Brain Imaging and Behavior
https://doi.org/10.1007/s11682-020-00308-4

ORIGINAL RESEARCH

Neural Modulation in Approach-Avoidance Conflicts in Externalizing Psychopathology

Allison J. Lake[1] · Peter R. Finn[2] · Thomas W. James[2,3,4]

Abstract

Externalizing psychopathology (EXT) is characterized by poor decision-making in situations that involve simultaneous cues for approach and avoidance behavior (i.e. approach-avoidance conflicts). Previous studies of EXT have examined these deficits primarily using tasks involving decisions between positive reward and negative punishment, suggesting that EXT is characterized by a general bias towards high salience (e.g. temporally proximal or reward) cues relative to low salience (e.g. temporally distal or loss) cues. However, in order to better characterize decision-making in approach-avoidance conflicts, the present study utilized a novel task to examine neural activation in contexts involving both positive reward and negative punishment as well as positive punishment and negative reward by manipulating physical proximity of affective cues. Neuroimaging results indicated that EXT was associated with deficits related to cue prioritization based on salience, suggesting that failure to differentiate relevant from less relevant information contributes to poor decision-making among individuals with EXT.

Keywords Externalizing psychopathology · Decision making · Emotion · Motivation

Externalizing psychopathology (EXT) is a unitary construct that reflects the shared variance across multiple disinhibitory disorders (Krueger et al. 2002; Krueger and Markon 2006). These disorders, which include conduct disorder, antisocial personality disorder, and substance use disorders, are highly comorbid and together share characteristically poor decision-making and low levels of behavior control (Bobova et al. 2009; Cantrell et al. 2008; Endres et al. 2011; Finn et al. 2015). In particular, these disorders are marked by decision-making processes that fail to adequately incorporate potential negative consequences and inhibit ongoing approach-related behavior (Cantrell et al. 2008; Endres et al. 2014). Resultant behavior, therefore, appears to be disinhibited and biased toward approach (Finn 2002; Gorenstein and Newman 1980; Iacono et al. 2008). Specifically, situations that present simultaneous signals for approaching a positive stimulus and avoiding an aversive stimulus (i.e. approach-avoidance conflicts) are characteristically difficult for individuals with EXT. Accordingly, understanding self-regulation failures in EXT requires a clear understanding of the component processes that comprise approach-avoidance conflicts.

Approach-avoidance conflicts are inherently complex scenarios involving opposing motivational, emotional, and behavioral cues. As such, they involve simultaneous opportunities for positive reward, positive punishment, negative reward, and/or negative punishment. Previous work with EXT populations has studied approach-avoidance conflicts mainly within a cognitive decision-making framework that specifically emphasizes the role of positive reward and negative punishment. Specifically, this work relates EXT to a general decision-making bias to approach appetitive cues (i.e. positive reward) despite long-term aversive consequences (i.e. negative punishment). These conclusions are largely based on studies using economic decision-making tasks such as the delay discounting (DDT; e.g. Kirby 1997) and Iowa Gambling Task (IGT; Bechara et al. 1994). For these tasks,

✉ Thomas W. James
thwjames@indiana.edu

[1] Department of Psychiatry, Indiana University School of Medicine, 355 W. 16th St., Suite 2800, Indianapolis, IN 46202, USA

[2] Department of Psychological & Brain Sciences, Indiana University, 1101 E. 10th St, Bloomington, IN 47405, USA

[3] Program in Neuroscience, Indiana University, 1101 E. 10th St, Bloomington, IN 47405, USA

[4] Cognitive Science Program, Indiana University, 819 Eigenmann, 1900 E. 10th St, Bloomington, IN 47406, USA

Published online: 01 August 2020

EXT individuals typically make more choices resulting in smaller, immediate rewards in the DDT (Bickel et al. 2012; 2014; Bobova et al. 2009; Finn et al. 2015; MacKillop 2011, 2013), and large potential gains but larger potential losses (i.e. high risk) in the IGT (Bechara et al. 2001; Cantrell et al. 2008; Gonzalez e al. 2007; Mazas et al. 2000). This EXT-related bias to approach cues that signal immediate reinforcement has been associated with a sensitivity for highly salient environmental cues. Specifically, models of decision-making based on these data contend that individuals with EXT are less likely to process low-salience cues when high-salience cues are present (Bechara & Martin 2004; Ersche et al. 2006; Finn 2002; Finn et al. 1999, 2009; Gunn and Finn 2013; Verdejo-García et al. 2006). In these contexts, salience is often manipulated via temporal immediacy, such that temporally proximal cues are more salient and temporally distal cues are less salient, irrespective of the cue's inherent motivational valence or value. In the DDT and IGT, immediate gains are more salient than distal losses, making it more likely that the high-salience cues will influence choice in EXT individuals. In this way, cue salience is likely a major contributing factor to the decision-making patterns observed in individuals with EXT. Neurally, atypical choice behavior displayed by individuals with EXT is commonly associated with abnormal patterns of activation of the prefrontal cortex (PFC), particularly the orbitofrontal cortex (OFC), ventromedial PFC (vmPFC), and dorsal anterior cingulate (dACC), coupled with strong motivational/emotional signals from subcortical regions including the amygdala and striatum (Bechara 2005; Bickel et al. 2007; Carroll et al. 2015; Ersche et al. 2012; Everitt and Robbins 2005; Goldstein and Volkow 2011; Li et al. 2010). Taken together, these data suggest that poorly planned and maladaptive behavior in EXT individuals is due to a relative imbalance between top-down cognitive control signals associated with prefrontal cortical areas and bottom-up motivational signals associated with subcortical structures.

While these models provide useful insight into elements of approach-avoidance conflicts in EXT populations, relatively little attention has been paid to other aspects of approach-avoidance conflicts that may provide additional insight into EXT-related deficits. First, the DDT and IGT heavily emphasize positive reward and negative punishment in decision-making behavior; however, approach-avoidance conflicts and, by extension, real-life decisions, also involve cues for positive punishment (e.g. legal consequences of drug use) and/or negative reward (e.g. removal from probation following prolonged abstinence; Bogg and Finn 2009; Finn et al. 2017; Gray and McNaughton 2000). To the extent that traditional economic decision-making tasks exclude these types of cues, extant models of decision-making biases in EXT are inherently limited and not reflective of the true scope of factors involved in decision-making. Second, in commonly used economic decision-making tasks, salience is highly confounded with temporal proximity. For example, in the DDT, highly salient cues are those most proximal, such as the possibility to receive a monetary reward immediately. However, salience is manipulated by a wide range of factors in addition to temporal proximity and monetary value, including physical proximity. Thus, in order to further clarify the behavioral and neural mechanisms associated with decision-making deficits in individuals with EXT, it is important to expand testing to both the types of reward and punishment in approach-avoidance conflict tasks as well as manipulating salience in ways beyond temporal proximity and incentive or disincentive value.

To address these limitations in extant decision-making literature among EXT populations, the present study utilized natural motivational biases (Aarts et al. 2008; Bradley et al. 2001; Chiew and Braver 2011; Lake et al. 2019; Pfister and Böhm 2008; Spielberg et al. 2008, 2011; Tooby et al. 2008) towards approaching positive stimuli and avoiding negative stimuli to create approach-avoidance conflicts. This novel task required both motivationally congruent actions (e.g. approaching positive stimuli) and motivationally incongruent actions (e.g. avoiding positive stimuli) to create scenarios involving positive reward, positive punishment, negative reward, and/or negative punishment. Additionally, simulated approach and avoidance actions from the participant changed the physical proximity of the stimulus to manipulate salience. fMRI methods were used to investigate the involvement of neural regions commonly implicated in cognitive models of decision-making in EXT within these novel contexts, including stimulus salience (i.e. physical proximity) as well as simultaneous conflicting cues.

To the extent that the amygdala has been associated with behavioral relevance detection and motivated action, it was hypothesized that individuals with EXT would display increased amygdalar activation in response to approached stimuli, reflective of hyper-reactivity in response to these high-salience conditions. It was similarly expected that these individuals, as compared to controls, would show poor amygdalar modulation in response to avoided stimuli; that is, these individuals would show poor neural discrimination between behaviorally relevant and irrelevant stimuli. Finally, it was hypothesized that conditions requiring motivationally conflicting actions (i.e. avoiding a positive stimulus or approaching a negative stimulus) would be particularly aversive for individuals with EXT. Along these lines, it was expected that individuals with EXT would display increased activation of limbic regions including the amygdala and insula during conflict trials. It was also expected that these individuals, as compared to controls, would show decreased activation in prefrontal conflict control

regions in these trials, specifically the OFC, vmPFC, and dACC, reflective of a diminished ability to control or moderate these affective responses to motivationally incongruent action (e.g. Ochsner, Bunge, Gross, & Gabrieli, 2002).

Method

Participants

Participants ($n = 40$; 22 women) were recruited from a larger study examining the role of personality and cognitive factors on substance use and other externalizing behaviors. Participants were primarily college-aged ($M = 21.35$, $SD = 2.46$) and Caucasian (72.50%), with the remaining participants endorsing African American (5.00%), Asian (12.50%), and other ethnicities (10.00%). All participants were right-handed as reported on a brief handedness questionnaire ($M = 14.11$, $SD = 2.09$; Chapman & Chapman, 1987). Sample size is consistent with what has been suggested elsewhere to produce robust and reliable effects (Desmond and Glover 2002; Seghier et al. 2008).

Group Inclusion Criteria The design included two equal groups (each $n = 20$) of individuals with low EXT and high EXT. Lifetime diagnoses of conduct disorder, antisocial personality disorder, alcohol use disorders, marijuana use disorders, and other drug use disorders as assessed by the Semi-Structured Assessment for the Genetics of Alcoholism (Bucholz et al. 1994) using DSM-IV-TR (American Psychiatric Association 2000) criteria were considered within a sample of 1041 participants from the larger study. Individuals meeting criteria for the low EXT group had no lifetime diagnosis within these categories, and thus serve here as control participants representing healthy functioning within these domains. Those meeting criteria for the high EXT group had a diagnosis of conduct disorder in addition to at least one other diagnosis within these categories, or greater than 50 total lifetime problems within these areas. Therefore, the high EXT group is reflective of significant problems in EXT domains across the lifespan (see Table 1).

