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Review

Anticipatory affect: neural correlates and consequences for choice

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'Anticipatory affect' refers to emotional states that people experience while anticipating significant outcomes. Historically, technical limitations have made it difficult to determine whether anticipatory affect influences subsequent choice. Recent advances in the spatio-temporal resolution of functional magnetic resonance imaging, however, now allow researchers to visualize changes in neural activity seconds before choice occurs. We review evidence that activation in specific brain circuits changes during anticipation of monetary incentives, that this activation correlates with affective experience and that activity in these circuits may influence subsequent choice. Specifically, an activation likelihood estimate meta-analysis of cued response studies indicates that nucleus accumbens (NAcc) activation increases during gain anticipation relative to loss anticipation, while anterior insula activation increases during both loss and gain anticipation. Additionally, anticipatory NAcc activation correlates with self-reported positive arousal, whereas anterior insula activation correlates with both self-reported negative and positive arousal. Finally, NAcc activation precedes the purchase of desirable products and choice of high-risk gambles, whereas anterior insula activation precedes the rejection of overpriced products and choice of low-risk gambles. Together, these findings support a neurally plausible framework for understanding how anticipatory affect can influence choice.

Keywords: anticipation; affect; accumbens; insula; reward; functional magnetic resonance imaging

1. BACKGROUND

In 1897, Wilhelm Wundt, the founding father of experimental psychology, proposed a dimensional scheme for affect. According to Wundt: 'In this manifold of feelings… it is nevertheless possible to distinguish certain different chief directions, including certain affective opposites of predominant character'. Wundt identified three bipolar dimensions: (i) pleasurable versus unpleasurable, (ii) arousing versus subduing, and (iii) strain versus relaxation. Wundt proposed that these dimensions laid the foundation for emotional experience. Despite subsequent research inspired by many of Wundt's ideas (most notably in the field of psychophysics), his theory of affect had lain dormant for a century. True to his physiological training (but in contrast to his competitor and contemporary William James), Wundt assumed that affect originated in the brain and not in the peripheral body. Thus, Wundt implicitly rued the lack of technology that might allow him to track neural activity and correlate it with affect when he stated: 'Which central regions are thus affected we do not know. But…the physiological substrata for all the elements of our psychological experience, are in all probability to be found in the cerebral cortex…'

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One contribution of 10 to a Theme Issue 'Neuroeconomics'.

Subsequent psychometric research during the twentieth century vindicated Wundt's notion that basic dimensions underlie emotional experience. For instance, several decades of psychological studies indicate that two independent dimensions can account for most of the variance in self-reported mood ratings (Osgood *et al.* 1957; Russell 1980; Watson & Tellegen 1985). As in Wundt's scheme, these dimensions have been called valence (running horizontally from good to bad) and arousal (running vertically from aroused to not aroused) (figure 1). Theorists have also proposed a quarter turn (45°) rotation that yields dimensions of positive arousal (i.e. positive affective states involving high arousal, e.g. 'excitement') and negative arousal (i.e. negative affective states involving high arousal, e.g. 'anxiety'). This two-dimensional 'affective circumplex' provides a simple and cross-culturally valid scheme for organizing different emotional states (Larsen & Diener 1992), consistent with the notion that its structure might reflect the operation of underlying physiological mechanisms.

Recent advances in neuroimaging techniques now allow investigators to begin to probe neural circuits that support affective experience. Were Wundt alive today, he might avail himself of these techniques. But where in the brain would he begin the search for affect? Over the twentieth century, neuroscience research has uncovered a few leads. In all mammalian species studied, stimulation of distinct brain circuits can unconditionally elicit either approach or avoidance behaviour. Most of these circuits are subcortical;

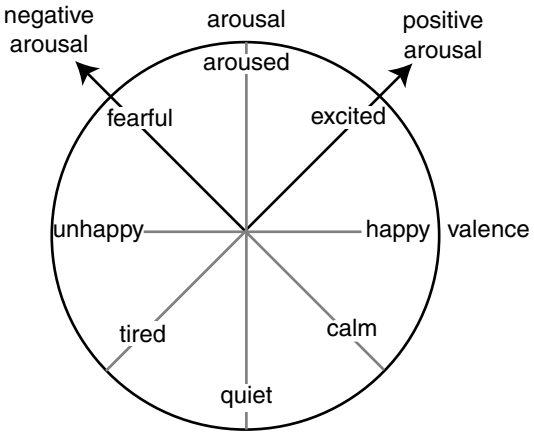

Figure 1. An affective circumplex (Watson *et al.* 1999).

however, they may also include some cortical components. Specifically, electrical stimulation of brain regions that lie along the projections of midbrain dopamine neurons (i.e. ascending from the ventral tegmental area to the lateral hypothalamus, ventral striatum (including the nucleus accumbens, NAcc) and mesial prefrontal cortex, MPFC) can unconditionally elicit approach behaviour (Olds & Fobes 1981; Shizgal 1997). On the other hand, electrical stimulation of other brain regions (i.e. descending from the anterior insula and basolateral amygdala through the stria terminalis to the medial hypothalamus and periaqueductal grey) can unconditionally elicit avoidance behaviour (Panksepp 1998). In humans, visualizing activity in small subcortical structures and small sections of larger cortical structures requires neuroimaging methods with adequate spatial resolution (i.e. of the order of millimetres; figure 2).

In addition to space, time also represents a critical dimension of incentive processing. Indeed, Wundt noted that affect could change rapidly over time and that past affect should influence present and future affect. Additionally, Wundt associated his third dimension (strain versus relaxation) with the passage of time and the resolution of affective episodes. At about the same time in history, ethologists distinguished between appetitive (i.e. when an organism anticipates incentives) and consummatory behaviour (i.e. when an organism responds to incentive outcomes) to describe the temporal dynamics of motivated behaviour (Craig 1918). More recent work has adopted learning models to characterize neural activity that occurs not only in response to incentive outcomes, but also during anticipation of incentives (Montague *et al.* 1996; Schultz *et al.* 1997; Knutson & Wimmer 2007). Based on these temporal distinctions, one can posit a simple scheme for incentive processing based not only on incentive quality (e.g. gain versus loss) but also on temporal phase (e.g. anticipation versus outcome; figure 3) (Knutson & Cooper 2005). Improved temporal resolution of neuroimaging now potentially allows investigators to disentangle brain activation that occurs at different stages of incentive processing—both immediately before and after choice.

Thus, recent advances in the spatial and temporal resolution of neuroimaging methods now make it possible for investigators to localize physiological substrates of affect. But what in the brain generates affect, does related activity correlate with affective experience and might this activity ultimately influence choice?

2. ANTICIPATORY AFFECT MODEL

Despite the popular notion that emotion can influence decisions, direct physiological evidence for such an influence remains elusive. Traditionally, investigators have focused on affective reactions to incentive outcomes (or consequential affect; Loewenstein *et al.* 2001). For instance, some of these 'consequentialist' models target the affect elicited by unexpected positive versus negative events, as well as by success or failure in achieving goals (Isen *et al.* 1988; Carver & White 1994). While more recent affective forecasting models focus on predicted affective responses, these models remain consequentialist in the sense that they refer to predictions about affective responses to outcomes rather than affect that occurs during anticipation (Wilson & Gilbert 2003). Affect that occurs during anticipation (or 'anticipatory affect'), however, is best situated in time to influence impending decisions.

