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Original article

Relationship of sensation seeking with the neural correlates of appetitive conditioning

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Abstract

Previous research has linked sensation seeking with a heightened risk for drug abuse and other risk-taking behavior. As appetitive conditioning presents a model for the etiology and maintenance of addictive behavior, investigating sensation seeking in a classical conditioning paradigm might elucidate possible pathways toward addiction within this model. Furthermore, the theoretical concept underlying sensation seeking proposes a negative relationship between reward processing and sensation seeking in only moderately arousing situations, which has been neglected by previous research. This study aimed to investigate this inverse relationship in moderately stimulating situations entailing reward processing using functional magnetic resonance imaging. Subjects ($N = 38$) participated in a classical conditioning paradigm in which a neutral stimulus (CS+) was repeatedly paired with a monetary reward, while another neutral stimulus (CS−) was not. Imaging results revealed a negative relationship between sensation seeking and neural responses in the insula, amygdala and nucleus accumbens during the early phase and in the dorsal anterior cingulate cortex during the late phase of conditioning. These findings suggest reduced reward learning and consequently diminished processing of outcome expectancy in appetitive conditioning in subjects with high sensation seeking scores. The results are discussed with respect to clinical implications.

Key words: fMRI; reward; classical conditioning; sensation seeking

Introduction

Appetitive conditioning is an important model for the development and maintenance of psychiatric disorders like addictions (Wanigaratne, 2006). Moreover, it can provide insight into how reward learning is altered in personality traits associated with a higher risk of developing these disorders. Investigating the role of individual differences regarding the neural underpinnings of appetitive conditioning might therefore further our understanding of dysfunctional human behavior. In addition, it might offer new approaches for individualized treatments (Lonsdorf & Merz, 2017; Insel & Cuthbert, 2015).

Differential appetitive conditioning paradigms allow for investigating reactions toward an initially neutral stimulus (conditioned stimulus, or CS+) that is repeatedly paired with an appetitive stimulus (unconditioned stimulus, or UCS; e.g. money) compared to a second neutral stimulus (CS−) that is never paired with the UCS. Only few pairings of CS+ and UCS are required to elicit increased responses to the CS+ compared to those to the CS− (conditioned responses, or CRs) (Blechert *et al.*, 2016). CRs may comprise increased valence and arousal ratings, skin conductance responses (SCRs) and blood oxygenation level-dependent (BOLD) responses in the reward network of the brain (Kruse *et al.*, 2017; Klucken *et al.*, 2013). Key brain regions within

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the reward network implicated in appetitive conditioning are the amygdala, nucleus accumbens (NAcc), insula, ventral and dorsal anterior cingulate cortex (dACC) and orbitofrontal cortex (OFC) (Martin-Soelch *et al.,* 2007; Haber & Knutson, 2010). While the amygdala is linked to the formation of CS/UCS associations (Balleine *et al.,* 2003; Martin-Soelch *et al.,* 2007; Klucken *et al.,* 2015), the NAcc is considered to play a pivotal role in reward anticipation and temporal difference learning (Spicer *et al.,* 2007; O'Doherty *et al.,* 2002; Tapia León *et al.,* 2018). The insula is associated with the processing of interoceptive information, saliency and its integration with emotional events (Sescousse *et al.,* 2013; Wang *et al.,* 2015; Kurth *et al.,* 2010). While the ventral ACC is ascribed a crucial role in early discriminative learning, the dorsal ACC is assumed to be important for the encoding of the outcomes of a CS+ (Gabriel *et al.,* 2003; Alexander & Brown, 2011; Kruse *et al.,* 2018). Finally, the OFC is thought to be involved in the encoding of expected UCS values (Cox *et al.,* 2005).

Sensation seeking is a personality trait defined by the need for varied, novel and complex sensations and experiences as well as the willingness to take physical and social risks for the sake of such experiences (Zuckerman, 1979, 2016). It is partly based on theories on the optimal level of stimulation and arousal (e.g. Lindsley, 1961; Wundt, 1893; Hebb, 1955). Importantly, situations that a low-sensation seeker finds pleasantly stimulating, a high-sensation seeker might not find stimulating enough, leading her/him to seek more intense but possibly harmful or addictive rewards (Norbury & Husain, 2015; Zheng & Liu, 2015).