Table 1 Lifetime problems and diagnoses related to externalizing psychopathology by group ($n = 36$)

	Low EXT	High EXT
Mean Lifetime Problems (SD)		
Childhood conduct	2.47 (1.74)	14.47 (3.95)
Adult antisocial	1.05 (.71)	10.82 (6.44)
Alcohol	2.21 (2.57)	31.89 (13.37)
Marijuana	.53 (.23)	11.76 (10.30)
Other drug	0.00 (0.00)	11.71 (23.14)
Diagnoses, %		
Childhood conduct	0.00	76.50
Adult antisocial	0.00	35.30
Alcohol abuse	0.00	23.50
Alcohol dependence	0.00	70.60
Marijuana abuse	0.00	11.80
Marijuana dependence	0.00	58.80
Other drug abuse	0.00	17.60
Other drug dependence	0.00	35.30

Procedure

Prior to testing, participants were required to abstain from alcohol and recreational drug use for at least 12 hours, get six or more hours of sleep the night before, and eat a meal within 3 hours of testing. Following informed consent, participants' breath alcohol was measured using an Alco Sensor IV (Intoximeters Inc., St. Louis, MO) to ensure they had not consumed alcohol prior to testing. Participants were then instructed on the approach-avoidance task and practiced the task outside the scanner with experimenter feedback. Broadly, participants pulled or pushed affective images (negative, neutral, and positive) towards or away from themselves, respectively, on a computer screen. Images were selected from the International Affective Picture System (IAPS; Lang et al. 2008). Negative images included those of threatening animals, injuries, and feces. Neutral images included occupational scenes and household objects. Positive images included adventurous images (e.g. skydiving), positive interpersonal interactions, and food[1] (see Table 2).

Following practice, participants were comfortably set up in the scanner with their head secured in the head coil with foam padding. Stimuli were projected onto a rear projection screen in the scanner bore and viewed through a mirror attached above the head coil. Trials were presented in an event-related experimental design using E-Prime 2.0 software (Psychology Software Tools, Pittsburgh, PA). On each trial, following fixation, a cue word ("push" or "pull") appeared for 2000 ms. Participants were instructed to push an MRI-safe joystick towards themselves following a "pull" cue; similarly,

[1] The following IAPS images were used: Negative: 1019, 1022, 1050, 1112, 1200, 1201, 1205, 1274, 1300, 1302, 1303, 1310, 1525, 2095, 2661, 2681, 2683, 2692, 2710, 2722, 2730, 2800, 2981, 3101, 3160, 3170, 3230, 3266, 3280, 3301, 3350, 3500, 3530, 3550, 6020, 6190, 6211, 6212, 6244, 6313, 6370, 6555, 6821, 6830, 6490, 7359, 7380, 8230, 8231, 8480, 9008, 9120, 9230, 9301, 9410, 9433, 9810. Neutral: 2025, 2191, 2200, 2210, 2214, 2235, 2270, 2280, 2381, 2383, 2393, 2480, 2485, 2493, 2495, 2499, 2500, 2514, 2575, 2579, 2580, 2635, 2840, 2850, 2870, 2880, 2890, 4605, 5130, 5395, 5535, 5750, 6150, 7000, 7002, 7004, 7010, 7020, 7025, 7035, 7036, 7037, 7040, 7041, 7090, 7095, 7096, 7100, 7140, 7205, 7217, 7233, 7493, 7560, 7590, 8311. Positive: 1340, 1463, 1710, 2057, 2091, 2303, 2346, 2352, 2650, 2655, 4533, 4598, 4599, 4601, 4603, 4608, 4676, 5621, 5623, 5626, 5628, 7200, 7220, 7260, 7282, 7340, 7400, 7430, 7460, 7475, 7480, 7481, 7503, 7640, 8030, 8031, 8034, 8041, 8160, 8161, 8178, 8180, 8185, 8186, 8190, 8200, 8210, 8320, 8350, 8370, 8400, 8490, 8496, 8500, 8503, 8540.

Table 2 Mean (SD) valence and arousal ratings for IAPS images across action conditions. All comparisons n.s

		Pull	Push
Positive	valence	6.96 (0.58)	7.01 (0.65)
	arousal	5.32 (0.87)	5.73 (0.85)
Neutral	valence	5.23 (0.49)	5.13 (0.46)
	arousal	3.26 (0.78)	3.23 (0.52)
Negative	valence	2.90 (0.81)	3.08 (0.95)
	arousal	5.74 (0.69)	5.96 (0.68)

they were instructed to push the joystick away from themselves following a "push" cue. Following the cue, an image appeared superimposed on a "hallway" in order to give the illusion of depth (van Dantzig et al. 2008). Participants were instructed to move the joystick as quickly as possible after the image appeared. Pull movements resulted in the image steadily increasing in size, making it appear to move towards the participant; push movements, conversely, steadily decreased the size of the image, making it appear to move away from the participant. Participants were instructed to maintain the motion of the joystick for the entirety of the 5000 ms picture presentation. A fixation cross then appeared on screen for a jittered duration. Image types (positive, negative, neutral) and action (push, pull) were fully crossed resulting in two valence-action congruent conditions (negative/push, positive/pull), two conflict conditions (negative/pull, positive/push), and two neutral conditions (neutral/push, neutral/pull; see Fig. 1). Participants completed 28 trials of each type, for a total of 168 trials. Trials were pseudorandomized and separated into four runs of 42 trials with short breaks between runs. Participants used their right hand to make joystick movements for the first two runs of the experiment, after which the joystick was moved to their left hand for the last two runs. The scanning session lasted approximately 45 min. Participants received approximately $50 for completing the study, which lasted approximately one and a half hours.

Image Acquisition

BOLD data were acquired with a Siemens Magetom TIM TRIO 3 T whole-body MRI using a 32-channel phased-array head coil. The field of view was 220 × 220 mm, with 35 axial slices of 3.8 mm per volume and an in-plane resolution of 64 × 64 pixels. Accordingly, voxels were 3.4 × 3.4 × 3.8 mm. Functional images were collected using a gradient echo EPI sequence with TE = 25 ms, TR = 2000 ms, and flip angle = 70°. High-resolution T1-weighted anatomical images were collected using a Turbo-flash 3D sequence of TI =

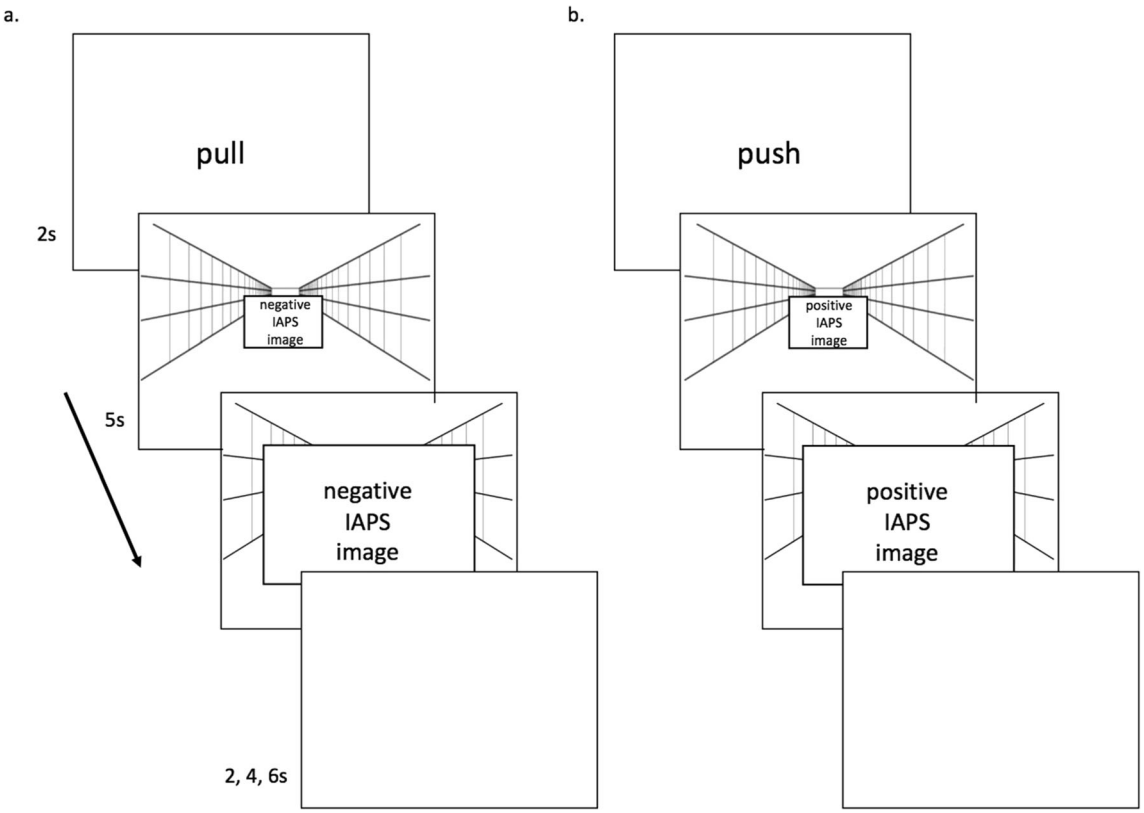

Fig. 1 Schematic of approach-avoidance task illustrating a negative-incongruent trial (**a**) and positive-congruent trial (**b**)

