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Thirst and the state-dependent representation of incentive stimulus value in human motive circuitry

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Abstract

Depletion imposes both need and desire to drink, and potentiates the response to need-relevant cues in the environment. The present fMRI study aimed to determine which neural structures selectively increase the incentive value of need-relevant stimuli in a thirst state. Towards this end, participants were scanned twice—either in a thirst or no-thirst state—while viewing pictures of beverages and chairs. As expected, thirst led to a selective increase in self-reported pleasantness and arousal by beverages. Increased responses to beverage when compared with chair stimuli were observed in the cingulate cortex, insular cortex and the amygdala in the thirst state, which were absent in the no-thirst condition. Enhancing the incentive value of need-relevant cues in a thirst state is a key mechanism for motivating drinking behavior. Overall, distributed regions of the motive circuitry, which are also implicated in salience processing, craving and interoception, provide a dynamic body-state dependent representation of stimulus value.

Key words: deprivation; drinking; fMRI; motivation; saliency network

Introduction

Thirst provides a powerful demonstration of motivation in action. Humans need to keep fluid levels in balance and even short periods without water endanger survival. Fluid ingestion thus provides a main biological imperative and strong motivation assures that drinking is prioritized in accordance with internal needs. Similar to other vital functional behavior systems for feeding, defense and sexual reproduction, a complex drinking/osmoregulation system controls stimulus sensitivities, motor responses and motivational conditions surrounding fluid ingestion (Timberlake et al., 2001; Watts, 2001). According to this behavior systems view, fluid depletion has motivational effects on multiple levels of the drinking system, ranging from the initiation of appetitive search behaviors to the modulation of anticipatory and consummatory responses.

In recent years, great progress has been made in identifying the neural mechanisms of thirst and the brain systems involved in osmoregulation. Numerous physiological studies have explored the interoceptive signals of dehydration and their sensing by key motivational structures such as the hypothalamus (Johnson and Thunhorst, 1997; Sternson, 2013). More recently, neuroimaging methods enabled the study of thirst- and drinking-related brain responses in humans (e.g. Denton et al., 1999b; Hallschmid et al., 2001). The majority of neuroimaging studies examined the drinking system by measuring activity changes commanded by hypertonic saline infusions, which trigger a decrease in plasma osmolality. These studies found that saline infusion led to increased brain activity in the anterior-, mid-cingulate (ACC, MCC) and insular cortices (INS; Denton et al., 1999a,b; Parsons et al., 2000; Egan et al., 2003; Farrell et al., 2008, 2006). Furthermore, activity in the ACC and posterior cingulate cortex (PCC) was correlated with both, feelings of thirst and plasma sodium concentrations, suggesting that these regions are implicated in the conscious representation of thirst (Denton et al., 1999a,b; Parsons et al., 2000; Farrell et al., 2008). A related line of research relied on water depletion to manipulate thirst and generally confirmed the findings obtained via saline infusion (Farrell et al., 2011).

Further studies explored the neural processes associated with the consummatory stage of motivated behaviors, i.e. the sensing and consuming of water. In these studies, administering small quantities of water prompted increased regional cerebral blood flow (rCBF) and blood-oxygen-level dependent (BOLD) responses in the insular cortex, especially in posterior and middle regions, as well as in the amygdala (AMY) and lateral orbitofrontal cortex (OFC; Frey and Petrides, 1999; Zald and Pardo, 2000; Wagner *et al.*, 2006; Yang *et al.*, 2008). Furthermore, the incentive value of water decreases during consumption, and this process plays an important role in the cessation of drinking. Possible neural correlates involve the mid-insular cortex and medial OFC, which showed a decrease in activation after the consumption of water when compared with the depleted state (de Araujo *et al.*, 2003). Moreover, the subjective pleasantness of water is positively correlated with BOLD activity in OFC, ACC and the insular cortex (de Araujo *et al.*, 2003; Saker *et al.*, 2014). Of note, these regions have also been shown to be involved in motivational processes by studies on fear, food, sexual behaviors or drugs (Kober *et al.*, 2008; van der Laan *et al.*, 2010; Kühn and Gallinat, 2011; Sescousse *et al.*, 2013). Overall, neural regions of the drinking system include core structures of the brain's motive circuitry.

