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Permalink

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Journal

Social Cognitive and Affective Neuroscience, 10(4)

ISSN

1749-5016

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Publication Date

2015-04-01

DOI

10.1093/scan/nsu091

Peer reviewed

Anticipation of high arousal aversive and positive movie clips engages common and distinct neural substrates

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The neural correlates of anxious anticipation have been primarily studied with aversive and neutral stimuli. In this study, we examined the effect of valence on anticipation by using high arousal aversive and positive stimuli and a condition of uncertainty (i.e. either positive or aversive). The task consisted of predetermined cues warning participants of upcoming aversive, positive, ‘uncertain’ (either aversive or positive) and neutral movie clips. Anticipation of all affective clips engaged common regions including the anterior insula, dorsal anterior cingulate cortex, thalamus, caudate, inferior parietal and prefrontal cortex that are associated with emotional experience, sustained attention and appraisal. In contrast, the nucleus accumbens and medial prefrontal cortex, regions implicated in reward processing, were selectively engaged during anticipation of positive clips (depicting sexually explicit content) and the mid-insula, which has been linked to processing aversive stimuli, was selectively engaged during anticipation of aversive clips (depicting graphic medical procedures); these three areas were also activated during anticipation of ‘uncertain’ clips reflecting a broad preparatory response for both aversive and positive stimuli. These results suggest that a common circuitry is recruited in anticipation of affective clips regardless of valence, with additional areas preferentially engaged depending on whether expected stimuli are negative or positive.

Keywords: expectation; valence; uncertainty; fMRI; films

Exaggerated anticipation is a central component of anxiety disorders. Besides feeling anxious in the presence of certain stimuli and situations, individuals with anxiety disorders often experience severe anxiety in expectation of confronting these stimuli/situations (Barlow, 2000). The neural correlates of anxious anticipation have been investigated, for the most part, using aversive stimuli such as generally aversive pictures (e.g. attack scenes, mutilated bodies; Nitschke *et al.*, 2006, 2009), phobogenic images (Simmons *et al.*, 2004; Straube *et al.*, 2007), noxious tactile stimuli (Chua *et al.*, 1999) and loud auditory stimuli (Carlson *et al.*, 2011b). The general paradigm used in these studies includes the following components: participants are instructed of cue-stimulus pairings in which one cue is predictive of a negative stimulus and a second cue is predictive of a control or neutral stimulus. The cue is followed by a brief anticipation period (during which participants passively focus on the screen or perform a distractor task). Next, the stimulus associated with the cue is presented. Across these studies, regions implicated, include the insula, anterior cingulate cortex (ACC), amygdala and the lateral (IPFC) and medial prefrontal cortex (mPFC). Given that similar regions are engaged whether visual (Carlson and Mujica-Parodi, 2010), auditory (Carlson *et al.*, 2011b) or tactile (Chua *et al.*, 1999) stimuli are employed, supports a common anticipatory circuit across modalities.

In most studies, aversive anticipation has been assessed by contrasting aversive and neutral trials; differences in activation explained in terms of affective valence. However, because the neutral condition contains images that are less arousing this interpretation is qualified

by a confound of valence and arousal (Onoda 2008). To address this limitation, it would be important to include a positive condition with images of comparable arousal levels to those presented in the aversive condition. The addition of a positive condition would also allow a broader examination of the effect of valence on anticipation and identification of common and selective regions engaged during aversive and positive anticipation. For example, the anticipatory affect model (Knutson and Greer, 2008) suggests that the (anterior) insula might be preferentially activated during aversive anticipation and the nucleus accumbens (NAcc) during positive anticipation. Herwig *et al.* (2007) incorporated positive trials in their anticipation paradigm. A comparison of the positive versus neutral condition showed activation in multiple regions including the ACC, extended amygdala, thalamus and superior frontal gyrus. However, the authors did not directly compare positive versus negative trials. Furthermore, arousal ratings for images in the negative condition were higher than those in the positive condition and relatively low overall. The study also included a condition in which the valence of target stimuli is unknown to participants (i.e. could be either negative or positive). Patterns of reactivity for this condition were similar to those observed during anticipation of negative images suggesting a negativity bias when the emotional valence of stimuli is unknown. This response also correlated with measures of depression and is expected to be high in anxious individuals based on their low tolerance for conditions of uncertainty.

