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Doctoral Thesis

Reward-Predictive Stimuli Enhance Post-Error Uncertainty in the Cingulate Cortex

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Experiment One Introduction

It is an awful winters evening with fog so thick you can barely see a full meter in front of you, but you are out driving on a narrow road and you come to a sharp corner. You stop for a while and look for potential headlights of cars approaching from the other direction. You see none and decide to brave the corner. After you put your foot back on the accelerator… do you stop looking for approaching cars? Hopefully not! In this case even after deciding to drive ahead it would be wise to continue monitoring perceptual information. This is because continued monitoring of perceptual information, even after we have committed to an action or response, has been shown to help us to process and thereby correct our mistakes (e.g. Hochman, Eviater, Breznitz, Nevat, & Shaul, 2015). For example, in this scenario the continued appraisal of perceptual information might help you to realize that you had made a mistake, and that there was in fact a car approaching, in which case you could quickly swerve your car to avoid a crash. Continued monitoring of perceptual information has also been shown to, in very worst cases, help us to prepare ourselves for impending aversive outcomes (Yu & Zhou, 2009), for example, it may help you to brace your body to deal with a crash.

Early on into the research of error-processing, it was suggested that this is similar to votes in a committee (Rabbitt & Vyas, 1981; Rabbitt, Cumming, & Vyas, 1978). The more votes that come in, the more likely the sum of these is to reflect the actual overall general consensus. Therefore, if one makes a decision too quickly before enough votes (evidence) have been accumulated, then they are more likely to come to the wrong conclusion (make an error). In this case, if one continues evaluating the incoming votes then eventually they

may find that their original decision was not in line with the overall general consensus (error-processing) and they may therefore have to adjust the conclusion (error correction). The key concepts of this analogy have since been formalized in computational models of the processing of error (for a summary of these models see Yeung & Summerfield, 2012).

A key premise for error-processing, as evident above, is that evidence must continue to be accumulated after a decision has been made. In support of this, Rabbitt and Vyas (1981) found that error correction rates, which naturally rely on the processing of errors, were reduced as stimulus duration decreased and therefore as continued processing of the evidence about stimuli became harder. Furthermore, Rabbitt (2002) found that participants were less likely to signal that they had made an error to a stimulus when it was immediately followed by another stimulus. This supports the above premise by indicating that interference of continued processing of the original stimulus prevents the detection of errors in response to it.

Neuroimaging studies have also shown evidence that the processing of errors occurs after a decision has been made. Many fMRI studies have found the anterior cingulate cortex (ACC) to be more active subsequent to erroneous compared to correct responses (Carter et al., 1998; Carter, et al., 2001; Garavan, et al., 2002; Kerns et al., 2004; Kiehl, et al., 2000; Menon, et al., 2001). This fMRI activation has been found to correlate with the size of the classic “error-related negativity” (ERN; Iannaccone et al., 2015; Mathalon, Whitfield, & Ford, 2003). The ERN is a negative deflection in ongoing encephalography measured from fronto-central sites on the scalp that occurs quickly, about 100ms, after an erroneous response (Falkenstein, Hohnsbein,

Hoormann, & Blanke, 1990; Gehring, Coles, Meyer, & Donchin, 1990). The ERN is thought to be sourced in or around the ACC (Herrmann, Rommler, Ehlis, Heidrich, & Fallgatter, 2004; Miltner, et al., 2003).

Related to this, fMRI studies have shown ACC activation to sometimes occur- not immediately after an erroneous response but rather- when a person subsequently receives feedback that response that they made was erroneous (e.g. Holroyd et al., 2004). This is related to another negative component in ongoing encephalography that is similarly found after feedback about errors (Miltner, Braun, & Coles, 1997). This component is often referred to as the "feedback ERN" and this is thought to be sourced in the same area as, and to share at least one major component with, the classic ERN (Potts, Martin, Kamp, & Donchin, 2011).

Together the error-related activity in the cingulate that occurs just after an erroneous response, and the error-related activity in the cingulate that occurs when feedback informs one that their response was an error, have been proposed to form a "generic error processing system" (Miltner et al., 1997). At which of these times an error is processed is thought to depend on when this cingulate system "first determines" that an error has been made (Holroyd & Coles, 2002). Therefore, in line with models of error-processing (e.g. see Yeung & Summerfield, 2012) this may depend on how much evidence is continued to be accumulated after a decision has been made.

Interestingly, the cingulate cortex is strongly connected to the mesencephalic dopamine system (Berger et al., 1991; Gaspar et al., 1989; Williams & Goldman-Rakic, 1993), which is part of the brains "reward processing system" (e.g. Bayer & Glimcher, 2005; Schultz, Dayan, &

Montague, 1997). Therefore, the “generic error processing system” is in a unique position where it may be able to combine processes related to error with those related to reward. Previous studies have shown that the reward value associated with stimuli can have drastic effects on information processing prior to decisions (Anderson, 2013; Marx & Einhauser, 2015; Stormer, Eppinger, & Li; 2014). Stimuli have been shown to be processed more when they are associated with reward than if they are not (Theeuwes & Belopolsky, 2012), and even when this is unnecessary or disadvantageous (Anderson, Laurent, & Yantis, 2011a, Anderson, Laurent, & Yantis, 2011b; Hickey, Chelazzi, & Theeuwes, 2010; Sali, Anderson & Yantis, 2014; Vaidya & Fellows, 2015). Therefore, if the reward value associated with stimuli can also increase their processing after decisions, then because error-processing depends on this, error-processing might be greater after decisions are made to stimuli that are associated with higher reward value.

Unfortunately, previous studies that have investigated reward value and error-processing have rewarded participants for correct responses but not for erroneous responses, thereby confounding response accuracy and value processes (e.g. Hajcak, Moser, Yeung, & Simons, 2005; Ichikawa, Siegle, Dombrovski, & Ohira, 2010; Martin & Potts, 2011). Furthermore, the design of these experiments meant that reward value was always associated with the accuracy of response rather than with stimuli, and therefore the distinct effects of stimulus value on error-processing remained unknown. In the first experiment of this thesis, we set out to investigate the effects of stimulus value on error-processing that might occur independent to effects caused by

response-outcome associations. Specifically we wished to see if error-processing is enhanced when responses are made to stimuli predictive of reward compared to when responses are made to stimuli predictive of non-reward. We therefore created an fMRI compatible task where the stimulus shown on each trial, rather than response accuracy, was predictive of the value of the outcome. This design yielded rewarded correct, unrewarded correct, rewarded error, and unrewarded error conditions and therefore we were able to properly dissociate the effects of reward value and response accuracy.

While error-related neural activity is commonly found just after decision response time or feedback time, it was recently proposed that neural activity related to response accuracy might also occur in the ACC prior to response (Hoffman & Beste, 2015). Therefore, we investigated error-related neural activity that occurred prior to response, after response, and after error feedback, to see if and when it might be affected by the reward value associated with stimuli. We used a perceptual decision making task with two conditions in which stimuli had higher and lower levels of expected perceivability. This meant that we were able to test error-processing under conditions where more or less evidence about the stimuli (reward predictive or non-reward predictive) was available to be processed.

Experiment One Materials and Methods

Ethics Statement

All participants were informed about the requirements of this study and completed written consent forms before it began. This study was approved by the ethics committee of Brain Science Institute of Tamagawa University.

Participants

The data of eighteen neurologically and psychologically healthy, right-handed, undergraduate students (9 female, 9 male, mean age 20 ± 1.2 years; this style indicates mean ± s.d.) were included this experiment. Data of nine other participants ware excluded from analyses due to excessive motion or low error rates. When required, participants were provided with MRI-compatible eyeglasses of the necessary strength. All participants were asked to refrain from eating for at least 10 hours before the beginning of the main experiment so as to maximize the value of the juice reward. Participants attended experiments for one hour on one day and then for two hours the next. They were compensated with a total of ¥7000.