Previous research investigating neural correlates of sensation seeking focused particularly on highly stimulating tasks entailing the processing of risks (Abler *et al.,* 2006; Kruschwitz *et al.,* 2012; Cservenka *et al.,* 2013). Structures repeatedly associated with sensation seeking in these paradigms are the insula and NAcc. Zuckerman (2016) suggested a central role of the reward system of the brain in sensation seeking. Furthermore, Joseph *et al.* (2009) found that while high-sensation seekers show greater activation in the insula and posterior mOFC when seeing high *vs* low-arousing stimuli, low-sensation seekers exhibit stronger BOLD responses in the anterior mOFC and ACC. However, investigating the trait only in highly stimulating tasks leads to an incomplete picture, as in everyday situations positive reinforcement is not necessarily associated with risks and high stimulation. Thus, in order to obtain a more comprehensive understanding of reward processing in sensation seeking, it is crucial to investigate its neural underpinnings in the absence of risk processing in only moderately stimulating situations as well. As different processes are proposed for the early and late phases of conditioning (Tabbert, Stark, Kirsch, & Vaitl, 2005; LaBar *et al.,* 1998), it is crucial to investigate the neural correlates of sensation seeking during the early and late stages separately.

This is particularly interesting since sensation seeking has been associated with addictive behaviors (Zuckerman, 2016). One theory suggests a reward deficiency syndrome (RDS), which might be a possible precursor or consequence of addictive disorders (Hommer *et al.,* 2011). The RDS theory (Blum *et al.,* 2000) proposes that individuals with addictions show a deficit in recruiting the reward network, leading them to perceive rewards as less pleasurable. Such individuals may thus engage in addictive behaviors to compensate for their reward deficiency. This is in line with recent data linking substance abuse and gambling addiction with decreased striatal responses in anticipation of rewards (Luijten *et al.,* 2017; Büchel *et al.,* 2017). Thus, one possible pathway toward addiction is reduced appetitive conditioning in at-risk individuals under moderately arousing circumstances. As fewer stimuli elicit strong CRs, this would then lead at-risk individuals to seek rewarding stimuli associated with higher stimulation and possibly risk.

This functional magnetic resonance imaging (fMRI) study thus aimed to examine the relationship between sensation seeking and the neural correlates of appetitive conditioning in a moderately stimulating task in the absence of risk processing. For this, a differential classical appetitive conditioning paradigm with monetary reward as moderately arousing UCS and colored rectangles as CS was used. We hypothesized a negative association between sensation seeking and differential BOLD responses in the CS+ > CS− contrast in the insula, amygdala, NAcc and dACC.

Materials and methods

Participants

Thirty-eight healthy participants (16 were female, age: *M* = 23.50 years, s.d. = 3.54 years) were recruited at the University of Giessen. All participants had normal or corrected-to-normal vision, had no current or prior psychiatric or neurological treatment and were right handed. Participants received either course credit or 10€/h in compensation for their time in addition to the monetary reward they won during the experiment. The study complies with the Declaration of Helsinki and was approved by the local ethical review board of the Department of Psychology and Sports Science at the University of Giessen. Written informed consent was obtained from all participants.

Questionnaire

Before the participants entered the scanner, they filled out the German version of the Sensation Seeking Scale V (SSS-V; Beauducel *et al.,* 2003). The total score (*M* = 22.18, s.d. = 4.55) is comparable to previous normative data (Beauducel *et al.,* 2003).