Anticipation paradigms have typically employed short anticipatory periods (2–6 s; Simmons *et al.*, 2004; Nitschke *et al.*, 2006; Simmons *et al.*, 2006). Recently, we tested an anticipation task with longer anticipatory periods (16 s) to investigate whether the same regions are engaged when the anticipated event is more distal and to examine the temporal dynamics of the anticipatory response. The task also included a self-report measure at the end of each trial to gauge participants’ subjective experience of anticipatory anxiety and its association with neural reactivity. We ran two versions of the task in healthy individuals, one with loud and soft auditory stimuli (Carlson *et al.*, 2011b) and a second with negative and neutral images from the international

Received 4 October 2013; Revised 2 June 2014; Accepted 26 July 2014

Advance Access publication 1 July 2014

We would like to thank Candida Royalle for providing the clips from ‘*Eyes of Desire 2*’ (Femme Productions Inc., 1999) for the fMRI task. This research was supported by the Office of Naval Research N0014-04-1-005 (L.R.M.P.) and the National Science Foundation 0954643 (L.R.M.P.).

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affective picture system (IAPS; Carlson and Mujica-Parodi, 2010). Results for the auditory version largely replicated previous findings, revealing activation in the insula, amygdala, brainstem, superior frontal gyrus and dorsolateral prefrontal cortex (dlPFC) during anticipation of loud (100 dB) versus soft (55 dB) white noise. In addition, the right anterior insula (aINS) was associated with participants' self-reported level of anxiety on a trial-by-trial basis, while the amygdala was selectively associated with feelings of anxiety during aversive trials. In the pictorial version, anticipation of negative versus neutral images engaged fewer brain regions including the insula, occipitotemporal visual areas and dlPFC and the amplitude and spatial extent of activation was smaller compared to the auditory task (observed only with a more liberal threshold of $\alpha = 0.005$ uncorrected). Participants' self-report ratings of anticipatory anxiety during the visual task were low as well. These findings suggest that affective pictures may not be optimal for eliciting a strong anticipatory response in healthy individuals, particularly for extended durations.

Given that anticipatory processing across the valence dimension has not been established, the aim of this study was to compare and contrast the sustained anticipatory response for high arousal aversive, positive and uncertain stimuli while controlling for arousal levels across conditions. On the basis of our findings of a restricted anticipatory response to affective pictures during long anticipation periods, we modified our previous anticipation task to include short movie clips (without sound) known to elicit a strong emotional response (Gross and Levenson, 1995). The movie clips are also more suitable than auditory stimuli for the loud scanner environment and for manipulating valence and arousal. The modified task included four conditions: an aversive condition with clips depicting a graphic medical procedure designed to elicit disgust, a positive condition with sexually explicit clips, an 'uncertain' condition in which either aversive or positive clips were presented and a neutral condition. We hypothesized that anticipation of aversive, positive and 'uncertain' clips would recruit a common circuitry involved in preparatory responses to affective stimuli and that regions associated with processing appetitive stimuli such as the NAcc and mPFC would be preferentially engaged during anticipation of positive clips (Knutson and Wimmer, 2007b). The insula, which has been previously implicated in aversive anticipation (Nitschke et al., 2006) as well as specifically linked to processing disgust (Phillips et al., 1997; Wright et al., 2004), was hypothesized to be preferentially active during anticipation of the aversive clips. Finally, we examined whether a negativity bias in neural reactivity previously reported when participants anticipate events of unknown valence (Herwig et al., 2007), would be present when the positive stimuli are highly arousing and motivationally significant.

METHOD

Participants

Twenty-five healthy women participated in the study (Mean age = 21.6; SD = 5.1). We recruited females only for this study to reduce gender-related heterogeneity in the sample based on previous evidence for gender differences in response to affective stimuli (Cahill et al., 2001; Hamann et al., 2004; Killgore and Yurgelun-Todd, 2001; Stevens and Hamann, 2012). All participants reported being right-handed except for one participant, who reported being ambidextrous. Participants were screened for absence of any current or past psychiatric illness with the Structured Clinical Interview for DSM-IV Axis I Disorders -Patient Edition, Version 2 (SCID-I/P; First et al., 2002) by doctoral candidates in clinical psychology. The study was approved by the Stony Brook University Institutional Review Board; all participants provided informed consent.