Materials

Visual stimulus presentation was controlled using the “psychophysics toolbox” (Brainard, 1997) running on Matlab 7.1 (Mathworks, Inc.). Visual stimuli were projected to an opaque screen set inside the scanner via a (CP-SX1350, HITACHI; frame rate = 60 Hz) projector and a mirror system. Responses were recorded using MRI compatible response pads (HHSC-2x2, Current Designs, Inc., PA, USA).

Experimental Procedure

Each participant completed the preliminary tasks and main task over a consecutive two-day period. On the first day after watching a video about MRI technology, participants completed a liquid-rating task, a practice task, a

psychophysical measurement task, and a training task. On the second day they completed the training task again, did the main task, and then once again briefly rated the two liquids that they had received in the main task.

Liquid-ratings

Six liquids (yoghurt-flavored water, apple juice, orange juice, and three ion water solutions) were rated in this task. The “juices” (yoghurt-flavored water, apple juice, and orange juice) were simply made from concentrates mixed with water. The aim in getting participants to rate these was to find a liquid that each participant liked a lot. The “ion waters” were made from different concentrations of ions and water (25 mM KCL and 2.5 mM NaHCO3 x 1, 2 or 3, with 1 liter of water). The aim in getting participants to rate these was to find a neutral tasting control (similar in content to human saliva, O’Doherty, Deichmann, Critchley, & Dolan, 2002) for each participant.

Six milliliters of each of these six liquids were provided to participants in disposable plastic cups. Participants were told that for each liquid, they were to pour all 6ml into their mouth, swish it around, and then spit it out into the provided spitting pot (following the design of De Araujo, Lin, Veldhuizen, & Small, 2013). They were told to then immediately rate what they thought about the liquid on a scale of -5 to +5 (**それぞれの飲み物について、どれぐら良いまたは嫌だと思いましたか。ー５から＋５で判断してください。該当する数字に丸をつけてください**). On this scale -5 represented very bad (とても嫌) 、0 represented neutrality (どちでもない), and +5 represented very good (とても良い). Participants were told to subsequently wash their mouth out well with water, and wait 30 seconds before moving onto the next

liquid. The order in which participants were presented with liquids was randomized.

Participants' most preferred juice was used as their "reward" in the training and main tasks. The most preferred juices were rated before the experiment with a mean of 4.3 (s.d.=0.8) and after the experiment with a mean of 3.1 (s.d.=1.7). Participants' most neutrally rated ion water was used as their "non-reward" in the training and main tasks. The most neutrally rated ion water solutions were rated before the experiment with a mean of -0.6 (s.d.=1.4) and after the experiment with a mean of −0.5 (s.d.=1.7). Juice ratings were significantly higher than ion water ratings ($F(1,17)=126.5$, $P<0.001$) and there was no main effect of time (before/after experiment) and no interaction between liquid (juice/ion water) and time (before/after experiment).

Practice task

Because we wanted the participants to properly understand the response mappings and task requirements before doing the psychophysical measurement task, we had them read instructions and then complete an approximately 4.5 minute task on a computer outside of the scanner. In this task the participants used the same fMRI response pads to respond that they would also use in the scanner in subsequent tasks. This "random dot motion discrimination" task involved basic discrimination between the global direction of motion of a cloud of small moving dots. Participants indicated on each trial whether they thought the global dot movement was leftwards, in which case they pressed a button on the response pad in their left hand, or rightwards, in which case they pressed a button on the response pad in their right hand. In reality all the dots in 50% of trials moved in a leftwards global direction and all

the dots in the other 50% of trials moved in a rightwards global direction (order determined using Optseq2 (Greve, 2002)).

There were 50 trials; in each trial the following sequence of events occurred. First, a red fixation point was presented in the center of the screen for 1 second. Second, a cloud of small white dots appeared around the fixation point and these had a global motion direction of leftwards or rightwards for 0.5 seconds (speed = 5 deg/s, density = 16.7 dots/deg, size of a dot = 0.10 × 0.07 deg^2, visual angle = 10°). Each small white dot was shown on a given video frame, and then shown three frames later, either displaced to the left or right (to indicate global motion while preventing the participants from following any one dot with their eyes). Third, the small white dots disappeared leaving only the fixation point onscreen. This remained onscreen for 2 seconds. The participants were able to respond their perceived dot motion direction at any point from the onset of the white cloud of dots until the offset of this 2-second fixation point (in total this made a 2.5 second response window). If participants responded the red fixation point changed to a darker red but the trial did not move on till the next screen until the response window was finished. Finally, participants were provided with feedback according to their response, either: “correct”, “incorrect”, or “you did not respond in time”. A 1 second inter-trial-interval (ITI) was inserted between all trials.

Psychophysical measurement task

After the practice task, participants completed another random dot motion discrimination task (Figure 1). No scans were taken but this task was completed in the scanner because we wanted to measure the psychophysical abilities of participants in the same environment as that in which they would

do the main task. Eight levels of coherence were used in this task (“coherence” refers to the percent of dots that move coherently in a given direction). These coherences were selected as representative of the full range of psychophysical abilities in preliminary testing and were 0, 5, 10, 15, 20, 40, 70, and 100%. In the practice task, coherence was 100% in all trials and so each small white dot was shown on a given video frame, and then shown three frames later, either displaced to the left or right. However, in this psychophysical measurement task, on each trial a given percent of the dots did this (depending on the coherence), and the rest reappeared after three frames in totally random positions. Participants were asked to indicate, using the left-hand and right-hand response pad buttons respectively, whether overall the dots appeared to be moving in a leftward or rightward global direction. The sequence of events and the timing in this task were the same as in the practice task except that no feedback was provided. Overall, each participant completed 160 trials. There were 20 trials of each coherence for each of which half of dots moved in a leftwards and half of dots moved in a rightwards global direction. This took 12 minutes. The results of this experiment were used to determine each individual's “high coherence” (90% accuracy threshold) and “low coherence” (65% accuracy threshold). On average, participants were found to respond with 90% accuracy when dots moved with a coherence of 20% (± 15%) and so this was the average high coherence. On average they were found to respond with 65% accuracy when dots moved with a coherence of 7% (± 6%) and so this was the average low coherence.

Figure 1.

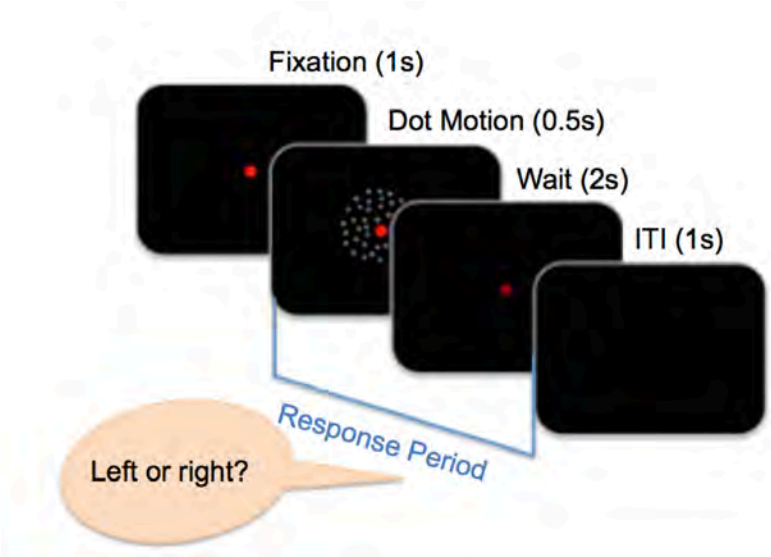

Figure 1. The sequence of events in each trial on the psychophysical testing task from experiment one. After initial presentation of a red fixation point for 1 second, a cloud of moving dots was presented for 0.5 seconds. This cloud then disappeared leaving the fixation point on screen for another 2 seconds. Finally a blank black screen was presented for 1 second as an inter-trial interval. Participants' task was to indicate whether the cloud of dots had a leftwards or rightwards global motion direction. They could respond any time from the onset of dot motion until the fixation point disappeared.