Here, we propose a model of anticipatory affect in which anticipation of incentive outcomes changes both affective arousal and valence. We make the simplifying assumption that, subjectively, all future outcomes are uncertain (i.e. probability <1 and >0), and all uncertain outcomes involve potential gains and losses. Future outcomes thus minimally vary in terms of uncertainty and the potential for gain versus loss. Cues signalling uncertain future gains or losses initiate anticipation, which resolves when uncertainty collapses as the outcome either occurs or fails to occur (i.e. probability $=1$ or 0). Uncertain cues increase arousal, while cues that signal potential gains increase valence and cues that signal potential losses decrease valence. Thus, anticipation of uncertain gains should increase positive arousal (e.g. feelings such as excitement), while anticipation of uncertain losses should increase negative arousal (e.g. feelings such as anxiety) (figure 1). Assuming that anticipatory affect serves an evolutionarily adaptive function (i.e. increases the probability of reproduction and decreases the probability of death), in addition to generating correlated affect, positive arousal should promote approach behaviour, while negative arousal should promote avoidance behaviour (figure 4).

Although initially inspired by brain stimulation research (Panksepp 1998), the anticipatory affect model shares some commonalities with 'somatic marker' and 'risk as feelings' models, both of which posit that anticipation of uncertain outcomes generates arousal (Bechara *et al.* 1996; Loewenstein *et al.* 2001). However, the anticipatory affect model does not postulate a mediating loop through bodily sensations (i.e. only a brain is necessary), and critically distinguishes anticipatory positive arousal from negative arousal, which can have opposing effects on subsequent behaviour. The anticipatory affect model also shares some commonalities with appraisal frameworks that invoke similar dimensions to describe emotional experience (Lerner & Keltner 2001).

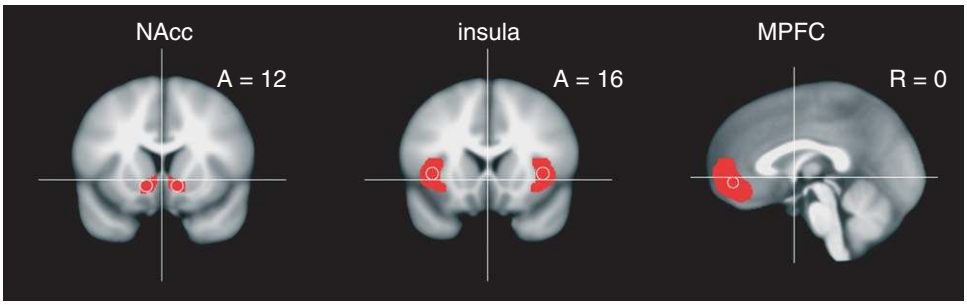

Figure 2. Brain regions (red area) and foci (white circles) of interest (i.e. nucleus accumbens, insula and MPFC).

At present, however, the anticipatory affect model primarily focuses on positive and negative arousal. This parsimonious restriction stays true to Wundt's notion that affect may provide foundational substrates for more complex emotions. For instance, while anger has traditionally been thought to involve negative arousal, it may also include a strong component of positive arousal, which may alter its impact on choice (Lerner & Tiedens 2006). In the future, investigators may use movement through affective space rather than static position in affective space to infer more complex emotional experiences (Nielsen *et al.* 2008).

Thus, while building upon and extending prior models, the anticipatory affect model generates novel predictions about how anticipatory affect might influence subsequent choice. For the purposes of this review, these predictions fall into three classes, which are as follows.

(i) *Spatio-temporal localization.* Circuits that generate positive and negative arousal should both show increased activation during anticipation of uncertain outcomes, but should differentially activate in response to anticipated gain versus loss.
(ii) *Experiential correlates.* Activation in circuits that generate positive and negative arousal (when strong enough to rise above the noise) should correlate with the self-reported experience of positive and negative arousal (assessed at the same time scale).
(iii) *Consequences for choice.* Activation in circuits that generate positive and negative arousal (however elicited) should promote approach towards or avoidance of an uncertain outcome, respectively.

Event-related functional magnetic resonance imaging (fMRI) offers adequate spatial (of the order of millimetres) and temporal (of the order of seconds) resolution to allow investigators to attempt to identify neural correlates of anticipatory affect. Since its development in the early 1990s, the focus of fMRI research has moved anatomically from sensorimotor cortical to less well-characterized subcortical and association cortical regions, with a parallel conceptual shift from mapping sensorimotor function to mapping cognitive and affective function. However, initial studies continue to provide methodological guidance for the current research. As illustrated by early mapping of the visual cortex, researchers must first localize brain regions in which activity correlates with a specific function. Following localization, researchers

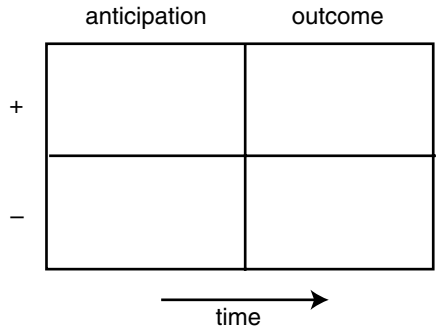

Figure 3. A minimal incentive processing scheme (Knutson & Cooper 2005).

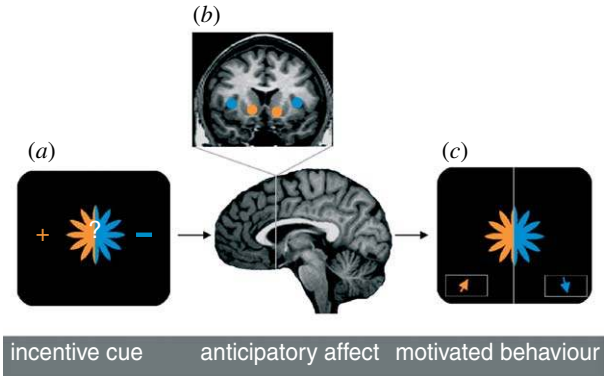

Figure 4. An anticipatory affect model. An incentive cue for (*a*) an uncertain future outcome first elicits activation in at least two brain regions (NAcc and anterior insula), which may correlate with (*b*) anticipatory affective experience (positive arousal (orange circles) and negative arousal (blue circles)). The balance of activation in related circuits then promotes (*c*) approach (orange) or avoidance (blue) of the cued outcome.

can vary experimental parameters to rule out alternative functional accounts. Eventually, researchers might examine not only how stimuli induce brain activation but also how brain activation might promote subsequent behaviour. Section 3 reviews and provides a meta-analysis of fMRI studies that attempted to elicit anticipatory brain activation. Section 4 examines whether activation in these regions correlates with affective experiences. Section 5 examines whether activation in these regions can be used to predict subsequent behaviour.

3. SPATIO-TEMPORAL LOCALIZATION

While brain stimulation findings implicate relevant circuits, which circuit components might provide neural markers of anticipatory affect in the context of

fMRI? As mentioned earlier, electrical stimulation of mesolimbic circuitry can elicit approach behaviour. The mesolimbic circuit receives dopamine projections from midbrain neurons (in the ventral tegmental area) and includes both subcortical (i.e. the lateral hypothalamus and the ventral striatum including the NAcc) and cortical components (i.e. the MPFC) (Olds & Fobes 1981). Furthermore, anatomical studies of both monkeys and humans indicate that striatal and prefrontal cortical regions interconnect in an 'ascending spiral' fashion. Thus, the NAcc projects to the MPFC via the thalamus, which then directly projects back to the medial caudate, which then back to more dorsal regions of the prefrontal cortex via the thalamus, and so forth (Haber *et al.* 2000; Ferris *et al.* 2004; Lehericy *et al.* 2004; Draganski *et al.* 2008). This ascending spiral of striatal–prefrontal connectivity eventually terminates in the premotor cortex, consistent with the notion that the NAcc can serve as a gate that translates motivation into motion (Mogenson *et al.* 1980). Thus, stimulation and connectivity literatures converge to implicate the NAcc (and interconnected MPFC) as a promising candidate neural marker of positive arousal. The connections of circuitry in which electrical stimulation elicits avoidance behaviour (e.g. descending from the insula to the amygdala, medial hypothalamus and periaqueductal grey of the brainstem) have received less characterization. In this circuit, the anterior insula is closest to and shares prominent connections with the prefrontal cortex (i.e. particularly with the lateral prefrontal cortex, but also with the MPFC; Mesulam & Mufson 1984). Thus, the anterior insula (and the interconnected amygdala) might provide a candidate neural marker of negative arousal. These patterns of connectivity not only imply that approach and avoidance circuits are partially distinct but also that their output may converge in the MPFC (and the interconnected medial caudate) to influence motor output.