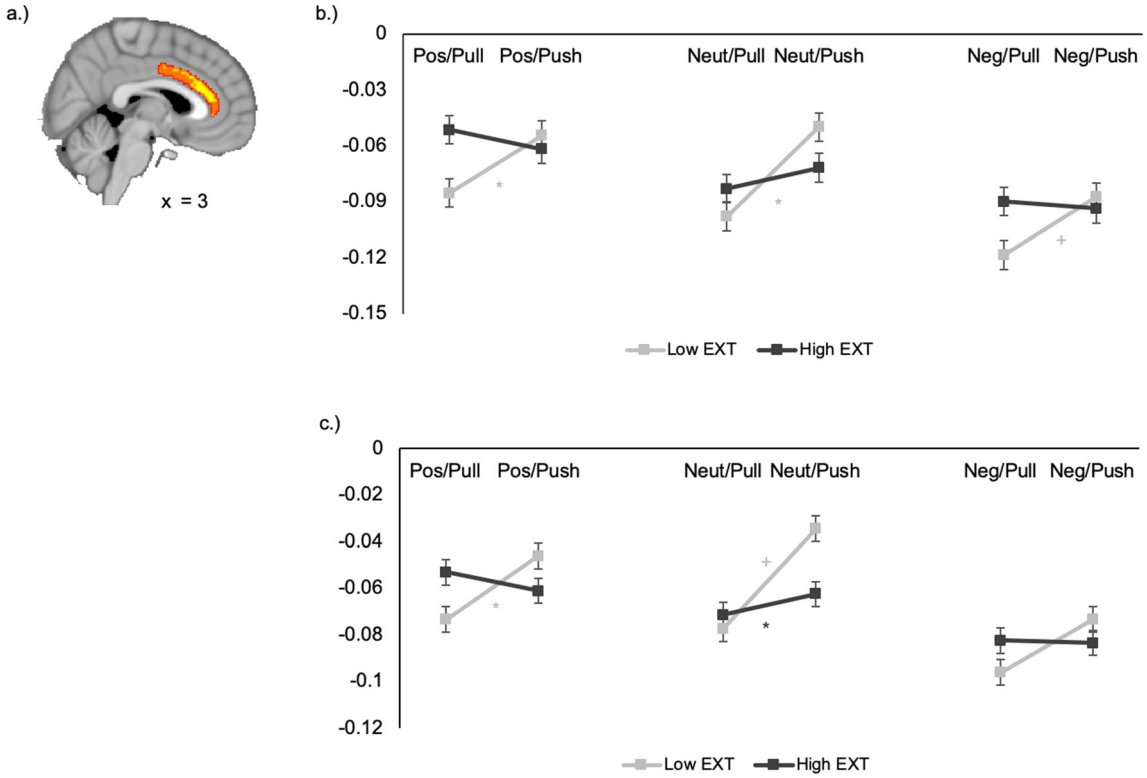

Fig. 2 Activation in the (**a**). dACC from the interaction between salience (i.e. push vs. pull) and group in the left (**b**) and right (**c**). hemisphere. Asterisks indicate significance at $p < .05$; crosses indicate trend-level significance

900 ms, TE = 2.67 ms, TR = 1800 ms, and flip angle = 9°. The field of view for anatomical images was 256 × 256 mm, contained 192 sagittal slices of 1 mm, and had an isometric voxel size of $1mm^3$.

Data Analysis Plan

First, to target group-related differences in activation within hypothesized regions, a priori regions of interest (ROIs) were identified in the bilateral insulae, amygdalae, OFC, vmPFC, and dACC. Second, whole-brain analyses were conducted with salience, conflict, and group as variables. All main effects and interactions of these three variables were assessed; however, the focus was on four specific contrasts: 1) the main effect of salience (i.e. physical proximity) and the interaction salience with group and 2) the main effect of conflict (i.e., conflicting motivational cues) and the interaction of conflict with group. Toward this end, stimulus salience was assessed by comparing conditions where stimuli approached (i.e. increasing salience) versus conditions where stimuli receded ("salience" contrast: [negative/pull + neutral/pull + positive/pull] > [negative/push + neutral/push + positive/push]). This contrast was performed as a main effect across all participants and also as an interaction with group. Additionally, motivational conflict was assessed by comparing conditions where valence and action were incongruent (conflict) versus conditions where valence and action were congruent ("conflict" contrast: [negative/pull + positive/push] > [negative/push + positive/pull]). This contrast was performed as a main effect across all participants and also as an interaction with group. Finally, betas were extracted from significant clusters to assess simple main effects that combined to produce the multi-factor main effects and interactions and to produce graphical representations of the multi-factor effects.

Data Processing

Imaging data were evaluated by inspecting the estimated motion parameters for individual participants. Individuals with estimated motion spikes greater than 3 mm were excluded from all analyses. By this criterion, three participants were removed (1 low EXT, 2 high EXT). One additional participant (high EXT) was removed from analyses due to a neuroanatomical abnormality that may have impaired the volume registration procedure. These exclusions resulted in 36 participants in the final dataset.

Imaging analyses were conducted with FMRIB Software Library (FSL; http://www.fmrib.ox.ac.uk) using the FMRI Expert Analysis Tool (FEAT) version 5.98 (Smith et al. 2004). Individual functional volumes were normalized to the

Table 3 Regions of activation associated with salience among all participants

Region Pull > Push	hemisphere	*t*-score	voxels	x	y	z
occipital pole	R	16.30	49,475	10	−96	4
precentral gyrus	L	5.20	988	−48	−6	60
supplementary motor cortex	R	3.86	255	8	4	56
anterior cingulate cortex	R	5.86	171	2	0	26
posterior cingulate cortex	L	8.06	138	−12	−20	38
precuneus	R	5.24	131	14	−46	50
posterior cingulate cortex	R	4.90	100	10	−20	40
frontal medial cortex	L	3.68	68	−6	32	−22
frontal medial cortex	L	3.53	53	−2	48	−26
parietal operculum cortex	L	3.58	42	−36	−36	18
precuneus	L	3.08	38	−8	−42	54
middle frontal gyrus	R	3.70	21	54	24	38
frontal medial cortex	R	3.03	18	8	46	−16
frontal pole	–	3.30	17	0	60	−10
middle temporal gyrus	L	2.82	16	−52	0	−22
frontal operculum cortex	L	2.76	14	−32	24	6
frontal pole	L	3.47	14	−12	46	−28
frontal pole	–	3.04	10	0	66	0
middle temporal gyrus	L	3.46	8	−62	−14	−30
Push > Pull						
angular gyrus	R	9.44	30,659	50	−50	46
middle frontal gyrus	R	9.68	11,540	34	14	44
cerebellum, I-IV	–	5.98	1133	0	−54	−6
cerebellum, crus I	L	4.76	441	−44	−68	−38
cerebellum, VIIIb	R	6.67	310	20	−58	−52
cerebellum, crus II	R	3.09	11	40	−58	−46
caudate	R	2.88	8	14	18	0
paracingulate gyrus	L	2.62	8	−8	42	−6
cerebellum, I-IV	R	2.58	8	12	−38	−20
Accumbens	R	2.56	6	10	8	−10
cerebellum, crus I	R	2.74	5	32	−84	−32

Coordinates are presented in MNI space and reflect the center of mass for each cluster

Montreal Neurological Institute (MNI) atlas and co-registered to the MNI 152 standard brain. First-level analyses were performed with a general linear model (GLM) for each functional run for each subject with explanatory variables (EVs) for each of the six task conditions using a set of boxcar functions based on the timing of the experimental protocol convolved with a double-gamma hemodynamic response function. Second-level analyses were performed to collapse run-level inputs from into subject-level outputs as beta coefficients. Third-level analyses combined subject-level inputs into groups using a random-effects model resulting in between-group contrasts across dependent variables from first-level contrasts. For a priori ROI analyses, regions were defined using the Harvard-Oxford probability atlas and thresholded (range: 65–85) to produce reasonably constrained areas. Neural activation within left and right hemispheres were analyzed separately. For whole brain analyses, maps produced from third-level analyses were cluster corrected with a permutation correction for multiple tests (Nichols 2012). In short, second-level betas (i.e. first-level dependent variables for each subject for each voxel) were randomly permuted across voxels 1000 times to build cluster-size distributions with a voxel-wise threshold of $t = 2.45$ ($p < .01$). For all three conflict contrasts of interest, the minimum cluster size required for a false positive rate of 5% varied from 4 to 6 voxels (32–48 1x1x1 mm^3 voxels), which is consistent with our experiences with other studies of similar effect sizes. These thresholds were applied to third-level maps. To visualize results, 3D thresholded surface maps were created using Surface Mapper (SUMA) within Analysis of Functional Neuroimages (AFNI; Cox 1996).

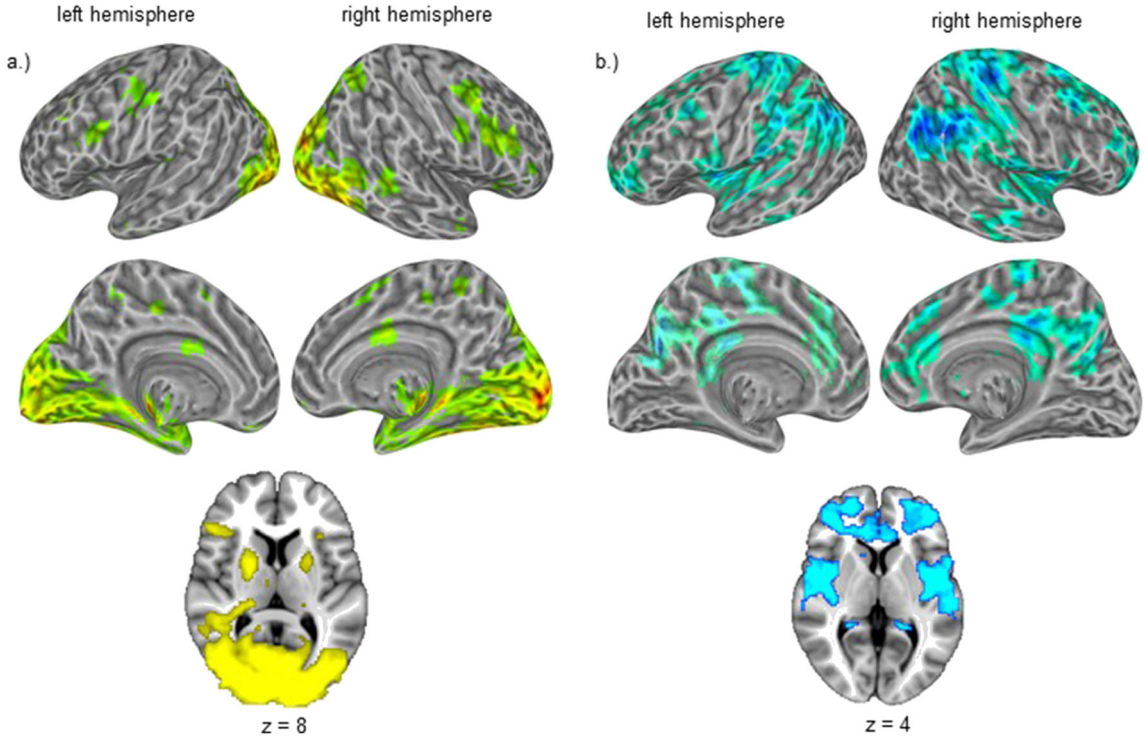

Fig. 3 Lateral, medial, and axial views of salience-associated (**a**) activation (**b**) and de-activation among all participants. Contrast examined (negative/pull + neutral/pull + positive/pull] > [negative/push + neutral/push + positive/push)

Results

Behavioral Results

Participants' reaction time (RT) was recorded during the approach-avoidance task. Behavioral data were missing for one participant (high EXT) due to equipment failure, resulting in $n = 35$ participants in the behavioral analyses. Correct responses were classified as trials in which the participant completed the action (i.e. pushing or pulling) as cued; the majority of responses ($M = 99.04\%$, $SD = 0.12\%$) were correct. For correct response trials, participants responded faster on pull trials ($M = 520.99$, $SD = 187.55$) than push trials ($M = 608.44$, $SD = 199.75$), $F(1, 34) = 93.27$, $p < .001$, likely reflective of ergonomic limitations of the task device in the scanner environment. There were no significant effects of valence, group, or interactions between these factors on RT.