Experimental procedure

A partial reinforcement appetitive acquisition paradigm as used in Tapia León *et al.* (2018) consisting of 40 trials was employed. Two isoluminant rectangles in blue and yellow (cross-balanced) served as conditioned stimuli (CS+, CS−). A monetary reward of 50 cents presented on a screen served as the UCS. The reinforcement rate was 50%; thus, half of the CS+ trials were paired with a monetary reward. Unnoticeable to the participants, the acquisition procedure was divided into an early phase (trials 1–20) and a late phase (trials 21–40). Trial sequence was pseudorandomized with the restrictions that (1) the first two trials of each half consisted of a CS+ and a CS− trial, (2) each CS would not be presented more than twice consecutively and (3) each conditioned stimulus (CS+; CS−) was presented in 10 trials of each half to allow for separate analysis of both halves. Participants were instructed regarding CS–UCS contingencies.

Ratings

After the acquisition procedure, participants provided ratings for valence and arousal regarding CS+, CS− and UCS on the nine-point Likert scale of the self-assessment manikin (valence: 1 'very unpleasant' to 9 'very pleasant'; arousal: 1 'calm and relaxed' to 9 'very aroused'). Differences in the valence and arousal ratings between conditions were examined via paired *t*-tests (CS+ − CS−) using SPSS 23 (SPSS 23.0 for

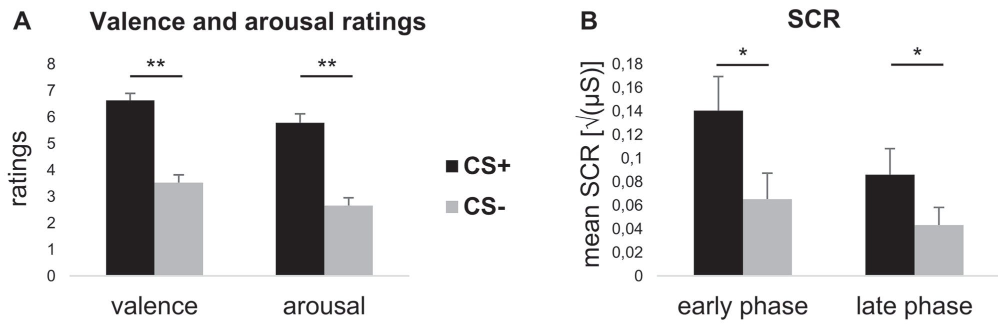

Figure 1. Analyses of ratings and SCR. (A) Differences in mean valence and arousal ratings. (B) Differences in mean SCRs in the early and late acquisition phases. ANOVA yielded the main effects of the CS type and time, qualified by a CS type × time interaction. The error bars represent the SEM. *$P < 0.05$; **$P < 0.01$; ***$P < 0.001$.

Windows, SPSS Inc., Chicago, IL, USA). To test the associations between sensation seeking and differential valence and arousal ratings (CS+ − CS−), one-tailed Pearson's correlations were performed. Furthermore, correlational analyses were conducted to check for correlations between sensation seeking scores and UCS ratings.

Skin conductance responses

SCRs were recorded throughout the experimental procedure and analyzed using Ledalab 3.4.4. (Benedek & Kaernbach, 2010) according to the procedure described in Tapia León *et al.* (2018). SCR data of three participants had to be discarded due to technical difficulties during data acquisition. Both SCRs and ratings for valence and arousal were measured as indicators of successful conditioning. To examine the relationship between SCRs and sensation seeking, correlational analyses were conducted analogous to the analyses of the ratings.

fMRI

Magnetic resonance data were acquired with a 3 T scanner (Magnetom Prisma; Siemens Healthineers, Erlangen, Germany) using a 64-channel head coil. The same scanning parameters, preprocessing pipeline and first-level analysis pipeline were used as described in Tapia León *et al.* (2018). For the second-level analyses, the CS+ − CS− contrast was investigated separately for the early and the late phases to more clearly discern between the early and late effects of learning, which is consistent with other studies (Kruse *et al.*, 2017; LaBar *et al.*, 1998; Lonsdorf *et al.*, 2017; Milad *et al.*, 2007; Phelps *et al.*, 2004). For this, one-sample *t*-tests in SPM12 (Wellcome Department of Cognitive Neurology, London, UK; 2012) were used. Regions of interest (ROIs) were the amygdala, NAcc, dACC and insula.