However, little is known about how motivation shapes brain responses during the appetitive stage of behavior and the responding to motivationally relevant stimuli (Craig, 1918; Konorski, 1967). In the case of the drinking system, the appetitive stage of motivated behavior consists of exploratory and approach behaviors that bring the organism into contact with fluid stimuli. This stage hosts a phenomenon everybody is familiar with: A glass of water looks more desirable when one is thirsty. Incentive motivation theory suggests that this effect reflects the dynamic shifting of stimulus value due to a body state of fluid depletion (Konorski, 1967; Bindra, 1978; Toates, 1986). Specifically, viewing a glass of water arouses relatively low motivation to drink in conditions of sufficient hydration. Conversely, viewing the same glass of water effectively arouses high motivation to drink in a fluid depleted organism. The significance of distinguishing between the appetitive and consummatory phases of ingestive behavior has been stressed recently. Specifically, in the food domain, appetitive behavior is cued by distinct environmental cues and acts on at least partially distinct neuroendocrine factors and neural structures when compared with consummatory behaviors (Keen-Rhinehart *et al.*, 2013). In this vein, research focusing on neural correlates related to drinking is complemented by this study with regard to thirst-modulated processing of drinking-related stimuli.

The main goal of this study was to determine which regions of the brain's motivational circuitry provide the dynamic and body state dependent representation of stimulus value most relevant to the organization of purposeful behavior. To examine the neural basis of motivation-dependent processing in the drinking system, we scanned participants who were either thirsty (7 h fluid-depleted) or not thirsty while they viewed pictures of beverages and chairs. We assumed that thirst selectively increases the processing of drinking-related stimuli in the anterior and PCC, insula, AMY and OFC. These neural structures were hypothesized based on previous findings regarding neural structures associated with body-state dependent regulation of consummatory behaviors towards water stimuli (de Araujo *et al.*, 2003; Wagner *et al.*, 2006; Saker *et al.*, 2014) as well as studies investigating the effects of hunger on neural responses towards appetitive food stimuli (LaBar *et al.*, 2001; Mohanty *et al.*, 2008; Goldstone *et al.*, 2009). A signed interaction term assured that the interaction effects were limited to voxels showing increased responding to drinking-related stimuli when thirsty rather than larger activations to chair stimuli when participants were not thirsty. Furthermore, main effects were analyzed to determine neural regions providing a state-independent representation of stimulus value and representing body state.

Materials and methods

Participants

Twenty-four participants (12 females, 1 left-handed) between 20 and 32 years of age ($M = 22.9$) with normal or corrected-to-normal vision participated in the study. Participants were recruited at the University of Konstanz and received either course credit or €8 per hour. The study was approved by the ethical review board of the University of Konstanz and informed consent was acquired from all participants. Participants were not included in the study when they had a history or currently suffered from psychiatric, neurological or endocrine diseases or taking medication that affects the endocrine or central nervous system.

Stimulus materials

The stimulus materials comprised pictures of beverages ($n = 24$) and chairs ($n = 24$), which were shown on a uniform gray-colored background. A pilot study ($n = 12$) revealed that water, apple juice and tea were regarded as the most potent thirst-quenching beverages. Accordingly, the beverage stimuli depicted glasses filled with water, apple juice and tea. None of the beverage pictures included commercial labels. Similar to previous studies on the neural correlates of object recognition (Haxby *et al.*, 2001; Downing *et al.*, 2006), pictures of chairs were chosen as control category. Chair pictures were selected to match the beverage pictures in terms of complexity, size and overall appearance.

Procedure

An initial screening session served to inform participants about the study, including the requirement to refrain from drinking to evoke thirst, and to check their eligibility for fMRI scanning. Participants were scanned in two sessions while being either thirsty or not thirsty. The order of these sessions was counterbalanced and ∼1 week apart. To control for variations in circadian rhythm, all sessions were scheduled at 6 pm. For the thirst session, participants had to completely refrain from drinking for 7 h. For the no-thirst session, participants were instructed to follow their normal drinking and eating habits. All participants reported that they had fully complied with these instructions.

At the start of both sessions, participants reconfirmed their informed consent and were prepared for MR scanning. Before entering the scanner, thirst and hunger were probed using rating scales. During fMRI scanning, participants viewed pictures of beverages and chairs, which were presented using a visual system (NordicNeuroLab, Bergen, Norway) positioned in front of the subject's eyes. The 48 pictures comprising both categories were repeated three times, resulting in 144 trials. In a slow event-related paradigm, pictures were shown for 2 s, followed by a variable inter-stimulus interval (ISI) showing a white fixation cross on a black background. The ISI was exponentially distributed with a mean of 7.5 s and a range of 6–12 s (see e.g. Amaro and Barker, 2006). After obtaining a second rating of thirst and hunger, a T1-weighted structural scan was recorded.