Imaging Results

A Priori ROIs With regard to hypothesized limbic regions, there were no two- or three-way interactions between EXT group and image valence or action (i.e. push or pull) in the bilateral amygdalae, insulae, OFC, or vmPFC ($ps > .17$). There was a significant EXT group x salience interaction in both the left dACC, ($F(1, 34) = 8.62$, $p = .006$) and right dACC ($F(1, 34) = 8.56$, $p = .006$). Within the left dACC, low EXT individuals demonstrated significantly increased neural activation during push vs. pull positive ($t(18) = -2.57$, $p = .02$) and neutral trials ($t(18) = -2.20$, $p = .04$), and trend-level increased activation during negative trials ($t(18) = -1.80$, $p = .09$). In contrast, high EXT individuals demonstrated no significant differences between push and pull trials of any image valence ($ps > .40$). A similar effect was observed in the right dACC, such low EXT individuals demonstrated significantly increased activation during push vs. pull positive ($t(18) = -2.39$ $p = .03$) trend-level neutral ($t(18) = -1.74$, $p = .10$) trials, whereas high EXT individuals demonstrated significant modulation of activation for neutral trials only ($t(18) = -2.35$, $p = .03$; see Fig. 2).

Salience Among all participants, approaching a stimulus (i.e. [negative/pull + neutral/pull + positive/pull] > [negative/push + neutral/push + positive/push]) was associated with activation in bilateral primary and higher-order visual processing areas, basal ganglia, amygdala, and dlPFC. In turn, pushing was associated with increased relative activation in precuneus, ACC, posterior insula, precentral and postcentral gyri, and frontal poles (see Table 3 and Fig. 3).

Group differences associated with salience were also explored. For low EXT individuals, greater activation was observed in the bilateral lateral frontal cortex, ACC, middle and inferior temporal cortices, and precuneus. In contrast, greater activation for high EXT individuals was observed in the left

Table 4 Regions of activation from the interaction of group and salience (i.e. push > pull)

Region	hemisphere	*t*-score	voxels	x	y	z
Low EXT > High EXT						
middle frontal gyrus	R	5.60	4703	32	12	44
frontal pole	L	4.14	723	−30	42	4
posterior cingulate gyrus	R	3.92	648	2	−30	28
occipital pole	–	4.03	232	0	−98	−10
inferior frontal gyrus	L	3.96	198	−56	−60	−10
middle frontal gyrus	L	4.14	192	−44	20	38
inferior frontal gyrus	L	4.07	188	−62	−20	−28
parahippocampus	R	4.73	177	22	−16	−32
angular gyrus	R	3.97	173	54	−52	36
middle temporal gyrus	R	3.97	173	64	−22	−14
superior frontal gyrus	L	3.97	151	−26	4	70
inferior temporal gyrus	R	3.87	132	58	−24	−32
cerebellum, crus II	R	3.91	126	46	−54	−46
postcentral gyrus	L	3.50	125	−4	−48	72
precuneus	R	3.49	116	2	−74	54
Heschl's gyrus	R	4.37	103	42	−26	6
superior frontal gyrus	R	3.36	101	4	30	62
postcentral gyrus	L	3.31	84	−52	−18	32
precentral gyrus	L	3.62	71	−6	−30	76
frontal pole	R	3.08	71	8	60	−14
frontal pole	R	3.54	67	0	58	34
cerebellum, VIIIb	L	4.09	67	−18	−60	−56
inferior frontal gyrus	R	3.76	66	52	−8	−36
middle frontal gyrus	L	3.47	64	−30	20	46
cerebellum, crus II	L	3.48	64	−14	−84	−34
middle frontal gyrus	L	3.26	63	−42	6	38
inferior temporal gyrus	R	3.64	59	56	−46	−24
cerebellum, crus II	L	3.20	58	−36	−42	−42
middle frontal gyrus	L	2.96	46	−24	36	32
superior temporal gyrus	L	3.39	45	−62	−22	−2
temporal pole	R	3.38	36	24	18	−32
middle temporal gyrus	R	2.76	35	54	−48	−6
precentral gyrus	L	3.17	32	−26	−16	58
middle temporal gyrus	L	3.68	31	−64	−30	−14
cerebellum, crus I	L	3.14	31	−40	−56	−38
temporal pole	R	3.45	27	52	18	−30
inferior temporal gyrus	L	3.29	24	−52	−42	−26
frontal operculum cortex	R	2.84	22	34	24	8
middle temporal gyrus	L	2.90	22	−58	−12	−12
superior parietal lobule	L	2.97	21	−36	−56	46
occipital pole	–	3.15	18	0	−94	20
temporal pole	R	3.32	18	40	26	−28
cerebellum, crus II	L	3.09	16	−40	−74	−52
supramarginal gyrus	R	3.23	15	62	−36	24
cerebellum, V	R	3.12	15	6	−62	−18
superior frontal gyrus	R	3.10	14	8	26	48
precentral gyrus	L	2.63	13	−26	−24	70

Table 4 (continued)

Region	hemisphere	*t*-score	voxels	x	y	z
lateral occipital cortex, superior division	L	2.80	13	−44	−66	40
temporal pole	L	2.91	13	−56	8	−8
cuneus	L	2.92	10	−8	−86	32
lateral occipital cortex, superior division	L	2.83	9	−46	−68	48
frontal pole	L	2.85	9	−22	48	28
temporal fusiform cortex	L	2.77	9	−32	−24	−30
temporal pole	L	2.87	9	−44	4	−34
middle temporal gyrus	R	3.25	8	64	−32	−18
middle temporal gyrus	R	2.79	7	48	−50	4
superior temporal gyrus	L	2.84	7	−48	−20	−6
superior temporal gyrus	R	2.81	7	60	6	−8
occipital pole	R	2.62	7	18	−100	−16
cerebellum, VIIIa	R	3.14	7	16	−60	−54
supramarginal gyrus	R	2.83	6	50	−38	60
posterior cingulate gyrus	R	2.69	6	4	−46	14
lateral occipital cortex, inferior division	R	3.07	6	52	−76	2
precentral gyrus	L	2.73	5	−8	−20	72
superior frontal gyrus	L	2.53	5	−22	26	58
superior frontal gyrus	L	3.03	5	−22	−84	52
planum temporale	L	2.70	5	−40	−34	14
subcallosal cortex	–	3.06	5	0	14	2
frontal orbital cortex	R	2.66	5	30	22	−18
cerebellum, crus I	R	2.83	5	48	−74	−24
middle temporal gyrus	R	2.83	5	60	−4	−28
High EXT > Low EXT						
occipital pole	L	3.33	55	−36	−92	14
hippocampus	R	3.78	42	24	−34	−2
occipital pole	L	3.08	25	−20	−90	34
lateral occipital cortex, inferior division	R	3.03	20	44	−72	−12
postcentral gyrus	R	3.81	17	52	−22	58
amygdala	L	3.27	13	−24	−10	−16
frontal medial cortex	–	3.00	13	0	46	−18
thalamus	R	3.28	11	2	−8	−4
frontal pole	L	3.16	8	−20	48	−12
intracalcarine cortex	L	2.56	7	−8	−76	10
occipital fusiform gyrus	L	2.74	5	−20	−86	−6
temporal fusiform cortex	R	2.57	5	42	−28	−18

Coordinates are presented in MNI space and reflect the center of mass for each cluster

amygdala, left frontal pole, right LOC, and left occipital pole (see Table 4 and Fig. 4). To clarify this interaction further, extracted betas were examined within targeted regions (see Fig. 5). Within the left frontal pole, the high EXT group displayed a similar pattern of activation as the low EXT group in the negative conditions, but an opposite pattern of activation in the positive and neutral conditions. In contrast, in the left amygdala, the high and low EXT groups displayed similar patterns of activation in the positive conditions, but opposite patterns in the neutral and negative conditions.

Conflict Among all participants, conflict (i.e. [negative/pull + positive/push] > [negative/push + positive/pull]) was associated with activation in the bilateral precuneus, supramarginal gyri, supplementary motor cortex, superior and inferior divisions of the left lateral occipital cortex (LOC), and the right

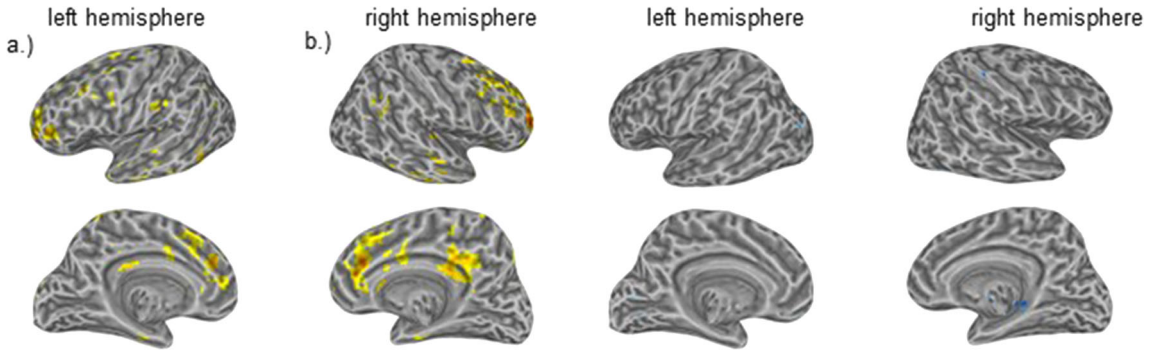

Fig. 4 Lateral and medial views of (**a**) regions activated and (**b**) deactivated by the interaction between salience (i.e. push > pull) and group

insula. Deactivation was observed in bilateral primary visual regions, amygdalae, hippocampi, orbitofrontal cortex (OFC), accumbens, temporal fusiform gyri, left precentral gyrus, and right caudate (see Table 5 and Fig. 6).