For ROI analyses, small volume correction implemented in SPM12 was used employing family-wise error (FWE)-corrected $P < 0.05$ and $k > 5$. Masks for the amygdala, NAcc and insula derived from the Harvard–Oxford cortical and subcortical structural atlases (Harvard Center for Morphometric Analysis). Masks for the dACC were created with MARINA (Walter *et al.*, 2003), which was aided by the anatomical parcellation of the brain published by Tzourio-Mazoyer *et al.* (2002).

In order to investigate the link between sensation seeking and neural activation during appetitive conditioning, contrast estimates of the peak voxel of pre-defined ROI were extracted for the $CS+_{early} - CS-_{early}$ and $CS+_{late} - CS-_{late}$ contrast for every subject and correlated with the sensation seeking score using SPSS (one-tailed Pearson's correlations).

Results

Ratings

Across participants, higher valence ratings [CS+: $M = 6.63$, s.d. = 1.63; CS−: $M = 3.53$, s.d. = 1.75; $t(37) = 7.10$; $P < 0.001$] and arousal ratings [CS+: $M = 5.79$, s.d. = 2.10; CS−: $M = 2.66$, s.d. = 1.82; $t(37) = 6.60$; $P < 0.001$] were revealed for the CS+ than for the CS− (see Figure 1A), showing overall successful conditioning.

Correlational analyses showed a negative association between sensation seeking scores and differential ratings (CS+ − CS−) for arousal ($r = -0.32$, $P = 0.025$) but not for valence ($r = 0.08$, $P = 0.308$).

For the UCS, there were no significant correlations between sensation seeking scores and valence ($r = 0.05$, $P = 0.764$) or arousal ratings ($r = -0.15$, $P = 0.359$). Mean ± s.d. ratings for the UCS were 8.24 ± 1.22 for valence and 6.53 ± 1.97 for arousal, indicating that the UCS was perceived as moderately arousing.

Skin conductance responsesv

Repeated-measures analysis of variance (ANOVA) yielded main effects of CS type [$F(1,34) = 9.31$; $P = 0.004$] and time [$F(1,34) = 29.83$; $P < 0.001$], which was qualified by a CS type × time interaction [$F(1,34) = 4.86$; $P = 0.034$]. A follow-up *t*-test showed a stronger differential CR in the early phase compared to the late phase of acquisition [$t(34) = 2.20$; $P = 0.034$; see Figure 1B]. This pattern is to be expected due to habituation and has been shown in several conditioning studies (Bacigalupo & Luck, 2018; Bulganin *et al.*, 2014; van Ast *et al.*, 2012). Overall, SCR results further indicate successful conditioning. There was no significant correlation between sensation seeking and SCR.

Hemodynamic responses

Main effect of conditioning (CS+ − CS−). Analyses of the main effects of appetitive conditioning (CS+ − CS−) in the pre-defined ROIs showed activation throughout the reward circuit in the early phase as well as in the late phase of acquisition. In the early phase, significant differential BOLD responses were observed in the NAcc, dACC, amygdala and insula in the contrast CS+ − CS−. In the late phase, analyses revealed significant CS+ − CS− BOLD responses in the NAcc, dACC and insula (see Table 1).

Correlation of BOLD responses with sensation seeking. Examining the relationship between sensation seeking and neural correlates of appetitive conditioning, we correlated SSS-V scores with the extracted contrast estimates of the peak voxels of the CS+ − CS− contrast for each ROI for the early and the late

Table 1. ROI results in the contrast CS+ − CS− for early and late phases

Structure	Side	k	x	y	z	z max	P corr
$CS+_{early} - CS-_{early}$							
Amygdala	L	46	−18	−6	−12	3.08	0.050*
dACC	L	1038	−10	16	38	4.04	0.010*
	R	208	8	−14	32	4.06	0.036*
Insula	L	126	−30	26	0	4.41	0.002**
	R	99	36	20	−6	3.61	0.037*
NAcc	L	75	−8	8	−6	5.20	<0.001***
	R	64	6	12	−4	6.43	<0.001***
$CS+_{late} - CS-_{late}$							
Insula	L	417	−40	4	2	3.50	0.048*
	R	340	32	26	0	3.44	0.055†
NAcc	L	69	−12	16	−6	3.15	0.017*
	R	84	10	10	−4	5.12	<0.001***
dACC	L	621	−6	24	28	4.38	0.002**
	R	544	12	16	36	4.16	0.006**

