers, had no neurological abnormalities, and met all safety requirements for MRI scanning. Informed consent was obtained from each participant before the experiment. The protocol of the study was approved by the University Institutional Review Board. Data collection took place from 20 January 2012 to 9 April 2014.

In a prescreening questionnaire, participants reported the frequency of CAI90, which ranged from 0 to 89 instances. To focus our investigation on motivated response inhibition behaviors, only participants reporting more than 0 instances (real-world risk-taking >0) were included in this analysis. In total, 113 participants met this criterion. In our analysis, we removed twenty-eight participants for the following reasons: (1) no valid structural data was collected (3 participants); (2) no Go/NoGo data was collected (5 participants); (3) bad behavioral performance (fewer than two correct responses in any of the four conditions, 12 participants); (4) outlier values of real-world risk-taking ($>$2.5SD, 4 participants); (5) excessive head motion during data collection (moved more than 3 mm, 4 participants). Thus, 85 participants remained (27 Caucasian, 22 Black, 39 Hispanic/Latino; age range: 18.2–30 years, $M = 25.1$ years) in our analysis.

2.2 | Materials

2.2.1 | The erotic Go/NoGo task

We adapted the design of the original Go/NoGo task (Murphy et al., 1999) to include both highly motivational stimuli (pictures of attractive, naked young men) and relatively less motivational stimuli (pictures of clothed middle-aged women) for our participants. In a pilot study, attractiveness, and sexual appeal of the male pictures were rated on a 10-point Likert scale by 141 self-identified men who have sex with men (MSM), aged 18–30. We created three versions of the task, one for each participating racial/ethnic group (Black/African-American, Latino, and White/Caucasian) in the study. For each version of the task we selected the 7 pictures with the highest ratings by the participants of the corresponding ethnicity out of 46 available images ($M_{attractiveness} = 8.05$, $M_{sex\ appeal} = 7.86$). Data from three men were excluded from the result because of data collection errors in this rating experiment.

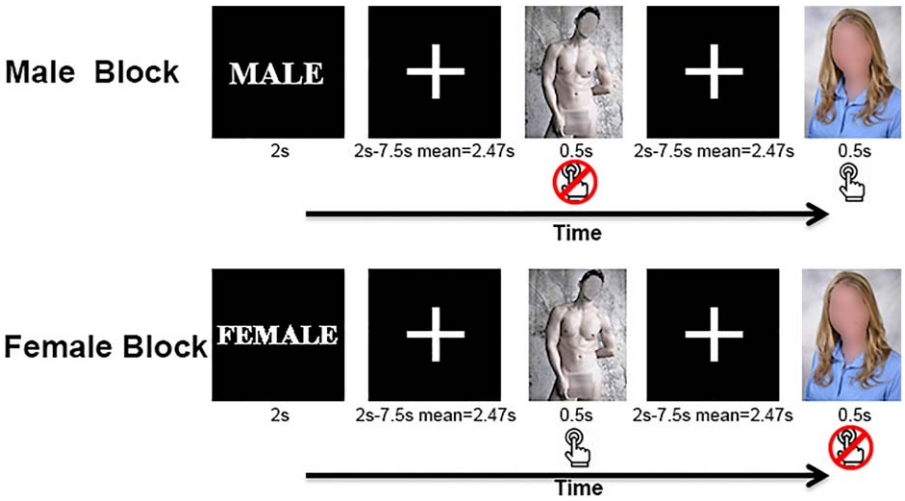

FIGURE 1 The erotic Go/NoGo task. Two types of task block were used in this task: the male block and the female block. In the beginning of each block, a word ("MALE" for male block and "FEMALE" for female block, respectively) was shown for 2 s. Participants were asked to ignore same gender pictures but press a key for opposite gender pictures. The word was then replaced by a fixation cross for a jittered period of 2–7.5 s (mean = 2.47 s). Following fixation, a picture—either male or female—was shown for 0.5 s. Participants responded as instructed. Faces and male genital areas have been blurred for publication but were visible to participants during the task [Color figure can be viewed at wileyonlinelibrary.com]

