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Neural correlates of aversive anticipation: An activation likelihood estimate meta-analysis across multiple sensory modalities

Jeremy A. Andrzejewski[1] · Tsafrir Greenberg[2] · Joshua M. Carlson[1]

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Abstract

Anticipation is a universal preparatory response essential to the survival of an organism. Although meta-analytic synthesis of the literature exists for the anticipation of reward, a neuroimaging-based meta-analysis of the neural mechanisms of aversive anticipation is lacking. To address this gap in the literature, we ran an activation likelihood estimate (ALE) meta-analysis of 63 fMRI studies of aversive anticipation across multiple sensory modalities. Results of the ALE meta-analysis provide evidence for a core circuit involved in aversive anticipation, including the anterior insula, anterior cingulate cortex, mid-cingulate cortex, amygdala, thalamus, and caudate nucleus among other regions. Direct comparison of aversive anticipation studies using tactile versus visual stimuli identified additional regions involved in sensory specific aversive anticipation across these sensory modalities. Results from complementary multi-study voxel-wise and NeuroSynth analyses generally provide converging evidence for a core circuit involved in aversive anticipation. The multi-study voxel-wise analyses also implicate a more widespread preparatory response across sensory, motor, and cognitive control regions during more prolonged periods of aversive anticipation. The potential roles of these structures in anticipatory processing as well as avenues for future research are discussed.

Keywords Aversive anticipation · fMRI · ALE meta-analysis · Anxiety · GingerALE

Anticipation, or the expectation of a future event or stimulus, is a universal preparatory response. Successful anticipation is an evolutionary advantage; recognizing contingencies that have led to reward and anticipating proper positive outcomes is adaptive. Likewise, preparing for an approaching or uncertain threat maximizes the likelihood of successfully mitigating the threat. Accordingly, anticipation research has primarily focused on two distinct subtypes: anticipation of reward and anticipation of aversive/anxiety-provoking stimuli. Perturbations of these anticipation subtypes have been linked to mood disorders (Dichter, Kozink, McClernon, & Smoski, 2012) and behavioral or substance addictions (Luijten, Schellekens, Kühn, Machielse, & Sescousse, 2017) as well as anxiety disorders (Grupe & Nitschke, 2013), respectively. The neural correlates of reward anticipation have been extensively studied with functional magnetic resonance imaging (fMRI) and have been subjected to recent fMRI-based meta-analyses, which implicate the striatum, medial prefrontal cortex (mPFC), dorsal lateral prefrontal cortex (dlPFC), nucleus accumbens (NAcc), insula, anterior cingulate cortex (ACC), and orbitofrontal cortex (Liu, Hairston, Schrier, & Fan, 2011; Luijten et al., 2017; Oldham et al., 2018). However, there is less consensus on the neural correlates of aversive anticipation, because there is no meta-analysis of the literature on this anticipation subtype. Considering the utility of aversive anticipation and its association with anxiety disorders (Grupe & Nitschke, 2013; Tovote, Fadok, & Lüthi, 2015), it is important to understand the underlying neural mechanisms associated with aversive anticipation.

Most studies on aversive anticipation have compared fMRI blood oxygen level dependent (BOLD) activity for aversive and neutral anticipatory periods. The task design employed typically features a cue followed by a timed anticipatory period before the anticipated stimulus is presented. Different cues indicate whether the forthcoming

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✉ Joshua M. Carlson
joshcarl@nmu.edu

[1] Department of Psychological Science, Northern Michigan University, Marquette, MI, USA

[2] Department of Psychiatry, University of Pittsburgh School of Medicine, Pittsburgh, PA, USA

stimulus will be aversive or neutral and thus leads to two different anticipation trial types. The BOLD data collected in these two trial types are compared to identify structures with increased activity during aversive anticipation (or vice versa). This neuroimaging research has implicated a number of structures in aversive anticipation, including the insula (Dalton, Kalin, Grist, & Davidson, 2005; Nitschke, Sarinopoulos, Mackiewicz, Schaefer, & Davidson, 2006; Onoda et al., 2008; Phelps et al., 2001; Simmons, Matthews, Stein, & Paulus, 2004; Waugh, Fredrickson, & Taylor, 2008), amygdala (Nitschke et al., 2006; Onoda et al., 2008; Phelps et al., 2001), and prefrontal cortex (PFC), comprising the medial, dorsolateral, orbitofrontal, and ventrolateral cortices, as well as the ACC (Nitschke et al., 2006; Onoda et al., 2008; Simmons et al., 2004; Simpson, Drevets, Snyder, Gusnard, & Raichle, 2001; Straube, Mentzel, & Miltner, 2007).

There is, however, a lack of consensus regarding the neural correlates of aversive anticipation—primarily due to the absence of a meta-analytic synthesis of the existing findings, unlike meta-analyses that exist for anticipation of reward versus loss (Liu et al., 2011; Luijten et al., 2017) as well as anticipation of pain (Palermo, Benedetti, Costa, & Amanzio, 2015). While the anterior insula (AI) has been consistently implicated, the role of the other areas is less clear, with inconsistent findings between studies. A potential reason for these inconsistent findings is that various aversive stimuli across multiple sensory modalities have been used to study aversive anticipation, including: auditory tones (Carlson, Greenberg, Rubin, & Mujica-Parodi, 2011; Bolstad et al., 2013), electric shocks (Chua, Krams, Toni, Passingham, & Dolan, 1999; Seidel et al., 2015), noxious heat stimuli (Smith et al., 2002; Seifert et al., 2013), tasting liquids (O'Doherty, Deichmann, Critchley, & Dolan, 2002; Liljeholm, Dunne, & O'Doherty, 2014), aversive visual images (Nitschke et al., 2006; Grupe, Oathes, and Nitschke, 2013), phobic-based visual images (Simmons et al., 2004; Straube et al., 2007), and movies (Greenberg, Carlson, Rubin, Cha, & Mujica-Parodi, 2015).

The purpose of this investigation was to provide a more comprehensive analysis of the neural structures involved in periods of anxious/aversive anticipation. To this end, we conducted activation likelihood estimation (ALE) meta-analyses on studies of aversive anticipation to identify (1) core areas commonly activated in aversive anticipation across sensory modalities and (2) secondary areas uniquely activated in a sensory-specific manner. The ALE-meta analysis was complemented by two supplementary approaches (i.e., Neurosynth and a combined voxel-wise analysis of three previously published fMRI datasets; Carlson et al., 2011; Carlson & Mujica-Parodi, 2010; Greenberg et al., 2015) to demonstrate convergence across methodological approaches for a core circuit involved in aversive anticipation.

Methods

Activation likelihood estimation meta-analysis

The activation likelihood estimation (ALE) analysis was performed using the meta-analytic software package BrainMap GingerALE (version 2.3.6, http://brainmap.org; Eickhoff et al., 2009; Eickhoff, Bzdok, Laird, Kurth, & Fox, 2012; Turkeltaub et al., 2012). GingerALE synthesizes coordinates from fMRI studies and utilizes a random effects algorithm (Eickhoff et al., 2009) to look for foci of consensus across experimental groups/contrasts. The benefit of the random effects algorithm is that it also considers the amount of subjects within each experiment to calculate more accurately the Full-Width Half-Maximum (FWHM) of a Gaussian probability distribution; more subjects in a study results in increased certainty and reduced FWHM, leading to increased likelihood that activation occurred in a specific voxel (Eickhoff et al., 2009; Eickhoff et al., 2012).