A third rating of thirst and hunger was obtained after participants left the scanner, and they additionally rated all pictures on emotional dimensions of valence and arousal. Finally, the participants were provided with as much water as desired.

Self-report data

Thirst and hunger ratings were collected using a 7-point Likert scale, ranging from not thirsty/not hungry to very thirsty/very hungry, respectively. Rating data were obtained immediately before, mid-term, and at the end of MR scanning. These data were entered into a two factorial repeated measures ANOVA with the factors 'Body State' (thirst vs no-thirst) and 'Time' (pre- vs mid-term vs post).

Participants used the Self Assessment Manikin (Bradley and Lang, 1994) to rate the stimuli on emotional dimensions of valence and arousal on a 9-point Likert scale, ranging from unpleasant over neutral to pleasant for valence and from calm to exciting for arousal. Valence and arousal ratings were entered into a two factorial repeated measures ANOVA with the factors 'Body State' (thirst vs no-thirst) and 'Category' (beverages vs chairs).

Where appropriate, the Greenhouse-Geisser procedure was used to correct for violations of sphericity. *Post-hoc* tests were corrected using the Bonferroni method.

MRI data acquisition and analysis

MR acquisition took place on a 1.5 Philips Intera MR system (Philips, Hamburg, Germany). For functional scanning, a T2*-weighted Fast Field Echo, Echo Planar Imaging sequence utilizing parallel scanning technique was used (SENSE; Pruessmann *et al.*, 1999). In plane resolution was 3×3 mm and slice thickness was 3.5 mm (32 axial slices; no gap; FOV = 240 mm; acquisition matrix = 80×80; TE = 40 ms; flip angle = $90°$; TR = 2500 ms). In addition, a standard T1-weighted high-resolution structural scan with $1 \times 1 \times 1$ mm voxel resolution was obtained.

Pre-processing and statistical analysis of the functional data were conducted using SPM8 (Wellcome Department of Imaging Neuroscience, University College London, UK; Friston *et al.*, 1994). Pre-processing steps included realignment and slice time correction for the functional images. No subject displayed head movements exceeding 3 mm or $3°$ on any axis and thus data from all participants were included in further analysis. Images were normalized to the MNI EPI template and resampled at $3 \times 3 \times 3$ mm voxel size. A Gaussian spatial kernel of full width at half maximum with an 8-mm radius was used for smoothing the data.

Single subject data were modeled with a thirst and a no-thirst session, each containing two covariates of interest representing beverage and chair condition onsets as well as covariates of no interest, including six movement parameters obtained during realignment and one covariate incorporating an overall intercept to the model. Group level random effects analysis combined all subjects' covariates of interest into a full factorial model with the factors 'Body State' (thirst vs no-thirst) and 'Category' (beverages vs chairs). Based on our a priori hypotheses, a linear contrast with (Beverages$_{Thirst}$ > Chairs$_{Thirst}$) vs (Beverages$_{No-thirst}$ > Chairs$_{No-thirst}$) was calculated to test for the interaction of 'Body State by Category'. A further constraint assured that the interaction examines a signed interaction, which is only sensitive for an enlarged activation of beverages over chairs during the thirst state, excluding voxels showing enlarged activation for chairs over beverages during the

no-thirst state. The signed interaction test was realized through (i) a cross interaction contrast with a statistical threshold of $P < 0.05$ (False discovery rate (FDR) corrected at voxel level) with a voxel extent of $k \geq 15$ voxels, and (ii) inclusively masking the result with the main effect of 'beverage > chair' at $P < 0.05$. To test for a reversed interaction effect, the linear contrast for (Chairs$_{Thirst}$ > Beverages$_{Thirst}$) vs (Chairs$_{No-thirst}$ > Beverages$_{No-thirst}$) was also calculated. As we did not have any a priori hypotheses, no further constraints were applied onto this contrast. Furthermore, linear contrasts were calculated for the main effects of 'Category' and 'Body State' (FDR $P < 0.05$, $k \geq 15$ voxel).