As depicted in Figure 1, a mixed design was used in the Go/NoGo task. Four task blocks were arranged in an ABBA fashion. Before each block, the word "MALE" or "FEMALE" was shown for 2 s. Participants were asked to press any key to indicate when they saw a picture with gender mismatching the word and to not respond when the gender matched (e.g., in a "MALE" block, participants would respond with a key press when a female picture appeared and inhibit their response when a male picture appeared). An event related design was used in each task block. Pictures were shown for 0.5 s, followed by a fixation cross until the next stimulus. The inter-trial-interval (ITI) was jittered from 2 to 7.5 s (M = 2.47 s). Task sequence was optimized using optseq2 (Dale, 1999). The ratio of NoGo trials versus Go trials was 1:3. Thus, there were four conditions: Go trials with a male picture (Male_Go, 60 trials), Go trials with a female picture (Female_Go, 60 trials), NoGo trials with a male picture (Male_NoGo, 20 trials), and NoGo trials with a female picture (Female_NoGo, 20 trials).

2.3 | Procedure

2.3.1 | Experimental procedure

Participants lay supine on the scanner table, and viewed visual stimuli back-projected onto a screen through a mirror attached to the head coil. Foam pads were used to minimize head motion. Stimulus presentation and timing of all stimuli and response events were controlled by Matlab (The Mathworks, Inc.), based on the Psychtoolbox extension (http://www.psychtoolbox.org) on a MacBook Pro. Participants' responses were collected online using an MRI-compatible button box.

MRI and fMRI scans were performed with a 3T Siemens MAGNETOM Tim/Trio scanner. Functional scans were performed using a z-shim gradient echo EPI sequence. This specific sequence is designed to reduce signal loss in the prefrontal and orbitofrontal areas. The parameters were: TR = 2000 ms; TE = 25 ms; FA = 90°; 64 × 64 matrix size with a resolution of 3 × 3 mm^2. Forty-one 3-mm axial slices were used to cover the whole cerebrum and most of the cerebellum with no gap. The slices were tilted about 30° clockwise from the AC–PC plane to obtain better signals in the orbitofrontal cortex. A total of 243 volumes were collected. The anatomical T1-weighted structural scan was acquired using an MPRAGE sequence (TI = 800 ms; TR = 2530 ms; TE = 3.1 ms; FA = 10°; 208 sagittal slices; 256 × 256 matrix size with spatial resolution at 1 × 1 × 1 mm^3).

2.3.2 | fMRI data preprocessing and statistical analysis

Image preprocessing and statistical analysis were carried out using FEAT (FMRI Expert Analysis Tool) version 6.00, part of the FSL package (FMRIB software library, version 5.0.9, http://www.fmrib.ox.ac.uk/fsl). The whole data analysis pipeline was managed using the XFSL package (http://xfsl.fmri.cn). The first four volumes before the task were automatically discarded by the scanner to allow for T1 equilibrium. The remaining images were then realigned to compensate for head movements (Jenkinson & Smith, 2001). Translational movement parameters never exceeded 1 voxel in any direction for any subject. The data were filtered in the temporal domain using a nonlinear high-pass filter with a 100 s cutoff, and spatially smoothed using a 5 mm full-width-half-maximum (FWHM) Gaussian kernel. A two-step registration procedure was used whereby EPI images were first registered to the MPRAGE structural image, and then into the standard MNI space (Montreal Neurological Institute, MNI), using affine transformations with FLIRT (Jenkinson, Bannister, Brady, & Smith, 2002; Jenkinson & Smith, 2001) to the avg152 2 mm T1 MNI template. Registration from MPRAGE structural images to standard space was further refined using FNIRT nonlinear registration (Andersson, Jenkinson, & Smith, 2007). Statistical analyses were performed in the native image space,

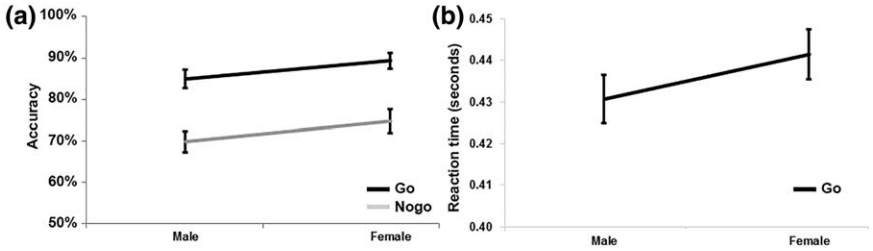

FIGURE 2 Behavioral results. (a) Accuracies on the four conditions. 2 × 2 ANOVA shows significant response inhibition (NoGo vs Go) and motivational (male vs female) effect but the interaction was not significant. (b) Reaction time on go trials. Significant difference was found between reaction time on Male_Go and Female_Go trials

with the statistical maps normalized to the standard space prior to high-level analysis. Melodic ICA was used to denoise the preprocessed functional data (Beckmann & Smith, 2004). The FIX software package was used to automatically identify noise components (Griffanti et al., 2014; Salimi-Khorshidi et al., 2014).