Initial fMRI studies that attempted to localize brain activation during anticipation of incentives used both primary incentives (e.g. pleasant tastes) and secondary incentives (e.g. money) (O'Doherty 2004; Knutson & Cooper 2005). Monetary incentives confer some experimental advantages over other types of incentives, since most people will work for money, and the magnitude, probability and timing of monetary outcomes can be easily controlled. Most importantly for the purposes of this review, however, monetary incentives can represent either gains or losses, and thus can be directly compared as a function of valence—a task more difficult in the case of primary incentives (e.g. how does one scale juice gains against shock avoidance?). Thus, this review focuses on monetary incentive research.

Investigators have primarily used two classes of monetary task to elicit anticipatory brain activation. One class involves consideration of mixed gambles, while the other class involves cued anticipation of response-contingent outcomes. While mixed gamble studies most closely approximate traditional economics experiments, they often simultaneously present potential gains and losses of different probabilities, and so implicitly assume linear additivity in neural responses to gains, losses and other factors (e.g. probability, certainty). Many mixed gamble studies also involve choice, which often is not modelled separately from anticipation. Cued response studies, on the other hand, have typically isolated anticipatory factors by presenting implicitly degenerate gambles (e.g. gain versus non-gain, loss versus non-loss), and separately manipulating relevant dimensions (e.g. magnitude, probability, certainty). Depending upon the elicited behavioural response (e.g. speeded reaction time, choice), however, investigators must take care not to confound anticipatory neural activation related to affect with that related to response preparation. In theory, both mixed gamble and cued response tasks can address similar research questions, but this remains to be established through experiments. Because cued response studies collectively offer the cleanest separation of anticipatory factors, this review focuses on their findings.

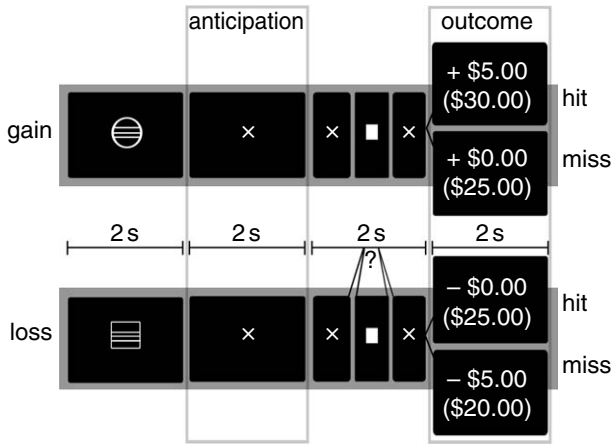

Figure 5. MID task gain and loss trial structure.

A prototypical cued response task called the monetary incentive delay (MID) task was developed to elicit anticipatory brain activation in the context of fMRI (Knutson *et al.* 2000). The design of the MID task was inspired by the historic observation that food cues could elicit salivation in dogs (Pavlov 1927), as well as more recent electrophysiological evidence that juice cues can elicit increased firing of dopamine neurons in monkeys (Schultz 1998). In a typical MID task trial, subjects initially see a cue indicating that they will have an opportunity to either gain or avoid losing a certain amount of money (2000 ms), followed by a fixation cross (2000–2750 s). Next, a target briefly appears on the screen (180–280 ms), and subjects attempt to press a button before the target is replaced by a fixation cross. Finally, subjects see the outcome of their performance on that trial and cumulative earnings (2 s).

The MID task trial structure allows investigators to separately visualize brain activity in response to incentive anticipation and outcomes by: (i) temporally separating anticipation and outcome phases, (ii) time-locking brain volume acquisition to the onset of each phase, and (iii) ensuring that each anticipatory condition leads to both types of outcomes (i.e. hit and miss; figure 5). The separation of gain and loss trials allows investigators to directly compare across these two types of incentives and thus to control for potential confounds related to sensory input, motor

output, arousal/salience and performance. Although fMRI provides better temporal resolution than other whole-brain neuroimaging techniques (i.e. positron emission tomography), the fMRI blood-oxygen-level-dependent signal is distributed over time from event onset, with a 4–6 s rise followed by a 8–12 s decay (Cohen 1997). Since this signal is linearly additive (in the range of seconds), investigators who use the MID task can overcome its temporal spread by employing orthogonalized analyses (due to full crossing of anticipation and outcome manipulations). In addition to examining statistical contrast maps to determine that activation occurred in predicted brain regions, investigators typically also scrutinize averaged activation time course data extracted from predicted regions to verify that peak activation differed at the predicted trial phase.

Initial event-related fMRI studies using the MID task suggested that anticipation of monetary gain proportionally increased NAcc activation (Knutson *et al.* 2001*a*). Anticipation of monetary gain proportionally increased activation in two other subcortical regions as well—the medial caudate and the dorsomedial thalamus—but activation in these regions also proportionally increased during anticipation of loss. By contrast, controlling for anticipatory activation, gain versus non-gain outcomes increased activation in a part of the MPFC (a cortical dopamine target) and the posterior cingulate (Knutson *et al.* 2003). In the NAcc and the MPFC, magnitude-proportional activations were not observed in the context of loss anticipation or outcomes. Since the turn of the twenty-first century, a sufficient number of these studies (i.e. using the MID task or similar cued response tasks) have been conducted and published to warrant meta-analysis of their combined findings.

(a) *Meta-analysis*

(i) *Rationale*

Examining the replicability of initial findings requires separate consideration of neural responses to anticipation and outcomes related to gain and loss (figure 3). Based on the anticipatory affect model, we expected increased NAcc activation during gain anticipation versus loss anticipation, as well as during gain anticipation versus in response to gain outcomes. Conversely, we expected increased anterior insula activation during loss anticipation versus gain anticipation. Finally, we expected increased MPFC activation in response to gain outcomes versus gain anticipation.

(ii) *Study selection*

Studies were identified using the sleuth interface for the BrainMap database (Laird *et al.* 2005*b*) by searching for experiments in the 'normal mapping' context and the 'reward task' paradigm class, as well as via Pubmed database searches using key phrases 'MID', 'reward anticipation' and 'fMRI (search date: 15 March 2008)'. We specifically searched for studies using the MID task or similar cued response tasks designed to isolate the four contrasts of interest (i.e. gain versus non-gain anticipation, loss versus non-loss anticipation, gain versus non-gain outcome, loss versus non-loss outcome). These searches identified approximately 50 studies for further consideration. Only studies that reported focus coordinates for at least one of the four contrasts of interest in healthy adult samples were included. We excluded studies with contrasts that did not separately model gain and loss (Critchley *et al.* 2001; Coricelli *et al.* 2005; Knutson *et al.* 2005; Preuschoff *et al.* 2006; Liu *et al.* 2007; Cooper & Knutson 2008), or that did not separately model anticipation and outcome periods of each trial (Elliott *et al.* 2000; Knutson *et al.* 2000; Ernst *et al.* 2004; Newman *et al.* 2004; Zink *et al.* 2004; Galvan *et al.* 2007; Tobler *et al.* 2007). We also excluded studies that reported contrasts that focused only on risk (i.e. in which models focused on probability rather than magnitude; Volz *et al.* 2003, 2004; Fukui *et al.* 2005; Huettel *et al.* 2006), as well as studies that included a dynamic learning component (i.e. in which anticipation of gain or loss changed over time; Pochon *et al.* 2002; Akitsuki *et al.* 2003; Bolla *et al.* 2005; Cox *et al.* 2005; Galvan *et al.* 2005; Remijnse *et al.* 2006). Activation foci coordinates from healthy adult samples in the remaining 21 studies were submitted to activation likelihood estimate (ALE) meta-analyses (table 1).