Results

Thirst and hunger ratings

Participants were significantly more thirsty in the thirst ($M = 5.9$, $SE = 0.15$) when compared with the no-thirst ($M = 2.9$, $SE = 0.22$) condition, $F(1, 23) = 193.7$, $P < 0.0001$, partial $\eta^2 = 0.89$. Furthermore, within sessions, thirst ratings varied across the three measurements, $F(2, 46) = 25.6$, $P < 0.001$, partial $\eta^2 = 0.53$. Specifically, ratings of thirst were larger for the second ($M = 4.7$, $SE = 0.17$) and third ($M = 4.7$, $SE = 0.21$) when compared with the first ($M = 3.8$, $SE = 0.15$) rating at the beginning of the session, $ts(23) > 5.3$, $P < 0.001$. Finally, a significant interaction of 'Body State' and 'Time' was obtained, $F(2, 46) = 6.4$, $P < 0.005$, partial $\eta^2 = 0.22$, indicating that the increase of thirst across the session was somewhat larger for the no-thirst (First: $M = 2.0$, $SE = 0.23$; Second: $M = 3.3$, $SE = 0.24$; Third: $M = 3.3$, $SE = 0.28$; $ts(23) > 5.7$ and 5.9, $P < 0.001$) than the thirst condition (First: $M = 5.5$, $SE = 0.17$; Second: $M = 6.1$, $SE = 0.17$; Third: $M = 6.0$, $SE = 0.19$; $ts(23) = 3.4$ and 2.6, $P < 0.05$.

The analysis of hunger ratings revealed a significant main effect of 'Time', $F(2, 46) = 17.6$, $P < 0.001$, partial $\eta^2 = 0.43$, indicating that hunger ratings increased from the first ($M = 2.5$, $SE = 0.20$) over the second ($M = 2.9$, $SE = 0.21$) to the third ($M = 3.2$, $SE = 0.25$) rating, [pre- vs mid-term: $t(23) = -3.8$, $P < 0.005$; pre- vs post: $t(23) = -5.0$, $P < 0.001$; mid-term vs post: $t(23) = -2.9$, $P < 0.05$]. However, no significant main effect of 'Body State', $F(1, 23) = 2.6$, n.s., nor an interaction involving the factor 'Body State', $F(2, 46) = 2.0$, n.s., was observed.

Stimulus valence and arousal

Significant main effects of 'Category' were obtained for valence and arousal ratings, Valence $F(1, 23) = 67.2$, $P < 0.001$, partial $\eta^2 = 0.75$, Arousal $F(1, 23) = 13.9$, $P < 0.001$, partial $\eta^2 = 0.38$. Specifically, beverage when compared with chair pictures were perceived as more pleasant ($M = 6.8$ and 5.0, $SE = 0.17$ and 0.13) and more arousing ($M = 4.1$ and 3.2, $SE = 0.25$ and 0.26, respectively). However, these main effects were qualified by significant interactions of 'Body State' × 'Category' for both valence and arousal ratings, Valence $F(1, 23) = 9.0$, $P < 0.01$, partial $\eta^2 = 0.28$, Arousal $F(1, 23) = 7.3$, $P < 0.05$, partial $\eta^2 = 0.24$. As shown in Figure 1, thirst selectively affected the evaluation of beverage pictures. When compared with the control condition, beverage pictures were perceived as more pleasant [$t(23) = 2.5$, $P < 0.05$] and arousing [$t(23) = 3.8$, $P < 0.001$] in the thirst condition. In contrast, valence and arousal ratings of chair pictures did not differ between thirst and no-thirst states, Valence: $t(23) = -1.0$, n.s., Arousal: $t(23) = 1.4$, n.s. Finally, a significant effect of 'Body State' was observed for arousal ratings, $F(1, 23) = 14.3$, $P < 0.001$,
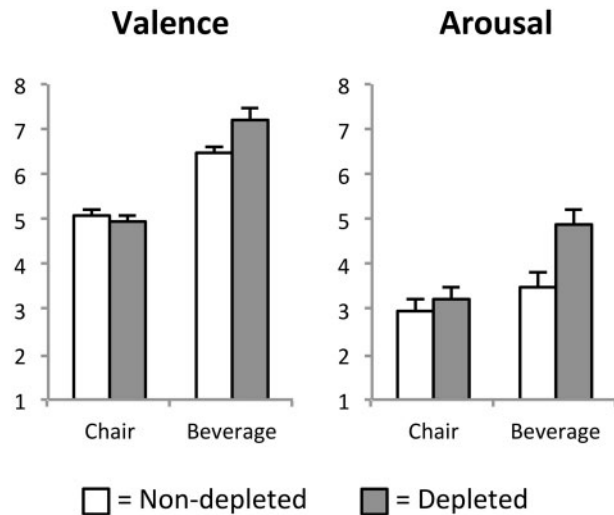
Fig. 1. Illustration of valence and arousal ratings for beverage and chair picture categories. Both valence and arousal ratings showed an interaction of 'Body State by Category'.