Data were modeled at the first level using a general linear model within FSL's FILM module. Correct trials (button press on Go trials within the response window and no response within the response window on NoGo trials) of the four conditions (Male_Go, Female_Go, Male_NoGo and Female_NoGo) were modeled separately. Error trials from the four conditions were also added to the model as separate nuisance covariates. No button press on the Go trial constitutes an Error Go trial. Button press on NoGo trials is considered an Error NoGo trial or False Alarm. Five main contrasts were tested in this model: (1) the overall response inhibition effect (NoGo - Go), (2) the overall motivational effect (Male - Female), (3) the response inhibition effect on trials of male pictures "Male_NoGo - Male_Go," (4) the response inhibition effect on trials of female pictures "Female_NoGo - Female_Go," and (5) the "motivationally relevant inhibition" interaction contrast [(Male_NoGo - Male_Go) - (Female_NoGo - Female_Go)], intended to measure additional inhibition during NoGo - Go with motivationally relevant stimuli (Males) compared to NoGo - Go with non-motivationally relevant stimuli (Females).

At the group level, we examined the group mean effect of the five contrasts. We also examined the relationship between a continuous measure of participants' real-world sexual risk-taking and those lower level contrasts by adding demeaned real-world risk-taking as a covariate in the higher level model. In this model, we used a random-effects model for group analysis using the FLAME (FMRIB's Local Analysis of Mixed Effects) Stage 1 simple mixed effect model (Beckmann, Jenkinson, & Smith, 2003; Woolrich, 2008; Woolrich, Behrens, Beckmann, Jenkinson, & Smith, 2004). Group images were thresholded using cluster detection statistics with a height threshold of $z > 2.3$ and a cluster probability of $p < .05$, corrected for whole-brain multiple comparisons using Gaussian Random Field Theory.

To isolate subregions of the IC involved (dAIC, vAIC & PIC), we first acquired probability masks of the PIC, dAIC, and vAIC for the right hemisphere from Chang el al. (2012) We then flipped the *x*-axial using the fslswapdim tool from FSL to generate masks for the left PIC, dAIC, and vAIC. The probability threshold for a voxel to be considered as part of the target region was set at 82%, which retains nonoverlapping regions while minimizing the number of overlapping voxels. Finally, these six masks were overlaid onto thresholded group images of those five contrasts mentioned above and results of correlational analyses between those five contrasts and CAI90 accordingly. Only images with valid overlap were reported here (Figures 3 and 4).

3 | RESULTS

3.1 | Behavioral results

A 2 [Response inhibition demand: High (NoGo) vs. Low (Go)] × 2 [Motivational strength: Highly motivational (Male) vs less motivational (Female)] ANOVA on the accuracy data found that the main effects of response inhibition demand and motivational strength were both significant, but the interaction between them was not [Figure 2a; response inhibition demand: $F(84,1) = 51.464$, $p < .001$; motivational strength: $F(84,1) = 35.519$, $p < .001$; interaction: $F(84,1) = 0.026$, $p = .871$]. Figure 2b shows a plot of the reaction times on the Male_Go condition and Female_Go condition. The difference between those two conditions is significant: [$F(84,1) = 4.503$, $p < .05$]. Taken together, the behavioral results show that participants responded more quickly but less accurately to highly motivationally relevant stimuli (naked male pictures) than to less motivationally relevant stimuli (female pictures). Lower accuracy here is referred to increased false alarm rate—the approach bias in "Male" block results in higher number of erroneous button presses on the NoGo trials. This pattern of behavioral data is supportive of the greater motivational significance of the male pictures. The combination of faster reaction times and reduced accuracy has been observed in response to salient stimuli in other Go/NoGo tasks (Teslovich et al., 2014). Correlational analysis between reaction times/accuracy and participants' real-world sexual risk-taking did not yield any significant result.