Structure, hemisphere (side), cluster size (k), x-/y-/z-coordinates, z-value, FWE-corrected P value (P_{corr}) are indicated. All coordinates are given in MNI (Montreal Neurological Institute) space.

*$P < 0.05$.
**$P < 0.01$.
***$P < 0.001$.
†$P < 0.10$.

phase of acquisition. The analysis showed significant negative correlations as hypothesized, indicating that higher sensation seeking was linked to decreased differential BOLD responses in reward-related brain areas. In the early phase, significant negative correlations in the right NAcc ([6/12/−4]; $r = -0.28$; $P = 0.046$), left insula ([−30/26/0]; $r = -0.32$; $P = 0.026$) and the right amygdala ([14/−8/−14]; $r = -0.29$; $P = 0.041$) were observed (see Figure 2A). In the late phase, analyses showed bilaterally negative correlations between sensation seeking and BOLD responses (CS+ − CS−) in the dACC (left: [−6/24/28]; $r = -0.38$; $P = 0.010$; right: [12/16/36]; $r = -0.29$; $P = 0.042$; see Figure 2B). The associations remain significant when controlling for valence ratings.

Discussion

This study focused on the relationship between the personality trait sensation seeking and the neural correlates of appetitive conditioning in healthy subjects. A classical appetitive conditioning paradigm with colored rectangles as CS and money as a moderately arousing UCS was employed. CRs were found across all subjects in ratings, SCRs and differential BOLD responses to the appetitive CS+ as compared to the CS−. We demonstrated a negative relationship between sensation seeking and BOLD responses in the appetitive CS+ − CS− contrast. In the early phase, while a CS–UCS association is still being established, negative correlations were found with the NAcc, insula and amygdala. In the late phase, in which previously formed contingencies are retrieved and outcome evaluation is central, a negative correlation was found in the dACC. The implications of the findings in early and late phases are first discussed separately and then regarding their clinical implications.

In the early phase, high sensation seeking was associated with blunted responses in the NAcc, insula and amygdala. Previous studies have shown that the NAcc plays a crucial role in reward processing, particularly regarding the encoding of the relative salience of a stimulus (Dillon *et al.*, 2008; O'Doherty *et al.*, 2006; Rademacher *et al.*, 2010). In the context of sensation seeking, this indicates that individuals with lower sensation seeking scores encode the appetitive CS+ as more salient than the CS− compared to high-sensation seekers. We observed the same pattern in the insula, which is associated with interoceptive processing and the integration of interoception and emotional processing (Sescousse *et al.*, 2013; Wang *et al.*, 2015; Kurth *et al.*, 2010). This indicates that sensation seeking is linked to reduced interoceptive processing of the appetitive CS+ compared to the CS−. In addition, the differential BOLD response in the amygdala was also negatively associated with sensation seeking. The amygdala is proposed to be crucial for emotional learning, particularly for establishing the link between CS and UCS (Balleine *et al.*, 2003; Martin-Soelch *et al.*, 2007; Klucken *et al.*, 2015). Thus, the negative relationship between sensation seeking and BOLD responses in the amygdala might indicate decreased associative learning in high-sensation seekers compared with low-sensation seekers. Taken together, the correlation of sensation seeking with lower differential responses to the appetitive CS+ as compared to the CS− in the early phase might reflect a reduced formation of CS+ salience in concert with reduced integration of interoceptive signals and CS–UCS association. Furthermore, higher sensation seeking scores were also associated with lower differential arousal ratings (CS+ − CS−). This indicates that subjects with high sensation seeking reported only small differences in arousal between CS+ and CS−, while subjects with low sensation seeking reported greater differences in arousal. This is in line with our assumption that the absence of risk in moderately stimulating situations leads to a reduced appetitive CS+ − CS− differentiation in individuals with high sensation seeking, as high-sensation seekers report lower differentiation in perceived arousal regarding CS+ and CS−.