Group differences associated with conflict were also examined. Greater activation was observed in the low EXT group in the right accumbens, left hippocampus, right superior temporal gyrus, and right paracingulate gyrus. Greater activation was observed in the high EXT group in the right dorsal anterior cingulate cortex, left precentral gyrus, and right angular gyrus (see Table 6 and Fig. 7). The pattern of activation (extracted betas) in target regions (see Fig. 8) was relatively consistent; specifically, while the low and high EXT groups showed similar patterns of activation for negative valence conditions, the difference in activation between push and pull for positive valence was the opposite for the two groups.

Other contrasts, including the three-way interaction contrast between salience, conflict, and group, did not produce any significant clusters that contributed to the interpretation of the findings.

Discussion

Externalizing psychopathology is characterized in part by poor resolution of approach-avoidance conflicts. Many extant theories of self-regulation failures in EXT (Bechara & Martin 2004; Finn 2002; Gorenstein and Newman 1980) contend that

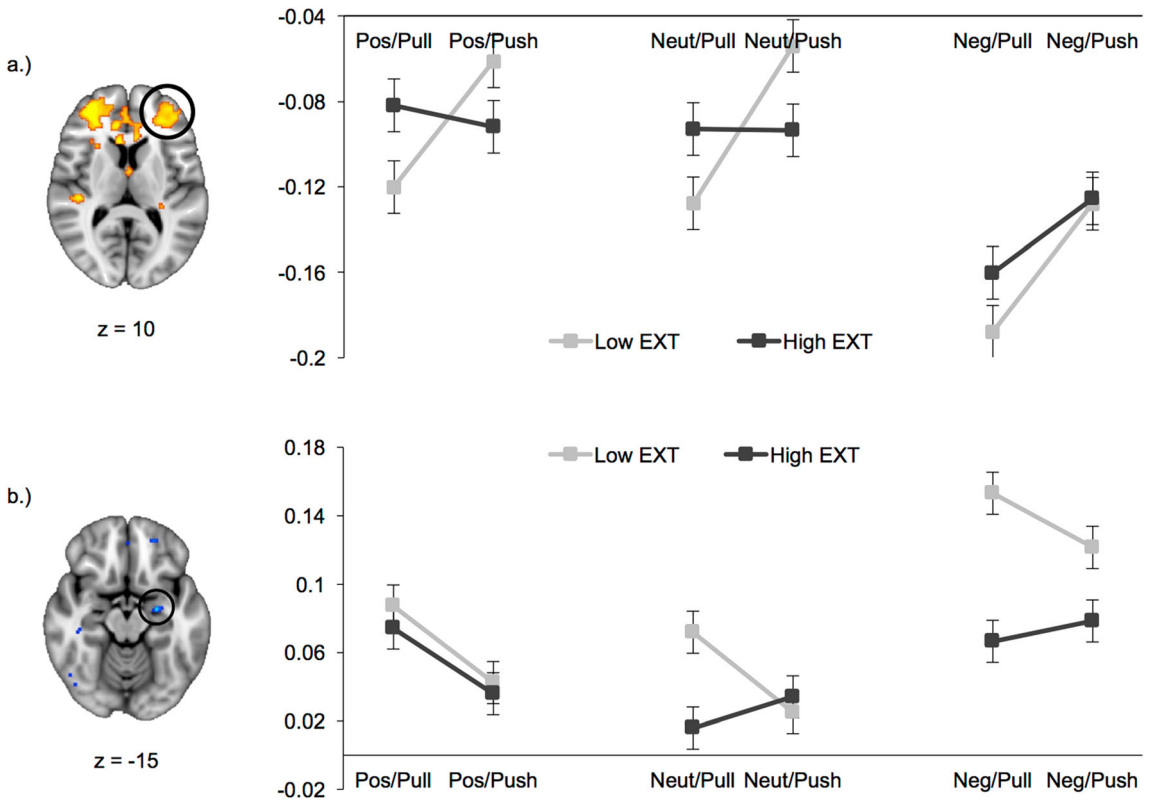

Fig. 5 Activation in the left frontal pole (**a**) and left amygdala (**b**) from the interaction between salience and group

Table 5 Regions of activation associated with conflict (i.e. [negative/pull + positive/push] > [negative/push + positive/pull]) in all participants

Region Conflict > Congruent	hemisphere	*t*-score	voxels	x	y	z
superior parietal lobule	L	6.23	1236	−30	−46	44
precentral gyrus	R	4.54	551	50	−6	34
precentral gyrus	L	4.65	476	−42	−4	26
superior parietal lobule	R	4.04	302	36	−44	52
precuneous	L	3.59	242	−8	−46	48
superior frontal gyrus	R	3.42	110	14	2	62
parietal operculum	R	3.00	69	58	−28	24
supplementary motor cortex	L	3.07	56	−6	0	56
lateral occipital cortex, superior division	L	4.10	55	−38	−88	30
inferior frontal gyrus, pars opercularis	L	3.50	55	−52	12	26
insula	R	3.00	52	28	18	−2
thalamus	L	3.72	50	−4	−22	−4
paracingulate gyrus	R	3.69	45	4	44	30
superior frontal gyrus	L	3.12	43	−18	−4	62
precentral gyrus	R	3.28	42	32	−6	54
frontal operculum	R	3.30	42	44	18	6
middle temporal gyrus	L	3.33	41	−50	−60	−2
frontal pole	R	3.75	40	22	62	26
supplementary motor cortex	L	3.17	20	−10	6	46
frontal pole	R	3.22	13	20	60	−18
superior parietal lobule	R	2.78	11	26	−56	62
Pallidum	R	2.87	10	18	0	0
supramarginal gyrus	R	2.87	9	60	−36	44
planum temporale	L	2.72	9	−50	−42	20
angular gyrus	R	2.87	8	58	−58	36
precuneus	L	2.96	7	−24	−52	4
frontal pole	L	3.18	7	−36	64	−2
cerebellum, I-IV	–	2.76	7	0	−42	−22
postcentral gyrus	R	2.88	6	54	−10	52
cerebellum, I-IV	L	2.98	6	−10	−36	−16
lateral occipital cortex, superior division	L	3.10	5	−20	−62	72
frontal pole	R	2.93	5	30	56	30
frontal pole	R	2.81	5	32	62	−12
Congruent > Conflict						
occipital pole	R	5.91	3735	18	−100	6
occipital fusiform gyrus	L	5.92	3575	−32	−74	−18
postcentral gyrus	L	4.65	328	−36	−24	68
amygdala	R	4.44	246	14	−10	−16
temporal pole	L	3.44	91	−46	18	−40
frontal pole	L	3.60	89	−10	56	28
frontal pole	R	3.56	49	20	44	44
lateral occipital cortex, inferior division	R	3.70	46	48	−74	10
temporal pole	R	3.80	42	52	14	−30
cerebellum, VIIIb	R	3.70	35	22	−52	−50
central opercular cortex	L	3.99	33	−34	−10	18
cerebellum, X	L	3.29	32	−18	−34	−48
temporal pole	L	3.24	30	−58	4	−22
middle frontal gyrus	L	3.47	26	−32	6	66

Table 5 (continued)

Region Conflict > Congruent	hemisphere	*t*-score	voxels	x	y	z
precentral gyrus	R	3.71	25	16	−26	46
superior frontal gyrus	L	3.47	23	−16	36	50
parahippocampal gyrus	R	3.70	23	22	2	−34
middle frontal gyrus	R	3.62	16	34	10	62
temporal pole	R	3.23	16	32	12	−38
thalamus	L	3.11	15	−20	−34	−4
superior frontal gyrus	L	2.90	13	−48	−40	2
frontal pole	L	2.86	13	−40	46	−2
paracingulate gyrus	L	3.44	13	−12	38	−8
temporal pole	L	3.36	12	−54	14	−30
temporal pole	R	3.02	12	46	20	−34
cerebellum, crus I	R	3.06	11	50	−68	−24
cerebellum, VIIIb	L	3.03	11	−24	−38	−56
paracingulate gyrus	L	3.12	10	−12	24	30
cerebellum, V	R	2.64	9	12	−56	−20
inferior temporal gyrus, posterior division	L	3.15	9	58	−22	−32
precentral gyrus	L	2.86	8	−8	−30	60
superior frontal gyrus	L	2.75	8	−18	28	58
middle frontal gyrus	R	2.81	8	38	20	56
temporal pole	R	2.82	8	44	16	−42
frontal pole	L	2.66	7	−4	44	52
frontal pole	L	2.67	7	−10	48	44
lateral occipital cortex, superior division	L	3.10	7	−16	−88	32
inferior temporal gyrus	R	2.65	7	54	−52	−14
central opercular cortex	L	2.85	6	−50	−20	16
frontal pole	L	2.68	6	−46	42	2
parahippocampal gyrus	L	2.90	6	−16	−28	−12
temporal pole	L	2.82	6	−28	6	−38
superior frontal gyrus	R	2.77	5	12	32	60
paracingulate gyrus	R	2.87	5	14	30	26
cerebellum, crus II	R	2.66	5	10	−84	−34
parahippocampal gyrus, anterior division	L	3.11	5	−20	0	−40

Coordinates are presented in MNI space and reflect the center of mass for each cluster

