Comparing cognitive and affective predictors of craving

Brendan Cullen
Krista DeStasio
Danielle Cosme
Elliot Berkman

Department of Psychology, University of Oregon

Address correspondence to:
Brendan Cullen
Department of Psychology
1227 University of Oregon Eugene, OR 97403-1227
bcullen@uoregon.edu

Abstract

Health-risking behaviors (HRBs), e.g., excessive consumption of alcohol, tobacco, drugs and energy-dense food, contribute to long-term health problems, particularly among individuals who experienced early life adversity (EA). Though traditional executive control tasks are commonly assumed to be relevant for predicting real-world HRBs, recent work has called into question the ecological and predictive validity of these tasks. This study explores the predictive validity of cognitive and affective neural measures derived from a more passive cue reactivity task in a community sample of adults with self-control problems and a history of early adversity. We extracted trial-level estimates of whole-brain expression of canonical "inhibitory control" and "craving" patterns while participants viewed images of personally relevant health-risking substances during the cue reactivity task. Statistical modeling showed that greater trial-level expression of the "craving" and "inhibitory control" patterns predicted higher and lower desire ratings, respectively, for cue reactivity stimuli. However, only "craving" pattern expression predicted measures of real-world craving in daily life. Taken together, these results suggest that, among individuals with self-control problems, the real-world predictive validity of passive neural measures of affective processes may be superior to that of neural measures of executive control.

Keywords: inhibitory control, craving, health-risking behaviors, cue reactivity, brain-as-predictor

Introduction

Health-risking behaviors (HRBs), such as excessive consumption of alcohol, tobacco, drugs and energy-dense food, increase risk for adverse health outcomes (e.g. cancer, heart disease, addiction), and can mark the beginning or escalation of life course trajectories towards long-term physical and mental health difficulties and early mortality. There is a clear need for identifying reliable predictors of HRBs that can be leveraged by researchers and clinicians in designing interventions that have the potential to reduce HRB prevalence. Previous research has found that deficits in inhibitory control (IC), defined here as the ability to suppress, stop, or otherwise prevent unwanted dominant responses, are associated with higher likelihood of HRBs. For example, individuals with low levels of IC are more likely to consume more alcohol (Cook, Young, Taylor, & Bedford, 1998) and engage in binge drinking and related harmful behaviors such as drunk driving (Gibson, Schreck, & Miller, 2004; Piquero, Gibson, & Tibbetts, 2000). Low levels of IC are also associated with greater consumption of energy-dense food (Hofmann, Friese, & Roefs, 2009; Hofmann, Rauch, & Gawronski, 2007; Polivy, Herman, Hackett, & Kuleshnyk, 1986) and increases in weight and BMI (Duckworth, Tsukayama, & Geier, 2010; Francis & Susman, 2009; Nederkoorn, Houben, Hofmann, Roefs, & Jansen, 2010). Furthermore, individuals with low IC are more likely to initiate and sustain tobacco use (Flory & Manuck, 2009; Wilson & Maclean, 2013) and are less likely to quit smoking in a given cessation attempt (Sheffer et al., 2012). Low IC has also been identified as a risk factor for substance abuse problems more broadly (Ivanov, Schulz, London, & Newcorn, 2006; King, Fleming, Monahan, & Catalano, 2011; Monterosso, Aron, Cordova, Xu, & London, 2005; Tarter, 1988). Given the evidence of the relationship between IC and a variety of health behaviors, laboratory studies on self-control often use classic executive functioning paradigms, such as stop signal or go/no-go

tasks, that probe behavioral and neural markers of IC with the assumption that these measures are relevant for predicting real-world HRBs.

However, recent work has called into question the real-world predictive validity of task-based measures of self-control. For example, (Eisenberg et al., 2018) found that a large battery of behavioral tasks related to self-control (e.g. temporal discounting, cognitive control, impulsivity, etc.) were on the whole unable to predict real-world behaviors and health outcomes (e.g. binge drinking, drug use, smoking, obesity, etc) in a large sample of adults. The authors suggest that executive control (EC) tasks either do not probe psychological processes that are relevant for real-world behaviors or that these tasks simply have poor ecological validity that limits the applicability of inferences derived from highly controlled experimental environments to real-world contexts. Similarly, Hedge et al. (2017) have proposed that standard EC tasks (e.g., Eriksen Flanker, Stroop, Stop Signal, Go/No-Go, etc.) are designed to maximize highly replicable experimental effects, which results in low between-subjects variability. In other words, the very nature of such tasks as highly robust tools in experimental contexts limits their ability to explain individual differences in real-world behaviors outside of the laboratory (Enkavi et al., 2018).

Though cognitive tasks measure top-down EC processes that are undoubtedly important for understanding basic mechanisms of self-control, bottom-up affective or motivational processes may also be relevant for predicting self-control failures (e.g. HRBs). For example, craving is an affective state characterized by strong appetitive motivation (Giuliani & Berkman, 2015) that has been shown to predict real-world cigarette smoking (Carpenter et al., 2009), unhealthy eating (Boswell & Kober, 2016), alcohol consumption (Flannery, Poole, Gallop, & Volpicelli, 2003; Higley et al., 2011) and drug use (Hartz, Frederick-Osborne, & Galloway,

2001). In contrast to EC, which is often measured using "active" tasks that require participants to follow a set of complex rules, another advantage of studying reward processes such as craving is that they can be measured by passive (or "reactive") tasks that have fewer artificial constraints and processing demands and thus may be better able to approximate real-world psychological processes. For example, cue-induced craving is typically measured using cue reactivity tasks (Courtney, Ghahremani, London, & Ray, 2014; Janes et al., 2010) in which participants passively view images on a screen rather than explicitly modifying their behavioral responses according to a set of rules. In contrast to highly contrived cognitive tasks that typically prioritize maximizing robust experimental effect sizes over capturing individual differences, the passive, open-ended structure of cue reactivity tasks might allow for greater between-subjects variability.