Training task I

In this task participants again completed a random dot motion discrimination task in the scanner but without being scanned (Figure 2 with 1s ITI). Coherence was 100%. The aim of this and the second training task was to help participants to understand that one direction of global dot motion was associated with delivery of the reward liquid and the other with delivery of the non-reward liquid. Importantly, which liquid they were given depended on the actual global dot motion direction, not on the participant's response. For half of the participants reward was associated with leftward global dot motion and for the other half of participants reward was associated with rightward global dot motion. In this task, there were 80 trials, which took a total of 12 minutes to complete. The same sequence of events as in the previous tasks occurred except that the response window was 4 seconds long; subsequent to this response window the participants were provided with either juice or ion water that took 2 seconds to be delivered via polythene tubes which were hooked up to a Multi-Phaser syringe pump system (New Era Pump Systems Inc.); and finally the fixation dot changed size and color for 0.5 seconds to indicate that the liquid could then be swallowed. Importantly, participants were told not to swallow the liquid until this cue appeared. As in the above tasks, a 1 second inter-trial interval (ITI) was inserted between all trials.

Figure 2.

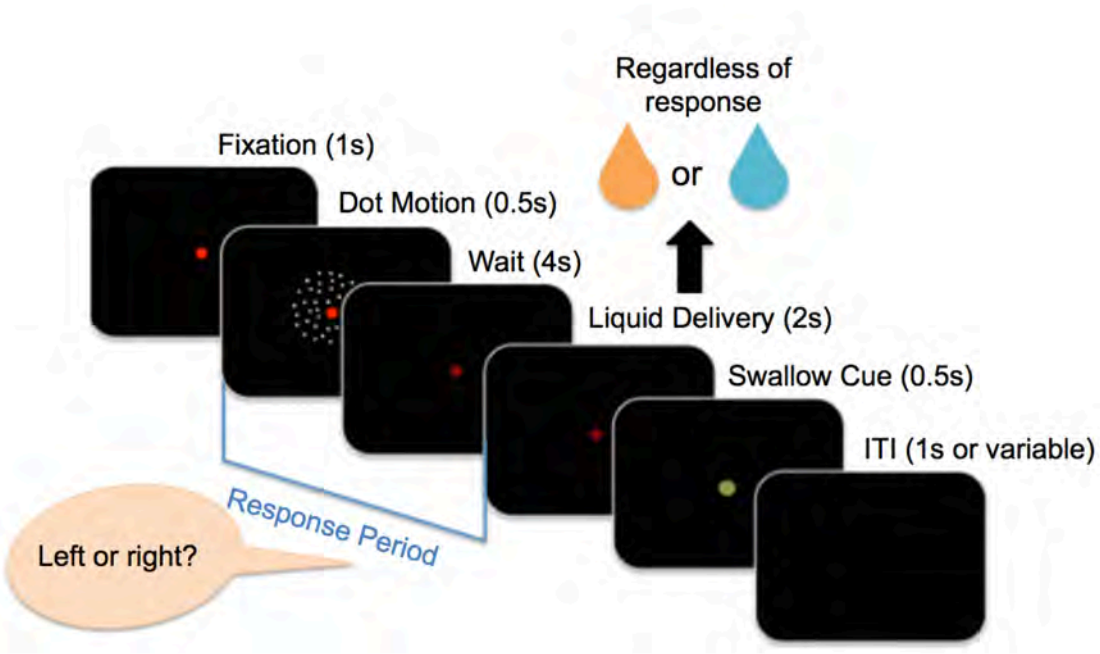

Figure 2. The sequence of events in each trial on the training and main tasks of experiment one. After initial presentation of a red fixation point for 1 second, a cloud of moving dots was presented for 0.5 seconds. This cloud then disappeared leaving the fixation point on screen for another 4 seconds. This was followed by delivery of juice or neutral tasting ion water which participants had to wait 2 seconds before swallowing. A change in size and color of the fixation point indicated when they could swallow. Finally, a blank screen was presented for 1 second in the training task/a variable length of time in the main task. Participants' task was to indicate whether the cloud of dots had a leftwards or rightwards global motion direction. They could respond any time from the onset of the dot motion until liquid was delivered**.**

Training task II

This was identical to the first training task except that it was completed on the second day (before the participant did the main task) while participants' T1 scans were taken. In total, the proportion of correct responses across the two training tasks was 0.998 (± 0.002) in trials where dots moved in the reward associated direction and 0.994 (± 0.004) in trials where dots moved in the non-reward associated direction. This shows that participants understood the task and could respond very well when coherence was 100%.

Main Experiment

The design of this task (Figure 2 with variable ITI) was similar to that of the training task except that (a) the dots moved with the high and low coherences determined for each participant individually in the psychophysical testing task, and (b) the ITI was of a variable length (0-23s, median = 3s, determined using Optseq2 (Greve, 2002)). In order to obtain enough error trials for a decent statistical analysis, an uneven number of high and low coherence trials were used. We planned for each participant to perform 10 sessions, each of which consisted of 32 trials and took 6 min in total (including ITIs). If there were 250 high coherence trials, and 70 low coherence trials completed across these 10 sessions, then because the high coherence was set at each individual's 90% accuracy threshold and the low coherence was set at each individual's 65% accuracy threshold, we expected participants to make around 25 error trials in total for each coherence condition. The ratio of high coherence to low coherence trials was therefore set to 78:22 accordingly. Due to fatigue and time limitations, some participants completed less than 10 sessions: 3 participants completed 9 sessions, 2 participants completed 8

sessions, and 2 participants completed 7 sessions. The data from these participants was still kept in our analyses because they all made over 2 errors in each of the 4 (reward/non-reward high/low coherence) conditions.

Imaging data acquisition

A Siemens Trio TIM 3T scanner with a 32-channel head coil was used for scanning acquisition. Anatomical images were acquired using a T1-weighted MP-RAGE protocol (TR = 2000 ms, TE = 1.98 ms, FA = 10°, FOV = 256 mm × 256 mm, resolution 1 × 1 × 1 mm^3). Subsequently, T2*-weighted images reflecting blood oxygen level-dependent (BOLD) signals were acquired using gradient-echo echo-planar imaging (EPI) (TR = 2000 ms, TE = 25 ms, 38 slices, FA = 90°, FOV = 192 mm × 192 mm, and resolution = 3.0 × 3.0 × 3.5 mm^3). Functional data were collected over a series of sessions, each of which took 360 seconds and consisted of 182 volumes. The first two volumes taken in each session were discarded to ensure steady-state magnetization.

Behavioral data analyses

Classical cognitive and behavioral experiments consider a person to be accurate if they correctly detect the presence of a signal (a ‘hit’), and to be inaccurate if they do not correctly identify the presence of a signal (a ‘miss’). However, the measure of accuracy does not account for the fact that people are also accurate if they correctly identify the absence of a signal (a ‘correct rejection’), and that they are also inaccurate if they say a signal is present when it is not (a ‘false alarm’). This means that whether a person's performance reflects sensitivity (the ability to discriminate between signal present and signal absent trials) or bias (the increased likelihood to select one response over the other) cannot be determined from traditional measures

alone. Application of Signal Detection Theory (SDT; Green & Swets, 1966) to data is useful because it considers 'false alarms' as well as 'hits', and therefore is informative about what type of errors (and correct responses) are made, and therefore what kinds of decision making strategies participants are using. We therefore conducted a SDT analysis to estimate participants' sensitivity and their bias.