The ALE meta-analytic method confers some advantages over traditional label-based meta-analytic methods, since it relies upon activation focus coordinates that show greater reliability across studies than do anatomical labels. Furthermore, the ALE method allows investigators to directly compare the likelihood of activation across contrasts. We conducted two ALE comparison analyses. The first identified areas that were significantly more likely to be active for gain versus non-gain anticipation contrasts than for loss versus non-loss anticipation contrasts, while the second identified regions that were significantly more likely to be active for gain versus non-gain anticipation contrasts than for gain versus non-gain outcome contrasts. Too few studies have reported coordinates for loss versus non-loss outcome contrasts to allow statistical comparison with the other contrasts. In order to conduct these comparisons, the 21 initially selected studies were filtered to match comparison contrasts within study. Thus, 12 studies were included in the gain anticipation versus loss anticipation contrast and a separate but overlapping set of 12 studies were included in the gain anticipation versus gain outcome contrast (groups A and B, respectively; table 1). Three studies that included only gain versus non-gain anticipation contrasts could not be included in either comparison analysis. This filtering ensured that ALE findings would not result from imbalanced observations (i.e. derived from the number of studies) across contrasts. Matching contrasts within study also minimized potential confounds that might vary across studies such as the number of subjects, the statistical threshold used to report foci or idiosyncrasies of analytic techniques (e.g. the spatial smoothing kernel or temporal model of the haemodynamic response function applied).

(iii) *Analysis*

Meta-analyses were conducted with the ALE algorithm implemented with GingerALE software available from www.brainmap.org (Laird *et al.* 2005*a*). In the ALE

Table 1. Studies included in the ALE meta-analysis and associated contrasts. (A, study included in the gain anticipation versus loss anticipation comparison; B, study included in the gain anticipation versus gain outcome comparison.)

study	gain anticipation	loss anticipation	gain outcome	loss outcome
Abler *et al.* (2007)[B]	x		x	
Abler *et al.* (2006)[B]	x		x	
Adcock *et al.* (2006)	x			
Bjork *et al.* (2004)[AB]	x	x	x	x
Bjork & Hommer (2006)[B]	x		x	
Breiter *et al.* (2001)[A]	x	x		
Cohen *et al.* (2005)[B]	x		x	
Dillon *et al.* (2008)[AB]	x	x	x	x
Juckel *et al.* (2006)[A]	x	x		
Kirsch *et al.* (2003)	x			
Knutson *et al.* (2008*a*)[AB]	x	x	x	x
Knutson *et al.* (2001*a*)[A]	x	x		
Knutson *et al.* (2003)[AB]	x	x	x	x
Knutson *et al.* (2004)[AB]	x	x	x	x
Knutson *et al.* (2001*b*)[B]	x		x	
Ramnani & Miall (2003)	x			
Samanez-Larkin *et al.* (2007)[AB]	x	x	x	x
Schlagenhauf *et al.* (2008)[A]	x	x		
Strohle *et al.* (2008)[B]	x		x	
Wrase *et al.* (2007*b*)[A]	x	x		
Wrase *et al.* (2007*a*)[A]	x	x		
total number of studies	21	12	12	6
total number of foci	255	119	87	32
foci in contrast A (gain anticipation > loss anticipation)	129	119		
foci in contrast B (gain anticipation > gain outcome)	133		87	

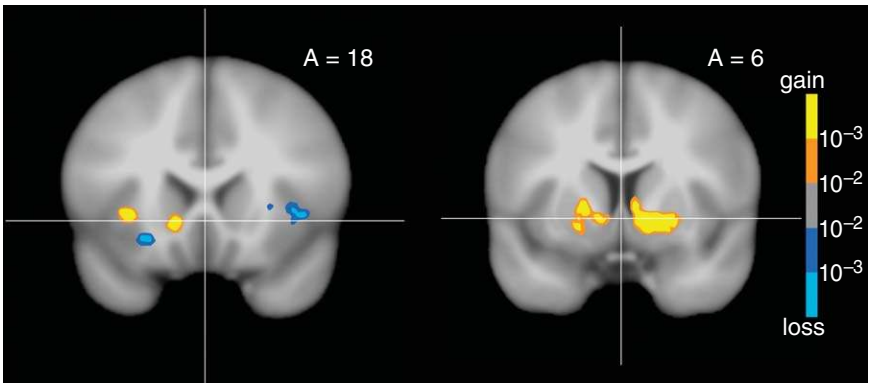

Figure 6. Gain anticipation contrast > loss anticipation contrast ALE maps. Contrast comparisons showing ALE values that are significantly greater for the gain anticipation contrast (129 foci) than for the loss anticipation contrast (119 foci; A, anterior). The same 12 studies were compared for gain and loss anticipation contrasts (group A marked in table 1).

analyses, each contrast focus was modelled as the peak of a Gaussian function that represents the probability of activation occurring (i.e. the ALE values). The ALE values were then aggregated in a whole-brain map and compared against the null hypothesis of random activation. Separate analyses were conducted for each of the four base contrasts (i.e. gain versus non-gain anticipation, loss versus non-loss anticipation, gain versus non-gain outcome and loss versus non-loss outcome; see the electronic supplementary material, S1). Next, in order to directly compare gain anticipation versus loss anticipation contrasts and gain anticipation versus gain outcome contrasts, ALE maps for the base contrasts of the reduced study sets were subtracted. Foci originally reported in Montreal Neurological Institute coordinates were converted to Talairach coordinates using the icbm2tal transformation prior to analysis (Lancaster *et al.* 2007). The ALE values were computed using a full width at half maximum of 8 mm. For the final two comparison analyses, statistical significance for the subtracted ALE values was assessed with a permutation test against 5000 permutations of randomly distributed foci. Statistical thresholds were computed using a false discovery rate procedure that corrected for multiple comparisons across the entire brain ($p < 0.01$, corrected, cluster criterion = 100 mm^3).

(iv) *Results*

The gain anticipation versus loss anticipation contrast comparison revealed relatively increased activation for the gain anticipation contrast in the medial frontal

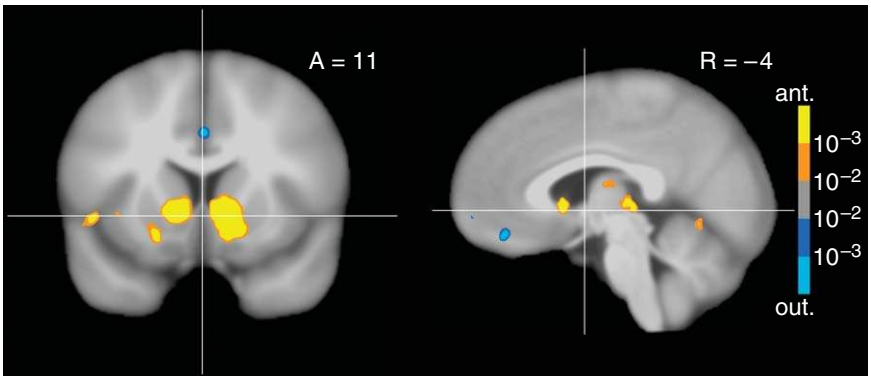

Figure 7. Gain anticipation contrast > gain outcome contrast ALE maps. Contrast comparisons showing ALE values that are significantly greater for the gain anticipation contrast (133 foci) than for the gain outcome contrast (87 foci; A, anterior; R, right). The same 12 studies were compared for gain anticipation and outcome contrasts (group B marked in table 1).