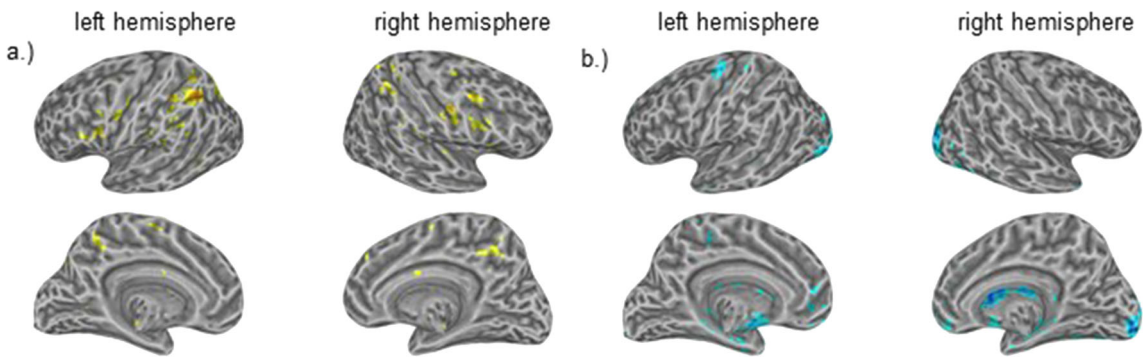

Fig. 6 Lateral and medial views of conflict-associated activation (**a**) and de-activation (**b**) among all participants. Contrast examined [negative/pull + positive/push] > [negative/push + positive/pull]

Table 6 Regions of activation from the interaction of group and conflict (i.e. conflict > congruent)

Region	hemisphere	*t*-score	voxels	x	y	z
Low EXT > High EXT						
accumbens	R	3.69	143	10	10	−12
caudate	R	3.60	120	12	18	10
thalamus	R	4.11	119	10	−2	−2
paracingulate gyrus	R	4.17	75	4	42	30
paracingulate gyrus	L	3.90	55	−14	52	8
lateral occipital cortex, superior division	R	3.28	53	48	−74	24
paracingulate gyrus	R	3.42	49	18	50	8
superior temporal gyrus, anterior division	R	3.33	45	54	−6	−16
cerebellum, VIIIa	L	4.23	45	−12	−62	−40
hippocampus	L	3.93	38	−22	−26	−8
lingual gyrus	R	2.90	35	6	−54	2
parahippocampal gyrus	R	4.73	29	28	−26	−28
lateral occipital cortex, superior division	L	2.94	26	−36	−82	18
middle frontal gyrus	R	3.39	24	34	4	36
frontal pole	L	3.56	23	−42	42	8
temporal occipital fusiform cortex	L	3.21	23	−32	−54	−10
parahippocampal gyrus	R	2.85	23	18	−38	−14
temporal fusiform cortex, posterior division	R	2.99	21	42	−34	−20
cerebellum, VIIIb	R	3.31	16	18	−58	−48
paracingulate gyrus	R	2.94	12	2	52	20
frontal pole	L	3.05	12	−14	48	−22
occipital fusiform gyrus	R	2.87	11	28	−76	−2
cerebellum, I-IV	L	3.98	11	−14	−36	−22
precuneus	R	2.67	10	14	−50	14
postcentral gyrus	R	3.20	9	14	−34	78
precuneus	R	2.80	9	22	−62	26
cerebellum, crus I	R	2.78	9	54	−50	−30
postcentral gyrus	R	2.95	8	42	−32	46
precentral gyrus	L	2.61	8	−32	8	26
precuneus	L	2.64	8	−20	−60	20
cerebellum, crus I	R	2.83	8	30	−76	−20
superior parietal lobule	R	2.73	7	26	−48	76
frontal pole	R	3.11	7	10	58	20
lateral occipital cortex, superior division	L	2.65	5	−24	−68	48
frontal pole	L	2.78	5	−14	58	38
cingulate gyrus, anterior division	R	2.69	5	10	30	18
occipital fusiform gyrus	R	2.70	5	30	−76	−8
cerebellum, I-IV	L	2.80	5	−6	−44	−8
temporal occipital fusiform cortex	R	2.75	5	32	−46	−10
frontal pole	R	3.07	5	28	8	−40
High EXT > Low EXT						
precentral gyrus	L	3.49	145	−8	−32	60
frontal pole	L	3.95	26	−34	58	−16
precentral gyrus	L	2.87	15	−6	−18	62
frontal pole	R	3.13	15	36	62	−6
cingulate gyrus, anterior division	R	3.42	13	6	−10	34
supramarginal gyrus, posterior division	R	2.74	11	58	−46	42

Table 6 (continued)

Region	hemisphere	*t*-score	voxels	x	y	z
postcentral gyrus	R	2.68	10	14	−32	52
frontal pole	L	3.10	10	−26	64	6
supramarginal gyrus, posterior division	R	2.69	8	46	−44	52
middle frontal gyrus	L	2.72	8	−28	28	34
inferior temporal gyrus, posterior division	L	2.89	8	−54	−38	−28
cingulate gyrus, anterior division	L	3.15	7	−6	−4	34
angular gyrus	R	3.06	6	46	−54	60
postcentral gyrus	L	2.63	6	−28	−32	54
superior frontal gyrus	R	2.98	6	10	32	50
frontal pole	L	2.84	6	−32	44	−14
middle temporal gyrus, anterior division	L	2.84	6	−56	0	−36
frontal pole	R	2.64	5	10	38	46
insula	R	2.69	5	38	2	0
orbitofrontal cortex	R	2.69	5	40	26	−22

Coordinates are presented in MNI space and reflect the center of mass for each cluster

a key mechanism is the inability to inhibit highly salient cues. In line with this view, robust differences between high and low EXT groups based on stimulus *salience* (i.e. pushing vs. pulling, approaching vs. avoiding) were observed in the current study in regions associated with emotion regulation, including frontal and limbic regions. Alternatively, previous work also suggests that abnormal decision-making in EXT is explained by an inability to resolve *conflict* between opposing motivational cues. However, in the present study, neural differences between externalizing groups related to differences in motivational conflict did not reach significance. Thus, these novel results indicate that poor prioritization based on cue salience is likely to contribute to problems with conflict resolution in high EXT individuals. This implies that a complex interplay between affective perception and motivated action contributes to multiple pathways to poor self-regulation among high EXT individuals.

Importantly, this study illustrated the networks associated with approach-avoidance conflicts in all participants. In particular, pulling (or approach) was associated with broad activation in regions associated with visual processing, visuospatial processing, and motivation (i.e. basal ganglia; Shirer et al. 2012). To the extent that objects moving towards an individual are highly motivationally relevant and thus receive priority of processing resources (Lang and Bradley 2010; Pessoa 2009), these data are consistent with other models of emotion, motivation, and behavior. In contrast, pushing (or avoidance) was associated with activation in regions commonly associated with the default mode network, executive control, and sensorimotor processing. Together, these findings suggest that changes in physical proximity are an effective manipulation of stimulus salience.

The present results suggest that poor regulation of frontal and limbic signals associated with cognitive control and emotional/motivational salience, respectively, in response to stimuli of varying levels of salience likely contributes to poor resolution of approach-avoidance conflicts among individuals with EXT. Specifically, in a priori ROI analyses in the

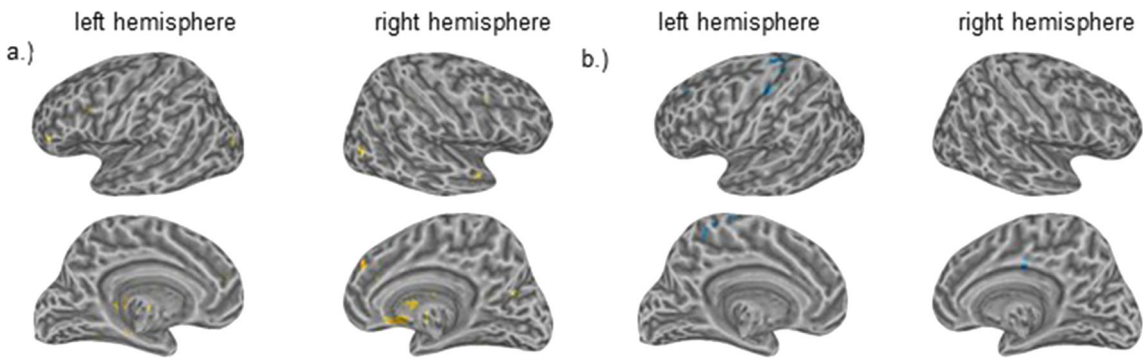

Fig. 7 Lateral and medial views of (**a**) regions activated and (**b**) deactivated by the interaction between task (i.e. conflict > congruent) and group