Identification and selection of studies Database searches were conducted using the following keywords in conjunction with "fMRI": "aversive and anticipation," "negative anticipation," "pain and anticipation," "anxious and anticipation," "aversion," "anticipatory," and "anxious." Keywords were selected based on their common occurrence in article titles and abstracts and were intended to provide a selection of studies for review and possible inclusion in the ALE meta-analysis. Database searches resulted in 113 studies, which were subsequently manually examined in-depth to determine eligibility with the following exclusionary criteria: a) did not focus on aversive anticipation (n = 19); b) contained no fMRI measure of anticipatory periods (n = 15); c) did not use fMRI (n = 7); d) involved drug administration to investigate effects on aversive anticipation (n = 2); e) reanalysis of previous datasets (n = 2); f) review article (n = 2); and/or g) did not provide any coordinates (n = 3). This resulted in 63 studies included for analysis.

ALE Analysis The 63 studies that were included for analyses were then manually examined, and any foci that were reported via contrasts of aversive anticipation activation over either neutral or positive anticipation were included. To conform to GingerALE formatting requirements, each of these contrasts was specified in a .txt file format with the reference space, number of subjects in the contrast, and the resulting foci. These files were then separately verified by another researcher (JA).

All studies that were reported in Talairach coordinate space were converted into Montreal Neurological Institute (MNI) space with the Lancaster transform (Lancaster et al., 2007), a transform that has been shown to be more reliable in reducing spatial disparity between these two coordinate spaces

when compared to the Brett transform (Laird et al., 2010). Once all of these studies were in MNI space and compiled, two separate ALE analyses were performed: one single dataset analysis for overall aversive anticipation regardless of stimulus type, and separate analysis for conjunctive and subtractive analyses involving aversive anticipation of tactile and visual stimuli. Comparisons between tactile (n = 26) and visual (n = 31) aversive anticipation were the only sensory modalities that could be compared, due to the small number of studies involving auditory (n = 3) and gustatory (n = 2) anticipation.

Each analysis was conducted with the nonadditive method, which calculates modeled activation (MA) maps by finding the maximum activation across each foci's Gaussian distribution (Turkeltaub et al., 2012). All of the MA maps are combined with the foci, the Gaussian blur, and the FWHM in order to create an ALE image. The ALE image determines the null distribution of activation estimates and is subsequently compared to the MA maps in order to calculate p values for each of the ALE scores (Eickhoff et al., 2012).

The resulting p values were then subjected to significance thresholds with a minimum cluster size of 200 mm^3. For the single dataset analyses, a conservative False Discover Rate (FDR) threshold (Genovese, Lazar, & Nichols, 2002; Laird et al., 2005) of $p < .05$ was used. For the analysis contrasting and comparing tactile and visual aversive anticipation, both a FDR $p < 0.05$ and an uncorrected threshold of $p < 0.005$ were used. Additionally, these subtractive and conjunctive analyses were subjected to 5,000 p-value permutations; these permutation numbers and thresholds have been used in a previous ALE meta-analysis (Oldham et al., 2018). P value permutations are used to collate ALE values and provide a more accurate statistical inference in differences between contrasts with Z scores being obtained for each voxel (Eickhoff et al., 2011). All visualizations of the ALE results were done using Multi-image Analysis GUI (Mango; http://ric.uthscsa.edu/mango).

Neurosynth meta-analysis

Neurosynth was used to create a custom meta-analysis of aversive anticipation. Neurosynth's literature database includes (as of July 2018) 11,406 studies. Neurosynth is an online platform that allows users to automatically synthesize the results of many different neuroimaging studies. Neurosynth was created as a way to analyze large amounts of data as a result of the advancement of non-invasive neuroimaging techniques (Yarkoni, Poldrack, Nichols, Van Essen, & Wager, 2011).

Identification and selection of studies Database searches were conducted using the same keywords and exclusionary criteria as the ALE analysis. The remaining 36 studies were included in the NeuroSynth analysis (see NeuroSynth supplementary materials for more details), which included 965 participants (female = 523), included both healthy and anxious samples, and utilized a variety of fMRI anticipation protocols (see Supplmentary Table S1 for more details on each included study). These 36 studies were also included in the ALE analysis.

Voxel-wise analysis of previously published datasets

Description of studies A voxel-wise analysis was conducted across three (N = 80, female = 51) fMRI datasets (Carlson et al., 2011, n = 35, age = 23.91 ± 6.64 years; Carlson & Mujica-Parodi, 2010, n = 20, age = 23.91 ± 6.64 years; Greenberg et al., 2015, n = 25, age = 21.6 ± 5.1 years) to test for common and distinct activity in anticipation of aversive sounds, images, and videos. While the detailed methods of each individual study can be seen in their respective publications, they will be explained briefly here. Each of the three studies featured affective stimuli (i.e., sounds, images, or videos) preceded by cues followed by a sixteen second countdown indicating subsequent stimulus presentation. The studies varied in stimulus type, featuring aversive and neutral tones (Carlson et al., 2011), International Affective Picture System (IAPS; Lang, Bradley, & Cuthbert, 1997) aversive and neutral images (Carlson & Mujica-Parodi, 2010) and positive, aversive, uncertain, and neutral video clips (Greenberg et al., 2015). Anticipatory periods were measured during the countdown period (always 16 sec) in each methodology utilizing fMRI, and it was these segments of aversive anticipation that were of interest for this analysis. These studies were also included in the ALE analysis.

Preprocessing and analysis MRI data were preprocessed with SPM12, which included image realignment for head movement corrections, slice timing corrections for order of slice acquisition, normalization to standard 2 × 2 × 2 mm MNI space, and spatial smoothing Gaussian 6-mm filter. Preprocessed images were entered into a general linear model with regressors for each anticipation period and stimulus onset for aversive and neutral stimuli. Additionally, six rigid body motion parameters were included as regressors of no interest. Serial autocorrelations were modeled with an autoregressive (AR) process. First-level single subject statistical parameter maps were created for the aversive > neutral anticipation contrast. In order to investigate areas of activation associated with anxious anticipation, a t-test for common activity in the aversive > neutral anticipation contrast was conducted at a family-wise error (FWE) rate of $p < 0.05$, and cluster size of $k \geq 20$. Additional contrasts to investigate sensory-specific activations were also performed (visual > auditory and auditory > visual) at a FWE rate of $p < 0.05$, and cluster size of $k \geq 20$.

Analysis comparing ALE and voxel-wise analysis

To compare the ALE and voxel-wise analyses, the ALE file was used as a mask to constrain the space and the coordinates of the peak z-score were used as input for a 6-mm sphere small volume correction (SVC) on the voxel-wise dataset. Images were initially thresholded at an uncorrected $p < 0.001$, and clusters resulting in a SVC $p < 0.05$ FWE were considered significant.

Results

ALE results

The single dataset analysis for overall aversive anticipation involved 963 foci across 104 contrasts involving 2,587 participants; the results can be observed in Table 1 and Fig. 1. These results suggest that overall aversive anticipation involves the AI, caudate, thalamus, amygdala, mid-cingulate cortex (MCC), ACC, and parahippocampal gyrus.

The conjunctive and subtractive analyses involved 434 foci across 40 contrasts with 995 participants in tactile aversive anticipation while visual aversive anticipation featured 364 foci across 47 contrasts with 1232 participants for a combined total of 798 foci across 87 contrasts with 2,227 participants. At the FDR $p < 0.05$ threshold, two separate clusters in the conjunction analyses were seen in the AI (38, 22, 0; 40, 24, 0) with ALE values of 0.02427 and 0.02226 with volumes (in mm^3) of 16 and 8, respectively. The results of the uncorrected $p < 0.005$ threshold images can be observed in Tables 2-4 and Fig. 2. Tactile anticipation demonstrated higher activation in the thalamus, the red nucleus of the midbrain, the post-central gyrus, as well as the right AI, right medial frontal gyrus (MFG), and right middle temporal gyrus (MTG) compared with visual anticipation (Table 2; Fig. 2). Visual anticipation featured higher activation likelihoods in the left parahippocampal gyrus, bilateral amygdala, right subcallosal gyrus, and bilateral MFG (Table 3, Fig. 2). The conjunctive analysis demonstrated activation likelihoods in the AI, claustrum, thalamus, fusiform gyrus, basal ganglia, inferior parietal lobule, and the left precentral gyrus and right supramarginal gyrus (Table 4; Fig. 2).