In this analysis, a 'hit' (H) was considered a trial in which participants correctly responded that dots moved in the reward associated direction. A 'false alarm' (F) was considered a trial in which participants responded incorrectly that the dots moved in the reward associated direction. The parameter *d'* was calculated to estimate sensitivity, and the parameter *c* was calculated to estimate bias.

$$d' = z(\mathrm{H}) - z(\mathrm{F}) \quad (1)$$

$$c = -0.5*(z(\mathrm{H}) + z(\mathrm{F})) \quad (2)$$

Imaging data analyses

SPM8 (Wellcome Trust Centre for Neuroimaging, University College London) was used to pre-process and analyze the imaging data. Standard pre-processing steps were completed in the following order: realignment, slice-timing correction, normalization to the EPI template (voxel-size re-sampled to 2 × 2 × 2 mm^3) and spatial smoothing using a Gaussian filter (FWHM = 8 mm). A high-pass filter of 128s was used to remove low-frequency noise.

Regressors of interest from different time points were found to have low orthogonality when they were all included in the same general linear model. Therefore, because we wished to analyze the brain activation from the dot

motion period, at response time, and from the outcome period, we performed three separate general linear model analyses looking at the regressors of interest at each of these times separately.

Our first whole-brain analysis model (EXPT1-GLM1) was a factorial design for brain activity that occurred during dot motion presentation time split by coherence (high/low), stimulus (reward/non-reward predictive), and accuracy (correct/error). This gave us the eight conditions in total. For each subject, the general linear model (GLM) was used to fit the fMRI time series. Each condition was modeled from the onset of dot motion until the offset of dot motion, 500 ms in total. In addition, six other trial-related regressors were included: left/right response (duration = 0 s), juice/ion water delivery (duration = 2s), and swallowing of juice/ion water (from swallow cue onset for 0 s).

Our second whole-brain analysis model (EXPT1-GLM2) was a factorial design for brain activity that occurred at response time split by coherence (high/low), stimulus (reward/non-reward predictive), and accuracy (correct/error). While these may appear the same as the eight regressors of interest in the EXPT1-GLM1 analysis, the current regressors occurred at the time that the participants made their response, which on average was 0.9 seconds (s.d. = 0.28, range = 0.2-4.5s) after the dot motion stimuli first appeared, and therefore on average 0.4s after these stimuli disappeared. This range of response times made a jittering effect on the analysis, which suggests that observed activation in EXPT1-GLM2 reflects different neural processes from that in EXPT1-GLM1. Each condition was modeled at the onset of response as an event (duration = 0 s). Six other trial-related regressors were also included: left/right dot motion (duration = 500 ms),

juice/ion water delivery (duration = 2s), and swallowing of juice/ion water (duration = 0 s).

For our third whole-brain analysis model (EXPT1-GLM3), a factorial design for brain activity that occurred at outcome time was completed and activity was divided by coherence (high/low), stimulus (reward/non-reward), and accuracy (correct/error). While these may appear the same as the regressors in the GLMs above, it is important to note that these regressors involved brain activations from a completely different time in the experiment. Each condition was modeled from the onset of liquid delivery until the offset of liquid delivery (i.e. duration = 2s). Two other trial-related regressors were included: dot motion leftwards and dot motion rightwards; these were modeled as starting at dot motion onset and lasting 500 ms until dot motion offset.

For all GLMs, random effect analyses at the group-level were conducted using an ANOVA design (Friston et al., 2002) that modeled the eight conditions of interest and the main effect of subjects. Significant clusters were identified using the voxel-level threshold of p-unc. = 0.001. The statistic threshold at cluster-level was set to p-FWE = 0.05. The six motion regressors were included as effects of no interest.

Experiment One Results

Behavioral Results

We examined the effects of coherence (high/low) and stimulus (reward/ non-reward predictive) on response accuracy and found that participants performed significantly better in high coherence trials (0.82 ± 0.15) than in low coherence trials (0.60 ± 0.15; $F(1,17)=47.1$, $P<0.001$; Figure 3a). Likewise,

their sensitivity in high coherence trials (d' = 2.27 ± 1.19) was better than that in low coherence trials (d' = 0.63 ± 0.52; t(17)=6.15, P<0.001, Figure 3b). However, sensitivity on low coherence trials was still better than chance (t(17)=5.15, P<0.001). An effect of stimulus (reward/non-reward predictive) was also found on accuracy. On average participants responded more accurately in trials with reward predictive stimuli (0.76 ± 0.15) than in trials with non-reward predictive stimuli (0.65 ± 0.16; F(1,17)=5.85, P<0.05, Figure 3a). This finding can likely be explained by response bias (c). The response bias across the experiment significantly differed from 0 in low coherence trials (one-sample t-test, t(17)=−2.40, P<0.05; Figure 3c), and approached significantly differing from 0 in high coherence trials (one-sample t-test, t(17)=−2.03, P=0.058; Figure 3c). On average it was -0.17 (± 0.35) in high coherence trials and -0.22 (± 0.39) in low coherence trials. Due to the way that we calculated c, any negative c reflects a bias for the response associated with reward predictive stimuli. Therefore because the average c for both high and low coherence conditions were negative, this shows that on average our participants had a bias for the response associated with reward predictive stimuli, and therefore that they tended to choose this response more than the other response. This may therefore explain why participants were correct more often on trials where stimuli were reward predictive. The level of bias did not differ significantly depending on coherence (t(17)=0.85, P=0.41).

Figure 3.

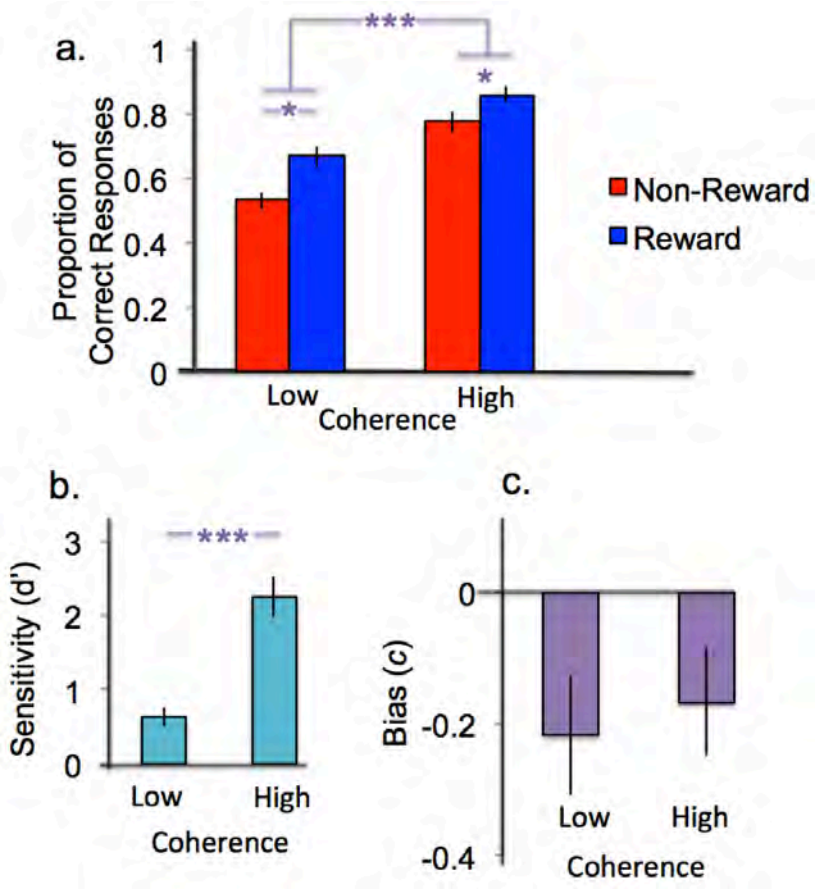

Figure 3. The accuracy and SDT results of the main task of experiment one. Asterisks indicate statistically significant differences. **a.** Accuracy: There were main effects of stimulus (reward/non-reward predictive) and coherence (high/low) on participants' dot motion direction discrimination performance. **b.** SDT Sensitivity: This (d') was significantly higher in high than in low coherence trials, and significantly greater than chance in low coherence trials. **c.** SDT Bias (*c*): On average, in both high and low coherence conditions, participants had a bias to select the response associated with reward predictive stimuli. Bias was significantly greater than chance in low coherence conditions and approached a significant difference from chance in high coherence conditions.