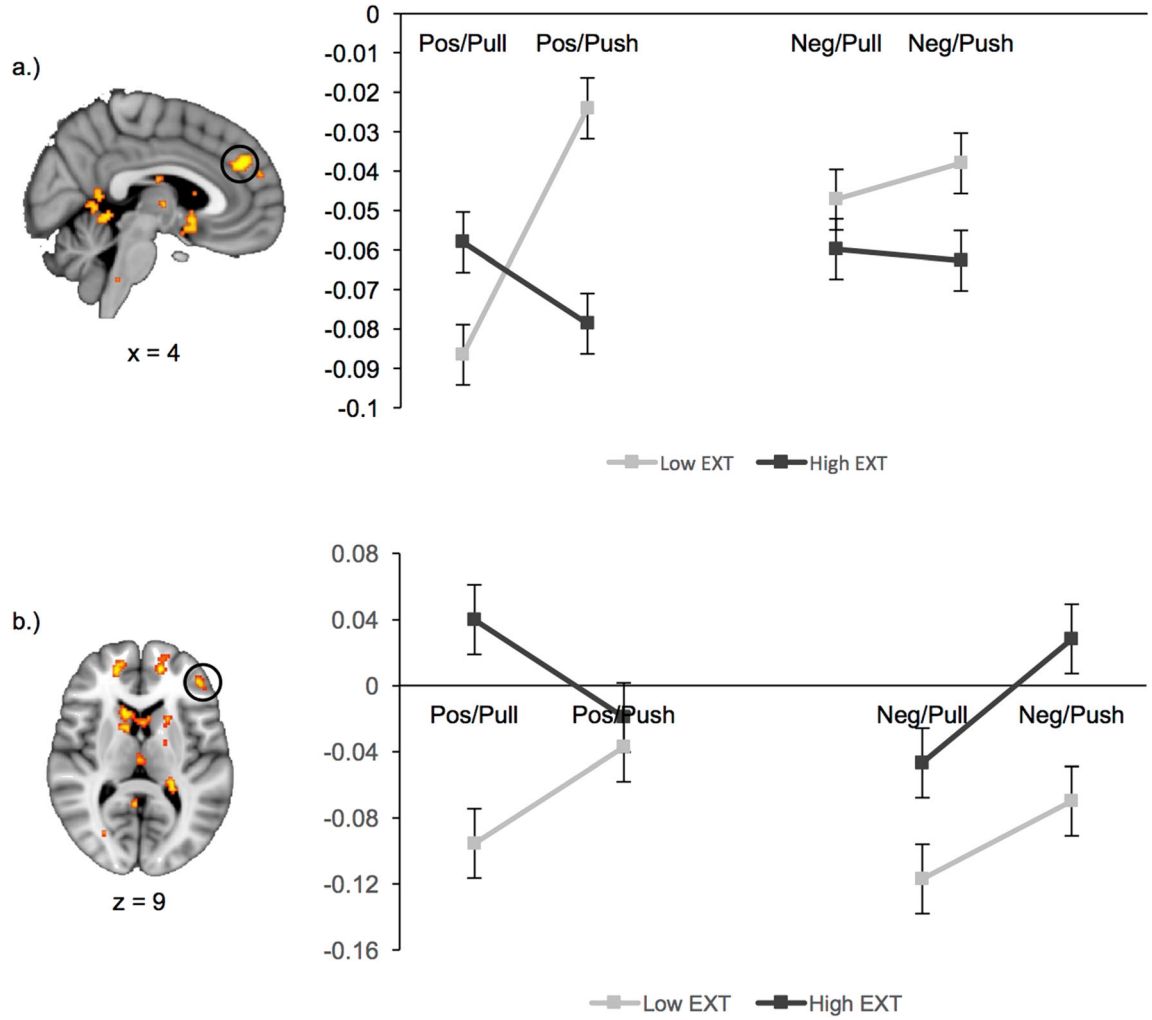

Fig. 8 Activation in the left paracingulate (**a**) and left frontal pole (**b**) from the interaction between conflict and group

bilateral dACC, low EXT individuals displayed similar patterns of neural modulation across push-pull conditions, while high EXT individuals displayed no significant modulation. A similar pattern was observed in a functionally-defined region of the frontal pole and amygdala, such that high EXT individuals displayed poor push-pull modulation in positive and neutral conditions, as well as neutral and negative conditions, respectively. Together, these data demonstrate poor neural differentiation between conditions that imply increasing salience (i.e. a pulled object moving closer) and decreasing salience (i.e. a pushed object moving away). Importantly, this deficit appears to be valence-specific across brain regions. That is, high EXT individuals displayed a relatively normal pattern of modulation in the negative condition in the frontal pole and in the positive condition in the amygdala. As such, valence likely influences detection of changes in motivational relevance in separate brain regions. Critically, poor modulation was observed in the neutral condition in both regions, suggesting that valence facilitates motivational neural modulation in some brain regions. To the extent that detecting changes in motivational relevance is critical to producing regulated, adaptive behavior, the present neural results argue that high EXT individuals may have difficulty with these processes, potentially contributing to poor decision-making. More specifically, highly salient cues should receive prioritization of processing resources; individuals with EXT appear to have difficulty differentiating cues of varying levels of salience and allocating resources appropriately. Thus, in contrast to extant theories that posit that individuals with EXT are hyper-reactive to highly salient cues, these data indicate that high EXT individuals have difficulty differentiating highly salient from less salient information.

Contrary to hypotheses, interpretable group differences associated with approach-avoidance conflicts were not demonstrated in this sample. In particular, observed activation from the interaction between conflict and group, which included both traditional positive reward/negative punishment trials as well as novel positive punishment/negative reward trials, had limited statistical reliability and was found outside hypothesized brain regions. These results do not lend support to the

assertion that poor decision-making among individuals with EXT is *specifically* related to fundamental differences in responding to simultaneously presented conflicting motivational stimuli, as compared to healthy controls.

While the present results provide novel insight into approach-avoidance resolution in EXT individuals, important considerations are worth noting. First, due to task design, neural differences in approach-avoidance conflicts between EXT groups may have been constrained. Specifically, participants were instructed to make actions congruent with the cue word ("push" or "pull") on each trial. While conflicts arose due to differences in naturalistic vs. instructed action, participants did not make free choices regarding their action on each trial. Thus, potential differences between groups may have been artificially limited to the extent that trials did not require a "decision" as traditionally conceptualized. However, in order to consistently induce approach-avoidance conflicts, instructed action was required. Future studies can address this issue by allowing participants a total percentage of push/pull actions, of which the participant freely chooses on any given trial. Additionally, a motivationally neutral movement (e.g. sideways) would be useful in future designs to further clarify the effects of action. Inclusion of self-reported perception of image size changes would also serve as a useful manipulation check of the task paradigm. Second, the sample size, though generally consistent with similar studies, is nonetheless modest. Accordingly, observed effects are likely to be limited to relatively large effects. This may be especially relevant to the interpretation of the three-way interaction effect (i.e. EXT group x salience x conflict) that would further elucidate the potentially complex interplay between salience and contrast in decision-making. While the interaction of salience with group and the lack of an interaction of conflict with group nonetheless remain important observations in clarifying the neural processes associated with EXT, future studies would benefit from a larger sample size. Finally, the sample was relatively limited in racial diversity, consistent with the demographics of the geographical region from which the sample was selected. However, future studies would likely benefit from inclusion of a more diverse sample.

The present results provide important insight into the processes associated with motivation among individuals with EXT. Specifically, these findings imply that individuals with EXT may inadequately differentiate between an object of increasing motivational relevance and one of decreasing motivational relevance. To the extent that appropriate resolution of an approach-avoidance conflict requires comparison between multiple conflicting cues, difficulty differentiating important from less important information is critical. These findings suggest that appropriate intervention in individuals with EXT may focus on identifying and clarifying relevant information in decisional contexts. Together, these results indicate that EXT is characterized by atypical modulation of brain regions associated with executive control and emotion during motivated action.

Conclusions

Externalizing psychopathology (EXT) is often associated with poor decision-making outcomes in situations involving simultaneous cues for approach and avoidance. Using a novel task to evoke such approach-avoidance conflicts, EXT-related differences in neural activation were associated with poor prioritization based on cue salience. These data suggest multiple, complex pathways to maladaptive behavior in EXT.

Acknowledgments This work was supported by a grant from the National Institute of Health and National Institute on Alcohol Abuse and Alcoholism (NIH/NIAAA RO1 AA13650) to P.R.F., a National Institute on Drug Abuse training grant fellowship (NIDA T32 DA024628) to A.J.L, and by the Indiana METACyt Initiative of Indiana University, which was funded in part through a major grant from the Lilly Endowment, Inc. The authors wish to thank Andrew Jahn and Kyle Gerst for technical and computer programming support; Tony Walker and Jeff Sturgeon for input device design and programming; and Sean Berry, Colleen McCracken, and Tiffany Barrios for assistance with data collection.

Funding information This work was supported by a grant from the National Institute of Health and National Institute on Alcohol Abuse and Alcoholism (NIH/NIAAA RO1 AA13650) to P.R.F., a National Institute on Drug Abuse training grant fellowship (NIDA T32 DA024628) to A.J.L, and by the Indiana METACyt Initiative of Indiana University, which was funded in part through a major grant from the Lilly Endowment, Inc.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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.

Informed consent Informed consent was obtained from all individual participants included in the study.

References

Aarts, H., Custers, R., & Veltkamp, M. (2008). Goal priming and the affective-motivational route to nonconscious goal pursuit. *Social Cognition, 26*, 555–577.

American Psychiatric Association (2000). *Diagnostic and statistical manual of mental disorders* (4th ed., Text Revision). Washington, DC: Author.

Bechara, A. (2005). Decision making, impulse control and loss of willpower to resist drugs: A neurocognitive perspective. *Nature Neuroscience, 8*, 1458–1463.

Bechara, A., Damasio, A. R., Damasio, H., & Anderson, S. W. (1994). Insensitivity to future consequences following damage to human prefrontal cortex. *Cognition, 50*, 7–15.

Bechara, A., Dolan, S., Denburg, N., Hindes, A., Anderson, S. W., & Nathan, P. E. (2001). Decision-making deficits, linked to a dysfunctional ventromedial prefrontal cortex, revealed in alcohol and stimulant abusers. *Neuropsychologia, 39*, 376–389.

Bechara, A., & Martin, E. M. (2004). Impaired decision making related to working memory deficits in individuals with substance addictions. *Neuropsychology, 18*, 152–162.

Bickel, W. K., Jarmolowicz, D. P., Mueller, E. T., Koffarnus, M. N., & Gatchalian, K. M. (2012). Excessive discounting of delayed reinforcers as a trans-disease process contributing to addiction and other disease-related vulnerabilities: Emerging evidence. *Pharmacology & Therapeutics, 134*, 287–297.

Bickel, W. K., Koffarnus, M. N., Moody, L., & Wilson, A. G. (2014). The behavioral-and neuro-economic process of temporal discounting: A candidate behavioral marker of addiction. *Neuropharmacology, 76*, 518–527.

Bickel, W. K., Miller, M. L., Yi, R., Kowal, B. P., Lindquist, D. M., & Pitcock, J. A. (2007). Behavioral and neuroeconomics of drug addiction: Competing neural systems and temporal discounting processes. *Drug and Alcohol Dependence, 90*, S85–S91.

Bobova, L., Finn, P. R., Rickert, M. E., & Lucas, J. (2009). Disinhibitory psychopathology and delay discounting in alcohol dependence: Personality and cognitive correlates. *Experimental and Clinical Psychopharmacology, 17*, 51–61.