partial $\eta^2 = 0.38$, with increased arousal ratings during a thirst when compared with a no-thirst state.

fMRI data

Interaction between stimulus category and a body state of thirst. The selective effect of thirst on the processing of beverage pictures was examined by the linear cross interaction contrast (Beverages$_{Thirst}$ > Chairs$_{Thirst}$) vs (Beverages$_{No-thirst}$ > Chairs$_{No-thirst}$). With regard to the a priori hypothesis, significant interactions were observed in the anterior MCC (aMCC), PCC, AMY (left) and anterior INS (right) (see Figure 2A). As shown in Figure 2B, increased BOLD responses to beverage when compared with chair pictures were observed in these brain regions during thirst state. In contrast, there were no differences between beverage and chair categories during the no-thirst state. Additional structures showing a significant interaction included the dorsal precentral gyrus (right), ventral postcentral gyrus (right), supramarginal gyrus (left) and inferior parietal lobule (left) (see Table 1).

Testing for effects in the opposite direction (Chairs$_{Thirst}$ > Beverages$_{Thirst}$) vs (Chairs$_{No-thirst}$ > Beverages$_{No-thirst}$) did not reveal any significant effects.

Main effects of stimulus category and body state. With regard to stimulus category, beverage when compared with chair pictures elicited increased brain activation in widespread brain regions (see Table 2). Testing for the opposite effect the contrast 'chairs > beverages' did not reveal any significant effects.

With regard to body state, neither the contrast of 'thirst state > no-thirst state' nor the contrast of 'no-thirst state > thirst state' did reveal any significant effects.

Discussion

Thirst can turn incentive stimuli, such as the sight of a glass of water, into powerful motivational magnets. This study investigated the neural correlates of such body state dependent value representations by asking participants in one experimental condition to refrain from drinking for seven hours. The neural processing of need-relevant beverage pictures and control stimuli
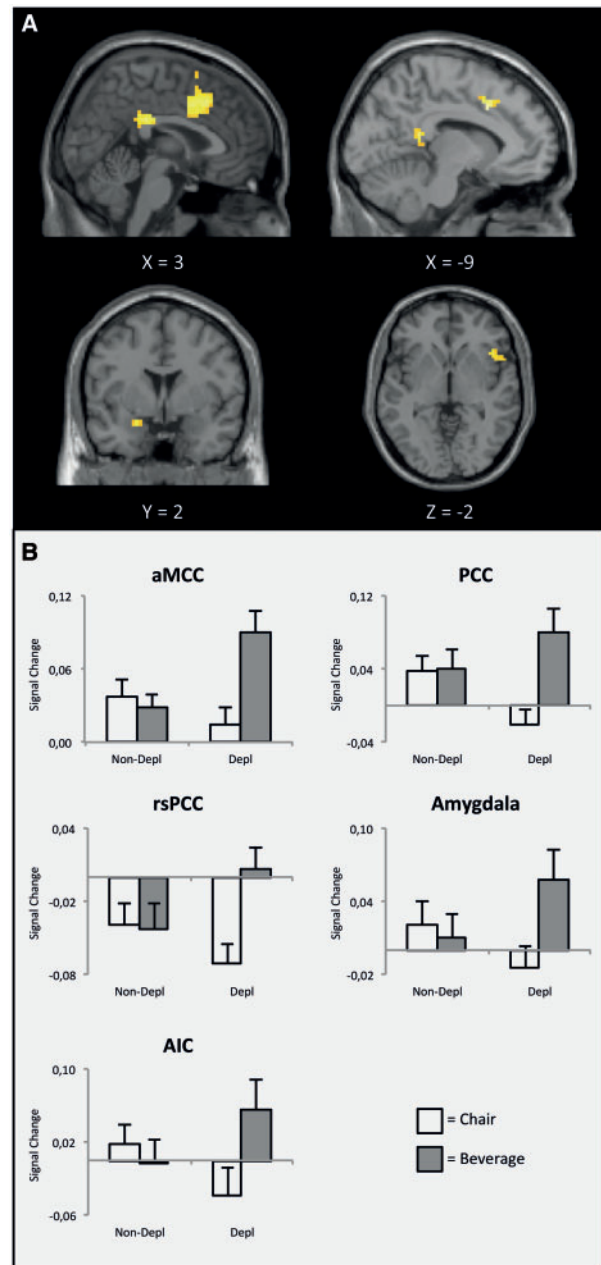