A coherence (high/low) by accuracy (correct/error) interaction was found when response times were investigated ($F(1,17)=9.04$, $P<0.01$). Post hoc t-tests showed that response times in high coherence correct trials (0.75s ± 0.18s) were faster than those in low coherence correct trials (0.88s ± 0.28s; $t(17)=-3.75$, $P<0.01$, Bonferroni corrected, Figure 4) and faster than those in high coherence error trials (1.01s ± 0.52s; $t(17)= -3.19$, $P<0.01$, Bonferroni corrected, Figure 4). Because participants were thereby shown to be fastest in high coherence correct trials, we wished to see if this was the same for both trials with reward and non-reward predictive stimuli. A paired sample t-test revealed that participants were significantly faster to respond in high coherence correct trials with reward predictive stimuli (0.73s ± 0.18s) than in high coherence correct trials with non-reward predictive stimuli (0.78s ± 0.18s; $t(17)= -3.07$, $P<0.01$, Bonferroni corrected). This finding means that when participants could identify the stimulus (high coherence correct trials), their speed in response discriminated between reward and non-reward conditions. This finding therefore provides evidence that participants had learned that stimuli with one direction of dot motion were associated with reward and that stimuli with the other direction were associated with non-reward

Figure 4.

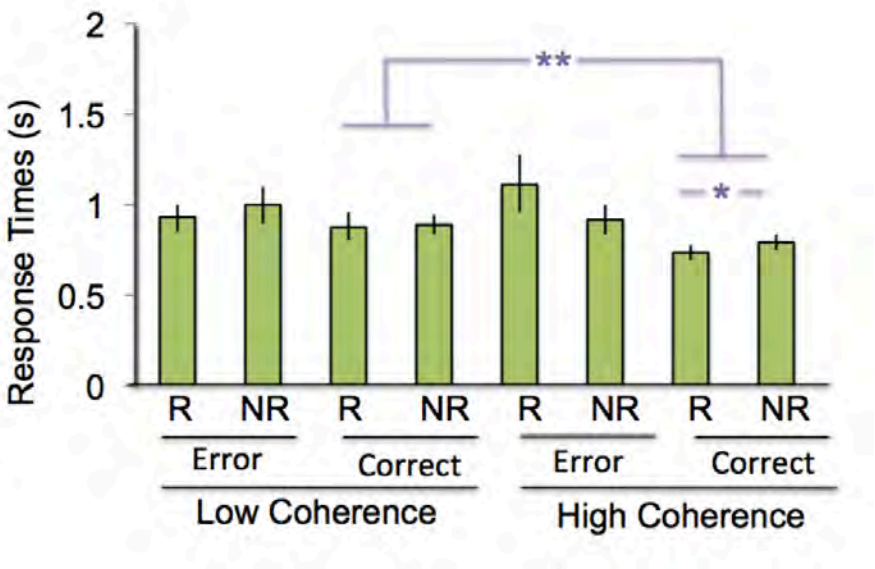

Figure 4. The response times of the main task of experiment one. Participants were faster to respond in correct high coherence trials than in any other trials. Responses were faster in correct high coherence trials with stimuli predictive of reward than in correct high coherence trials with stimuli predictive of non-reward. R = reward trials, NR = non-reward trials. Asterisks indicate statistically significant differences.

When we investigated the relationship between response times and the SDT measures of response bias and sensitivity, we found that the greater a person's bias for the response associated with reward predictive stimuli was on high coherence trials, the faster they erroneously responded on high coherence reward trials, (n=18, r=0.59, *P* =0.01). Similarly, the greater a person's bias for the response associated with reward predictive stimuli was on low coherence trials, the faster they erroneously responded on low coherence reward trials, (n=18, r=0.54, *P* <0.05) and the faster they correctly responded on low coherence reward trials (n=18, r=0.56, *P* <0.05). No other correlations reached significance.

fMRI Results

Dot Motion Duration BOLD Contrasts: EXPT1-GLM1

We investigated brain activation that occurred during the 0.5 second time period in which dot motion stimuli were displayed (Table 1, Figure 5). Significantly increased activity in trials where participants subsequently made a correct compared to an erroneous response (correct > error) was seen in visual areas, including the putative middle temporal area (MT), which is associated with visual motion perception (Krug, Cicmil, Parker, & Cumming, 2013). Significantly increased activity in trials where participants subsequently made an erroneous compared to a correct response (error > correct) was seen in the bilateral inferior frontal gyrus (IFG) and medial frontal cortex (MFC; including a cluster from the ACC). None of these activities were found to differ depending on whether stimuli were reward or non-reward predictive. Finally, significantly increased activity in the midcingulate cortex (MCC), insula, cerebellum, precentral gyrus was found in trials with non-reward

compared to reward predictive stimuli (non-reward > reward). None of these activities were found to differ depending on whether the subsequently made response would be correct or incorrect. No areas were found to have significantly increased activity for reward compared to non-reward predictive stimuli (reward > non-reward).

Table 1. Summary of brain activation found in EXPT1-GLM1.

Contrast / Region	Peak in MNI coordinates			Hemisphere	z-score (peak)	Cluster size
	x	*y*	*z*			
Correct > Error						
Visual areas	−22	−94	−8	Left	5.73	2414
	−44	−66	0	Left	5.06	
	−22	−86	12	Left	4.87	
Visual areas	22	−96	−4	Right	5.41	2580
	40	−56	−14	Right	5.20	
	32	−82	6	Right	4.67	
Thalamus	4	−28	−4	Right	4.40	338
	−4	−26	−4	Left	4.30	
	8	−14	2	Right	3.82	
MCC	0	0	58		3.85	352
	-6	6	52	Left	3.63	
Error > Correct						
IFG	44	46	2	Right	4.59	844
	40	44	14	Right	3.90	
	14	58	8	Right	3.76	
MTG	64	−36	−12	Right	4.50	278
	66	-30	−6	Right	4.30	
SFG	−22	56	12	Left	4.41	1041
	−10	50	30	Left	4.08	
	−34	54	8	Left	4.02	
MTG	−58	−32	−6	Left	3.98	375
	−58	−32	−22	Left	3.84	
	−56	−40	6	Left	3.60	
MFC	8	46	24	Right	3.74	223
	14	54	28	Right	3.74	
Non-Reward> Reward						
MCC	−2	−10	42	Left	5.14	2072
Insula	−46	−8	30	Left	4.80	2421
Cerebellum	46	−56	−38	Right	4.54	283
Insula	60	6	4	Right	4.49	724
Precentral gyrus	44	−16	38	Right	4.44	318
MCC	0	−42	52		4.15	458

MCC = midcingulate cortex, IFG = inferior frontal gyrus, MTG = middle temporal gyrus, SFG = superior frontal gyrus, MFC = medial frontal cortex.

Figure 5.