Task design

The task consisted of 40 trials presented pseudorandomly: 10 aversive trials (anticipation of an aversive movie clip), 10 positive trials (anticipation of a positive movie clip), 10 'uncertain' trials (anticipation of either a positive or aversive movie clip; 50% each) and 10 neutral trials (anticipation of a neutral movie clip). Each trial began with a white fixation crosshair presented in the center of a black screen (jittered 10–14 s). The fixation crosshair was followed by an anticipation period during which a countdown from 16 to 1 was numerically presented in the center of the screen with a specific cue associated with each trial type presented above it (16 s duration). The cues were: '▼' for a negative clip, '▲' for a positive clip, '?' for an 'uncertain' clip and '—' for a neutral clip. A movie clip was presented next (6 s) and then participants rated the strength of the anticipatory response they experienced during the countdown period on a four-point scale (4s). Participants were explicitly asked to rate the level of their anticipatory response rather than the content of the image or their response to the image. Ratings ranged from 1 = 'weak' to 4 = 'strong' and were not valence specific. The task was programmed with Experiment Builder (SR Research Ltd.; Ontario, Canada) and presented with an MRI-compatible 60 Hz projector with 1024 × 768 resolution. The duration of the task was 25 min and 30 s.

Stimuli

The aversive clips were taken from a noncommercial surgery film of an arm amputation, which was previously shown to reliably elicit disgust (Gross and Levenson, 1995) and a similar film of a thigh surgery found online. The positive clips were sexually explicit and taken from two scenes featured in 'Eyes of Desire 2' (Femme Productions Inc., 1999) and 'Island Fever 2' (Digital Playground Inc., 2003). The neutral clips were taken from a scene in the movie 'Quiet Earth' (Cinepro and Mr Yellowbeard Productions Limited & Company, 1985) showing a man driving. All clips were appraised for arousal and valence prior to testing by eight women. Aversive and positive clips were appraised equally high on arousal and low (i.e. negative) and high (i.e. positive) on valence, respectively. Neutral clips were appraised low on arousal and with intermediate valence.

Post-task rating of clips

Outside the scanner immediately following the task, participants rated each clip for arousal and valence using two nine-point scales. The valence scale ranged from 1 = 'negative' to 9 = 'positive'. The arousal scale ranged from 1 = 'calm' to 9 = 'excited' (participants were instructed that a high score on this scale could reflect either negative or positive arousal/excitement).

Image acquisition

We acquired a total of 760 T2*-weighted echoplanar images with an oblique coronal angle and Repetition Time (TR) = 2100 ms, Echo Time (TE) = 23 ms, Flip Angle = 83°, Matrix = 96 × 96, FOV = 224 × 224 mm, Slices = 37 and Slice Thickness = 3.5 mm. In addition, we obtained T1-weighted structural scans with TR = 1900 ms, TE = 2.53, Flip Angle = 9°, FOV = 176 × 250 × 250 mm and Matrix = 176 × 256 × 256 mm.

Image analysis

Preprocessing procedures were performed in SPM8 and included slice time correction, motion correction, normalization and smoothing with a 6-mm full width at half maximum Gaussian kernel. Preprocessed images were entered into a general linear model with one regressor for each anticipation period and clip type (aversive, positive, 'uncertain' and neutral). In addition, we included six rigid body motion

parameters as regressors of no interest. Serial autocorrelations were modeled with an autoregressive (AR)1 process. First-level single subject statistical parameter maps were created for the *aversive anticipation*, *positive anticipation*, *'uncertain' anticipation*, *neutral anticipation*, *aversive clip*, *positive clip*, *'uncertain' clip* and *neutral clip*. These contrasts were used in a 2 (process: *anticipation*, *clip presentation*) \times 4 (valence: *aversive*, *positive*, *'uncertain'*, *neutral*) second-level random effects repeated measures analysis. In addition, we conducted conjunction analyses, detailed below, using the minimum statistic compared to the conjunction null (Nichols *et al.*, 2005).

RESULTS

Self-report ratings of anticipatory response

Data for one participant was not available due to technical difficulties. A repeated measures analysis of variance (ANOVA) showed differences in self-reported anticipatory ratings across conditions ($F_{(3,69)} = 68.75$, $P < 0.001$). As presented in Figure 1, anticipatory ratings for the aversive ($M = 3.06$; $SD = 0.71$), positive ($M = 2.54$; $SD = 0.79$) and 'uncertain' ($M = 2.8$; $SD = 0.64$) conditions were all higher than the ratings for the neutral condition ($M = 1.2$; $SD = 0.22$; all $P_s < 0.001$). These results confirm that, on average, participants experienced a stronger emotional response in anticipation of the affective clips. Anticipatory ratings for the aversive condition were marginally higher than the ratings for the positive condition ($P = 0.055$). There were no significant differences in ratings between the 'uncertain' condition and either the aversive or positive conditions (both $P_s > 0.13$).