Fig. 2. Sagittal, coronal, and axial sections showing the interaction of 'Body State by Category' in the cingulate cortex, AMY and anterior insula. Statistical maps are thresholded at $P < 0.05$ (FDR) with a voxel extent of $k \geq 15$ (A). Extracted signal changes relative to baseline activation corresponding to the regions presented under A, illustrating an interaction effect of 'Body State by Category' (B). Abbreviations: aMCC, anterior middle cingulate cortex; PCC, posterior cingulate cortex; rsPCC, retro-splenial cingulate cortex; AIC, anterior insular cortex.

in a thirst state was then compared with that during a no-thirst state. Reflecting body state dependent changes in incentive value, the data revealed the selective increase of neural responses towards beverage pictures during thirst in the aMCC, PCC, INS and AMY. Using drinking as important survival-related motivational behavior system, this study contributes to the decomposition of motivation processes and distinct representations of incentive value in key motivational regions (Salamone and Correa, 2012).

Table 1. Regions showing a significant 'State by Category' interaction

No.	Region	Side	BA	Coordinates			Size	PeakZ
				x	y	z		
1	aMCC	L	24	−3	14	37	244	5.21
2	PCC	L / R	23	0	−28	28	60	4.32
3	rsPCC	L	29	−6	−43	16	21	4.25
4	Anterior insula	R	13	57	14	−5	36	4.10
5	AMY	L		−21	2	−20	16	3.74
6	Ventral postcentral gyrus	R	3	54	−13	31	25	4.31
7	Dorsal precentral gyrus	R	1	45	−19	58	29	4.12
8	Inferior parietal lobule	L	40	−36	−49	37	31	4.06
9	Supramarginal gyrus	L	40	−63	−31	28	48	4.05

Thresholds for activated clusters were set to $P < 0.05$ (FDR) with a voxel extent of $k \geq 15$.

Abbreviations: aMCC, anterior middle cingulate cortex; PCC, posterior cingulate cortex; rsPCC, retro-splenial cingulate cortex; AMY, amygdala.

Neural regions showing body state by picture category interactions

A related view on dynamic stimulus representations is emerging in the rapidly growing literature on the functional role of the ACC, which also responded in a body-state-dependent manner in the current study. The ACC acts as major neural site for the integration of internal and external events (Paus, 2001; Craig, 2002; 2010; Medford and Critchley, 2010). In the current dataset, regions exhibiting state-dependent responses towards beverage pictures were located in the aMCC, which a large number of previous studies associated with negative affect, pain and cognitive control, and which is regarded as an important hub for the expression of affect and the organization of goal-directed behaviors (Etkin *et al.*, 2011; Shackman *et al.*, 2011). Interestingly, activation of the aMCC is particularly apparent during stimulus anticipation as brought out by an array of experimental paradigms, including conflict, divided attention, response selection and threat-of-shock (Liu *et al.*, 2011). The present data are generally consistent with these findings. However, they also add important evidence by showing that aMCC responding is not only sensitive to top-down processes, such as goals and intentions, but also modulated by 'motivational' interactions, i.e. the interplay of bottom-up and top-down processes during which internal factors (thirst) bias the processing of incoming stimuli on the basis of their need relevance.