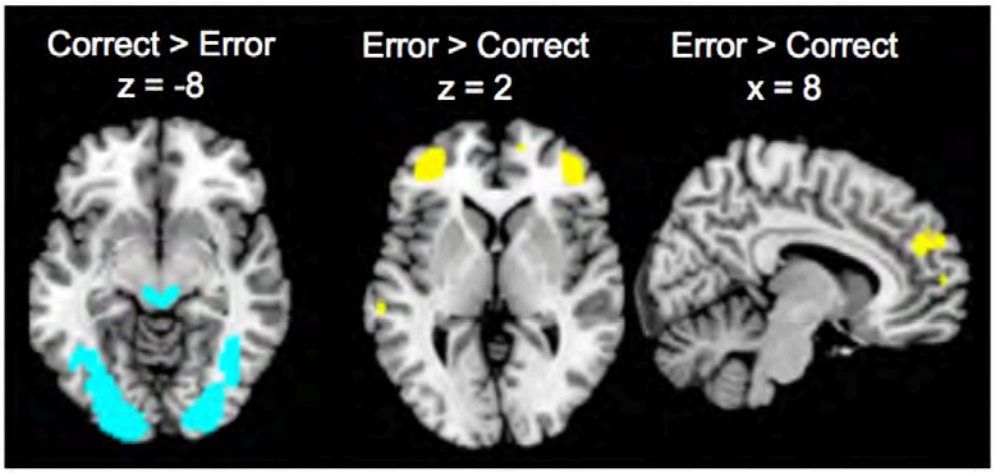

Figure 5. The results of EXPT1-GLM1, i.e. activity during the dot motion period, are shown rendered on the template of SPM with *P* <0.001, uncorrected. The correct > error contrast revealed significant activation in the visual cortex including the MT. The error > correct contrast revealed significant activation in the IFG and MFC, including part of the ACC.

Response Time BOLD Contrasts: EXPT1-GLM2

We next examined neural activation that occurred at the time participants made a response (Table 2, Figure 6). Note that at this time participants had already committed to a decision but had not yet received feedback about its accuracy. Activations for erroneous responses (error > correct) were found in the left posterior medial frontal cortex (PMFC), the left IFG, the bilateral insula, and an array of bilateral visual areas. We split these trials by stimulus type (reward/non-reward predictive). When we re-did the same contrast exclusively using trials with reward predictive stimuli (reward error > correct) we found that activity in the bilateral PMFC, the right IFG, the left precentral gryus, and an array of bilateral visual areas was significantly increased at this time. Doing the same contrast exclusively using trials with non-reward predictive stimuli (non-reward error > correct) revealed no significant activity. Therefore, the error-related activity we found was much more broadly and significantly active in reward compared to non-reward trials. No areas were more active at this time in correct compared to erroneous responses.

Table 2. Summary of brain activation found in EXPT1-GLM2.

Contrast / Region	Peak in MNI coordinates			Hemisphere	z-score (peak)	Cluster size
	x	*y*	*z*			
Error > Correct						
PMFC	−8	14	48	Left	4.97	1465
	−8	6	56	Left	4.72	
	−6	−2	60	Left	4.62	
IFG	−44	0	32	Left	4.87	658
	−44	−6	50	Left	4.24	
	−34	−8	48	Left	3.90	
Insula	−30	26	0	Left	4.34	293
	−32	18	6	Left	4.14	
	−26	20	−8	Left	3.50	
Insula	34	24	6	Right	4.61	212
Visual Areas	−22	−92	6	Left	4.63	1291
	−22	−92	−10	Left	4.51	
	−22	−86	18	Left	4.19	
Visual Areas	36	−74	20	Right	4.28	399
	22	−70	34	Right	4.00	
Reward Error > Reward Correct						
PMFC	−6	14	50	Left	5.30	1621
	4	10	56	Right	5.00	
	−6	2	58	Left	4.93	
IFG	44	6	26	Right	4.96	513
	46	4	36	Right	4.60	
	52	4	42	Right	4.49	
Precentral Gyrus	−46	2	32	Left	4.79	870
	−32	2	32	Left	4.61	
	−44	−6	50	Left	4.22	
Visual Areas	−22	−90	−8	Left	4.67	1108
	−22	−92	6	Left	4.54	
	−20	−90	14	Left	4.46	
Visual Areas	36	−74	18	Right	4.63	773
	22	−70	36	Right	4.07	
	24	−90	0	Right	4.02	
Interaction between Reward and accuracy						
MCC	−10	6	52	Left	4.02	282
	14	10	52	Right	3.88	
	−8	16	52	Left	3.63	

PMFC = posterior medial frontal cortex, IFG = inferior frontal gyrus, MOG = middle occipital gyrus, MCC = midcingulate cortex.

Figure 6.

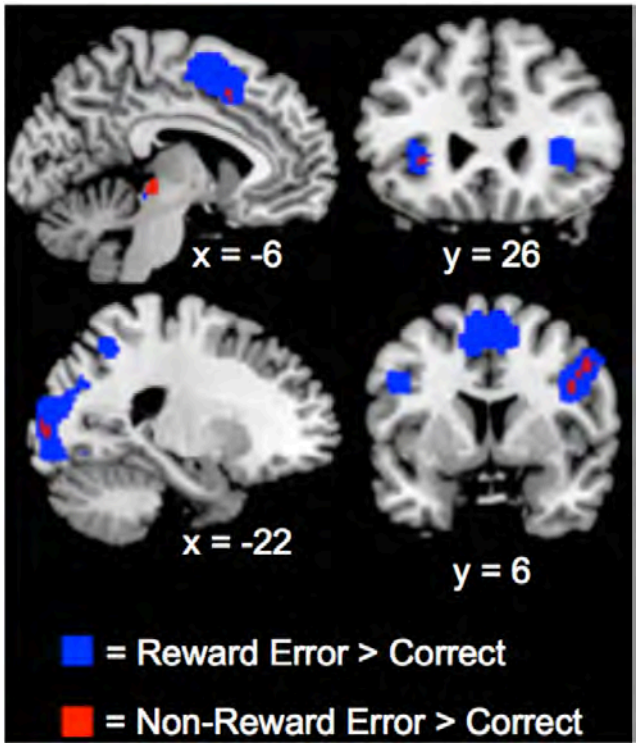

Figure 6. The results of EXPT1-GLM2, i.e. activity at the time of response, are shown rendered on the template of SPM with *P* <0.001, uncorrected. The error > correct contrast revealed significant activation in the PMFC, IFG, bilateral insula, and visual areas. Activity in these same areas was more significant and broad in reward trials (reward error > correct; blue) than in non-reward trials (non-reward error > correct; red).

Interestingly, part of the PMFC, specifically part of the bilateral MCC, survived an interaction between accuracy (correct/error) and stimulus (reward/non-reward predictive). This area had increased activity for error compared to correct responses in reward compared to in non-reward trials (Table 2, Figure 7).

Figure 7.