Post-task valence and arousal ratings for the movie clips

Ratings for two participants were not available due to software malfunction. Figure 2 shows mean valence and arousal scores for the aversive, positive, 'uncertain' aversive, 'uncertain' positive and neutral clips, respectively. Valence scores were highest for the positive ($M = 5.83$; $SD = 1.17$) and 'uncertain' positive clips ($M = 5.86$; $SD = 1.31$) and lowest for the aversive ($M = 2.93$; $SD = 1.45$) and 'uncertain' aversive clips ($M = 3.11$; $SD = 1.58$). Valence scores for the neutral clips were 5.08 ($SD = 0.77$). Arousal scores for the aversive ($M = 5.77$; $SD = 2.08$), 'uncertain' aversive ($M = 5.40$; $SD = 2.14$), positive ($M = 5.36$; $SD = 1.58$) and 'uncertain' positive clips 5.67 ($SD = 1.87$) did not differ (all $P_s \geq 0.16$) and were all higher than arousal scores for the neutral clips ($M = 1.46$; $SD = 0.62$; all $P_s < 0.001$).

Brain activation during anticipation of affective clips

Comparisons of activation during aversive, positive and 'uncertain' anticipation versus neutral anticipation are presented in Table 1. The *aversive anticipation > neutral anticipation* contrast showed activation in the aINS and mid-insula, thalamus, caudate, ACC, lateral prefrontal cortex (IPFC) and inferior parietal area (BA40). The *positive anticipation > neutral anticipation* contrast showed activation in the aINS, thalamus, caudate, putamen, NAcc, amygdala, ACC (including supracallosal and perigenual sectors), mPFC, IPFC, inferior parietal area (BA40), superior temporal gyrus and midbrain. The *'uncertain' anticipation > neutral anticipation* contrast showed activity in the aINS, thalamus, caudate, NAcc, amygdala, ACC, mPFC, IPFC, middle temporal gyrus, inferior parietal area (BA40) and midbrain.

Conjunction analyses for the anticipation contrasts

In order to identify regions commonly activated for the aversive anticipation, positive anticipation and 'uncertain' anticipation (versus neutral anticipation) we conducted a conjunction analysis for

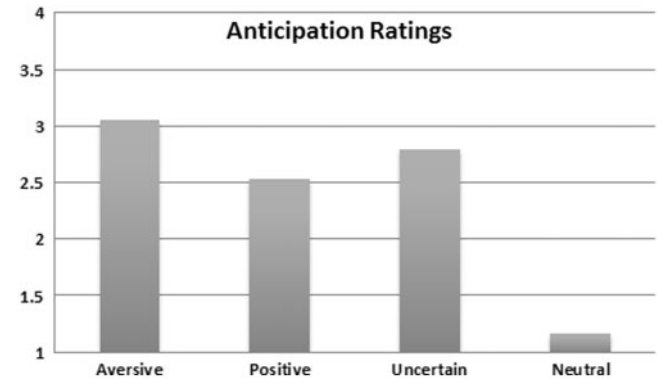


Fig. 1 Mean anticipatory ratings for the aversive, positive, 'uncertain' and neutral conditions ($N = 24$).

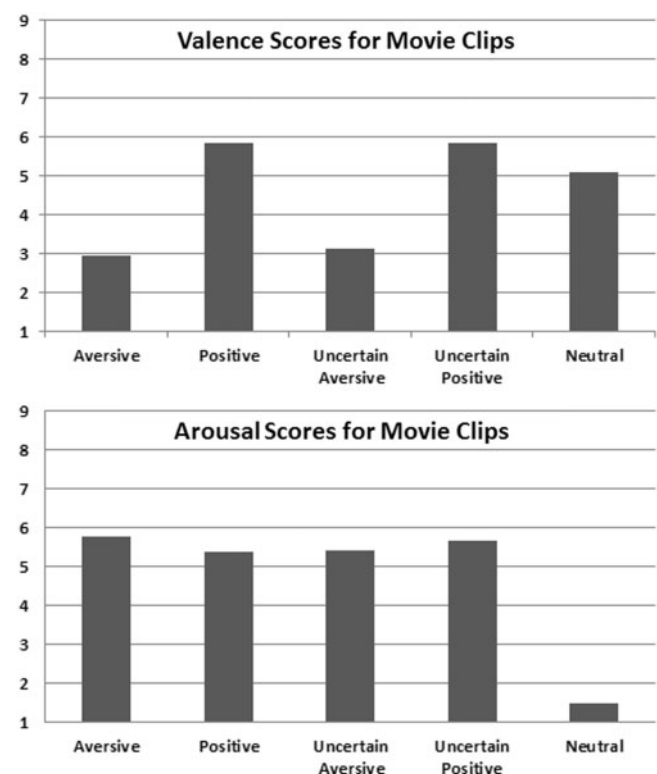


Fig. 2 Mean valence (top) and arousal (bottom) scores for the aversive, positive, 'uncertain' aversive, 'uncertain' positive and neutral clips ($N = 23$).

these three contrasts (see Figure 3). This analysis showed shared activation in the aINS, thalamus, caudate, dorsal anterior cingulate cortex (dACC), IPFC and inferior parietal area (BA40).