Table 2. Gain anticipation contrast > loss anticipation contrast ALE foci table (R, right; A, anterior; S, superior).

region	ALE ($\times 10^{-3}$)	R	A	S
gain anticipation > loss anticipation				
right medial frontal gyrus	19.24	2	26	36
right anterior insula	24.35	30	20	2
right NAcc	24.41	12	20	−2
left NAcc	59.43	−10	10	−2
right putamen	21.39	20	10	−6
right NAcc	26.15	10	8	0
right putamen	23.67	16	4	4
right medial frontal gyrus	21.12	2	−2	48
right thalamus	21.61	4	−10	14
right thalamus	20.00	8	−28	6
loss anticipation < gain anticipation				
right superior frontal gyrus	−20.32	20	58	−12
right anterior insula	−18.70	24	20	−8
left anterior insula	−19.05	−36	16	2
left caudate	−17.06	−14	−4	16
right caudate	−20.45	12	−4	16
left thalamus	−20.06	−14	−4	10
right red nucleus	−18.09	6	−16	−6
left superior temporal gyrus	−18.93	−50	−32	8

gyrus, NAcc, anterior insula, putamen and thalamus. This comparison conversely revealed relatively increased activation for the loss anticipation contrast in the right superior frontal gyrus, anterior insula, dorsal caudate, thalamus, red nucleus and left superior temporal gyrus (figure 6; table 2).

The gain anticipation contrast versus gain outcome contrast comparison revealed relatively increased activation for the gain anticipation contrast in the right anterior cingulate, NAcc, insula, caudate, supplementary motor area, thalamus and culmen. This comparison conversely revealed relatively increased activation for the gain outcome contrast in the MPFC, caudate, putamen and amygdala (figure 7; table 3).

(v) *Summary*

Consistent with initial findings, gain anticipation contrasts showed greater activation in the NAcc than loss anticipation contrasts of the same magnitude.

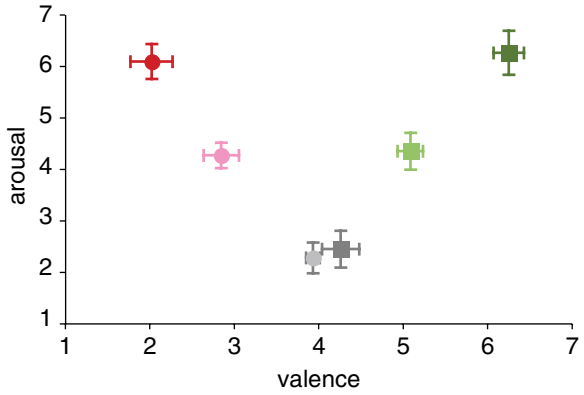

Figure 8. Affect dynamics during incentive anticipation in the MID task ($n=12$) (Samanez-Larkin *et al.* 2007). Lose (circles): grey, \$0.00; rose, \$0.50; red, \$5.00. Win (squares): black, \$0.00; light green, \$0.50; dark green, \$5.00.

Additionally, loss anticipation contrasts elicited greater activation in some (but not all) regions of the anterior insula and the medial caudate. Gain anticipation contrasts also elicited greater activation in the NAcc than gain outcome contrasts of the same magnitude, while gain outcome contrasts elicited greater activation in the MPFC than gain anticipation contrasts. Notably, both component contrasts for anticipation alone (e.g. gain versus non-gain anticipation, loss versus non-loss anticipation) showed some evidence of NAcc activation, but neither contrast by itself controlled for arousal or other related confounds (see the electronic supplementary material, S1). A direct comparison of these contrasts, however, revealed relatively increased NAcc activation for gain anticipation. This finding concurs with those of excluded studies in which direct contrasts of anticipated gain against anticipated loss revealed correlated NAcc activation (Ernst *et al.* 2004; Knutson *et al.* 2005; Preuschoff *et al.* 2006). The appearance of different anterior insula regions in both the gain anticipation versus loss anticipation contrast and its reverse is consistent with increased anterior insula activation during anticipation of uncertain outcomes in general (which might either involve gains or losses; Critchley *et al.* 2001; Volz *et al.* 2004; Huettel 2006). Together, these findings suggest that activation in the NAcc and the anterior insula increases during anticipation of uncertain incentives. For the NAcc at least, this activation most robustly occurs during gain

Table 3. Gain anticipation contrast > gain outcome contrast ALE foci table.

region	ALE ($\times 10^{-3}$)	R	A	S
gain anticipation > gain outcome				
right anterior cingulate	21.56	6	40	12
right NAcc	19.23	14	18	−2
right insula	30.19	32	18	0
right insula	17.17	46	12	−2
left caudate	60.55	10	10	2
left NAcc	65.25	−12	10	−2
left NAcc	23.53	18	8	−8
left medial frontal gyrus	22.68	0	−2	48
right thalamus	34.67	4	−12	14
left thalamus	22.28	−6	−22	4
left thalamus	20.79	−18	−22	20
left culmen	25.00	0	−60	−6
gain outcome < gain anticipation				
left mesial prefrontal cortex	−20.06	−2	42	−12
right caudate	−19.02	6	18	2
left amygdala	−27.89	−16	−2	−10
left putamen	−20.46	−26	−14	−2

anticipation. Section 4 reviews whether anticipatory activation correlates with affective experience.

4. EXPERIENTIAL CORRELATES

To assess affective experience, researchers have primarily relied upon self-report. Despite challenges posed by measuring fleeting and subjective experiences, assessment of self-reported affect can be compared with psychophysical assessment of other sensory impressions. For instance, in vision research, subjects rate the brightness of stimuli most reliably when compared against other stimuli. As with sensory impressions, people can easily and rapidly report how much they like different stimuli (for instance, the speed of liking judgments is typically faster than olfactory discrimination but slower than visual discrimination; Kahneman 1999). Thus, in the case of affect, investigators might compare a single individual's affective reactions to several different stimuli in two dimensions (e.g. bad–good, not aroused–aroused).

Assessment of affective experience inevitably requires trade-offs. One trade-off involves semantic (e.g. number of indices) versus temporal resolution (e.g. number of occasions). Semantically comprehensive measurements have more stable psychometric properties but take more time to acquire than fast probes. A second trade-off involves reference to specific versus general events. Affective responses to specific events may capture focused variations but miss general trends captured by more general assessments. A third trade-off involves online versus retrospective ratings. Online ratings show less degradation or distortion due to memory, but may disrupt an ongoing task and alter the affect to be measured, unlike retrospective assessments. Thus, affective measurement in the midst of an engaging task might require sampling fewer indices more frequently online in reference to specific events. On the other hand, a general affective assessment might require sampling a larger number of indices retrospectively after an extended period of time in reference to no specific event. In either case, repeated probes of affect might allow investigators to chart an individual's 'affect dynamics' or trajectory through affective space over time (Nielsen *et al.* 2008).

In the context of the MID task, affect dynamics have been probed in response to incentive anticipation versus outcomes. These dynamics have been confirmed with both online probes of valence and arousal dimensions, as well as retrospective but more semantically comprehensive ratings of emotion adjectives. In either case, subjects rate their reactions to specific events on seven-point Likert scales (running from 'not at all' to 'extremely'). Ratings of valence and arousal are then mean corrected across stimuli within an individual and mathematically rotated through affect space (by 45°) to derive indices of positive and negative arousal (Knutson *et al.* 2005) (figure 1). Ideally, affect probes might allow investigators to assess both affective experience and brain activation at the same second-to-second time scale.