Despite the advantages of studying bottom-up motivational or affective processes using passive tasks, there is one notable disadvantage of this approach. Unlike cognitive EC tasks, which often generate behavioral measures (e.g. reaction times, percent inhibition, etc.) that can be used as independent variables for predicting various outcomes, passive cue reactivity tasks do not produce as much behavioral data. Neuroimaging methods such as functional magnetic resonance imaging (fMRI) are well suited to address the lack of behavioral measures because neural measures can be used as independent variables even in the absence of an overt behavioral response, following a "brain-as-predictor" approach (Berkman & Falk, 2013)

Additionally, neural measures gathered during cue reactivity tasks can generate an index of EC processes even without explicit instructions to regulate. Classic EC tasks directly elicit a regulatory processes of interest (e.g. IC), by explicitly instructing participants to withhold responses to specific stimuli. This type of paradigm assesses EC capacity, or the ability to engage EC processes when actively attempting to regulate according to explicit instructions in an

experimental context. Cue reactivity tasks, on the other hand, have the ability to assess implicit EC, or EC tendency (Milyavskaya, Berkman, & De Ridder, 2017), which represents the degree of spontaneous engagement of EC in an uninstructed context. For example, as others have argued in the parallel context of emotion regulation (Doré et al., 2019; Doré, Jochen, & Ochsner, 2017; Shahane, Lopez, & Denny, 2018), neural activity in canonical EC regions while passively viewing highly desirable images during a cue reactivity task can be interpreted as spontaneous regulation (Lopez et al., 2017). In these cases, activity during passive tasks in neural regions specific to EC can serve as one index of EC processes.

Given recent evidence of the limited ecological and predictive validity of cognitive tasks of self-control, the primary aim of the current study is to determine the extent to which spontaneous expression of neural patterns related to EC and reward processes during a more open-ended, ecologically valid cue reactivity task predict real-world HRBs. More specifically, this analysis explores the relationship between these neural patterns and craving for personally-relevant health-risking substances, characterized in two different contexts: 1) "proximal" craving as measured in the lab within the context of a cue reactivity task and 2) "distal" craving as indexed by self-reported levels of real-world craving in daily life. We recruited a large sample of adults from the community with a history of early adversity and self-control problems across a variety of domains (e.g. disinhibited intake of alcohol, tobacco, drugs or energy-dense food). Participants completed a cue reactivity task during which they passively viewed both neutral images and personalized risk images tailored to their specific self-reported HRBs and rated how desirable they found each image. We combined a trial-by-trial modeling approach with pattern expression analysis using whole-brain Neurosynth maps (Yarkoni, Poldrack, Nichols, Van Essen, & Wager, 2011) corresponding to canonical "inhibitory control" (IC) and "craving"

patterns. For each trial, we calculated whole-brain expression of "IC" and "craving" patterns, regressed desire rating on these pattern expression values (PEVs), and used multilevel modeling to determine how well each of these neural patterns predicted proximal, in-task measures of craving. We then aggregated PEVs across trials and used multiple regression to compare how well "IC" and "craving" pattern expression predicted distal, real-world craving. Our analysis plan was pre-registered and is available online at https://osf.io/n9e2y/?view_only=2319cc39123441c493ae5059caaaf22a.

Methods

Participants

A sample of 143 adults between the ages of 35 and 55 were recruited from the Eugene, OR community. The specific population of interest for this study is adults who experienced adversity in childhood and have current difficulties with self-control because these individuals are at elevated risk of health problems related to behavior (Lovallo, 2013). Thus, eligibility criteria included reporting experience of early adversity (EA) before age 18, i.e. a score of 4 or higher on the Adverse Childhood Experiences (ACEs) questionnaire (Felitti et al., 1998) and current difficulties with self-control, including problematic use of energy-dense foods, alcohol, tobacco, or drugs, including marijuana, cocaine, heroine, methamphetamine or prescription pills. Exclusion criteria included current diagnoses of psychiatric, eating, neurological, or substance use disorders and contraindications for an MRI scan, e.g., metal implants or fragments, pacemakers, claustrophobia, pregnancy, and weight greater than 550 lbs. Of the 143 participants enrolled, 10 dropped out of the study before the baseline session. Data from an additional 16 participants were excluded, resulting in a final sample of 117. Reasons for data exclusion included noncompliance with task instructions, sleeping during the task, structural brain

abnormalities, initially unreported neurological disorders, and excessive motion artifacts in fMRI data.