Neurosynth results

Analysis of the 36 included studies for the Neurosynth can be observed in Supplementary Materials (Supplementary Table S2; Figure S1); results from this analysis suggest that anticipatory activity is seen in the bilateral AI, amygdala, caudate nucleus, ACC, MCC, MFG, as well as the left mOFC and right inferior frontal gyrus (IFG).

Voxel-wise results

Results from the voxel-wise analysis revealed widespread activity in the bilateral AI, dorsolateral prefrontal cortex, MCC, right medial supplementary motor area, premotor area, left inferior occipital cortex, right superior occipital cortex, auditory cortex, and postcentral gyrus (Table 5; Fig. 3). Results in both sensory contrasts (auditory > visual and visual > auditory) yielded no significant sensory-specific results. Results in the opposite contrast of neutral > aversive yielded no significant results.

Comparison of ALE and voxel-wise analyses

Results from the comparison analysis suggest areas of consensus within the bilateral AI, amygdala, caudate, and MCC (Table 6).

Table 1 Overall anticipation ALE results at FDR $p < 0.05$

Region	Hemisphere	MNI coordinates			ALE (10^{-3})	Volume (mm^3)
		X	Y	Z		
Amygdala	Right	22	-2	-14	42.71	3920
Caudate body	Right	12	4	12	37.38	
Caudate head	Right	10	6	-4	36.86	
Thalamus	Right	10	-12	4	35.43	
Thalamus	Right	8	-4	2	30.88	
Anterior insula	Right	36	26	0	64.29	3392
Anterior insula	Left	-32	22	8	54.18	2608
Claustrum	Left	-32	22	-6	41.90	
Amygdala	Left	-20	-2	-14	49.84	1344
Mid cingulate	Left	2	18	34	39.27	848
Anterior cingulate	Right	4	32	-6	39.28	360
Caudate body	Left	-10	0	14	35.47	360
Parahippocampal gyrus	Right	28	-52	-10	33.40	208

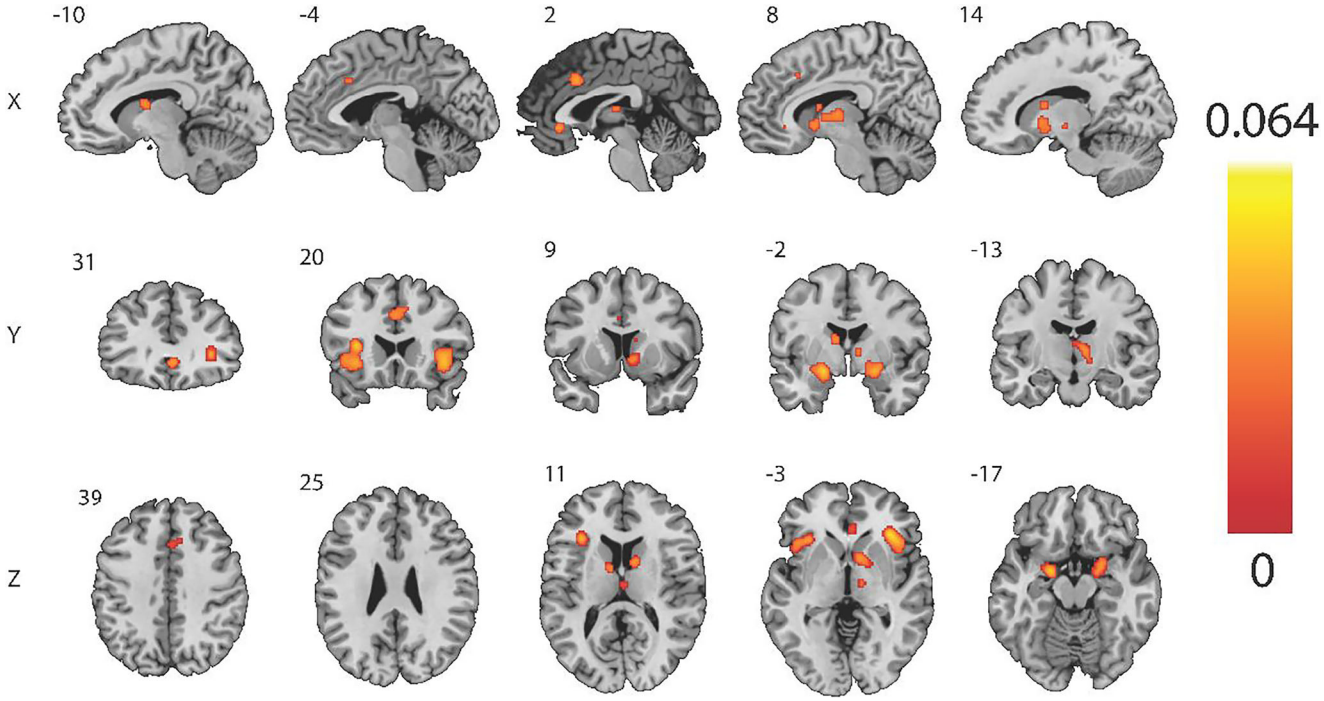

Fig. 1. ALE results for overall aversive anticipation. Bar on the right indicates the range of ALE values

Discussion

The purpose of this investigation was to use meta-analytic and integrative voxel-wise approaches to identify areas of common and unique activity in aversive anticipation across a variety of sensory modalities. ALE meta-analysis results provide evidence for a core circuit involved in aversive anticipation including the AI, amygdala, ACC, MCC, thalamus, and caudate nucleus (Fig. 1). A direct comparison between anticipation of aversive tactile and visual stimuli (which were the two most common sensory modalities utilized in the aversive anticipation literature) indicate that there are both similarities and differences across sensory modalities (Fig. 2). In particular, conjunction analysis indicates that the AI, thalamus, caudate, and a number of other regions are commonly engaged across sensory modalities. On the other hand, anticipation of aversive visual stimuli was associated with greater activation in the amygdala and MFG, whereas anticipation of aversive tactile stimuli resulted in greater activation in the midbrain, thalamus, somatosensory cortex, insula, and several other regions. Results from complementary multi-study voxel-wise and NeuroSynth analyses generally provide converging evidence for a core circuit involved in aversive anticipation (Supplementary Figure S2). Yet, the multi-study voxel-wise

Table 2 Tactile > visual anticipation ALE contrast at uncorrected $p < 0.005$

Region	Hemisphere	MNI coordinates			ALE (10^{-3})	Volume (mm^3)
		X	Y	Z		
Thalamus	Right	9	-14	1	3540.08	2304
Mammillary body	Right	14	-16	-2	3238.88	
Thalamus	Right	6	-16	0	3155.91	
Red nucleus of midbrain	Right	5	-24	-12	2820.16	
Red nucleus of midbrain	Right	5	-20	-8	2747.78	
Postcentral gyrus	Left	-61.5	-23.9	22.9	2947.84	1056
Postcentral gyrus	Left	-60.3	-20	17.7	2706.48	
Postcentral gyrus	Left	-54	-22	18	2589.91	
Claustrum	Right	44	6	5	3238.88	528
Anterior insula	Right	44	11	8	2770.33	
Thalamus	Left	-10	-2	8	3352.80	456
Middle temporal gyrus	Right	60	-38	-2	3035.67	240
Middle temporal gyrus	Right	60	-40	4	2911.24	
Medial frontal gyrus	Right	4	44	30	3352.80	240

Table 3 Visual > tactile anticipation ALE contrast at uncorrected $p < 0.005$

Region	Hemisphere	MNI coordinates			ALE (10^{-3})	Volume (mm^3)
		X	Y	Z		
Parahippocampal gyrus	Left	-17.7	-9.4	-26.9	3719.02	1384
Amygdala	Left	-20	-7	-19	3155.91	
Amygdala	Right	26	-2	-16	2988.88	288
Amygdala	Right	30	-2	-16	2911.24	
Subcallosal gyrus	Right	30	2	-16	2878.16	
Subcallosal gyrus	Right	30	6	-18	2847.96	
Medial frontal gyrus	Right	5	58	-2	2947.84	208
Medial frontal gyrus	Left	1	54	2	2878.16	
Medial frontal gyrus	Right	6	52	4	2747.78	

results also implicate more widespread activity in the occipital cortex, superior/inferior parietal, dlPFC, supplementary motor area, auditory cortex, and somatosensory cortex.