Bogg, T., & Finn, P. R. (2009). An ecologically based model of alcohol-consumption decision making: Evidence for the discriminative and predictive role of contextual reward and punishment information. *Journal of Studies on Alcohol and Drugs, 70*, 446–457.

Bradley, M. M., Codispoti, M., Cuthbert, B. N., & Lang, P. J. (2001). Emotion and motivation I: Defensive and appetitive reactions in picture processing. *Emotion, 1*, 276–298.

Bucholz, K. K., Cadoret, R., Cloninger, C. R., Dinwiddie, S. H., Hesselbrock, V. M., Nurnberger, J. I., et al. (1994). A new, semi-structured psychiatric interview for use in genetic linkage studies: A report on the reliability of the SSAGA. *Journal of Studies on Alcohol, 55*, 149–158.

Cantrell, H., Finn, P. R., Rickert, M. E., & Lucas, J. (2008). Decision making in alcohol dependence: Insensitivity to future consequences and comorbid disinhibitory psychopathology. *Alcoholism: Clinical and Experimental Research, 32*, 1398–1407.

Carroll, A. J., Sutherland, M. T., Salmeron, B. J., Ross, T. J., & Stein, E. A. (2015). Greater externalizing personality traits predict less error-related insula and anterior cingulate cortex activity in acutely abstinent cigarette smokers. *Addiction Biology, 20*, 377–389.

Chiew, K. S., & Braver, T. S. (2011). Positive affect versus reward: Emotional and motivational influences on cognitive control. *Frontiers in Psychology, 2*, 1–10.

Cox, R. W. (1996). AFNI: Software for analysis and visualization of functional magnetic resonance neuroimages. *Computers and Biomedical Research, 29*, 162–173.

Dalley, J. W., Everitt, B. J., & Robbins, T. W. (2011). Impulsivity, compulsivity, and top-down cognitive control. *Neuron, 69*, 680–694.

Desmond, J. E., & Glover, G. H. (2002). Estimating sample size in functional MRI (fMRI) neuroimaging studies: Statistical power analyses. *Journal of Neuroscience Methods, 118*, 115–128.

Endres, M. J., Donkin, C., & Finn, P. R. (2014). An information processing/associative learning account of behavioral disinhibition in externalizing psychopathology. *Experimental and Clinical Psychopharmacology, 22*, 122–132.

Endres, M. J., Rickert, M. E., Bogg, T., Lucas, J., & Finn, P. R. (2011). Externalizing psychopathology and behavioral disinhibition: Working memory mediates signal discriminability and reinforcement moderates response bias in approach–avoidance learning. *Journal of Abnormal Psychology, 120*, 336–351.

Ersche, K. D., Clark, L., London, M., Robbins, T. W., & Sahakian, B. J. (2006). Profile of executive and memory function associated with amphetamine and opiate dependence. *Neuropsychopharmacology, 31*, 1036–1047.

Ersche, K. D., Jones, P. S., Williams, G. B., Turton, A. J., Robbins, T. W., & Bullmore, E. T. (2012). Abnormal brain structure implicated in stimulant drug addiction. *Science, 335*, 601–604.

Everitt, B. J., & Robbins, T. W. (2005). Neural systems of reinforcement for drug addiction: From actions to habits to compulsion. *Nature Neuroscience, 8*, 1481–1489.

Finn, P. R. (2002). Motivation, working memory, and decision making: A cognitive-motivational theory of personality vulnerability to alcoholism. *Behavioral and Cognitive Neuroscience Reviews, 1*, 183–205.

Finn, P. R., Gerst, K., Lake, A., & Bogg, T. (2017). Decisions to attend and drink at party events: The effects of incentives and disincentives and lifetime alcohol and antisocial problems. *Alcoholism: Clinical and Experimental Research, 41*, 1622–1629.

Finn, P. R., Gunn, R. L., & Gerst, K. R. (2015). The effects of a working memory load on delay discounting in those with externalizing psychopathology. *Clinical Psychological Science, 3*, 202–214.

Finn, P. R., Justus, A., Mazas, C., & Steinmetz, J. E. (1999). Working memory, executive processes and the effects of alcohol on go/no-go learning: Testing a model of behavioral regulation and impulsivity. *Psychopharmacology, 146*, 465–472.

Finn, P. R., Rickert, M. E., Miller, M. A., Lucas, J., Bogg, T., Bobova, L., & Cantrell, H. (2009). Reduced cognitive ability in alcohol dependence: Examining the role of covarying externalizing psychopathology. *Journal of Abnormal Psychology, 118*, 100–116.

Goldstein, R. Z., & Volkow, N. D. (2011). Dysfunction of the prefrontal cortex in addiction: Neuroimaging findings and clinical implications. *Nature Reviews Neuroscience, 12*, 652–669.

Gonzalez, R., Bechara, A., & Martin, E. M. (2007). Executive functions among individuals with methamphetamine or alcohol as drugs of choice: Preliminary observations. *Journal of Clinical and Experimental Neuropsychology, 29*, 155–159.

Gorenstein, E. E., & Newman, J. P. (1980). Disinhibitory psychopathology: A new perspective and a model for research. *Psychological Review, 87*, 301–315.

Gray, J. A., & McNaughton, N. (2000). *The neuropsychology of anxiety: An enquiry into the functions of the septo-hippocampal system*. Oxford: Oxford University Press.

Gunn, R. L., & Finn, P. R. (2013). Impulsivity partially mediates the association between reduced working memory capacity and alcohol problems. *Alcohol, 47*, 3–8.

Iacono, W. G., Malone, S. M., & McGue, M. (2008). Behavioral disinhibition and the development of early-onset addiction: Common and specific influences. *Annual Review of Clinical Psychology, 4*, 325–348.

Kirby, K. N. (1997). Bidding on the future: Evidence against normative discounting of delayed rewards. *Journal of Experimental Psychology-General, 126*, 54–70.

Krueger, R. F., & Markon, K. E. (2006). Reinterpreting comorbidity: A model-based approach to understanding and classifying psychopathology. *Annual Review of Clinical Psychology, 2,* 111–133.

Krueger, R. F., Hicks, B. M., Patrick, C. J., Carlson, S. R., Iacono, W. G., & McGue, M. (2002). Etiologic connections among substance dependence, antisocial behavior and personality: Modeling the externalizing spectrum. *Journal of Abnormal Psychology, 111*(3), 411.

Lake, J. I., Spielberg, J. M., Infantolino, Z. P., Crocker, L. D., Yee, C. M., Heller, W., & Miller, G. A. (2019). Reward anticipation and punishment anticipation are instantiated in the brain via opponent mechanisms. *Psychophysiology*, 1-14.

Lang, P. J., & Bradley, M. M. (2010). Emotion and the motivational brain. *Biological Psychology, 84*, 437–450.

Lang, P.J., Bradley, M.M., & Cuthbert, B.N. (2008). International affective picture system (IAPS): Affective ratings of pictures and instruction manual. Technical report A-8. University of Florida, Gainesville, FL.

Li, X., Lu, Z. L., D'argembeau, A., Ng, M., & Bechara, A. (2010). The Iowa gambling task in fMRI images. *Human Brain Mapping, 31*, 410–423.

MacKillop, J. (2013). Integrating behavioral economics and behavioral genetics: Delayed reward discounting as an endophenotype for addictive disorders. *Journal of the Experimental Analysis of Behavior, 99*, 14–31.

MacKillop, J., Amlung, M. T., Few, L. R., Ray, L. A., Sweet, L. H., & Munafò, M. R. (2011). Delayed reward discounting and addictive behavior: A meta-analysis. *Psychopharmacology, 216*, 305–321.

Mazas, C. A., Finn, P. R., & Steinmetz, J. E. (2000). Decision-making biases, antisocial personality, and early-onset alcoholism. *Alcoholism: Clinical and Experimental Research, 24*, 1036–1040.

Seghier, M. L., Lazeyras, F., Pegna, A. J., Annoni, J. M., & Khateb, A. (2008). Group analysis and the subject factor in functional magnetic resonance imaging: Analysis of fifty right-handed healthy subjects in a semantic language task. *Human Brain Mapping, 29*, 461–477.

Shirer, W. R., Ryali, S., Rykhlevskaia, E., Menon, V., & Greicius, M. D. (2012). Decoding subject-driven cognitive states with whole-brain connectivity patterns. *Cerebral Cortex, 22*, 158–165.

Nichols, T. (2012). Multiple testing corrections, nonparametric methods, and random field theory. *Neuroimage, 62*, 811–815.

Pessoa, L. (2009). How do emotion and motivation direct executive control? *Trends in Cognitive Sciences, 13*, 160–166.

Pfister, H.-R., & Böhm, G. (2008). The multiplicity of emotions: A framework of emotional functions in decision making. *Judgment and Decision making, 3*, 5.

Spielberg, J. M., Heller, W., Silton, R. L., Stewart, J. L., & Miller, G. A. (2011). Approach and avoidance profiles distinguish dimensions of anxiety and depression. *Cognitive Therapy and Research, 35*, 359–371.

Smith, S. M., Jenkinson, M., Woolrich, M. W., Beckmann, C. F., Behrens, T. E., Johansen-Berg, H., et al. (2004). Advances in functional and structural MR image analysis and implementation as FSL. *Neuroimage, 23*, S208–S219.

Spielberg, J. M., Stewart, J. L., Levin, R. L., Miller, G. A., & Heller, W. (2008). Prefrontal cortex, emotion, and approach/withdrawal motivation. *Social and Personality Psychology Compass, 2*, 135–153.

Tooby, J., Cosmides, L., Sell, A., Lieberman, D., & Sznycer, D. (2008). 15 internal regulatory variables and the Design of Human Motivation: A computational and evolutionary approach. In *Handbook of approach and avoidance motivation* (Vol. 251). Lawrence Erlbaum Mahwah, NJ.

van Dantzig, S., Pecher, D., & Zwaan, R. A. (2008). Approach and avoidance as action effects. *Quarterly Journal of Experimental Psychology, 61*, 1298–1306.

Verdejo-García, A., Bechara, A., Recknor, E. C., & Perez-Garcia, M. (2006). Executive dysfunction in substance dependent individuals during drug use and abstinence: An examination of the behavioral, cognitive and emotional correlates of addiction. *Journal of the International Neuropsychological Society, 12*, 405–415.