Procedure Overview

An initial 30-minute intake session took place at the Social and Affective Neuroscience Lab at the University of Oregon (UO), during which participants gave written informed consent. This study was approved by the UO's Institutional Review Board, and participants were compensated for their participation. A unique stimulus set of personalized risk cues (PRCs) was compiled for each participant containing images corresponding to his or her specific HRB categories. For participants who endorsed more than one HRB category, the relative proportion of PRCs was determined by their score on a 5-question adaptation of the Brief Self-Control Scale (Tangney, Baumeister, & Boone, 2004); questions 1, 2, 5, 9, & 12) for each HRB category (e.g. "I am good at resisting alcohol/drugs/tobacco/unhealthy food"). For example, if a participant endorsed only alcohol and tobacco and rated each with equal severity, he or she would view an equal number of alcohol and tobacco images. PRCs were selected from a database of ~24,000 images collected from the internet for use in this study. All images were scaled to cover an equal area of the display screen.

Cue Reactivity Task

The cue reactivity task was adapted from a task used by (Giuliani, Mann, Tomiyama, & Berkman, 2014) and consisted of two runs of 26 trials each. During this task, participants were shown PRCs and neutral images (e.g., common household objects) and were asked to "look and respond naturally" to the images shown (see Figure 1). Instructions appeared on the screen at the start of each run for 2s, after which either a PRC or a neutral image (1:1 ratio) appeared on the screen for 5s. Participants were then shown a blank screen for 0.5s, followed by a rating screen

for 4s, which asked them to rate on a scale of 1-5 (1 = "Not desirable", 5 = "Very desirable") how desirable they found whatever image they had just seen. The rating screen was followed by a jittered inter-trial interval ranging from 1.5-4s (mean, 2 sec).

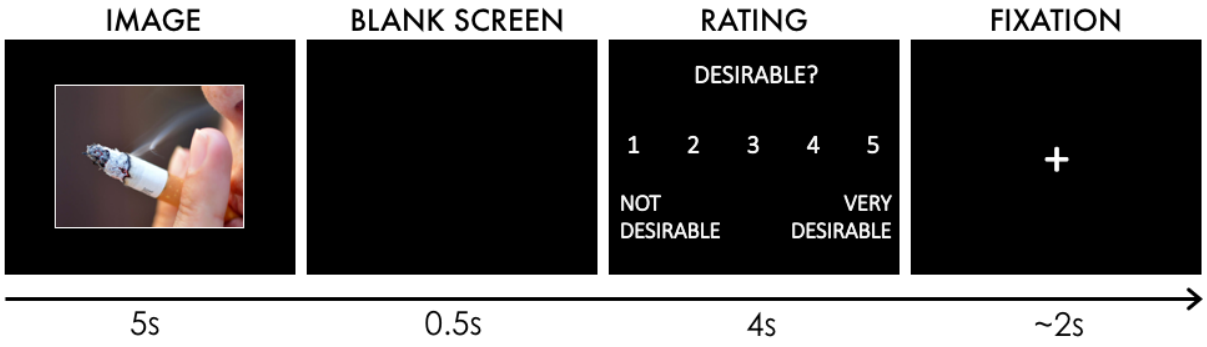

Figure 1. Task design. Each trial consisted of a five second image presentation, followed by a blank screen for 0.5s and a rating period. Images were either neutral (e.g., common household objects) or personalized risk cues (e.g., alcohol, tobacco, drugs, unhealthy food). All trials ended with a jittered fixation cross presented for a mean of 2s.

Self-report Measures

Self-report measures related to self-control were included as covariates in regression models. These included the Brief Self Control Scale (13 items, 1 = "Not at all" to 5 = "Very much") (Tangney et al., 2004), Barratt Impulsiveness Scale (30 items, 1 = "Rarely/Never", to 4 = "Almost always/Always") (Patton et al., 1995), and Behavioral Avoidance/Inhibition Scale (20 items, 1 = "Strongly disagree" to 5 = "Strongly agree") (Carver and White, 1994). In order to reduce multicollinearity between these scales in our statistical models that are described below, we used principal components analysis (PCA) for data reduction. Using the criteria of eigenvalue greater than 1, PCA with varimax rotation extracted three components that together accounted for 34.5% of the total variance. Based on factor loadings, these components corresponded to impulsivity (e.g., "I act on the spur of the moment"; "I buy things on impulse"; "I spend or charge more than I earn"), lack of planning (e.g., "I plan for the future"; "I am able to work effectively toward long-term goals"; "I am a careful thinker", all reverse scored), and negative

emotional reactivity (e.g., "I feel worried when I think I have done poorly at something"; "Criticisms or scolding hurts me quite a bit" ; "If I think something unpleasant is going to happen I usually get pretty 'worked up'").

Health-Risking Behavior Outcomes

Participants reported their everyday levels of craving for and consumption of their endorsed HRB categories (e.g., energy-dense foods, alcohol, tobacco and/or drugs) via a battery of surveys. Measures of craving included the Brief Substance Craving Scale (3 items regarding craving in last 24 hours: "intensity", 1 = "None at all" to 5 = "Extreme"; "frequency", 1 = "Never" to 5 = "Almost constantly"; "length of time spent craving", 1 = "None at all" to 5 = "Very long") (Baker et al., 1996); Alcohol Craving Questionnaire-Short Form (12 items, 1 = "Strongly disagree" to 7 = "Strongly agree") (Singleton, Tiffany, & Henningfield, 1998); Penn Alcohol Craving Scale (5 items, 1-7 scale, various scale anchors) (Flannery, Volpicelli, & Pettinati, 1999); Cocaine Craving Questionnaire-Brief (10 items, 1 = "Strongly disagree" to 7 = "Strongly agree") (Sussner et al., 2006); Heroin Craving Questionnaire-Short Form (14 items, 1 = "Strongly disagree" to 7 = "Strongly agree") (Heinz et al., 2006); Marijuana Craving Questionnaire-Short Form (12 items, 1 = "Strongly disagree" to 7 = "Strongly agree") (Heishman et al., 2009); Craving Experience Questionnaire (prescription pills subscale; 10 items, 0 = "Not at all" to 10 = "Extremely/constantly") (May et al., 2014); Questionnaire of Smoking Urges-Brief (10 items, 1 = "Strongly disagree" to 7 = "Strongly agree") (L. S. Cox, Tiffany, & Christen, 2001); Food Craving Inventory (7 items, 1 = "Never" to 5 = "Always/Almost every day") (White, Whisenhunt, Williamson, Greenway, & Netemeyer, 2002) and a single item about meth craving ("Rate how intense your most severe craving was yesterday"; 0 = "No Craving" - 100 = "Worst Craving Ever Experienced"). Measures of consumption included the Alcohol Use