To identify regions commonly activated for 'uncertain' and aversive anticipation we conducted a conjunction analysis using the following four contrasts (adapted from Herwig *et al.*, 2007): (i) *'uncertain' anticipation > neutral anticipation* (ii) *'uncertain' anticipation > positive anticipation* (iii) *aversive anticipation > neutral anticipation* (iv) *aversive anticipation > positive anticipation*. This analysis showed activation in the right mid-insula. Similarly, to identify regions commonly activated for 'uncertain' and positive anticipation we conducted a conjunction analysis with these four contrasts: (i) *'uncertain' anticipation > neutral anticipation* (ii) *'uncertain' anticipation > aversive anticipation* (iii) *positive anticipation > neutral anticipation* (iv) *positive*

anticipation > *aversive anticipation*. This analysis showed activation in the NAcc and mPFC. There was no significant activation for the *aversive anticipation* > *'uncertain' anticipation* and the *positive anticipation* > *'uncertain' anticipation* contrasts.

Table 1 Brain activation during aversive, positive and 'uncertain' anticipation versus neutral anticipation

Analysis and region	Hemisphere	MNI coordinates			Maximum voxel	T value
		x	y	z		
Aversive anticipation > neutral anticipation						
Anterior insula	R	32	28	-4	387	4.52
	L	-34	24	10	275	4.09
Thalamus	R-L	-10	-14	4	1071	4.07
Caudate	R	14	6	14	348	4.08
	L	-14	2	18	364	3.53
Anterior cingulate cortex	R-L	-2	8	28	419	4.57
Superior/middle frontal gyri*	R	24	58	28	55	3.49
	L	-46	36	28	307	3.76
Inferior parietal area (including BA40, BA3)*	R	34	-38	44	725	4.52
	L	-32	-40	38	1082	4.56
Positive anticipation > neutral anticipation						
Anterior insula	R	30	22	-8	589	4.74
	L	-32	24	0	606	4.65
Thalamus	R-L	-2	-18	10	547	4.34
Caudate	R	-10	6	6	680	6.15
	L	10	8	8	713	5.52
Nucleus accumbens	R	10	8	-4	32	4.24
	L	-12	6	-8	58	5.03
Amygdala	R	18	4	-16	19	3.89
	L	-14	0	-16	75	4.41
Anterior cingulate cortex	R-L	10	20	28	1811	4.81
Medial/superior/middle frontal gyri*	R-L	4	48	38	6469	5.81
Inferior parietal area (BA40)*	R	30	-50	60	348	4.33
	L	-38	-40	46	1133	4.53
'Uncertain' anticipation > neutral anticipation						
Anterior insula	R	32	22	-10	449	4.37
	L	-32	24	-2	762	5.27
Thalamus	R-L	4	-18	4	1177	4.36
Caudate	R	10	10	4	520	4.82
	L	-12	2	12	573	4.86
Nucleus accumbens	L	-12	4	-8	71	4.1
Amygdala	R	18	2	-16	30	3.83
	L	-12	-2	-16	85	4.19
Anterior cingulate cortex	R-L	10	22	28	1203	4.73
Medial/superior/middle frontal gyri*	R-L	6	44	34	7916	5.53
Superior/middle temporal gyrus*	R	48	-30	4	92	4.3
	L	-52	-28	-4	71	3.99
Inferior parietal area (BA40)*	R	28	-52	58	1461	4.93
	L	-34	-48	56	1797	5.73

Note: BA = Brodmann area.

* $P < 0.05$ small volume correction (SVC); ** $P < 0.001$.

Differential activation for aversive and positive anticipation

To identify regions that were selectively activated during aversive anticipation we conducted a conjunction analysis using the *aversive anticipation* > *neutral anticipation* and *aversive anticipation* > *positive anticipation* contrasts. In addition, we applied exclusive masking with the *positive anticipation* > *neutral anticipation* contrast to remove any voxels that were significant for this contrast from the final results. This analysis showed activation in the right mid-insula (see Figure 4).