Core neural circuitry for aversive anticipation

Our findings provide ALE meta-analytic evidence that the AI, amygdala, ACC, MCC, thalamus, and caudate are commonly involved in the anticipation of aversive stimuli across sensory modalities. Activation of this circuit enables an organism to prepare for an undesirable outcome and ready an action response. Previous research has frequently implicated the AI in aversive anticipation (Dalton et al., 2005; Nitschke et al., 2006; Onoda et al., 2008; Phelps et al., 2001; Simmons et al., 2004; Waugh et al., 2008), which we confirmed in our meta-analysis. Consistent with the notion that the AI is involved in aversive anticipation across a variety of sensory modalities, the insula receives thalamic input from all sensory modalities (Gogolla, 2017). These afferents include interoceptive signals of bodily states, which may underlie interoceptive and affective awareness (Craig, 2009; Critchley, Wiens, Rotshtein, Öhman, & Dolan, 2004; Menon & Uddin, 2010). This likely includes the feeling-state associated with anxious anticipation (Carlson et al., 2011). Current theory posits that the AI utilizes afferent sensory information to detect salience, appraise stimulus valence, evaluate risk, and predict likely outcomes (Greenberg et al., 2015; Grupe & Nitschke, 2013; Liu et al., 2011; Gogolla, 2017), which are all central to preparatory processing.

Beyond thalamic sensory inputs, the insula is highly connected — serving as an integrative hub across widespread brain regions including bidirectional connections with the thalamus, amygdala, ACC, MCC, as well as outputs to the caudate and other basal ganglia structures (Gogolla, 2017). These

Table 4 Conjunctive tactile and visual anticipation ALE analyses at uncorrected $p < 0.005$

Region	Hemisphere	MNI coordinates			ALE (10^{-3})	Volume (mm^3)
		X	Y	Z		
Anterior insula	Right	38	22	0	24.27	1936
Claustrum	Left	-34	20	-4	15.22	1216
Anterior insula	Left	-34	24	8	15.21	
Inferior frontal gyrus	Left	-42	20	-8	13.15	
Putamen	Left	-22	0	-12	17.37	288
Inferior frontal gyrus	Right	42	10	26	13.76	184
Thalamus	Left	-8	-12	0	12.31	168
Fusiform gyrus	Right	30	-56	-8	14.20	112
Caudate body	Left	-14	2	18	13.46	80
Caudate head	Right	8	6	-6	12.89	64
Claustrum	Right	40	-14	0	13.00	48
Putamen	Right	24	2	-8	10.93	24
Anterior insula	Left	-46	16	-2	11.02	16
Thalamus	Right	6	-4	0	11.26	16
Inferior parietal lobule	Right	50	-40	42	10.90	16
Lateral globus pallidus	Right	20	0	-10	11.16	8
Lateral globus pallidus	Right	22	2	-10	11.20	8
Lateral globus pallidus	Right	22	0	-8	11.47	8
Precentral gyrus	Left	-44	18	2	10.10	8
Supramarginal gyrus	Right	48	-40	40	11.59	8

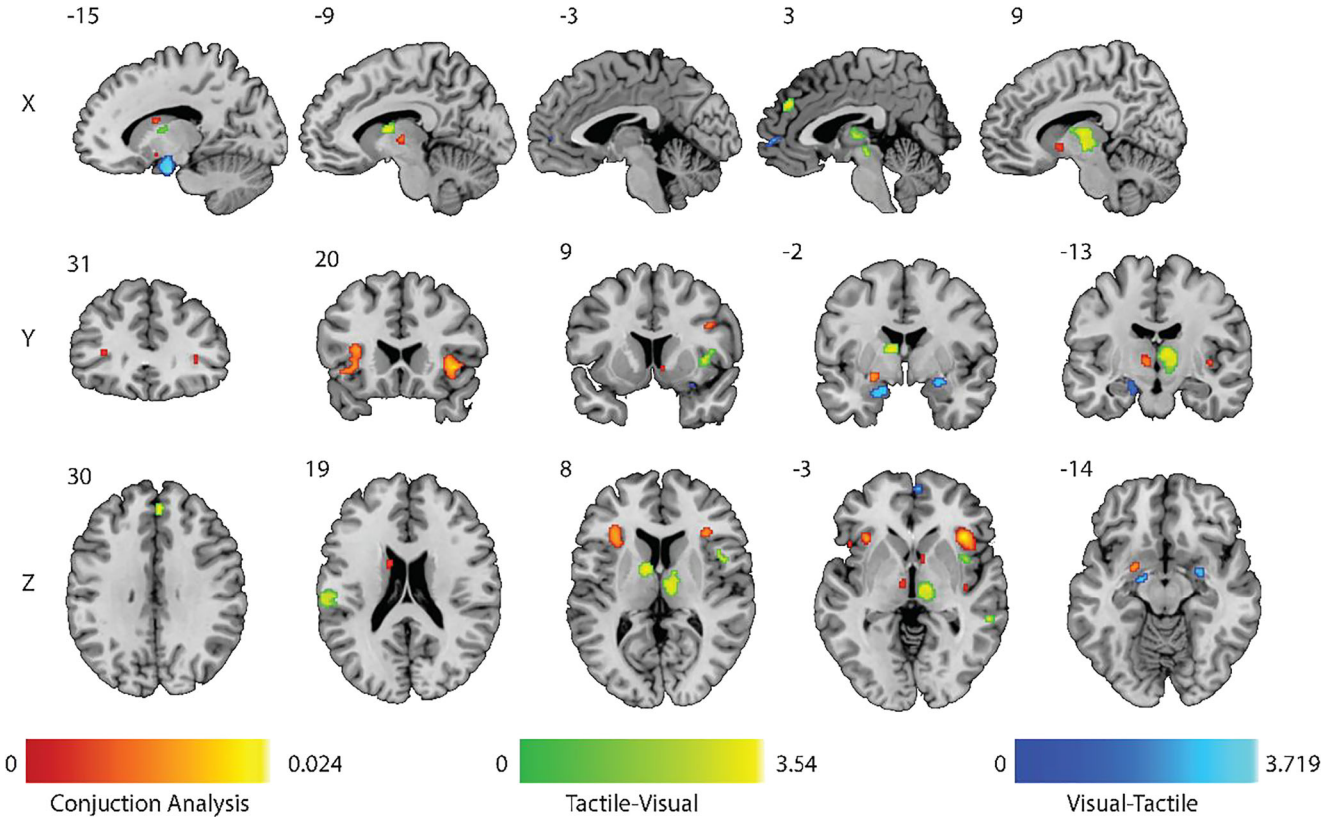

Fig. 2. ALE results (values represented as Z scores) for the tactile and visual conjunctive and subtractive analyses

integrative connections are aptly suited to allow the AI to mediate a coordinated anticipatory response in preparation of an impending aversive stimulus. In particular, the amygdala and MCC are thought to modulate and initiate appropriate defense responses (Grupe & Nitschke, 2013), including generation of autonomic nervous system responses (Critchley et al., 2003; Davis & Whalen, 2001). Additionally, the caudate nucleus is involved in initiating motor responses to affectively salient