During the MID task, both online and retrospective probe data indicate that when subjects anticipate gains, positive arousal increases, and when they anticipate losses, negative arousal increases. This anticipatory affect increases proportional to the magnitude of anticipated gain or loss (Samanez-Larkin *et al.* 2007; figure 8). Accordingly, peripheral indices of arousal (i.e. skin conductance) also increase when subjects anticipate gains and losses (Nielsen *et al.* 2004). When subjects receive incentive outcomes, however, changes in valence are more prominent than changes in arousal. In the case of gain outcomes, receiving a gain increases valence, while not receiving a gain (i.e. getting nothing) decreases valence, while in the case of loss outcomes, the reverse pattern applies. Together, these findings suggest not only that incentive cues elicit anticipatory affect but also that anticipatory affect can qualitatively differ from outcome-elicited affect, with anticipation eliciting more arousal than outcomes (figure 8). Interestingly, when young adults (age 20–40) are asked to predict their affective responses during the MID task before playing, they accurately predict changes in valence, but mistakenly predict that they will feel more arousal in response to incentive outcomes than during anticipation (Nielsen *et al.* 2008).

These findings suggest that in addition to altering brain activation, anticipation of incentives elicits reliable changes in self-reported affective experience within subjects. But do individual differences in affective response also correlate with brain activation across subjects? Addressing the relationship of self-reported affect to brain activation raises several technical issues. First, activity in brain regions activated during incentive anticipation (e.g. NAcc, anterior insula) fluctuates on a second-to-second basis, and is often plagued by artefacts and noise. Large incentives, however, might invoke a sufficiently robust signal in these regions to rise above the noise and thus correlate with affective ratings. Second, correlating activation in the entire brain with affective self-report involves many statistical tests, and thus would require a conservative criterion for significance. Focusing on regions activated

during incentive anticipation constrains the number of tests, and so can provide greater sensitivity for detecting associations. In the light of these considerations, investigators have attempted to correlate anticipatory brain activation with self-reported affect in a number of studies. Strictly interpreted, the anticipatory affect model might predict that NAcc activation should correlate with positive arousal but not negative arousal, while anterior insula activation should correlate with negative arousal but not with positive arousal (since positive and negative arousal are psychometrically independent).

Several of the cued response studies reviewed above have explored correlations between cue-elicited brain activation and retrospective cue-elicited affect ratings. The first studies used emotional adjectives rather than ratings of valence and arousal. In an initial study of young adults (age 20–40, $n=8$), large gain (i.e. +\$5.00) cue-elicited right NAcc activation correlated with large gain cue-elicited happiness (assessed retrospectively). This correlation was not significant in the right caudate, and activation in these regions also did not correlate with large gain cue-elicited unhappiness (Knutson *et al.* 2001*a*). In a second study of both adolescents (age 12–17, $n=12$) and young adults (age 20–40, $n=12$), large gain (+\$5.00) cue-elicited right NAcc activation correlated with large gain cue-elicited excitement and happiness but not with fear or unhappiness, controlling for age (figure 9) (Bjork *et al.* 2004). In a third study of young adults (age 20–40, $n=8$), gain cue-elicited NAcc activation correlated with gain cue-elicited excitement but not with loss cue-elicited excitement (Knutson *et al.* 2004). In a fourth study of young adults (age 20–40, $n=14$), affect was assessed with ratings of valence and arousal in response to each cue (rather than emotional adjectives), which were transformed into measures of positive and negative arousal. As with previous methods, large gain (+\$5.00) cue-elicited bilateral NAcc activation correlated with large gain cue-elicited positive arousal, but not with negative arousal (Knutson *et al.* 2005). Together, these findings suggest that NAcc activation correlates with positive arousal but not with negative arousal (figure 9).

A fifth study of younger (age 20–40, $n=12$) and older (age 60–80, $n=12$) adults examined correlations between brain activation and anticipatory affect with more comprehensive assessments in terms of both affective indices and brain regions of interest (Samanez-Larkin *et al.* 2007). This study again replicated the association between large gain (+\$5.00) cue-elicited bilateral NAcc activation and large gain cue-elicited positive arousal across both age groups, and further revealed no correlation between large loss (−\$5.00) cue-elicited bilateral NAcc activation and large loss cue-elicited negative arousal. The medial caudate showed an opposite pattern, with no correlation of large gain cue-elicited medial caudate activation with large gain cue-elicited positive arousal, but a significant correlation of large loss cue-elicited activation with large loss cue-elicited negative arousal. Anterior insula activation showed an intermediate pattern of correlations, since large gain cue-elicited activation correlated with large gain cue-elicited positive arousal, and large loss cue-elicited activation correlated with large loss cue-elicited negative arousal. Thus, while NAcc activation selectively correlated with positive arousal, anterior insula activation apparently correlated more with general arousal (i.e. both positive and negative). These findings further suggest that NAcc and medial caudate activation, while both occurring in the striatum, may correlate with different affective experiences.

Consistent with the anticipatory affect model, NAcc activation correlated with positive arousal and anterior insula activation correlated with negative arousal. Anterior insula activation, however, also correlated with positive arousal in the most comprehensive of the reviewed studies, suggesting that activation in this region may index general arousal more than negative arousal. These correlations appear to hold across different affect terms (e.g. specific emotion terms versus arousal and valence) and across different time scales (e.g. online versus retrospective probes, so long as the referent is clear). More research is needed, however, to comprehensively examine the relationship between activation in all the regions of interest for both positive and negative arousal (see the electronic supplementary material, S2). While most peripheral physiological measures (e.g. skin conductance, pupillary dilation) primarily index arousal, brain activation (at least in the NAcc) also partially indexes valence, which provides critical information for the prediction of choice, as described in §5.

Associating self-reported affect with brain activation raises the tantalizing possibility of reverse inference. Specifically, could investigators infer increased positive arousal from increased NAcc activation? In fact, we first observed brain activation during anticipation of incentives, and only later verified correlated changes in anticipatory affect. Reverse inference poses hazards, however, since many factors other than those related to NAcc activation might influence the self-reported experience of positive arousal (Poldrack 2006; Knutson & Gibbs 2007). The physiological events that increase NAcc activation might represent a necessary but not sufficient feature for the generation of self-reported positive arousal. Other prerequisites might involve a capacity for reflection, attention to affective experience and an ability to communicate those experiences (LeDoux 2000). Research has yet to determine whether reflective awareness is required for NAcc activation, but this requirement seems unlikely given the prominent functional role of the NAcc in stimulating approach behaviour in non-human species (Berridge & Robinson 1998; Ikemoto & Panksepp 1999). Conversely, the events that generate NAcc activation may provide necessary input for the self-reported experience of positive arousal. As implied by the anticipatory affect model, activity in these circuits might also influence subsequent choice, either in the presence or absence of reflective awareness (Zajonc 1980).

5. CONSEQUENCES FOR CHOICE

To ensure adaptive function (i.e. promote survival and procreation), anticipatory affect should not only generate neural activity and correlated experience, but

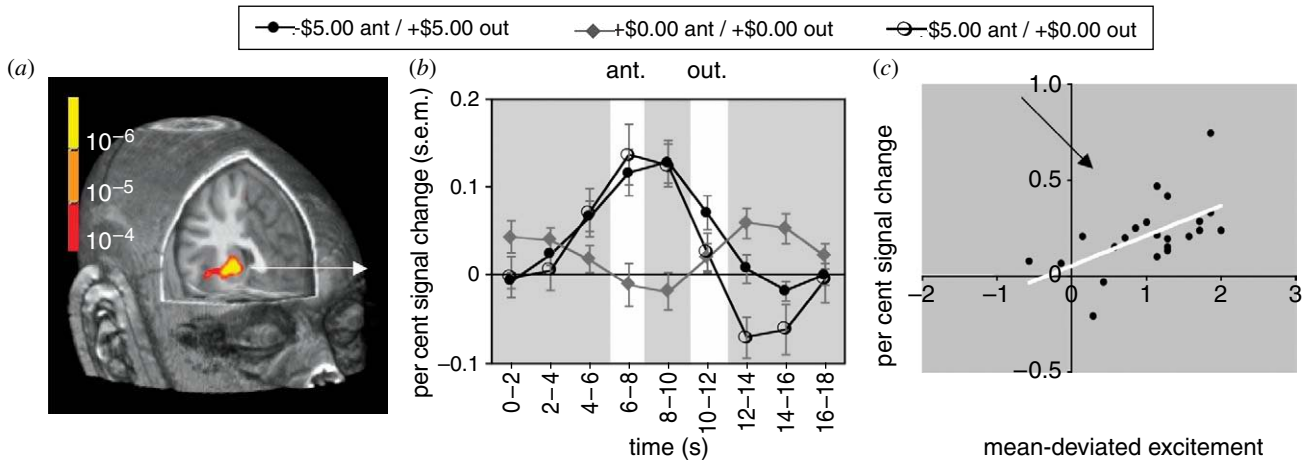

Figure 9. (*a*) NAcc activation elicited by anticipation of monetary gain ($) versus non-gain (zero). (*b*) NAcc activation time courses for large gains and non-gains (s.e.m.). (*c*) Correlation of individual differences in NAcc response to large gain cue and cue-elicited positive arousal (i.e. 'excitement'; $n=24$ and $r=0.58$; Bjork *et al.* 2004; Knutson & Gibbs 2007).