Disorders Identification Test (10 items, 1 = "Never" to 5 = "4 or more times a week") (Babor & Grant, 1988); Fagerstrom Test for Nicotine Dependence (6 multiple choice questions) (Heatherton, Kozlowski, Frecker, & Fagerstrom, 1990); Dutch Eating Behavior Questionnaire (20 items, 1 = "Never" to 5 = "Very Often") (van Strien, Frijters, Bergers, & Defares, 1986) and a single item about drug use ("On average, how many times per day do you use alcohol/ cocaine/ marijuana/ heroin/ meth/ prescription pills?").

Participants only completed surveys that pertained to their endorsed HRB categories, and a mean score was calculated for each scale they completed. Since participants endorsed different HRB categories, some of which were measured with multiple scales, separate composite scores were created for craving ($HRB_{craving}$) and consumption ($HRB_{consumption}$) scores, as follows. First, for each scale, participant means were converted to z-scores with respect to the subset of individuals who completed that scale. For example, a positive z-score indicates higher than average craving or consumption of that substance with respect to the rest of sample. Then, for each participant who endorsed more than one HRB category, an average z-score was calculated and weighted by the extent to which participants rated each category as problematic, as measured by a 5-item adaptation of the Brief Self Control Scale (Tangney et al., 2004) (see "Overview of Procedure" above).

Image Acquisition

Experimental stimuli were presented to participants using a magnet-compatible, rear-projection system controlled by an Apple MacBook Pro using Psychtoolbox software run on the MATLAB platform. Participants' button presses were collected on a 10-key button box capable of recording responses to the millisecond level. fMRI scans were acquired in the Siemens Skyra 3 Tesla scanner at University of Oregon's Lewis Center for Neuroimaging (LCNI), a research-

dedicated, whole-body system optimized for functional brain imaging. First, a shimming protocol maximized homogeneity in the field, and a 30s, T2-weighted scout allowed slice prescriptions for all subsequent scans. Between functional runs, we acquired a high-resolution anatomical T1- weighted MP-RAGE scan (TR/TE = 2300/2.1 ms, 192 x 192 matrix, 1 mm thick, 160 sagittal slices, FOV = 256). Task-based functional images used a T2*-weighted echo-planar scan (33 axial slices, TR/TE = 2000/30, 90-deg flip, 64 x 64 matrix, 4 mm thick, FOV = 200), and in-plane gradient echo field magnitude and phase maps partially corrected for inhomogeneities in the magnetic field (33 axial slices, TR/TE = 345/8.06 ms, 40-deg flip, 64 x 64 matrix, 4 mm thick, FOV = 200). After acquisition, images were transferred to LCNI's computation grid for analysis.

fMRI Analyses

Pre-processing/GLM. Neuroimaging data were preprocessed using FMRIPREP version 1.0.0 (Esteban et al., 2018). In brief, each participant's functional images were realigned, coregistered to the high-resolution anatomical image, unwarped to reduce susceptibility artifacts, and smoothed using a $2mm^3$ FWHM Gaussian smoothing kernel. First-level models were constructed in SPM12 using a "beta series" approach to extract trial-level estimates of brain activity (Koyama, McHaffie, Laurienti, & Coghill, 2003; Rissman, Gazzaley, & D'Esposito, 2004) to be used in multilevel statistical models. Specifically, each image-viewing period during the task was modeled as a separate boxcar function convolved with the canonical hemodynamic response, resulting in trial-level estimates of brain activity for each voxel in each participant, relative to implicit baseline. Trial duration was specified as the 8.5s from image onset to fixation (see Figure 1).

Realignment parameters were transformed into five motion regressors, including absolute displacement from the origin in Euclidean distance and the displacement derivative for both translation and rotation, and a single trash regressor for images with motion artifacts (e.g., striping) identified using automated motion assessment version v0.2-alpha (Cosme, Flournoy, & DeStasio, 2018) and visual inspection. A single regressor for the response period (i.e. desire rating), in addition to these five motion regressors, were included in the statistical models as regressors of no interest.