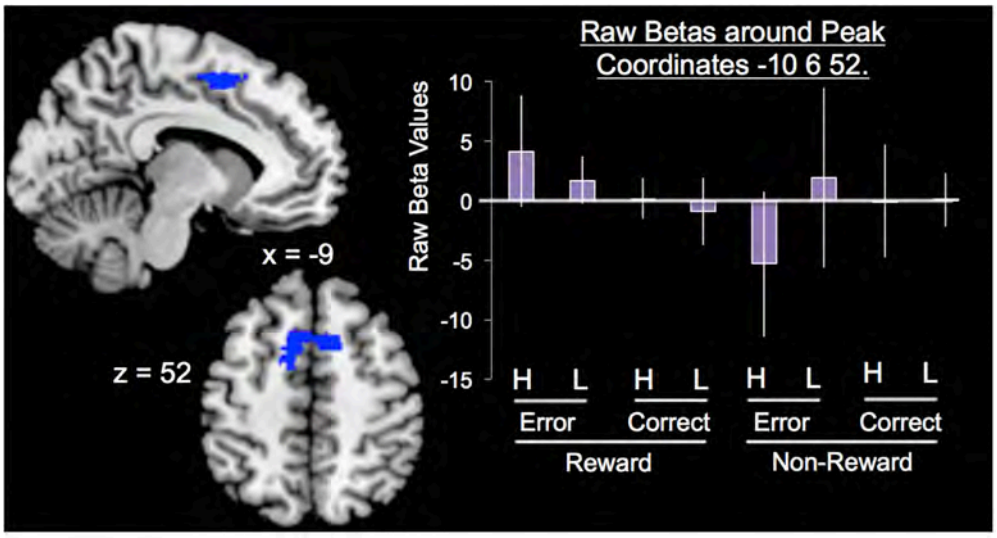

Figure 7. The results of an interaction found in the MCC in EXPT1-GLM2, i.e. during the response period, are shown rendered on the template of SPM with *P* <0.001, uncorrected. This interaction revealed increased error-related activity in reward compared to non-reward trials. Raw beta values from each condition are shown. H = high coherence, L = low coherence.

Because certain models predict that error-related neural activity should differ depending on decision boundaries (to be discussed in the general discussion), we analyzed averaged beta values from 4mm spheres around each of the three MCC peaks found in this interaction for each participant for each of the 8 conditions. We correlated the betas from high coherence conditions with participants' response bias in the high coherence trials (calculated using SDT as reported in the above behavioral result section). Similarly, we correlated the betas from low coherence conditions with participants' response bias for the low coherence trials. Betas in high coherence reward error trials from two of these spheres were found to correlate negatively with high coherence response bias (n=18, r = -0.483, *P* <0.05 for the sphere around the peak coordinates 14 10 53; n = 18, r = -0.514; *P* <0.05 for the sphere around the peak coordinates -8 16 52). Because in our analyses a negative *c* indicates a bias for the response associated with reward predictive stimuli, this means that the more biased a participant was for the response associated with reward predictive stimuli, the more activity they had in their MCC during high coherence reward error trials. No other correlations were found to reach significance.

Outcome Time BOLD Contrasts: EXPT1-GLM3

Brain activation that occurred when participants were presented with an outcome (reward/non-reward) was examined (Table 3). It is important to note that at this time, the outcome was dependent on the direction in which the dots had moved rather than on the accuracy of the participants' response (e.g. if dots moved leftwards then you get the juice reward regardless of whether you correctly responded that they moved leftwards or incorrectly

responded that they moved rightwards). The outcome therefore informed participants of the correct dot motion direction in the current trial (e.g. if you receive juice then you know that the dots must have moved leftwards). Participants could then use this information to determine if they had made the correct response or not. At this time, we did not find any overall effects of error. However, when we split these trials by stimulus type (reward/non-reward predictive) and looked only at trials with non-reward predictive stimuli (non-reward error > correct), we found significant error-related activation in part of the MFC, the ACC (Figure 8). No significant error-related activity was found at this time when we looked at trials with reward predictive stimuli (reward error > correct).

Table 3. Summary of brain activation found in EXPT1-GLM3.

Contrast / Region	Peak in MNI coordinates			Hemisphere	z-score (peak)	Cluster size
	x	*y*	*z*			
Error Non-Reward > Correct Non-Reward						
ACC	−2	44	16	Left	4.25	590
	−4	36	32	Left	3.83	
	10	40	16	Right	3.36	

ACC = anterior cingulate cortex.

Figure 8.

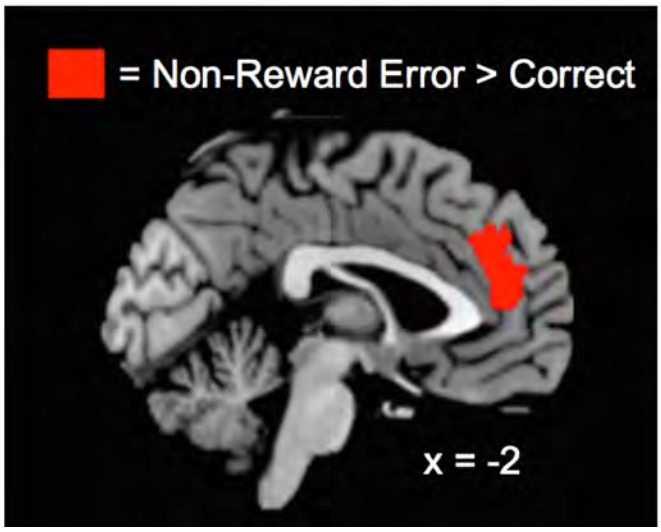

Figure 8. The results of EXPT1-GLM3, i.e. activity at outcome time, rendered on the template of SPM. The ACC was found to be activated in an error > correct contrast using only non-reward trials. These results are shown rendered on the template of SPM with *P* <0.001, uncorrected.

Experiment One Discussion

In our first experiment we set out to determine if error-processing would differ after decisions were made to stimuli associated with different reward values. Therefore, we designed a task in which participants' goal was to distinguish between reward and non-reward predictive stimuli after which they received the outcome (reward or non-reward) corresponding to the stimulus, regardless of whether they made the correct or incorrect response. Behaviorally, despite the fact that its selection did not determine whether reward or non-reward would be delivered, participants were biased for the response associated with reward predictive stimuli. Because this means that participants selected the response associated with reward predictive stimuli more often overall, they were consequently more accurate in responding when stimuli were reward predictive rather than non-reward predictive. In addition, participants made correct responses faster to reward predictive compared to non-reward predictive stimuli. This effect was only significant for high coherence trials, which makes sense because information about the reward value associated with stimuli should have been more available in high than in low coherence trials. Overall, these results show that the reward value associated with stimuli can affect behavior. We next looked to see if the reward value associated with stimuli could also affect error-related neural processing at three different periods in time. At the time of stimulus presentation, neural activity that was related to the subsequent accuracy of response was found but this did not differ dependent on the reward value associated with stimuli. In addition, neural activity that discriminated between reward and non-reward predictive stimuli was also found at this time (it was

greater in non-reward trials), but this did not differ depending on the subsequent accuracy of response. Therefore, at stimulus presentation time neural activity that signaled the reward value associated with stimuli was not related to neural activity that signaled the subsequent accuracy of response.

These factors were found to interact, however, at a subsequent point in time where participants had committed to their decision and were therefore no longer able to change it, but had not yet received feedback about its accuracy. At this time error-related neural activity (defined as activity in error trials minus activity in correct trials) in the MCC was significantly greater in reward than in non-reward trials. This indicates that, as hypothesized, even when reward outcome is unrelated to the accuracy of decision response, the reward value associated with stimuli can enhance the neural processing of errors after a decision is made. Finally, in the third time period that we investigated, when participants received feedback that essentially informed them about the accuracy of their response, the only error-related neural activity found was in non-reward trials in the MFC.

The main finding of this experiment was the interaction between stimulus (reward/non-reward predictive) and accuracy (correct/error) in the MCC at response time (Figure 7). This interaction showed that, even though response did not affect whether or not a reward would be obtained, error-processing in the MCC was significantly greater in trials where responses were made to reward predictive compared to non-reward predictive stimuli. In fact, when trials with non-reward predictive stimuli were examined alone error-processing was not significant at all at this time. This indicates that the reward value associated with stimuli can affect information processing after a decision has

been made. However, the reward we used in this experiment was a primary reward, and because primary and secondary rewards are often associated with processes in different areas of the brain (e.g. see Sescousse, et al., 2013) we have to be cautious and note that it remained undetermined whether or not this effect was generalizable to all types of reward.