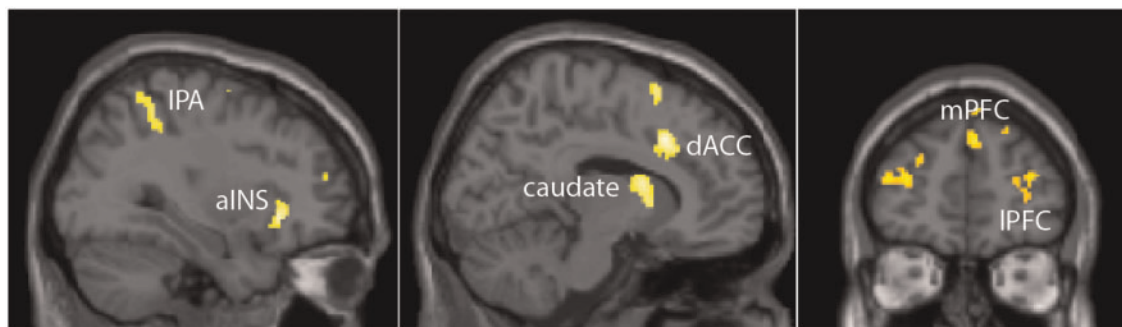
To identify regions that were selectively activated during positive anticipation we conducted a conjunction analysis using the *positive anticipation* > *neutral anticipation* and *positive anticipation* > *aversive anticipation* contrasts. Results were exclusively masked with the *aversive anticipation* > *neutral anticipation* contrast. This analysis showed activation in the left NAcc and mPFC (see Figure 4).

Brain activation in response to the clips

Regions activated for the *aversive clip* > *neutral clip* contrast included the insula (both anterior and mid-posterior regions), thalamus, dACC, globus pallidus, bilateral precentral gyrus (BA6), bilateral fusiform gyrus, superior and inferior parietal areas, precuneus (BA7) and cerebellum. Regions activated for the *positive clip* > *neutral clip* contrast included the aINS, cingulate gyrus (including dorsal and anterior sections), NAcc, caudate, mPFC, thalamus, amygdala, parahippocampal gyrus (BA34), bilateral fusiform gyrus, superior and inferior parietal areas, precuneus (BA7), midbrain and cerebellum. Regions activated for the *'uncertain' clip* > *neutral clip* contrast included the aINS, cingulate cortex (including dorsal and anterior sections), NAcc, amygdala, mPFC, bilateral fusiform gyrus, superior and inferior parietal areas, precuneus (BA7) and cerebellum.

Differential activation for the aversive and positive clips

To identify regions that were selectively activated in response to the aversive clips, we conducted a conjunction analysis using the *aversive clip* > *neutral clip* and *aversive clip* > *positive clip* contrasts. In addition, we applied exclusive masking with the *positive clip* > *neutral clip* contrast. This analysis showed activation in the bilateral mid-posterior insula, precentral gyrus (BA4) and a subsection of the left fusiform area. To identify regions that were selectively activated in response to the positive clips we conducted a conjunction analysis using the *positive clip* > *neutral clip* and *positive clip* > *aversive clip* contrasts. Results were exclusively masked with the *aversive clip* > *neutral clip* contrast. This analysis showed activity in the NAcc, mPFC, amygdala, medial thalamus, superior temporal gyrus and precuneus (BA7).



aINS = anterior insula; IPA = inferior parietal area (BA 40); dACC = dorsal anterior cingulate cortex; mPFC = medial prefrontal cortex; IPFC = lateral prefrontal cortex
Whole brain threshold $\alpha = .001_{uncorrected}$, extent threshold = 10 voxels

Fig. 3 Brain activation for the conjunction of aversive, positive and 'uncertain' anticipation versus neutral anticipation contrasts.