also motivate behaviour (Dawkins 1989). The anticipatory affect model (figure 4) implies that positive arousal (indexed by NAcc activation) promotes approach, while negative arousal (indexed by anterior insula activation) promotes avoidance. Thus, investigators might predict upcoming choices by measuring brain activation indicative of anticipatory affect, and might possibly even alter choice by manipulating anticipatory affect (reflected by intermediate changes in brain activation). Theoretically, confirming these predictions requires reversing the traditional logic of brain imaging. Instead of examining how sensory input correlates with brain activation, investigators must instead examine how brain activation correlates with subsequent behavioural output. Methodologically, confirming these predictions requires development of new analytic techniques. Rather than the general linear modelling approach traditionally used to correlate stimuli with brain activation (Friston 2005), predicting trial-to-trial choice with brain activation requires new analytic tools including (but not limited to) classification and mediation approaches. At present, only a few studies have implemented these novel methods.

Some studies have used brain activation to predict choice in the context of purchasing. In an initial study, subjects participated in a shopping task while undergoing fMRI. During each task trial, subjects saw a product, followed by an associated price, and then prompts for indicating whether they wanted to purchase the displayed product at its associated price or not. Subjects evaluated a total of 80 products and two of their choices were randomly selected to count 'for real' after scanning. Subjects also rated their preference and willingness to pay for each product after scanning. Analyses indicated that while NAcc activation correlated with viewing preferred products, right anterior insula activation and MPFC deactivation correlated with viewing excessive prices (i.e. the displayed price was higher than subjects were willing to pay). This pattern of findings was replicated for buying and extended into the realm of selling in a follow-up study (Knutson *et al.* 2008*c*). Importantly, NAcc activation during product presentation predicted that subjects would be more likely to buy a product, whereas insula activation and MPFC deactivation during price presentation predicted that subjects would be less likely to buy a product (Knutson *et al.* 2007). By entering the brain activation variables alone into a logistic regression, trial-to-trial purchases could be predicted at approximately 60 per cent, a rate significantly greater than chance (i.e. 50%, confirmed by cross-validation). New analytic techniques that account for multivariate correlations, however, can increase this prediction rate to 67 per cent (Grosenick *et al.* in press). These analyses also established that anticipatory activation, rather than activation at the time of choice, contributed the most information about upcoming purchases in regions of interest. In the future, extension of these techniques to whole-brain data may allow researchers to isolate the most informative regions as well as time points for predicting upcoming choice.

Other studies have used brain activation to predict choice in the context of investing or gambling. The first study that used fMRI activation to predict choice on a trial-to-trial basis did so in the context of investing (Kuhnen & Knutson 2005). The choice to take financial risk requires determining that potential gains outweigh potential losses. Thus, relative to a low-risk option, increasing gain anticipation should increase people's willingness to choose a high-risk option while increasing loss anticipation should decrease people's willingness to choose a high-risk option. While earlier studies had associated NAcc activation with risk seeking and anterior insula activation with risk aversion, they could not establish whether this activation occurred before or after choice due to limited temporal resolution (Paulus *et al.* 2003; Matthews *et al.* 2004). In a study designed to mimic the process of financial investing, investigators examined subjects' anticipatory activation before they made high-risk (i.e. stock) or low-risk (i.e. bond) investment choices. In addition, the investigators determined whether the subjects' choices optimally matched those of a rational (i.e. risk-neutral Bayesian updating) agent or not. Controlling for econometric variables (i.e. uncertainty, overall wealth, previous

actual earnings and previous counterfactual earnings), results indicated that anticipatory NAcc activation predicted both optimal and suboptimal high-risk (i.e. stock) choices, while anticipatory right anterior insula activation predicted both optimal and suboptimal low-risk (i.e. bond) choices. Interestingly, these effects were most evident before investors switched from one strategy to another, implicating these circuits more prominently in decisions involving uncertainty than habitual responding. On an individual difference basis, subjects with greater overall insula activation tended to select the low-risk option more often (Kuhnen & Knutson 2005).

A second study used brain activation to predict choice in the context of a gambling task (Hampton & O'Doherty 2007). This 'reversal learning' task required subjects not only to learn which of two cues signalled a higher probability of potential gain than potential loss, but also to reverse their choice after the value assigned to the cues switched. The investigators found that anticipatory activation in the NAcc, MPFC and anterior cingulate predicted that subjects were about to reverse their choice, or switch from choosing a cue increasingly associated with loss to a cue potentially associated with gain. Particularly in the case of the NAcc, these findings are consistent with the investment findings that NAcc activation precedes switching to a high-risk option.

While the above studies suggest that spontaneous (or endogenous) changes in brain activation can be used to predict upcoming choice, they cannot establish a causal connection between brain activation and choice. The anticipatory affect model, however, also implies that (exogenous) manipulations of activation prior to choice should causally influence subsequent choice. One study has explored whether irrelevant affective stimuli can influence financial risk taking by influencing anticipatory brain activation (Knutson *et al.* 2008*b*). In each trial of a gambling task, heterosexual males first viewed positive (e.g. erotic couples), negative (e.g. snakes or spiders) or neutral (e.g. office supplies) pictures and then chose between unrelated high-risk (i.e. 50% chance of gaining or losing $1.00) and low-risk (i.e. 50% chance of gaining or losing $0.10) gambles while undergoing fMRI scanning. Subjects were informed that pictorial stimuli were unrelated to the outcome of each subsequent gamble, and all gambles had the same expected value (i.e. $0.00). Nonetheless, viewing positive pictures increased subjects' likelihood of subsequently switching to the high-risk gamble. Furthermore, NAcc activation statistically mediated the influence of positive pictures on subjects' tendency to switch to the high-risk gamble. These findings are thus consistent with a causal model in which increasing NAcc activation (even with informationally irrelevant stimuli) can increase approach towards a high-risk choice.

Anticipatory activation might also predict preferences for social stimuli, although trial-based prediction has yet to be implemented in this domain. For instance, one study found that even in the absence of relevant judgments, NAcc activation in response to novel faces correlated with later preference judgments for those faces (Kim *et al.* 2008). Other evidence potentially implicates anticipatory activation in social choice, although those studies lacked the temporal precision to support formal prediction analyses. For instance, in the context of economic exchange games, NAcc (and adjacent medial caudate) activation precedes the choice to invest in a cooperating partner (Rilling *et al.* 2002, 2004; King-Casas *et al.* 2005), but anterior insula activation precedes the choice to defect against an unfair partner (Sanfey *et al.* 2003).