Pattern expression analysis. Pattern expression of meta-analytic brain maps has been used successfully as an analytical tool in the context of studies on working memory (van Ast et al., 2016), emotion regulation (Doré et al., 2019, 2017; Shahane et al., 2018), picture-induced negative affect (Chang, Gianaros, Manuck, Krishnan, & Wager, 2015) and pain (Wager et al., 2013; Woo et al., 2017). Here, we used pattern expression analysis to determine the degree to which trial-level expression of whole-brain, meta-analytic Neurosynth maps related to EC and reward processes could predict desire for PRC images during the cue reactivity task ("proximal" craving) and whether overall expression of these neural patterns across trials could predict real-world craving for HRB categories ("distal" craving). Specifically, we used the Neurosynth search terms "inhibitory control" and "craving", respectively, and downloaded the corresponding "uniformity test" (i.e., forward inference) maps, both thresholded for a false discovery rate of .01 (Yarkoni et al., 2011). Using the *"3ddot -dodot"* function from Analysis of Functional NeuroImages (AFNI) software (R. W. Cox, 1996), we calculated the dot product of the activation image (β map) for each trial with both the Neurosynth "IC" and "craving" maps, resulting in scalar PEVs for each participant representing the degree to which each trial-level β map expressed the "IC" and "craving" patterns (PEV_{IC} and $PEV_{craving}$, respectively) during the

image-viewing period of the cue reactivity task (see Figure 2). Extreme outliers (defined as ± 3 standard deviations from the mean) were removed from raw PEVs, which were then standardized within subjects for later use in statistical models.

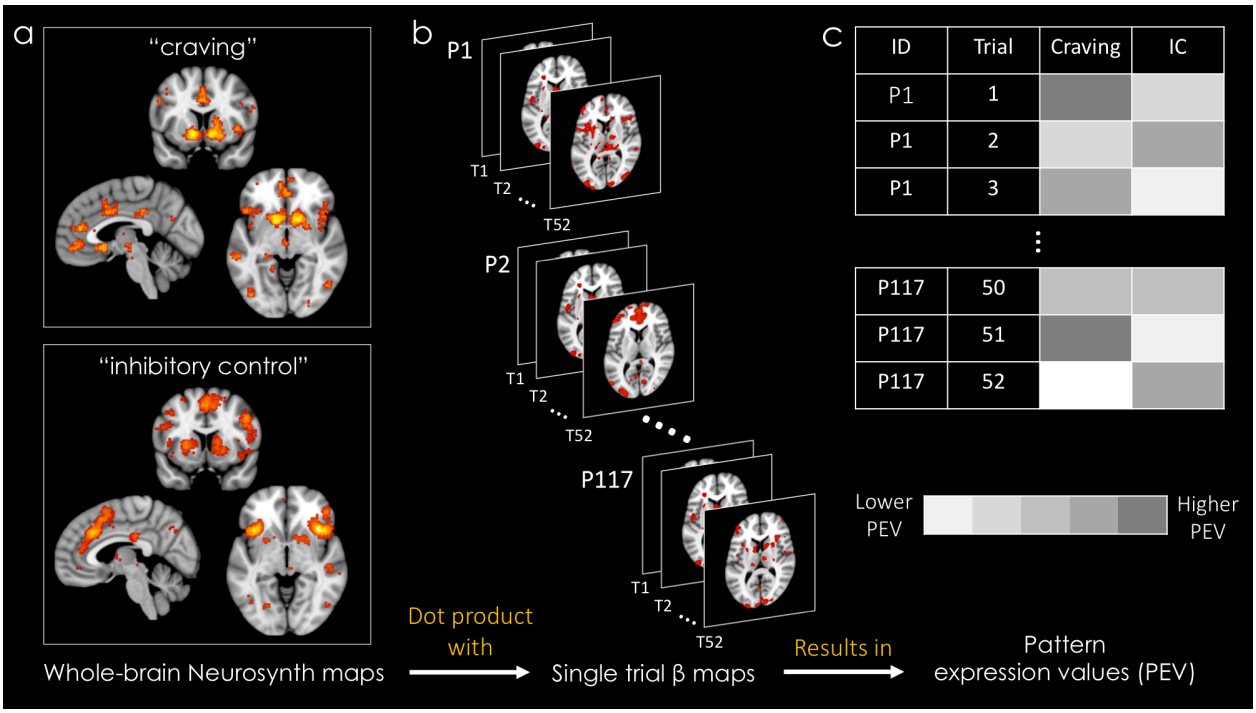

Figure 2. Pattern expression analysis. The dot product between whole-brain Neurosynth maps corresponding to "inhibitory control" (IC) and "craving" patterns (*a*) and each participant's trial-level *β* maps (*b*) resulted in scalar pattern expression values (PEVs) for each trial for each participant (*c*). Higher PEVs indicate greater expression of a given brain pattern. Individual participants and trials are denoted with "P" and "T", respectively. Figure adapted from Shahane et al. (2018)

Statistical Analysis

Multilevel modeling. Multilevel models were used to determine whether PEV_{IC} and $PEV_{craving}$ predicted "proximal" craving (i.e. desire ratings) on a trial-by-trial basis. Statistical analyses were conducted in R 3.5.2. (R Core Team, 2018; https://www.r-project.org/) using the lme4 package (Bates, Mächler, Bolker, & Walker, 2013). Only PRC trials were included in this analysis, as estimates of brain activity related to craving and IC in response to neutral images are

difficult to interpret. The bound optimization by quadratic approximation (BOBYQA) optimizer was used to maximize model convergence.