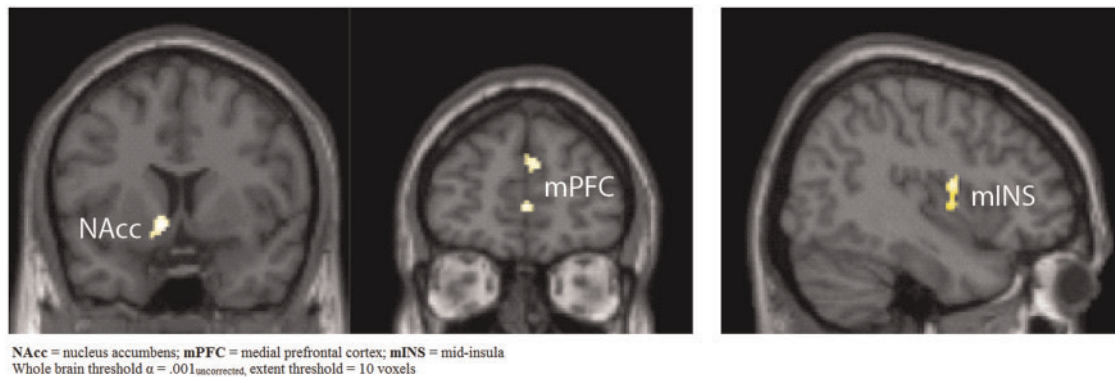


Fig. 4 Selective activation during aversive (right) and positive (left) anticipation.

DISCUSSION

Anticipation of aversive, positive and ‘uncertain’ clips engaged common regions consisting of the bilateral aINS, thalamus, bilateral caudate, dACC, lateral prefrontal cortex (IPFC; including clusters in superior, middle and inferior frontal gyri) and bilateral inferior parietal area (BA40). The NAcc and mPFC, on the other hand, were selectively activated during anticipation of positive clips and the mid-insula was selectively activated during aversive anticipation; all three regions were also activated in the ‘uncertain’ condition in which either aversive or positive clips were forthcoming. These results suggest that a common circuitry is recruited in anticipation of affective clips regardless of valence, with additional areas preferentially engaged depending on whether expected stimuli are negative or positive.

Recruitment of common regions across affective conditions supports their involvement in a general preparatory response, which likely includes multiple processes such as vigilance, appraisal of upcoming stimuli and one’s response to them (i.e. self-referential processing), generation of an affective state and initiation of regulatory mechanisms. The aINS has been frequently implicated in aversive anticipation (Chua *et al.*, 1999; Phelps *et al.*, 2001; Simmons *et al.*, 2004, 2006; Nitschke *et al.*, 2006; Onoda *et al.*, 2008); reactivity in this region across affective conditions is consistent with its broader role in processing and awareness of interoceptive signals associated with salient stimuli (Craig, 2002; Menon and Uddin, 2010). This information is relayed to other regions such as the dACC and IPFC where it can modulate attentional and regulatory processes and is also thought to contribute to the rise of conscious feeling states (Craig, 2009). Indeed, trial-by-trial levels of anticipatory aINS activation have been shown to correlate with trial-by-trial levels of participants’ subjective experience of anxious anticipation (Carlson *et al.*, 2011b). The dACC, inferior parietal cortex and IPFC mediate attentional control/sustained attention (Bush *et al.*, 2000; Thakral and Slotnick, 2009). The observed activation in these regions before presentation of the affective clips may reflect enhanced vigilance and focus on predictive affect cues. In addition, the dACC is involved in generation of autonomic responses (Critchley *et al.*, 2003). Activity within dACC correlates with measures of skin conductance (Critchley *et al.*, 2001), blood pressure (Critchley *et al.*, 2000) and sympathetic cardiovascular influences (Critchley *et al.*, 2003). The thalamus is also involved in the arousal response. Reactivity in the dorsomedial region, in particular, is associated with subjective ratings of arousal (Colibazzi *et al.*, 2010) and intensity of emotional arousal (Lane, 1999). The caudate (especially the head portion) is often implicated in emotional processing. It is part of an output system of affective circuitry involved in motor behaviors (Rolls, 2000) and may contribute to implicit preparatory motor

responses to the clips. Additional PFC regions activated during affective anticipation such as the middle and superior frontal gyri have been linked to appraisal processes of expected stimuli and one’s reaction to them (Ochsner *et al.*, 2004) as well as automatic (Mauss *et al.*, 2007) and volitional emotion regulation (Ochsner *et al.*, 2002; Ochsner and Gross, 2005).

The NAcc and mPFC, which were selectively activated during anticipation of positive clips, are part of the mesocorticolimbic pathways associated with reward and motivation. Both regions are involved in perception of pleasant stimuli (Berns *et al.*, 2001; Gottfried *et al.*, 2002; Karama *et al.*, 2002; Bartels and Zeki, 2004) and reward processing (McClure *et al.*, 2004). Research on reward anticipation has focused on monetary incentives. This work has implicated the NAcc and mPFC in anticipation of monetary gains (Knutson and Wimmer, 2007a) and emphasized their role in assessment of expected value based on gain magnitude and probability (Knutson *et al.*, 2005). Activity in NAcc before delivery of monetary rewards is also associated with self-reported positive arousal (Knutson and Peterson, 2005) and increases in self-reported happiness that may be due in part to dopamine release in this area (Knutson *et al.*, 2001). Anticipatory positive affect has been posited to promote approach behavior to primary (and secondary) rewards (Knutson and Greer, 2008), which is critical for survival and reproduction.