In summary, anticipatory brain activation can predict choices in the context of purchasing, investing and gambling. Consistent with a gain anticipation account, NAcc activation predicts purchasing desirable products and choice of high-risk investments. Consistent with a loss anticipation account, anterior insula activation predicts avoidance of purchasing overpriced products and choice of low-risk investments. Anticipatory activation appears to predict choice when people both conform to and deviate from the optimal choices of a rational actor. Intriguingly, irrelevant affective cues may alter subsequent choice, partially as a function of their ability to increase activation in regions associated with anticipatory affect.

6. IMPLICATIONS AND ISSUES

Nearly a decade of research has verified the robustness of initially observed brain activation during anticipation of incentives (Knutson *et al.* 2001*a*). In the present synopsis, (i) a meta-analysis of cued response studies indicates that neural activation increases during incentive anticipation, with NAcc activation primarily occurring during gain anticipation, but anterior insula and medial caudate activation occurring during both loss and gain anticipation, (ii) a review of cued response studies including affect probes suggests that NAcc activation correlates with gain cue-elicited positive arousal, while anterior insula activation correlates with both loss cue-elicited negative arousal and gain cue-elicited positive arousal across subjects, and (iii) a review of trial-to-trial prediction studies suggests that NAcc activation promotes approach towards uncertain outcomes, while anterior insula activation promotes avoidance of uncertain outcomes (i.e. in the context of both purchasing and investment). Together, these findings have begun to support a nascent model of the influence of anticipatory affect on choice.

The meta-analytic findings clearly localize regions implicated in anticipatory affect. One continuing mystery involves the relative asymmetry of neural markers for gain versus loss anticipation. Even in experiments that control incentive magnitude, analyses tend to more consistently identify areas whose activation correlates with anticipated gain than with anticipated loss, unlike behavioural findings in which 'losses loom larger than gains' (Kahneman & Tversky 1984). One way of accounting for this asymmetry involves assuming a single neural mechanism in which high levels of activity promote approach, while low levels of activity promote avoidance (Tom *et al.* 2007). However, neither the human evidence reviewed above nor most of the animal literature (e.g. brain stimulation studies) support such a monolithic mechanism (Panksepp

1998). At present (i.e. 2008), fMRI is still a relatively new method, and many technical details might interfere with researchers' abilities to visualize signals that specifically correlate with loss anticipation. These technical details include (but are not limited to) the timing (including the appropriateness of temporal models), the spatial distribution (e.g. which might occur either in very small regions or very large regions) and the physiological basis of the blood-oxygen-level-dependent signal (e.g. the strength of the coupling of whichever neurotransmitter carries the loss anticipation signal to fMRI activation). The present absence of evidence is not evidence of absence, and future research will have to determine how to better resolve loss anticipation signals.

Regions implicated in anticipatory affect doubtless represent limited 'neural markers' for more extensive circuits. If fMRI activation indexes changes in postsynaptic activity (Logothetis *et al.* 2001), increased neurotransmitter release might increase activation in these regions. Elsewhere, we have argued that dopamine release in the NAcc (and subsequent postsynaptic D1 receptor agonism) increases activation detectable with fMRI in that region (Knutson & Gibbs 2007). This argument was based on anatomical projections of ventral tegmental dopamine neurons to the NAcc, the brief half-life of extrasynaptic dopamine in the NAcc (i.e. of the order of seconds) and the effects of dopaminergic manipulations on the fMRI signal. Although the anterior insula includes more territory, the best candidate for a neuromodulator of anterior insula function may be noradrenaline (in addition to dopamine), based on the density of locus coeruleus noradrenaline projections to the anterior insula (Gaspar *et al.* 1989) and the half-life of extrasynaptic noradrenaline. Future studies will have to determine whether noradrenaline release actually modulates fMRI activation in the anterior insula. Combined with anatomical localization findings, these neurochemical speculations suggest physiological mechanisms that might support anticipatory affect. Specifically, the rate of NAcc dopamine release might modulate positive arousal, whereas the rate of anterior insula noradrenaline release might modulate negative arousal.

fMRI researchers have adopted various theoretical frameworks to account for activation in regions implicated in anticipatory affect (i.e. the NAcc and the anterior insula). For instance, early fMRI studies alluded to reinforcement learning (McClure *et al.* 2003; O'Doherty *et al.* 2003), reward anticipation (Knutson *et al.* 2001*a*), expected value (or utility) (Knutson & Peterson 2005; Knutson *et al.* 2005) and reward/risk accounts (Kuhnen & Knutson 2005; Preuschoff *et al.* 2006, 2008). While complementary to these accounts, the anticipatory affect model might explain a broader range of phenomena. First, reinforcement accounts model brain activation as people learn affective reactions to stimuli, but do not model brain activation that occurs in the absence of learning. Even after learning cue values, however, subjects continue to show robust anticipatory brain activation (Knutson *et al.* 2001*a*). Also, incidental affective stimuli with no relevance to choice outcomes can still alter NAcc activation and subsequent financial risk taking (Knutson *et al.* 2008*b*). Second, reward anticipation and expected value (or utility) accounts can explain NAcc activation during anticipation of gains (whether learned or not) but do not traditionally separately model anticipation of losses. A number of studies now suggest that although NAcc activation scales proportional to anticipated gains, the same is not generally true for anticipated losses (either in a clearly increasing or decreasing manner; Knutson *et al.* 2001*a*). Third, reward/risk accounts incorporate an additional component that might be related to loss anticipation (i.e. risk) and which can counteract gain anticipation, but (as with expected value accounts) cannot account for choices that deviate from this model. For instance, NAcc activation predicts high-risk choices and anterior insula activation conversely predicts low-risk choices even when those choices deviate from those of a financially optimal actor as specified by reward/risk accounts (Kuhnen & Knutson 2005). Fourth, the anticipatory affect model can explain individual differences in brain activation during anticipation. Given identical incentives, the more positive arousal subjects experience, the more NAcc activation they should show, and the more negative arousal subjects experience, the more anterior insula activation they should show. The mounting evidence that anticipatory affect can drive learning and choice implies that affect stands at the centre rather than the periphery of decision making.

Future issues include both methodological and conceptual questions. Methodologically, the increased spatio-temporal resolution of fMRI has made possible the present findings. Further advances in spatio-temporal resolution seem inevitable and will probably yield more revelations, both in terms of where and when relevant signals occur. Since fMRI signals only indirectly index changes in postsynaptic neural activity, triangulation with other methods that provide chemical resolution (e.g. positron emission tomography) or that support causal inference (e.g. lesions, transcranial magnetic stimulation) remains essential. Conceptually, future research will also focus on how 'low-level' gain and loss anticipation signals interact with 'high-level' processes related to attention, reflection, planning and control. Markers for many of these processes might reside in the prefrontal cortex. For instance, activation in the MPFC might integrate anticipated gain and loss, and predict choice (e.g. in the context of shopping and investing; Kuhnen & Knutson 2005; Knutson *et al.* 2007), while activation in the dorsolateral prefrontal cortex might allow people to strategically modulate anticipatory affect (Delgado *et al.* 2008).

In conclusion, over the span of less than a decade, neuroscientists have begun to build evidence for consistent and reproducible neural markers of anticipatory affect. Activation in these brain regions correlates with self-reported anticipatory affective experience in predictable ways, and may support prediction of impending approach and avoidance behaviours. More work remains to be done in solidifying this evidence, particularly in the domains of affective experience and influence on choice. However, the anticipatory affect model provides a useful framework for both integrating existing findings and generating new

predictions. Importantly, the anticipatory affect model highlights a temporal path from cued responses to resolution of outcomes. Investigators must take care to temporally dissociate different stages of incentive processing in order to understand how decisions unfold. fMRI provides a method with sufficient spatial and temporal resolution to dissociate these stages of decision making. Although Wundt's ideas about affect are among the oldest in psychology, they also remain among the most enigmatic. After a century of technical advances, the time is right to begin again where Wundt ended and elucidate the mechanism of affect.

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