Anterior and ventral regions of the PCC also showed increased activations to beverage when compared with chair pictures in thirst state. This finding may appear surprising given the partial overlap with PCC regions comprising the default mode network, which shows decreased activations during tasks that demand external stimulus processing (Raichle, 2010). However, research regarding the cue-reactivity to cocaine as well as self-reported craving in nicotine addiction showed activations in the PCC (Kühn and Gallinat, 2011). Although it is tempting to relate the present PCC findings to the urge to drink, a Neurosynth meta-analysis (Yarkoni *et al.*, 2011) indicates that this region is also associated with recollection, self-referential processing and imagery. Furthermore, the functional role of the PCC is not yet clear and current theories incorporate broad concepts of regulation of arousal, attention, and internal/external focus (Leech and Sharp, 2013). Functionally distinct regions within the PCC may also be dynamically connected to large scale neural networks (Leech *et al.*, 2011; Torta *et al.*, 2013).

Table 2. Regions showing a significant 'Category' effect for 'beverage vs chair'

No.	Region	Side	BA	Coordinates			Size	PeakZ
				x	y	z		
1	OFC	R	47/11	21	32	−17	5732	5.20
	Inferior temporal gyrus	L	37	−48	−49	−20		
		R	37	51	−46	−23		
	Primary visual cortex	L/R	17/18	0	−76	−20		
	PCC	L/R	23	0	−31	40		
	Caudate/VSTR	R		12	5	4		
	DLPFC	R	44	48	14	31		
	ACC	L/R	32	0	38	16		
	MCC	L/R	24	0	14	43		
	Supramarginal gyrus	L	40	−54	−31	43		
	Anterior insula	R	13	42	5	−11		
	VLPFC	R	46	51	35	13		
2	Brainstem	L		−6	−25	−14	315	4.31
		R		6	−31	−11		
	AMY	L		−27	−1	−20		
3	OFC	L	47/11	−30	35	−17	156	5.84
4	DLPFC	L	44	−45	8	31	331	4.62
5	Fusiform gyrus	R	36	39	−25	−20	151	4.19
6		L	36	−39	−16	−29	29	3.68
7	Postcentral gyrus	R	4	27	−28	64	171	3.99
8		L	4	−21	−31	67	28	3.26
9	Supramarginal gyrus	L	48	−66	−22	34	32	3.85
10		R	40	57	−34	49	55	3.82
11		R	48	24	−28	22	56	3.66
12	VLPFC	L	46	−48	41	10	135	3.80
13	Caudate/VSTR	L		−18	23	10	57	3.78
14	Anterior PFC	L	10	−18	62	4	125	3.74
15		R	10	18	65	19	21	3.23
16	AMY	R		21	−4	−20	45	3.46
17	Precuneus	L	7	−3	−58	58	148	3.38
18	Anterior insula	L	13	−30	20	4	26	3.21
19		L	13	−45	14	−11	42	3.07
20	Inferior Occipital gyrus	R	18	27	−94	−14	19	2.98

Thresholds for activated clusters were set to $P < 0.05$ (FDR) with a voxel extent of $k \geq 15$. Conjoined clusters are listed on top of the table with the cluster peak corresponding to the first listed region.

Abbreviations: OFC, orbitofrontal cortex; ACC, anterior cingulate cortex; MCC, middle cingulate cortex; PCC, posterior cingulate cortex; VSTR, ventral striatum; DLPFC, dorsolateral prefrontal cortex; VLPFC, ventrolateral prefrontal cortex; AMY, amygdala.

Furthermore, the insular cortex, another key region involved in processing salient external or internal stimuli, showed a significant interaction effect in the right anterior INS. This finding concurs with a large number of studies showing that the insula seems to act as an interface between feelings and cognitions, or as a site of integration between internal and external relevant stimuli (Craig, 2009; 2010; Menon and Uddin, 2010; Chang *et al.*, 2013). Influential accounts of insula function have suggested a functional division, according to which the anterior insular cortex responds more to salient external input, whereas the posterior insula is more responsive to homeostatic and somatosensory processes (Craig, 2010; Menon and Uddin, 2010). A recent meta-analytic study generally provided support for these subdivisions (Chang *et al.*, 2013). Our data add to this issue by showing that insula responses towards externally salient stimuli are modulated by internal factors. Overall, these data

are consistent with the view that the insula plays a key role in the motivational integration of interoceptive and homeostatic signals with incoming external stimuli.