3.2 | Neuroimaging results

3.2.1 | Involvement of the AIC in response inhibition and motivational information processing

On both the "Male_NoGo - Male_Go" contrast and the "All NoGo - Go" contrast, NoGo trials yielded stronger activity than Go trials in bilateral dAIC and vAIC (Figure 3a,c). On the "Female_NoGo - Female_Go" contrast, only the right dAIC and the right vAIC showed stronger activity (Figure 3b). On the "Male - Female" contrast, both

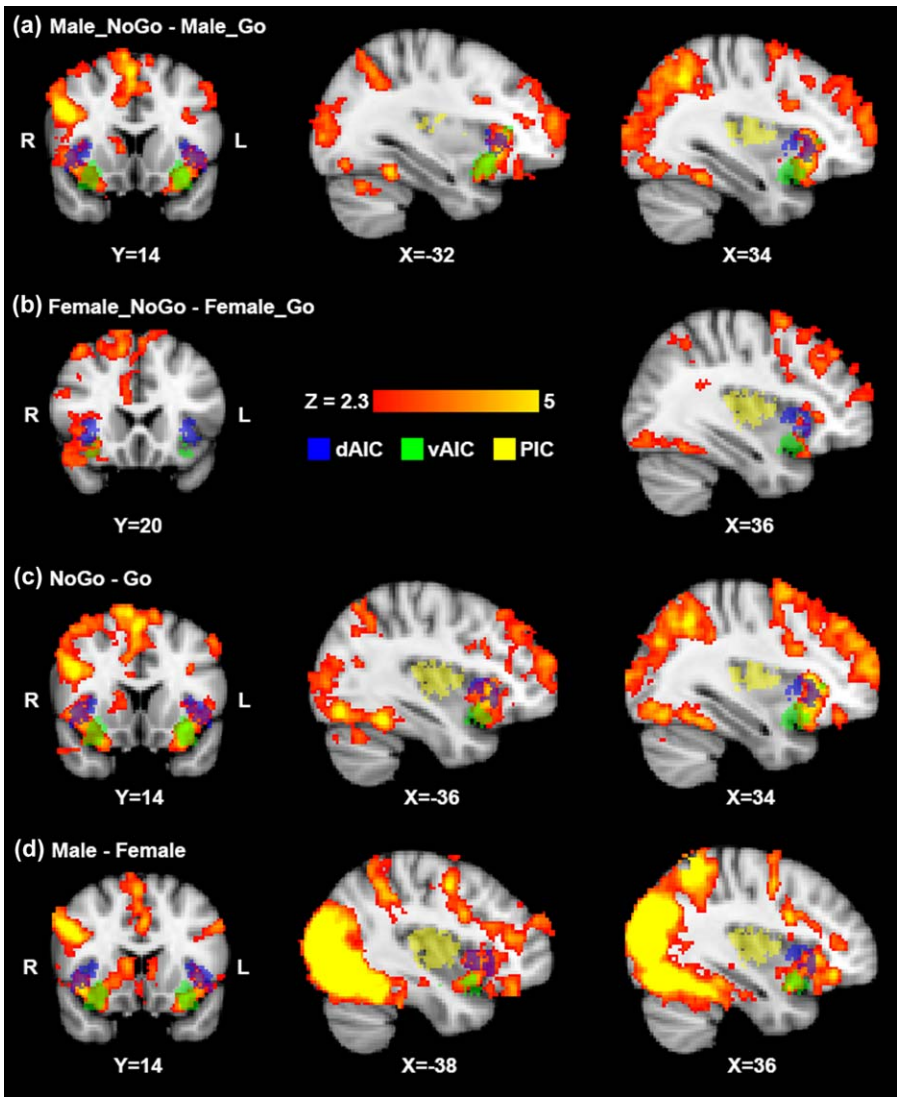

FIGURE 3 AIC activation on the four contrasts. (a) Activation in AIC on the "Male_NoGo - Male_Go" contrast. (b) Activation in AIC on the "Female_NoGo - Female_Go" contrast. (c) Activation in AIC on the "NoGo - Go" contrast. (d) Activation in AIC on the "Male - Female" contrast. Light blue color means dAIC, light green color means vAIC, and light yellow color means PIC [Color figure can be viewed at wileyonlinelibrary.com]

bilateral dAIC and bilateral vAIC showed stronger activity on Male trials than on Female trials (Figure 3d). No significant result in AIC was found after thresholding on the "motivationally relevant inhibition" interaction contrast [(Male_NoGo - Male_Go) - (Female_NoGo - Female_Go)]. No significant result in PIC was found on any of the contrasts.