Table 5 Results from voxel-wise analysis

Region	Hemisphere	MNI coordinates				Maximumvoxel	Peak voxel
		X	Y	Z	Cluster Size	T value	Z Score
Fusiform gyrus	Left	-28	-82	-16	592	6.11	5.59
Inferior occipital cortex	Left	-26	-92	-2	743	7.64	6.72
Inferior parietal lobule	Left	-34	-40	44	48	5.9	5.43
Anterior insula	Left	-32	26	6	51	6.81	6.13
	Right	44	14	-2	66	5.24	5.24
Lobule VI of Cerebellar hemisphere	Left	-32	-54	-34	242	6.68	6.03
	Right	24	-66	-18	46	5.98	5.49
Midcingulate area	Right	10	20	38	476	6.47	5.87
Supplementary Motor area[a]	Right	8	8	66		6.03	5.53
Middle frontal Gyrus	Left	-32	50	22	274	6.66	6.01
	Right	26	58	26	87	5.87	5.4
Middle occipital Gyrus	Left	-48	-74	2	29	5.47	5.09
Precentral gyrus	Left	-36	-4	46	108	5.91	5.44
Superior frontal Gyrus	Left	-22	4	68	20	5.68	5.25
Superior occipital	Right	24	-76	38	25	5.41	5.04
Superior parietal Lobule	Left	-26	-56	54	416	6.54	5.92
	Right	26	-54	64	220	5.83	5.37
Superior temporal Gyrus	Right	48	-26	4	28	6.2	5.66

[a] This region is a subcluster of the above cluster

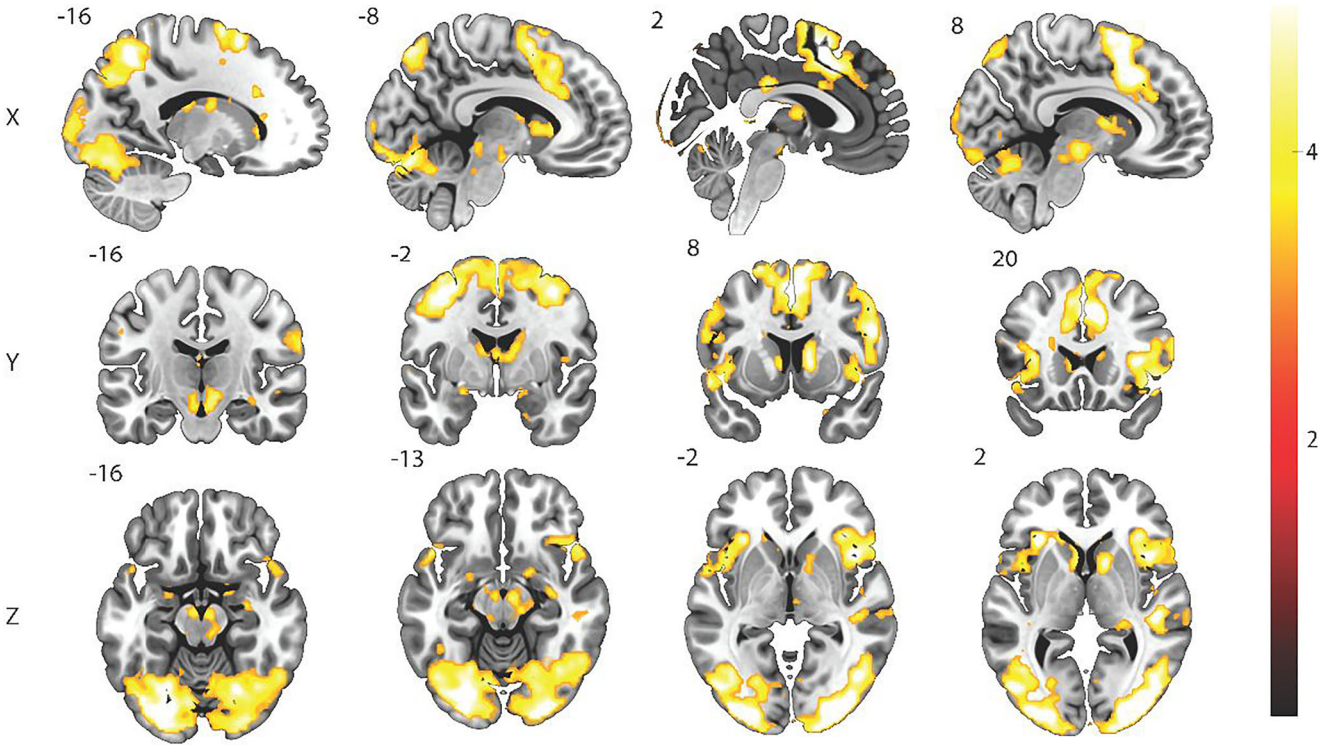

Fig. 3. Areas of activation for aversive anticipation relative to neutral anticipation from the voxel-wise analysis. For visualization purposes, results are displayed at a threshold of $p < 0.001$ uncorrected. Bar on the right indicates t values

stimuli (Rolls, 2000; Greenberg et al., 2015). Thus, in the context of aversive anticipation, connections between the AI, amygdala, MCC, and caudate nucleus appear to represent a core network for initiating preparatory responses across autonomic and motor systems to a wide range of potential threats.

Results from our Neurosynth and multi-study voxel-wise analyses provide converging evidence that the AI, amygdala, ACC, MCC, thalamus, and caudate are commonly involved in the anticipation of aversive stimuli across sensory modalities (Fig. 3; Supplementary Table S3). However, the results from the multi-study voxel-wise analyses also implicate a more widespread preparatory response across sensory (visual, auditory, and somatosensory cortex), motor (supplementary motor area), and cognitive control regions (dlPFC). The reason for these discrepancies is unclear. However, one possibility is the relatively long anticipation period used in our multi-study voxel-wise analyses (i.e., 1 sec cue + 16 sec countdown). Comparatively, it is common for anticipation studies to have much shorter anticipation periods (e.g., 2-6 secs; Grupe, Wielgosz, Davidson, & Nitschke, 2016; Simmons et al., 2012; Yoshimura et al., 2014). Therefore, it is not unreasonable to speculate that the additional areas of widespread activation in the multi-study voxel-wise analysis are unique to the extended anticipation period used. Taken together, these results may indicate that during an extended period of aversive anticipation more widespread preparatory processes are engaged to better prepare the individual to confront the expected threat. Indeed, previous research has shown that the neural

Table 6 Regions of consensus activation from both the ALE and voxel-wise analyses

Region	Hemisphere	MNI coordinates			Voxels	Maximal voxel	Peak-level
		X	Y	Z		Z score	pFWE
Amygdala	Left	-22	-2	-14	25	3.63	0.004
	Right	18	0	-14	20	4.06	0.001
Caudate	Right	12	4	8	46	5.05	0.000
	Left	-10	-2	12	29	3.67	0.000
Anterior Insula	Left	-32	26	6	94	6.81	0.000
	Right	36	28	2	120	4.69	0.000
Midcingulate area	Left/right	6	20	38	66	5.30	0.000

substrates of aversive anticipation evolve over the duration of the anticipation period (Grupe et al., 2013; McMenamin, Langeslag, Sirbu, Padmala, & Pessoa, 2014). However, this broad preparatory response may also be accompanied by a (secondary) sensory specific response.