Multiple linear regression. In addition to the trial-by-trial multilevel model, we also examined the between-subjects association between brain activity and craving. To do this, we estimated a multiple linear regression model at the subject level to compare the extent to which average, standardized "IC" and "craving" PEVs across PRC trials in the cue reactivity task predicted "distal" real-world craving (i.e., $HRB_{craving}$). In a first step in the hierarchical regression, relevant covariates were added to the regression model, including demographics (i.e., age, gender, race/ethnicity); number of PRC categories endorsed (representing complexity of self-control problems); factor scores corresponding to individual differences in self-reported self-control ability (see "Self-report Measures" above) and number of early life adverse events, measured by the ACEs scale (Felitti et al., 1998), as early life stress is known to influence IC (Skowron, Cipriano-Essel, Gatzke-Kopp, Teti, & Ammerman, 2014). We controlled for these variables in order to isolate the unique effects of the neural pattern expression variables on craving. In a second step, average PEV_{IC} and $PEV_{craving}$ were added to the model to determine the extent to which they predicted $HRB_{craving}$. As an additional, exploratory analysis, we also tested a linear model using all the same independent variables listed above, with $HRB_{consumption}$ as the dependent variable.

Results

Descriptives

As a manipulation check, we confirmed that participants reported significantly higher desire ratings for PRC images (M = 3.68, SD = 1.26) compared to neutral images (M = 2.00, SD = 1.17) during the cue reactivity task (Figure 3; b = -0.84, 95% CI [-0.86, -0.81], $p < .001$).

Standardized PEV_{IC} and $PEV_{craving}$ variables were both approximately normally distributed after removing extreme outliers from raw scores ($PEV_{craving}$: *M* = -0.03, *SD* = 0.99, *range* = -5.11 to 4.59; PEV_{IC}: *M* = 0.18, *SD* = 0.97, *range* = -3.98 to 3.68).

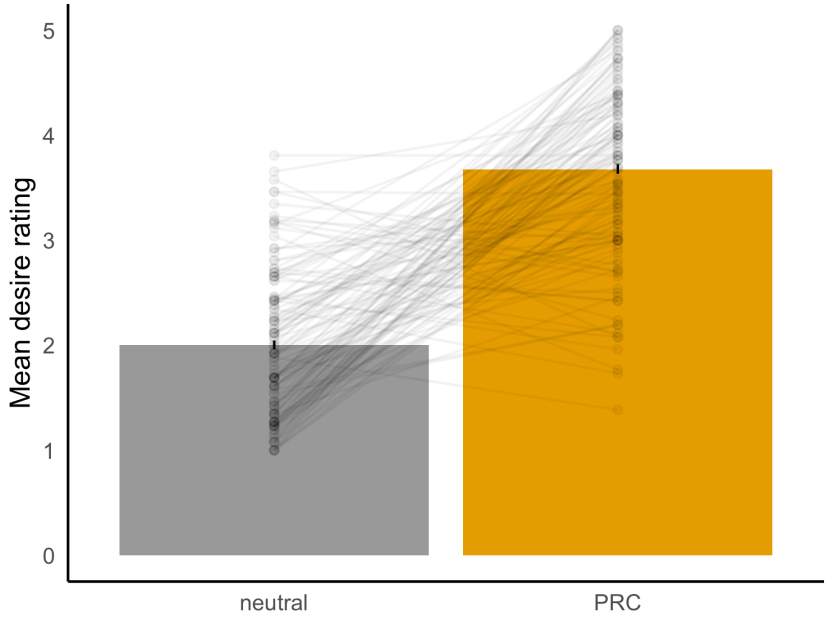

Figure 3. Average desire rating per participant for each condition in the cue reactivity task. On average, participants rated personalized risk cue (PRC) images (e.g. alcohol, tobacco, drugs, unhealthy foods) as more desirable than neutral images. Error bars are 95% confidence intervals across trials.

Model comparison

To determine the relationship between desire ratings and trial-level PEVs, we first compared model fit indices across a series of theoretically-defined multilevel models. Models were compared based on the Akaike information criterion (AIC), where smaller AIC indicates greater predictive accuracy. The best-fitting model is summarized below:

First level equation:

Y_{ij} (desire rating of stimulus presented in trial *i* by person *j*) = $\beta_{0j} + \beta_{1j}PEV_{cravingij} + \beta_{2j}PEV_{ICij} + \beta_{3j}PEV_{craving} \times PEV_{ICij} + \varepsilon_{ij}$

Second level equations:

$\beta_{0j} = \gamma_{00} + \gamma_{01}HRB_{craving} + \gamma_{02}HRB_{consumption} + \mu_{0j}$
$\beta_{1j} = \gamma_{10} + \mu_{1j}$
$\beta_{2j} = \gamma_{20} + \mu_{2j}$
$\beta_{3j} = \gamma_{30}$

Inspection of the multilevel model revealed that higher $PEV_{craving}$ predicted higher desire ratings (b = 0.26, 95% CI [0.18, 0.35], p < .001), while, higher PEV_{IC} predicted lower desire ratings (b = -0.24, 95% CI [-0.34, -0.15], p < .001; Figure 4). Furthermore, $HRB_{craving}$ and $HRB_{consumption}$ (second-level predictors) were both positively related to desire ratings (craving: b = 0.55, 95% CI [0.33, 0.77], p < .001; consumption: b = 0.19, 95% CI [0.01, 0.38], p = .038).