3.2.2 | Negative relationship between real-world sexual risk-taking and neural activity in the right dAIC

We found a significant negative relationship for the right dAIC between participants' real-world sexual risk-taking and neural activity on three contrasts: the "Male_NoGo - Male_Go" contrast (Figure 4a), the "Male - Female" contrast (Figure 4b), and the "motivationally relevant inhibition" interaction contrast (Figure 4c). No significant result was found in vAIC and PIC.

4 | DISCUSSION

In this study, we used our newly developed erotic Go/NoGo task to investigate the possible role of the IC in motivated response inhibition by sexually risky MSM, and to examine how it may relate to their real-world sexual risk-taking. Significantly, our correlational results showed that activity in the right dAIC was negatively correlated with participants' real-world sexual risk-taking. Participants reporting more sexually risky behavior (condomless anal intercourse) in real-world had weaker activity in the right dAIC in the motivationally relevant condition on the three contrasts described above ("Male – Female," "Male_NoGo - Male_Go," and "motivationally relevant inhibition" interaction). The relationship with the contrast between motivational and nonmotivational conditions may suggest increased arousal and/or urge generation. However, this mechanism does not explain the

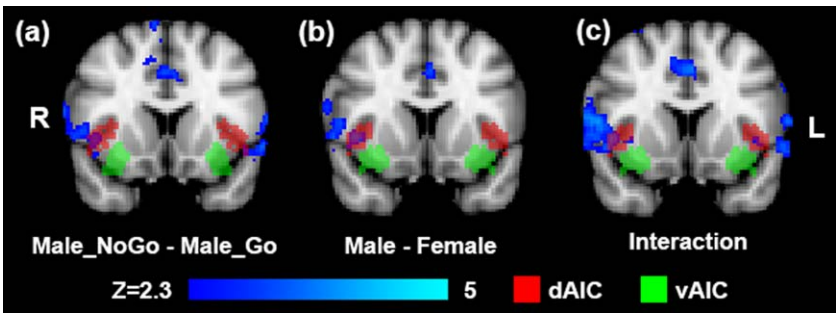

FIGURE 4 Negative relationship between group result on the three contrasts and participants' real-world risk-taking (CAI90). (a) Results in the right dAIC on the "Male_NoGo - Male_Go" contrast. (b) Results in the right dAIC on the "Male - Female" contrast. (c) Results in the right dAIC on the "motivationally-relevant inhibition" interaction contrast. Light blue color means dAIC and light green color means vAIC [Color figure can be viewed at wileyonlinelibrary.com]

correlation with the "Male_NoGo - Male_Go" contrast (as arousal should be consistent for all male stimuli) or the "motivationally relevant inhibition" interaction contrast [(Male_NoGo - Male_Go) - (Female_-NoGo - Female_Go)]. The most parsimonious explanation of all three contrasts is the reactivity of the right dAIC to the more salient stimuli (the stimuli would be more salient if it is either more motivationally relevant as in "Male - Female" contrast, or behaviorally more relevant as a NoGo condition and thus required to evoke inhibition. Thus, our findings suggest that sexual risk-taking may be partially related to a deficit in salience processing that reduces the likelihood that sexually risky men will sufficiently engage executive control. However, due to the limitations of this study the causality between deficit in salience process and reduced executive control cannot be directly tested.