Sensory-specific neural circuitry for aversive anticipation

The two most common sensory modalities within the aversive anticipation literature were visual (31 studies) and tactile (26 studies). Within these two sensory modalities, there were more similarities than differences in the neural circuity associated with anticipation of aversion across their respective sensory modalities. Indeed, conjunction analyses indicate that the AI, thalamus, caudate, and a number of other regions are commonly engaged across visual and tactile sensory modalities (Table 3; Fig. 2). However, sensory-specific differences were found. In particular, anticipation of aversive visual (relative to tactile) stimuli was associated with greater activation in the amygdala and MFG (BA 10). Conversely, anticipation of aversive tactile (relative to visual) stimuli was associated with greater activation in the thalamus, midbrain, somatosensory cortex, AI, MTG, and MFG (BA 9). Thus, anticipation of aversive tactile stimuli appears to recruit distinct (or at least greater) activation in sensory specific regions (i.e., thalamus & somatosensory cortex). This pattern of results was not observed for the anticipation of aversive visual stimuli, which may be due to the recruitment of visual cortical processing across both sensory modalities (Table 3). Given that humans are a highly vision dominated species, it may be evolutionarily advantageous to initiate a preparatory facilitation of visual cortical processing regardless of the threat domain as detection of a visual stimulus may allow for avoidance of the threat. An additional consideration is the nature of the cue, which often is visual and may therefore recruit visual processing resources even when the anticipated aversive stimulus is in another sensory modality. These findings also indicate that the amygdala is less involved in the anticipation of aversive tactile stimuli, which is consistent with a prior meta-analysis of pain anticipation showing deactivation of the amygdala (Palermo et al., 2015).

Many of the structures implicated by our meta-analysis in aversive tactical anticipation (i.e., AI, thalamus, midbrain, MTG, and mPFC/BA 9) are consistent with the results of an earlier meta-analyses on pain anticipation (Palermo et al., 2015). However, two notable differences were observed. First, Palermo et al. (2015) found increased activation in the MCC in their meta-analysis of pain anticipation. MCC activity was not observed in our ALE meta-analytic tactile > visual aversive anticipation contrast but was implicated in our ALE meta-analysis across all sensory modalities. This pattern of results suggests that the role of the MCC during aversive anticipation is not pain specific, but more general (e.g., initiation/modulation of the autonomic response to threat). Second, we found increased activity in the somatosensory cortex in anticipation of aversive tactile stimuli, which was not observed in the meta-analysis by Palermo et al. (2015). This may either be due to the fact that our meta-analysis includes a number of studies published since the Palermo et al. (2015) meta-analysis, or because we included a comparison with aversive visual anticipation. Regardless, our meta-analytic results add novel insight into the role of these two structures during aversive anticipation: (1) the involvement of the MCC in aversive anticipation is not specific to pain, and (2) anticipation of aversive tactile stimuli recruits somatosensory cortex.

An unexpected finding was that anticipation of aversive visual and tactile stimuli recruit distinct regions of the MFG/mPFC (i.e., BA 10 & BA 9, respectively). This may indicate that distinct sub-regions of mPFC are coded in a sensory specific manner. The mPFC is reciprocally connected with the AI (Gogolla, 2017) and may — speculatively — be the node(s) in which sensory specific anticipatory responses are recruited. Yet, this hypothesis remains untested. More research directly comparing the neural systems engaged in aversive anticipation across multiple sensory modalities is needed to directly test this hypothesis. Regardless, our ALE meta-analysis findings suggest that distinct regions of the mPFC are recruited during the anticipation of aversive tactile and visual stimuli.

Although gustatory and auditory anticipation have been studied with fMRI, the number of studies (2 and 3, respectively) in these areas is not sufficient for meta-analysis and to the best of our knowledge no research has explored the anticipation of aversive olfactory stimuli. We expect that across these sensory modalities that both core anticipation and sensory specific regions will be involved. Our multistudy voxel-wise analysis comparing differences in visual and auditory aversive anticipation did not reveal any significant differences. However, this may be due to this analysis being underpowered. Further research is needed to better understand the common and distinct structures involved in aversive anticipation across auditory, gustatory, and olfactory sensory modalities. We anticipate that the results and masks made available through this meta-analysis will assist in such future research.

Comparison to reward anticipation

To elucidate these results further in the context of aversive anticipation, they should be compared to recent meta-analyses of reward anticipation (Liu et al., 2011; Luijten et al., 2017; Oldham et al., 2018). Our meta-analytic results implicate the AI, thalamus, amygdala, MFG, and ACC, which

are all also reported in the anticipation of reward (Liu et al., 2011; Luijten et al., 2017). Furthermore, experimental evidence directly comparing aversive and reward anticipation has implicated activity within the AI, thalamus, caudate, ACC, and PFC in anticipation of aversive and rewarding video stimuli (Greenberg et al., 2015). Therefore, it appears that these areas comprise a universal anticipatory system.

Additional regions of activation are also seen in anticipation of reward that are not seen in aversive anticipation, such as the NAcc/ventral striatum and mPFC (Greenberg et al., 2015; Liu et al., 2011; Luijten et al., 2017). The NAcc and mPFC are part of the mesolimbic and mesocortical dopamine circuits, respectively (Liu et al., 2011). NAcc activity has been shown to mediate positive and negative outcomes related to reward, with the mPFC providing additional facilitation of response selection (Greenberg et al., 2015; Knutson & Greer, 2008). The ventral striatum has been associated with the assessment of valence for positive/rewarding events and is also associated with the value representation and anticipation of reward, which contributes to reward-related approach behavior (Liu et al., 2011; Knutson & Greer, 2008). These findings compared with our own suggest that there are separate and distinct neural systems for the anticipation of positive or aversive outcomes.

Limitations, strengths, and future directions

Some caveats and limitations to these results need to be considered. First, the nature of our analyses indicate that these structures are involved in aversive anticipation but do not provide information about the functional significance of these structures or the dynamic communication between these structures during anxious anticipation (Mujica-Parodi, Carlson, Cha, & Rubin, 2014; Mujica-Parodi, Cha, & Gao, 2017). Additionally, the studies included in the multi-study voxel-wise analyses all contained anticipation periods with a one second fixation cue followed by a sixteen second anticipatory countdown. However, the anticipation periods in the ALE meta-analysis varied much more widely. Thus, this discrepancy may account for differences observed across the two approaches. This is of potential concern considering that research into the time-course of aversive anticipation demonstrates different areas of activation are dependent upon the anticipatory phase (early, middle, or late; McMenamin et al., 2014. Future research that features longer anticipation periods is needed to determine (at a meta-analytic level) if there is any variation in activations/deactivations over periods of sustained anticipation.

A major strength of this work is that it represents the first ALE-based meta-analysis of aversive anticipation considering both common and unique anticipatory activation across sensory modalities. In an effort to guide future research in aversive anticipation, the ALE files of our results are available for download to be used as masks for region of interest analyses (see Supplementary Materials). Such *a priori* masks could be used to facilitate investigations into aversive anticipation in studies that have smaller sample sizes such as clinical studies into PTSD and anxiety, or studies that look into how pharmacological interventions can reduce hyperactive aversive anticipation as a method of treatment (Acheson et al., 2012; Aupperle et al., 2011). Additionally, the diverse methods used by the studies included in our meta-analyses can be seen as a strength, as it provides evidence for the neural mechanisms of aversive anticipation as observed across a wide variety of operationalizations. This provides evidence for the neural correlates of aversive anticipation independent of the duration of anticipation and consequence of anticipation. The understanding of the areas of activation featured in aversive anticipation across multiple sensory modalities identified in the current meta-analysis can inform future investigations and enable modality-specific anticipation distinctions to be made. It should be noted, however, that very few fMRI studies of aversive anticipation have utilized aversive stimuli in the gustatory (2; Liljeholm et al., 2014; O'Doherty et al., 2002), auditory (3; Bolstad et al., 2013; Carlson et al., 2011; Simmons et al., 2012), or olfactory (0) domains. Future fMRI research is needed in these areas of aversive anticipation to better understand the sensory-specific responses that may occur in these domains.

Conclusions

When utilizing both the meta-analytic approach as well as a combined multi-study voxel-wise analysis, the AI, amygdala, ACC, MCC, thalamus, and caudate were identified as structures that comprise a core network involved in aversive anticipation across a variety of sensory modalities. In addition, direct comparison of aversive anticipation for tactile and visual stimuli identified regions involved in sensory specific aversive anticipation across these modalities (Tables 2-3). Our identification of common and distinct activation will aid future anticipation research by providing evidence for *a priori* region of interest analyses. In an effort to aid these future analyses, the masks of our results are available for download (see *Supplementary Materials*).