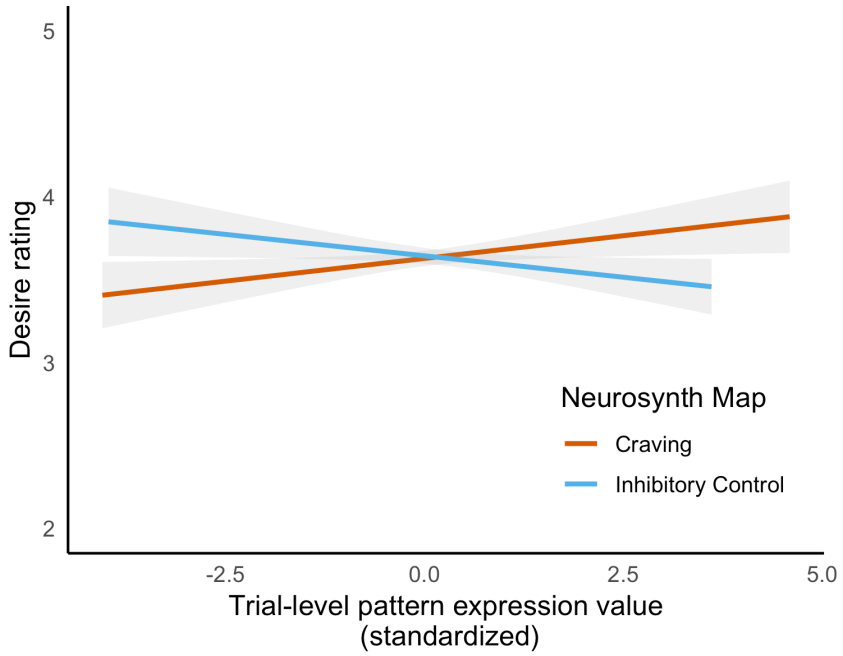

Figure 4. Relationship between standardized "craving" and "inhibitory control" pattern expression values (PEVs) and desire ratings of personalized risk cues (PRC) from the cue reactivity task.

To quantify the degree to which $PEV_{craving}$ and PEV_{IC} predicted measures of craving outside the context of the cue reactivity task, we tested a linear regression model, including $HRB_{craving}$ as the dependent variable and mean $PEV_{craving}$ and PEV_{IC} (collapsed across PRC trials)

as independent variables. Covariates included age, gender, race/ethnicity, number of PRC categories endorsed, factor scores representing self-reported impulsiveness, lack of planning, and negative emotional reactivity and number of early life adverse events. Overall, the model we specified explained 7.4% of the variance in $HRB_{craving}$ scores ($F(13,79) = 1.57$, $p = .11$). Higher levels of $HRB_{craving}$ were predicted by higher impulsivity ($b = 0.24$, 95% CI [0.09, 0.39], $p = .003$) and higher $PEV_{craving}$ ($b = 0.61$, 95% CI [.04, 1.2], $p = .04$), but there was no significant relationship between $HRB_{craving}$ and PEV_{IC} ($b = -0.28$, 95% CI [-0.78, 0.22], $p = 0.28$; Figure 5). Furthermore, there was no significant relationship between $HRB_{consumption}$ and either PEV_{IC} or $PEV_{craving}$ (p's > .05)

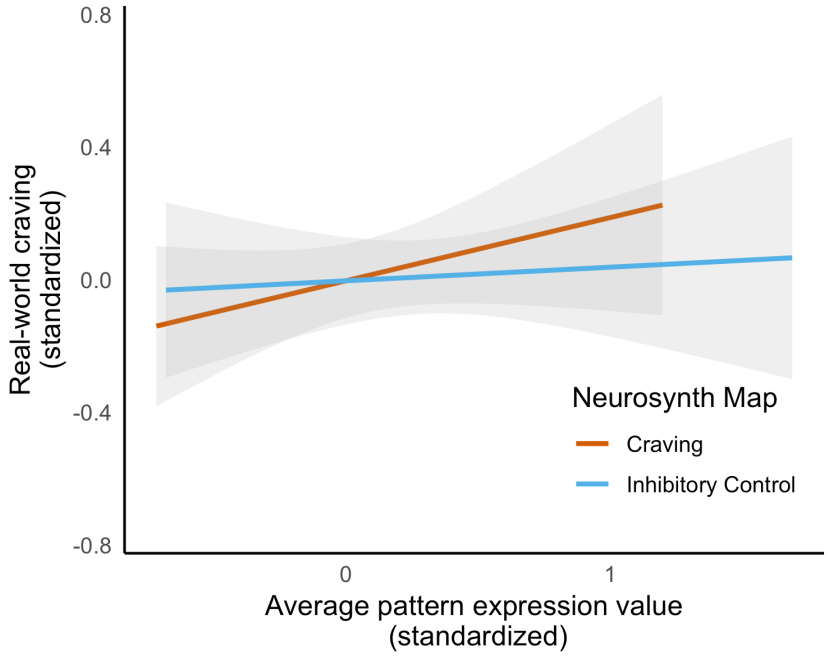

Figure 5. Relationship between standardized "craving" and "inhibitory control" pattern expression values (PEVs) averaged across personalized risk cue (PRC) trials from the cue reactivity task and real-world craving (indexed by a composite score of self-report health-risking behavior measures).

Discussion

This study tested the predictive validity of a cue-reactivity with respect to craving for unhealthy substances. Our data speak to whether a more passive, neural measure of responses to experimental stimuli might shed light on the processes that drive craving and consumption of unhealthy substances. This question is particularly pressing given the societal importance of health-risking behaviors, particularly among people who are at elevated risk because of their life history, as well as recent revelations about the lack of reliability and predictive validity of more active, task-based measures of EC processes.