In addition, we found that both the bilateral dAIC and vAIC were more active when contrasting the higher motivational condition with the lower motivational condition, likely due to their role in arousal tracking and urge generation. Consistent with prior findings (Swick et al., 2011), higher activation in the bilateral dAIC and vAIC was evident when contrasting higher response inhibition demand with lower response inhibition demand. Interestingly, we found possible laterality differences in AIC involvement, that is, the right dAIC and vAIC were involved in inhibition processing on both motivationally relevant and non-motivationally relevant stimuli, while inhibition processing of motivationally relevant stimuli also recruited left dAIC and vAIC. This finding resonates with prior work which found that the left AIC (both dorsal and ventral) was a unique predictor of speed and accuracy of correct inhibition responses in a Go/NoGo task (Boehler, Appelbaum, Krebs, Hopf, & Woldorff, 2010). On the other hand, the right AIC has been identified as an initiator of salience processing (Ham, Leff, de Boissezon, Joffe, & Sharp, 2013; Sridharan et al., 2008). These findings may suggest that the role of the right AIC in inhibition may be to support salience processing (activating the executive control network), which may be sufficient for performance on easier, nonmotivationally relevant trials; however, more challenging, motivationally relevant trials require recruitment of the left AIC to sustain appropriate efficacy. However, this hypothesis has not been tested in this study.

Our findings that attenuated IC reactivity corresponds to higher risk-taking are consistent with neuroimaging addiction research that shows reduced activation in IC in drug users (Nestor, Hester, & Garavan, 2010; Stewart et al., 2014a, 2014b). However, lesion research findings are contradictory at first glance: brain damage that destroys IC eradicates nicotine (Naqvi, Rudrauf, Damasio, & Bechara, 2007) and gambling (Clark, Studer, Bruss, Tranel, & Bechara, 2014) addictions. We examined this apparent paradox (Droutman et al., 2015b) and suggested a network-based explanation: IC damage leads to changes or reconfiguration in neural networks in which it is a key component, which may result in the contradictory findings. Several functional connectivity studies provide initial evidence for this hypothesis and suggest that addiction is characterized by salience network deregulation (Gu et al., 2010; Sutherland, McHugh, Pariyadath, & Stein, 2012; Sutherland, Carroll, Salmeron, Ross, & Stein, 2013; Upadhyay et al., 2010; Xie et al., 2011). Thus, SN deregulation may be the common basis of risky behaviors such as unprotected sex and substance use.

5 | LIMITATIONS

This neuroscience project is unique in focusing on a high risk group of MSM—a population that is at high risk for STDs and HIV (CDC, 2014, 2015a, 2015b). Therefore, constrained by our project goals to study risky sexual decision-making in MSM, we only recruited MSM as participants. It is unclear how well our results generalize to other populations (i.e., to women, to men who have sex with only women). Future studies should extend this work by recruiting non-MSM samples with appropriate task modifications.

Although our erotic Go/NoGo task successfully introduced motivational information in the task, it does not closely resemble real-life sexual situations. Future studies may benefit from more naturalistic experimental approaches to study risky sexual behavior, such as using virtual reality techniques. In other work, we are examining young MSM as they play a virtual "hookup" game while in the scanner.

Additionally, we did not match lower-level visual specifications (such as illuminance and hue of the picture, size of the head, etc.) of images used as stimuli in the erotic Go/NoGo task. One may argue that differences in lower-level visual specifications may result in different impacts on the lower-level visual cortex, such as occipital cortex, fusiform, and so on, hence cause different level of neural activity in those

cortices (e.g., those parameters may contribute to larger activation in occipital cortex in "Male_NoGo - Male_Go" contrast compared to "Female_NoGo - Female_Go" contrast). However, we are not focusing on those visual cortices but higher order cognition cortices instead. So, our main findings reported above should be free from this argument.

6 | CONCLUSION AND FUTURE DIRECTIONS

Using the erotic Go/NoGo task, we provide evidence that the insula and especially the dAIC and vAIC play important roles in risky sexual response inhibition, particularly in exerting inhibitory control in response to motivationally relevant stimuli. The current findings are consistent with a growing literature suggesting that the insula, especially the anterior insula, plays an important role in risky behaviors. The results from this study may shed light on mechanisms of risky sexual decision-making, specifically, and also potentially inform future HIV and STD intervention development. Moreover, greater attention to the role of the insula in motivated response inhibition, sexual and otherwise, is likely to shed further light on its complex functions.

ACKNOWLEDGMENT

The content is solely the responsibility of the authors and does not necessarily represent the official views of NIDA or NIMH.

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How to cite this article: Xue F, Droutman V, Barkley-Levenson EE, et al. The role of the dorsal anterior insula in sexual risk: Evidence from an erotic Go/NoGo task and real-world risk-taking. *Hum Brain Mapp*. 2018;39:1555–1562. https://doi.org/10.1002/hbm.23931