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References

References marked with an asterisk indicate studies included in the ALE meta-analysis. References marked with a double asterisk were included in both the ALE analysis and the Neurosynth analysis.

Acheson, D. T., Stein, M. B., Paulus, M. P., Ravindran, L., Simmons, A. N., Lohr, J. B., & Risbrough, V. B. (2012). Effects of anxiolytic treatment on potentiated startle during aversive image anticipation. *Human Psychopharmacology*, *27*(4), 419–427. https://doi.org/10.1002/hup.2243

Aupperle, R. L., Tankersley, D., Flagan, T., Ravindran, L., Paulus, M. P., Stein, N. R., … Stein, M. B. (2011). Pregabalin influences insula and amygdala activation during anticipation of emotional images. *Neuropsychopharmacology*, *36*(7), 1466–1477. https://doi.org/10.1038/npp.2011.32

**Bolstad, I., Andreassen, O. A., Reckless, G. E., Sigvartsen, N. P., Server, A., & Jensen, J. (2013). Aversive event anticipation affects connectivity between the ventral striatum and the orbitofrontal cortex in an fMRI avoidance task. *PLoS ONE, 8*(6), e68494. https://doi.org/10.1371/journal.pone.0068494

*Carlson, J. M., & Mujica-Parodi, L. R. (2010). A disposition to reappraise decreases anterior insula reactivity during anxious anticipation. *Biological Psychology, 85*(3), 383–385. https://doi.org/10.1016/j.biopsycho.2010.08.010

**Carlson, J. M., Greenberg, T., Rubin, D., & Mujica-Parodi, L. R. (2011). Feeling anxious: Anticipatory amygdalo-insular response predicts the feeling of anxious anticipation. *Social Cognitive and Affective Neuroscience, 6*(1), 74–81. https://doi.org/10.1093/scan/nsq017

Chua, P., Krams, M., Toni, I., Passingham, R., & Dolan, R. (1999). A functional anatomy of anticipatory anxiety. *NeuroImage*, *9*(6 I), 563–571. https://doi.org/10.1006/nimg.1999.0407

Craig, A. D. (2009). How do you feel - now? The anterior insula and human awareness. *Nature Reviews Neuroscience*, *10*(1), 59–70. https://doi.org/10.1038/nrn2555

Critchley, H. D., Mathias, C. J., Josephs, O., O'Doherty, J., Zanini, S., Dewar, B. K., … Dolan, R. J. (2003). Human cingulate cortex and autonomic control: Converging neuroimaging and clinical evidence. *Brain, 126*(10), 2139–2152. https://doi.org/10.1093/brain/awg216

Critchley, H. D., Wiens, S., Rotshtein, P., Öhman, A., & Dolan, R. J. (2004). Neural systems supporting interoceptive awareness. *Nature Neuroscience, 7*(2), 189–195. https://doi.org/10.1038/nn1176

Dalton, K. M., Kalin, N. H., Grist, T. M., & Davidson, R. J. (2005). Neural-cardiac coupling in threat-evoked anxiety. *Journal of Cognitive Neuroscience*, *17*(6), 969–980. https://doi.org/10.1162/0898929054021094

Davis, M., & Whalen, P. J. (2001). The amygdala: Vigilance and emotion. *Molecular Psychiatry*, *6*(1), 12-34. https://doi.org/10.1038/sj.mp.4000812

Dichter, G. S., Kozink, R. V., McClernon, F. J., & Smoski, M. J. (2012). Remitted major depression is characterized by reward network hyperactivation during reward anticipation and hypoactivation during reward outcomes. *Journal of Affective Disorders*, *136*(3), 1126–1134. https://doi.org/10.1016/J.JAD.2011.09.048

Eickhoff, S. B., Bzdok, D., Laird, A. R., Kurth, F., & Fox, P. T. (2012). Activation likelihood estimation meta-analysis revisited. *NeuroImage*, *59*(3), 2349–2361. https://doi.org/10.1016/j.neuroimage.2011.09.017

Eickhoff, S. B., Bzdok, D., Laird, A. R., Roski, C., Caspers, S., Zilles, K., & Fox, P. T. (2011). Co-activation patterns distinguish cortical modules, their connectivity and functional differentiation. *NeuroImage*, *57*(3), 938–949. https://doi.org/10.1016/j.neuroimage.2011.05.021

Eickhoff, S. B., Laird, A. R., Grefkes, C., Wang, L. E., Zilles, K., & Fox, P. T. (2009). Coordinate-based activation likelihood estimation meta-analysis of neuroimaging data: A random-effects approach based on empirical estimates of spatial uncertainty. *Human Brain Mapping*, *30*(9), 2907–2926. https://doi.org/10.1002/hbm.20718

Genovese, C. R., Lazar, N. A., & Nichols, T. (2002). Thresholding of statistical maps in functional neuroimaging using the false discovery rate. *NeuroImage*, *15*(4), 870–878. https://doi.org/10.1006/nimg.2001.1037

Gogolla, N. (2017). The insular cortex. *Current Biology*, *27*(12), R580-R586. https://doi.org/10.1016/j.cub.2017.05.010

**Greenberg, T., Carlson, J. M., Rubin, D., Cha, J., & Mujica-Parodi, L. (2015). Anticipation of high arousal aversive and positive movie clips engages common and distinct neural substrates. *Social Cognitive and Affective Neuroscience, 10*(4), 605–611. https://doi.org/10.1093/scan/nsu091

Grupe, D. W., & Nitschke, J. B. (2013). Uncertainty and anticipation in anxiety: An integrated neurobiological and psychological perspective. *Nature Reviews Neuroscience*, *14*(7), 488–501. https://doi.org/10.1038/nrn3524

**Grupe, D. W., Oathes, D. J., & Nitschke, J. B. (2013). Dissecting the anticipation of aversion reveals dissociable neural networks. *Cerebral Cortex, 23*(8), 1874–1883. https://doi.org/10.1093/cercor/bhs175

*Grupe, D. W., Wielgosz, J., Davidson, R. J., & Nitschke, J. B. (2016). Neurobiological correlates of distinct post-traumatic stress disorder symptom profiles during threat anticipation in combat veterans. *Psychological Medicine, 46*(9), 1885–1895.https://doi.org/10.1017/S0033291716000374

Knutson, B., & Greer, S. M. (2008). Anticipatory affect: Neural correlates and consequences for choice. *Philosophical Transactions of the Royal Society of London. Series B, Biological Sciences*, *363*(1511), 3771–3786. https://doi.org/10.1098/rstb.2008.0155

Laird, A. R., Fox, P. M., Price, C. J., Glahn, D. C., Uecker, A. M., Lancaster, J. L., … Fox, P. T. (2005). ALE meta-analysis: Controlling the false discovery rate and performing statistical contrasts. *Human Brain Mapping, 25*(1), 155–164 https://doi.org/10.1002/hbm.20136

Laird, A. R., Robinson, J. L., McMillan, K. M., Tordesillas-Gutiérrez, D., Moran, S. T., Gonzales, S. M., … Lancaster, J. L. (2010). Comparison of the disparity between Talairach and MNI coordinates in functional neuroimaging data: Validation of the Lancaster transform. *NeuroImage, 51*(2), 677–683. https://doi.org/10.1016/j.neuroimage.2010.02.048

Lancaster, J. L., Tordesillas-Gutiérrez, D., Martinez, M., Salinas, F., Evans, A., Zilles, K., … Fox, P. T. (2007). Bias between MNI and Talairach coordinates analyzed using the ICBM-152 brain template. *Human Brain Mapping, 28*(11), 1194–1205. https://doi.org/10.1002/hbm.20345

Lang, P.J., Bradley, M.M., & Cuthbert, B.N. (1997). *International affective picture system (IAPS): Technical manual and affective ratings*. Gainesville, FL: University of Florida.