We used a novel trial-by-trial modeling approach to compare the predictive validity of whole-brain expression of canonical "IC" and "craving" patterns during a cue reactivity task in which participants rated how much they desired personally relevant health-risking substances (e.g. alcohol, tobacco, drugs and/or unhealthy foods). Specifically, we compared the extent to which these neural PEVs predicted both "proximal" cue-induced craving during the cue reactivity task and "distal" real-world craving in daily life. In order to determine the extent to which PEV_{IC} and $PEV_{craving}$ predicted "proximal" craving, we fit a multilevel model with desire ratings from the cue reactivity task as the outcome variable. We found that greater expression of the "craving" pattern during PRC trials predicted higher desire ratings, while greater expression of the "IC" pattern during those trials predicted lower desire ratings. Together, these results indicate that both top-down, executive control and bottom-up, affective reward processes predict craving in the expected direction in the context of an experimental task.

The analyses relating average neural responses to overall real-world craving at the person level present a different pattern of results. Greater average $PEV_{craving}$ predicted greater $HRB_{craving}$, but there was no relationship between $HRB_{craving}$ and average PEV_{IC}. Additionally, we found no

significant relationship between our neural predictors and $HRB_{consumption}$ after controlling for demographic variables and relevant individual differences. However, and consistent with previous comparisons of the predictive validity of task-based and questionnaire measures, self-report factor scores predicted both $HRB_{craving}$ and $HRB_{consumption}$. Specifically, greater impulsivity corresponded to higher $HRB_{craving}$, while greater lack of future planning corresponded to higher levels of $HRB_{consumption}$. Similarly, recent work comparing the real-world predictive validity of task-based and self-report measures of self-regulation found that self-report survey measures largely outperformed task-based measures in terms of predicting real-world health behaviors (Eisenberg et al., 2018; Enkavi et al., 2018)

Taken together, the data presented here support the predictive validity of passive neural measures of affective processes among individuals with self-control problems. It is also notable that both pattern expression measures related to proximal indices of craving though neither measure predicted real-world consumption above and beyond self-reported individual differences. Participants were given no explicit instructions to regulate their reactions to the stimuli they were exposed to during the cue reactivity task, so neural expression of the "IC" pattern might best be interpreted as engagement of spontaneous or *implicit* IC, i.e., IC initiated without an explicit exogenous cue. Participants in this study shared the explicit goal of reducing their HRBs by improving their IC ability, which is consistent with the explanation that PRC-related activity in canonical EC regions in these participants might signify an ongoing motivation to regulate craving and consumption of their PRC substances (Lopez et al., 2017). Accordingly, our results suggest that, while implicit IC predicts less craving within a controlled experimental task, it shows no relationship with real-world HRBs.

Limitations

There are several limitations to consider when interpreting the results of this study. First, though our primary aim was to compare real-world predictive validity of cognitive and affective neural predictors, real-world health-risking behaviors were assessed via self-report measures. It would be more ecologically valid in future research to use methods such as ecological momentary assessment to get more direct behavioral measures. Nonetheless, the validity of the measures we used is well established. Also, the fact that our neural measures were significantly related to responses to the self-report measures means that shared measurement error cannot explain the observed results. Second, our sample consisted of individuals with a heterogeneous variety of self-control problems. For example, some participants endorsed only one HRB category while others endorsed all four, and to varying degrees of severity. Though the heterogeneous nature of the sample reduces specificity, it increases the generalizability of our findings. There is an inherent tradeoff between specificity and generalizability in sampling, and we chose to focus on the latter given the relevance of craving of unhealthy substances to a broad section of the population. Finally, it should be recognized that craving is not a unitary construct across substances. For example, desire for appetitive stimuli such as food and alcohol is different than craving for drugs of abuse. Thus, while we were able to create standardized measures of craving and consumption that allowed us to compare participants on the same scale, these outcome measures represent potentially diverse psychological processes.

Despite these limitations, this study contributes to the current self-control literature in three primary ways. First, this study has strong translational relevance given our sample of adults with self-control problems who experienced early adversity, which is known to contribute to a range of harmful physical and mental health outcomes extending well into adulthood. For

example, adults who experienced adverse situations such as poverty, abuse, neglect, pre- or postnatal substance exposure or stress during childhood are more likely to develop depression and anxiety disorders (Phillips, Hammen, Brennan, Najman, & Bor, 2005), are at increased risk for obesity and heart disease (Repetti, Taylor, & Seeman, 2002), and are more likely to die prematurely (Power, Hyppönen, & Smith, 2005). Thus, the composition of our community sample imbues our findings with greater clinical relevance for at-risk populations. Furthermore, we simultaneously assessed EC and reward processes using an ecologically valid, open-ended cue reactivity task without the artificial constraints of traditional cognitive tasks that increase the risk of "theoretical overfitting" (Eisenberg et al., 2018) and limit approximation of real-world conditions. Lastly, the trial-by-trial modeling approach used in this analysis captures greater within-subject variability in neural processes related to craving and IC at a finer time scale than is traditionally available with neuroimaging data.

Conclusion

We observed that neural expression of both "IC" and "craving" patterns predicted craving during a cue reactivity task, but only "craving" pattern expression predicted real-world craving. Future work should further explore whether task-based measures of affective or motivational processes have better real-world predictive validity than executive functioning measures in other domains, as this may be informative for researchers or clinicians who would benefit from more precise specification of reliable predictors of real-world health behaviors.

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