Saliency: a neural network perspective

Complementary to the focus on the individual structures, a brain system perspective emphasizes connectivity across large-scale neural networks. The MCC and the anterior insula are often coactivated, exhibit strong functional connectivity in the resting state, and have been suggested to form a functional network involved in salience processing (Seeley *et al.*, 2007; Menon and Uddin, 2010). This network is thought to be involved in assessing the salience of stimuli in order to guide adaptive behavior. Specifically, the saliency network comprises several hubs, which enable autonomic response generation, access the motor system and shift processing priorities in the large scale networks implicated in working memory and attention processes (Menon and Uddin, 2010). Salience, or relevance, has been defined in this line of research fairly broadly and includes internal saliency assessments, such as interoceptive signals and feelings, as well as external saliency commanded by stimulus or task characteristics. Drinking adds to this evidence the demonstration of the integration of internal and external stimuli in structures of the saliency network. At a gross level, regions of the ACC and anterior insular cortex, consistently implicated in previous research focusing on consummatory behaviors were also observed to be relevant to the anticipatory stage of motivated behaviors. However, comparisons across studies are not sufficient to address the issue of common and distinct neural correlates across appetitive and consummatory stages of motivated behavior. As such, future studies should examine the two stages of motivated behavior simultaneously.

The present findings concur with findings studying the effects of hunger on neural responses towards food pictures. Specifically, significant effects of body state by stimulus category (food-related *vs* control pictures) have been observed with regard to the AMY (LaBar *et al.*, 2001; Mohanty *et al.*, 2008; Goldstone *et al.*, 2009), insular cortex (Goldstone *et al.*, 2009; Haase *et al.*, 2009), ACC (Goldstone *et al.*, 2009) and PCC (Mohanty *et al.*, 2008). However, the considerable variability of findings across food-based studies presumably reflects the complexity of the food system as well as methodological differences across the studies (Schupp and Renner, 2011). Furthermore, the present findings show commonalities and differences to effects associated with craving. Specifically, meta-analysis suggests that craving is most reliably associated with ACC, AMY and ventral striatum activity (Kühn and Gallinat, 2011), although few studies directly contrasted deprived and non-deprived conditions (McClernon *et al.*, 2005; 2009; McBride *et al.*, 2006; David *et al.*, 2007; Stippekohl *et al.*, 2010). Overall, the saliency network may comprise a large scale neural network implicated in the dynamic representation of stimulus value across domains of emotion and motivation.

Neural regions responding to beverage stimuli

Several regions showed stronger activations to beverage when compared with chair pictures. Thus, these regions responded similarly in thirst and no-thirst state, suggesting that they represent more abstract and generalized value signals. Interestingly, the OFC and the ventral striatum were among the regions that did not show a state-depended representation of stimulus value, whereas previous findings have linked them to state-dependent representations. Specifically, studies of sensory-specific satiety show the involvement of OFC and ventral striatum contrasting the activation before and after eating a food to satiety (Small *et al.*, 2001; Gottfried *et al.*, 2003). Furthermore, monkey studies revealed the increased neuronal firing in OFC and ventral striatum during the anticipation of rewarding water trials (Simmons *et al.*, 2007) and the magnitude of neuronal firing in the OFC varied with the quantity of water anticipated (Roesch and Olson, 2007). Another recent study demonstrated that rats experiencing a sodium deficit instantaneously approached a conditioned stimulus (CS) lever which they avoided in non-depleted body state with the OFC and ventral striatum were among the structures showing increased Fos activity (Robinson and Berridge, 2013). One possible explanation for the discrepancies between previous and the current findings involves the temporal organization of motivated behaviors. Specifically, neural representations of moment-to-moment value representations may vary depending on whether an animal is in an appetitive or consummatory stage (Timberlake *et al.*, 2001). Thus, future research investigating the anticipatory and consummatory stages of drinking behavior would enable the capture of the dynamics of moment-to-moment incentive value across temporal stages of motivated behaviors.

Conclusion

At its core, incentive motivation theory holds that the power of external stimuli is calibrated dynamically based on the current body state of the organism. The present findings demonstrate that key regions of the saliency network, i.e. aMCC, PCC, anterior insular cortex and AMY, show selectively enhanced activations in response to need-relevant pictures of beverages in thirst when compared with no-thirst state. Studying the effects of thirst on the neural processing of motivational cues offers a potent model system to examine the neural correlates of moment-to-moment incentive stimulus value. Arguably, drinking represents a less complicated behavior system than eating since the body has very little means to compensate the deficit and the influence of circadian rhythms and cognitions appears less pronounced. Overall, the current study offers insights into the neural systems that implement such powerful motivational forces in the drinking system.

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