**Liljeholm, M., Dunne, S., & O'Doherty, J. P. (2014a). Anterior insula activity reflects the effects of intentionality on the anticipation of aversive stimulation. *Journal of Neuroscience, 34*(34), 11339–11348. https://doi.org/10.1523/JNEUROSCI.1126-14.2014

Liu, X., Hairston, J., Schrier, M., & Fan, J. (2011). Common and distinct networks underlying reward valence and processing stages: A meta-analysis of functional neuroimaging studies. *Neuroscience and*

Biobehavioral Reviews, 35(5), 1219-1236. https://doi.org/10.1016/j.neubiorev.2010.12.012

Luijten, M., Schellekens, A. F., Kühn, S., Machielse, M. W. J., & Sescousse, G. (2017). Disruption of reward processing in addiction. *JAMA Psychiatry*, *74*(4), 387. https://doi.org/10.1001/jamapsychiatry.2016.3084

**McMenamin, B. W., Langeslag, S. J. E., Sirbu, M., Padmala, S., & Pessoa, L. (2014). Network organization unfolds over time during periods of anxious anticipation. *Journal of Neuroscience, 34*(34), 11261–11273. https://doi.org/10.1523/JNEUROSCI.1579-14.2014

Menon, V., & Uddin, L. Q. (2010). Saliency, switching, attention and control: A network model of insula function. *Brain Structure & Function, 214*(5-6), 655-667. https://doi.org/10.1007/s00429-010-0262-0

Mujica-Parodi, L. R., Carlson, J. M., Cha, J., & Rubin, D. (2014). The fine line between 'brave' and 'reckless': Amygdala reactivity and regulation predict recognition of risk. *NeuroImage*, *103*, 1–9. https://doi.org/10.1016/j.neuroimage.2014.08.038

Mujica-Parodi, L. R., Cha, J., & Gao, J. (2017). From anxious to reckless: A control systems approach unifies prefrontal-limbic regulation across the spectrum of threat detection. *Frontiers in Systems Neuroscience*, *11*, 18. https://doi.org/10.3389/fnsys.2017.00018

**Nitschke, J. B., Sarinopoulos, I., Mackiewicz, K. L., Schaefer, H. S., & Davidson, R. J. (2006). Functional neuroanatomy of aversion and its anticipation. *NeuroImage, 29*(1), 106–116. https://doi.org/10.1016/j.neuroimage.2005.06.068

O'Doherty, J. P., Deichmann, R., Critchley, H. D., & Dolan, R. J. (2002). Neural responses during anticipation of a primary taste reward. *Neuron*, *33*(5), 815–826. https://doi.org/10.1016/S0896-6273(02)00603-7

Oldham, S., Murawski, C., Fornito, A., Youssef, G., Yücel, M., & Lorenzetti, V. (2018). The anticipation and outcome phases of reward and loss processing: A neuroimaging meta-analysis of the monetary incentive delay task. *Human Brain Mapping*, *39*(8), 3398–3418. https://doi.org/10.1002/hbm.24184

**Onoda, K., Okamoto, Y., Toki, S., Ueda, K., Shishida, K., Kinoshita, A., … Yamawaki, S. (2008). Anterior cingulate cortex modulates preparatory activation during certain anticipation of negative picture. *Neuropsychologia, 46*(1), 102–110. https://doi.org/10.1016/j.neuropsychologia.2007.08.006

Palermo, S., Benedetti, F., Costa, T., & Amanzio, M. (2015). Pain anticipation: An activation likelihood estimation meta-analysis of brain imaging studies. *Human Brain Mapping*, *36*(5), 1648–1661. https://doi.org/10.1002/hbm.22727

Phelps, E. A., O'Connor, K. J., Gatenby, J. C., Grillon, C., Gore, J. C., & Davis, M. (2001). Activation of the human amygdala to a cognitive representation of fear. *Nature Neuroscience*, *4*(437), 437–441.

Rolls, E. T. (2000). On the brain and emotion. *Behavioral and Brain Sciences*, *23*(2), 219-228. https://doi.org/10.1017/S0140525X00512424

**Seidel, E.-M. M., Pfabigan, D. M., Hahn, A., Sladky, R., Grahl, A., Paul, K., … Lamm, C. (2015). Uncertainty during pain anticipation: The adaptive value of preparatory processes. *Human Brain Mapping, 36*(2), 744–755. https://doi.org/10.1002/hbm.22661

**Seifert, F., Schuberth, N., De Col, R., Peltz, E., Nickel, F. T., & Maihöfner, C. (2013a). Brain activity during sympathetic response in anticipation and experience of pain. *Human Brain Mapping, 34*(8), 1768–1782. https://doi.org/10.1002/hbm.22035

*Simmons, A. N., Fitzpatrick, S., Strigo, I. A., Potterat, E. G., Johnson, D. C., Matthews, S. C., … Paulus, M. P. (2012). Altered insula activation in anticipation of changing emotional states: Neural mechanisms underlying cognitive flexibility in special operations forces personnel. *NeuroReport, 23*(4), 234–239. https://doi.org/10.1097/WNR.0b013e3283503275

**Simmons, A., Strigo, I., Matthews, S. C., Paulus, M. P., & Stein, M. B. (2006). Anticipation of aversive visual stimuli is associated with increased insula activation in anxiety-prone subjects. *Biological Psychiatry, 60*(4), 402–409. https://doi.org/10.1016/j.biopsych.2006.04.038

Simpson, J. R., Drevets, W. C., Snyder, A. Z., Gusnard, D. A., & Raichle, M. E. (2001). Emotion-induced changes in human medial prefrontal cortex: II. During anticipatory anxiety. *Proceedings of the National Academy of Sciences*, *98*(2), 688–693. https://doi.org/10.1073/pnas.98.2.688

Smith, K. A., Ploghaus, A., Cowen, P. J., Mccleery, J. M., Goodwin, G. M., Smith, S., … Matthews, P. M. (2002). Cerebellar responses during anticipation of noxious stimuli in subjects recovered from depression. *British Journal of Psychiatry, 181*(05), 411–415. https://doi.org/10.1192/bjp.181.5.411

**Straube, T., Mentzel, H. J., & Miltner, W. H. R. (2007). Waiting for spiders: Brain activation during anticipatory anxiety in spider phobics. *NeuroImage, 37*(4), 1427–1436. https://doi.org/10.1016/j.neuroimage.2007.06.023

Tovote, P., Fadok, J. P., & Lüthi, A. (2015). Neuronal circuits for fear and anxiety. *Nature Reviews Neuroscience*, *16*(6), 317–331. https://doi.org/10.1038/nrn3945

Turkeltaub, P. E., Eickhoff, S. B., Laird, A. R., Fox, M., Wiener, M., & Fox, P. (2012). Minimizing within-experiment and within-group effects in activation likelihood estimation meta-analyses. *Human Brain Mapping*, *33*(1), 1–13. https://doi.org/10.1002/hbm.21186

Waugh, C. E., Fredrickson, B. L., & Taylor, S. F. (2008). Adapting to life's slings and arrows: Individual differences in resilience when recovering from an anticipated threat. *Journal of Research in Personality*, *42*(4), 1031–1046. https://doi.org/10.1016/j.jrp.2008.02.005

Yarkoni, T., Poldrack, R. A., Nichols, T. E., Van Essen, D. C., & Wager, T. D. (2011). Large-scale automated synthesis of human functional neuroimaging data. *Nature Methods*, *8*(8), 665–670. https://doi.org/10.1038/nmeth.1635

**Yoshimura, S., Okamoto, Y., Yoshino, A., Kobayakawa, M., Machino, A., & Yamawaki, S. (2014). Neural basis of anticipatory anxiety reappraisals. *PLoS ONE, 9*(7), e102836. https://doi.org/10.1371/journal.pone.0102836