The amygdala was also active during positive anticipation. Amygdala activation to appetitive stimuli (Carlson *et al.*, 2011a; Fitzgerald *et al.*, 2006; Hamann and Mao, 2002; O’Doherty *et al.*, 2002) including erotic films (Beauregard *et al.*, 2001; Karama *et al.*, 2002; Hamann *et al.*, 2004) has been previously demonstrated. Interestingly, however, amygdala deactivation has been observed during orgasm in both women (Georgiadis *et al.*, 2006) and men (Georgiadis and Holstege, 2005). These contrary amygdala reactivity patterns may reflect increased vigilance in the early phase of the sexual response followed by attenuated vigilance during the consummatory phase (Georgiadis and Holstege, 2005). Our finding provides support for sustained engagement of the amygdala in women early on in this process.

A small area in the mid-insula was selectively activated during anticipation of the aversive clips. Preferential activation in the (anterior) insula has been reported for facial expressions of disgust (Phillips *et al.*, 1997) and disgust-inducing pictures of contamination and mutilation (Wright *et al.*, 2004; but see Phan *et al.*, 2004). In addition, the insula is involved in perception of pain in self and others (i.e. pain empathy; Jackson *et al.*, 2006). The aversive clips depicted medical procedures that elicit high levels of disgust (Gross and Levenson, 1995) but due to their graphic nature they may also prompt regions associated with pain processing. The location of insular activation we observed is more

compatible with the latter. Interestingly, there was no amygdala activation during aversive anticipation. Amygdala reactivity is less consistently reported for disgusting relative to fearful stimuli (Murphy et al., 2003; Vytal and Hamann, 2010) and is also known to habituate rapidly (Breiter et al., 1996).

All regions selectively activated during aversive and positive anticipation were also engaged during 'uncertain' anticipation. This finding does not support a negativity bias for anticipated events of unknown valence but rather a preparatory response for both aversive and positive stimuli. The discrepancy with previous results (Herwig et al., 2007) may be due to the use of high arousal sexually explicit clips in the current study. These clips are more emotionally intense and have higher motivational value (i.e. motivate approach to a greater extent) than the low arousal positive stimuli presented by Herwig et al., which included pictures of animals, scenery and babies. In circumstances when both the aversive and positive stimuli are highly potent, they might be processed equally during the anticipation phase. However, because the aversive stimuli presented by Herwig et al., (e.g. pictures of attacks/mutilations) were potentially more threatening than the disgusting clips used here (though it should be noted that these clips had lower arousal ratings than the current stimuli), our results should be replicated in a paradigm that includes sexual and fear-inducing clips.

Neural response to the affective clips was strong and widespread across temporoparietal visual areas and limbic and paralimbic structures. A comparison of positive and aversive clips showed activity in mesolimbic regions in response to the positive clips and mid-insula activity in response to the aversive clips. This parallels the differential response pattern observed for these two conditions during anticipation. Reactivity to the clips was more extensive than reactivity during the anticipatory phase; however, there was overlap in regions engaged consistent with previous findings that implicate similar networks in both processes (Nitschke et al., 2006). Early recruitment of regions (i.e. during the anticipatory phase) subsequently involved in the response to aversive and other affective stimuli may expedite processing and execution of appropriate action/behavior to these stimuli. Selective activation to the clips was observed in areas involved in visual processing including subsections of the superior and inferior parietal cortices and fusiform area. In contrast, sections in the right superior frontal gyrus and IPFC, associated with appraisal of stimuli and one's affective state as well as emotion regulation processes, were selectively activated during anticipation.

Self-report anticipatory ratings during the task confirmed that the manipulation was successful in eliciting stronger anticipation to the affective clips compared to the neutral clips. In addition, post-task valence and arousal scores indicate that participants perceived the positive clips as more pleasant than the aversive clips and both as equally arousing. This is important for interpretation of valence effects because it implies that comparisons between the positive and aversive conditions were not confounded by arousal.

In summary, our results show that anticipation of affective clips recruits common regions, involved in various preparatory processes, regardless of valence and that additional areas are preferentially engaged depending on whether expected stimuli are negative or positive. Anticipation of clips with 'uncertain' valence reflected a preparatory response for both aversive and positive stimuli suggesting that when both types of stimuli are highly motivating, they are equally processed during the anticipation phase.

Conflict of Interest

None declared.

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