In the late phase, sensation seeking is linked with reduced BOLD responses in the dACC, a structure mainly linked with outcome evaluation (Gabriel *et al.*, 2003; Alexander & Brown, 2011; Kruse *et al.*, 2018). This suggests that in the late phase when retrieval of learned associations and outcome evaluation plays a crucial role, high-sensation seekers show reduced processing

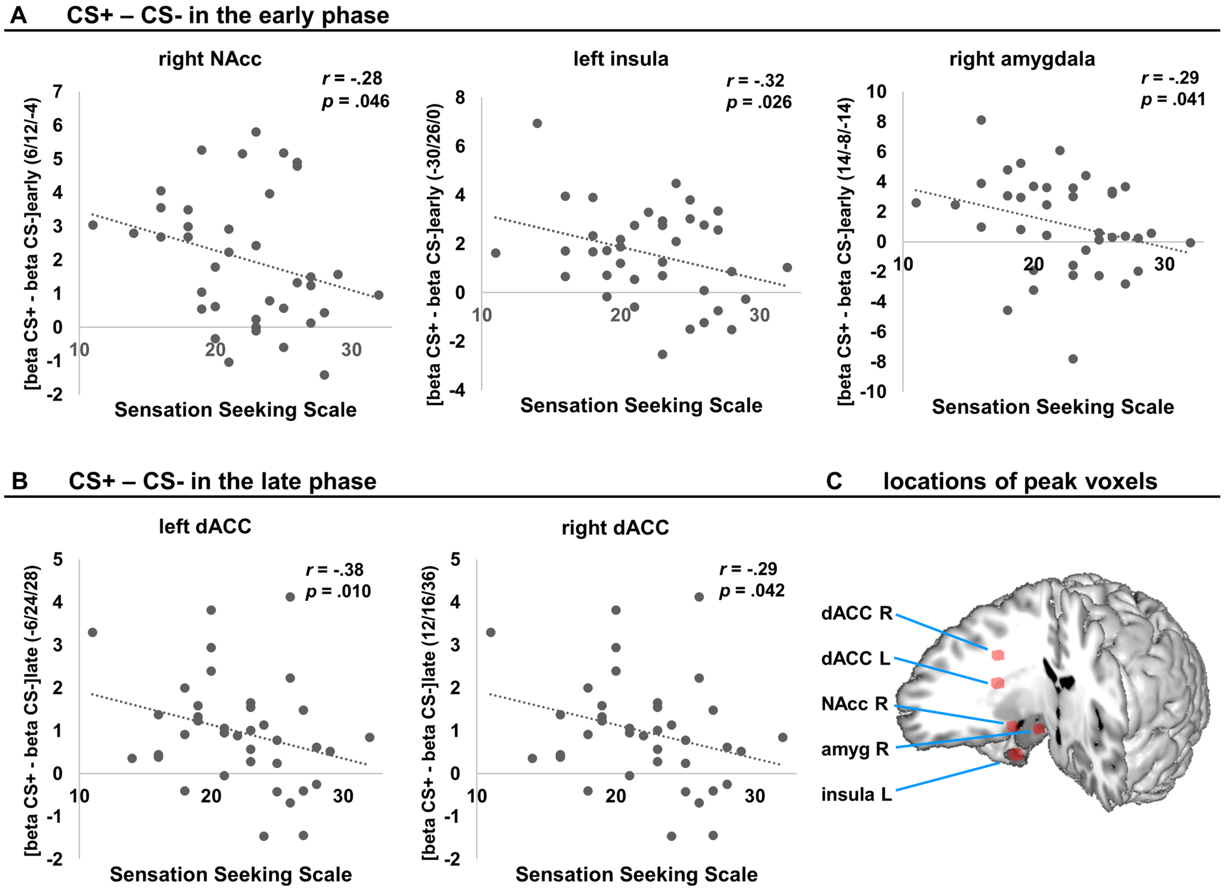

Figure 2. Negative correlations of sensation seeking and neural activity in the CS+ – CS– contrast during the early (A) and the late (B) phases of acquisition. Significant correlations were found in the NAcc, insula, amygdala and dACC (bilateral). (C) Locations of peak voxels used for correlational analyses are plotted as red cubes.

of outcome expectancy toward the appetitive CS+ compared with the CS–. This might be following the reduced differential BOLD responses in brain areas crucial for the formation of differential learning in the early phase. To conclude, we found high-sensation seekers to show an inverse relationship between sensation seeking and reward learning during a classical appetitive conditioning paradigm.

Previous research employed highly stimulating tasks containing risky decision making or stimuli associated with highly arousing situations, in contrast to small amounts of money used as a UCS in the current study. Under those highly stimulating circumstances, high sensation seeking was associated with increased neural activation in these areas (e.g. Abler et al., 2006; Cservenka et al., 2013). This is in line with the concept of an optimal level of stimulation, which suggests that based on the individual trait level of sensation seeking, different levels of stimulation are optimally stimulating (Zuckerman, 2016). Because risky situations are optimally stimulating for high-sensation seekers but less so for low-sensation seekers, these situations reveal positive correlations. In moderately arousing situations, the level of stimulation is more optimal for low-sensation seekers but less so for high-sensation seekers, revealing negative correlations. Thus, our results are in line with the theoretical concept of sensation seeking, demonstrating a modified pattern of reward processing in a moderately stimulating situation compared with previous risk processing paradigms. Indeed, Kruschwitz et al. (2012) found that the neural processing of relatively high rewards and losses differs distinctly from relatively low rewards and losses in the insula and the NAcc. This might be due to the specific trials with relatively low rewards and losses being less stimulating.

Our results are consistent with the RDS theory (Blum et al., 2000), linking high scores of sensation seeking to reward deficiency on a neural level in moderately stimulating contexts. Due to the reward deficiency, individuals might seek out situations more stimulating and thus providing more reward as suggested by previous studies (Abler et al., 2006; Cservenka et al., 2013; Kruschwitz et al., 2012). This is in line with previous research showing that sensation seeking is associated with risk-taking behaviors like substance use and gambling (Zuckerman, 2007). During appetitive conditioning, neutral stimuli become rewarding themselves. Reduced salience processing of conditioned stimuli might effectively reduce the number of stimuli that are perceived as rewarding. Additionally, seeing stimuli associated with reward in everyday life allows us to pursue gaining this reward. Reduced salience processing, as seen in high-sensation seekers, might preclude that, again limiting the number of low risk rewards that appear available in high sensation seeking. This might be a pathway leading high-sensation seekers to seek more stimulating rewards, thus inducing risky behavior.

As a limitation, this study did not vary the degree of arousal the situation entails experimentally. This would seem to be an important next step to further assess the role of sensation seeking in appetitive conditioning. Furthermore, if the separate ROIs were treated as a family of hypotheses, it can be argued that stricter corrections are needed.

As effects of online ratings of the CS might affect the conditioning process, we did not collect any ratings during the acquisition phase. However, as SCR and imaging results reveal different patterns in early and late phases, collecting online ratings might provide helpful insights in future studies.

In addition, future research might further explore the complex interplay of trait sensation seeking, the degree of stimulation the situation comprises and the degree of arousal due to the UCS.

In conclusion, in the present study, we investigated the role of sensation seeking in classical appetitive conditioning. In the early phase of acquisition, sensation seeking was linked to lower differential hemodynamic responses in the NAcc, insula and amygdala, indicating reduced reward processing and learning. In the late phase, sensation seeking was negatively associated with differential activation in the dACC, indicating reduced retrieval of outcome expectancy. This highlights the importance of the individual level of optimal stimulation for appetitive conditioning.

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Conflicts of interest

None declared.

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