Because the value of the outcome on each trial on this task was not related to response accuracy, this finding is problematic for the popular idea that error-processing occurs specifically when the learning of response-outcome associations is useful for obtainment of future reward (e.g. Holroyd & Coles, 2002). Instead, because error-processing at response time (after committing to a decision but before receiving feedback about its accuracy) is thought to occur as a result of continued monitoring of evidence after a decision is made (for an related theories see the general discussion and Yeung & Summerfield, 2012), our result perhaps indicates the reward value associated with stimuli can affect the degree to which decision evidence continues to be monitored after a decision is made. If this explanation were true, then the brain would need to be able to distinguish between reward and non-reward predictive stimuli prior to this. Consistent with this idea, activity prior to response (at stimulus presentation time) was found to be different for reward and non-reward conditions. While this activity did not differ according to subsequent accuracy, and therefore was likely not processed explicitly enough to be used to make the correct response, it may have provided enough information for the brain to determine whether or not, or how much, to continue evidence monitoring after making a decision response.

In further support of the idea that reward enhances error-processing at response time, we found activity in a variety of other regions of the brain (including the bilateral insula, IFG, and posterior medial prefrontal cortex) to be somewhat differentially activated after erroneous responses in reward compared to non-reward trials. These areas are often found to be active after errors (e.g. Garavan et al., 2002; Klein et al., 2007; Menon et al., 2001). In our study, an error > correct contrast conducted on activity exclusively from reward trials showed these areas to be broadly and significantly active. In contrast, a similar error > correct contrast conducted on activity exclusively from non-reward trials did not show any significantly active areas at all (although the same areas must have been a *little* active in non-reward trials, albeit non-significantly, or else they would have survived the interaction, and this can be seen in Figure 6 where the p-value is reduced to <0.001 uncorrected). This result therefore indicates that *overall* error-processing may be stronger in conditions with reward predictive stimuli (Figure 6).

In our first experiment, because outcome was associated with dot motion direction (e.g. left = juice, right = ion water), when participants received the outcome of the current trial they should have been able to infer the direction in which dots had moved (e.g. “I got juice so the dots must have moved left”). Based on this they should have been able to infer the accuracy of their response (e.g. “I got juice so the dots must have moved left but I responded that they moved right so I was wrong”). In this way the outcome of each trial was informative about response accuracy. One explanation for our finding of ACC activity in non-reward trials at feedback time is that the brain simply did not recognize that an error had been made in these trials until this point. In

reward trials, perhaps due to better continuation of evidence accumulation, error had already been signaled at response time. On the contrary, on non-reward trials error was not signaled (significantly) at response time and so when feedback effectively informed participants that their response had been erroneous, the generic error processing system proposed to exist in the cingulate (Holroyd & Coles, 2002) may finally have then received the evidence it needed to process these errors properly.

Our result that increased activity was found in the MFC (including the part of the ACC) and IFG prior to erroneous compared to correct response is interesting because it is the first time, to our knowledge, that such activity has been reported. A popular theory claims that activity in the ACC might be used in difficult situations for the recruitment of cognitive control to improve response accuracy (e.g. Hoffman & Beste, 2015; Shenhav, Botvinick, & Cohen, 2013). Problematic for this, we found this activity, on average to occur prior to errors compared to prior to correct responses. Nevertheless, because this was not our goal we did not directly test this and so cannot rule out the possibility that this activity might have occurred and lead to correct response in a small amount of correct trials. Therefore further studies are required to determine the function of the activity we found to precede erroneous responses in this experiment.

Overall, the results of our first experiment showed that error-related activities in the MCC and (to a lesser extent) in an array of other classic error regions were enhanced at response time by reward value. This was found even though the reward value of outcome in our task was simply related to the provided stimuli rather than to the accuracy of response. In situations of non-

reward, error-related processing did not significantly occur until feedback that an error has been made was effectively provided. These results therefore indicate that whether error is processed at response time, or not until external source provides evidence that an error was made, may depend on the value associated with the stimuli to which the erroneous response was made.

Experiment Two Introduction

In our first experiment we found that error-processing at response time (prior to feedback) particularly in the MCC, was enhanced in conditions with reward predictive stimuli. Because the reward used in experiment one was a primary reward we wished to test whether or not the same result could be found with a secondary reward. In addition to this, because the processing of response accuracy has been proposed to reflect confidence and uncertainty (see Yeung & Summerfield, 2012), we wished to see if the results found in experiment one were related to these. We therefore conducted a follow-up experiment.

The “common currency" hypothesis is the proposal that all types of reward are converted to a common currency and then similarly processed in the brain (Levy and Glimcher, 2012; Montague & Berns, 2002; Sugrue, Corrado, & Newsome, 2005). However, secondary rewards only acquire value after they have been associated with primary rewards (see Knutson & Bossaerts, 2007). For example money, a secondary reward, may acquire value after one learns that they can use it to buy food, a primary reward. Therefore, because this suggests that the processing of secondary rewards may be more convoluted than the processing of primary reward, it suggests

that the neural regions which process them might differ somewhat. Consistent with this, a recent activation likelihood estimate meta-analysis investigating 33 neuroimaging studies on reward showed that while some areas were indeed commonly activated for both primary and secondary rewards (including the ventromedial prefrontal cortex and striatum), other areas were more activated for certain types of rewards (e.g. the orbitofrontal cortex for secondary reward; Sescousse, et al., 2013). This paper did not discuss whether or not primary and secondary rewards are processed in the cingulate. Therefore, whether or not the results our first experiment are generic to all types of reward remained questionable and thus did the scope of our finding. To test the generalizability of this effect, we conducted another similar experiment where a secondary reward (money) was associated with stimuli.

If we are able to replicate the effect found in experiment one using a secondary reward, then we would have the chance to further probe the mechanisms underlying this effect. In experiment one, we measured and compared neural activity that occurred after correct and erroneous responses. This type of binary analysis was enough to show that processing in erroneous compared to correct responses was greater when stimuli were associated with reward than non-reward. However, some studies have suggested that rather than processing actual error per se, this type of cingulate activity instead depends on some other process that occurs more often in erroneous than in correct responses (Scheffers & Coles, 2000; Vidal, Hasbroucq, Grapperon, & Bonnet, 2000).

One likely candidate for a process that occurs more often in erroneous than in correct trials is decision uncertainty (Yeung & Summerfield, 2012). This is

often defined as one's perceived likelihood of having made an erroneous decision (rather than their actual processing of an error), and has been considered the opposite of decision confidence, which is the perceived likelihood of having made the correct decision (e.g. Kepecs, et al., 2008; Kepecs & Mainen, 2012). For simplicity, in this paper we shall adhere to these definitions. There is some support for the idea that post-error processes that occur in the cingulate cortex might reflect decision confidence/uncertainty rather than just the processing of error. For example, several studies have had participants self-report their perceived confidence in their decisions and found that event related potentials (thought to be sourced in the cingulate) which were originally thought to signify error-processing, actually differed in a graded fashion as decision confidence decreased, i.e. as decision uncertainty increased (Boldt & Yeung, 2015; Scheffers & Coles, 2000). Importantly, when participants reported feelings of uncertainty, this activity has been found to occur even in correct trials in which error-processing, by nature, should be impossible (Boldt & Yeung, 2015; Scheffers & Coles, 2000). Therefore, many findings of the error-processing literature might be better explained as reflecting decision uncertainty (Yeung & Summerfield, 2012). If the results that we found in the MCC in experiment one reflect the processing of uncertainty rather than simply the processing of error, then if we get participants to self-report decision confidence, this MCC activity should correlate negatively with these. Furthermore, this correlation should withstand even in correct trials.

Overall, in experiment two we wished to further study the effect found in experiment one. Therefore, we had participants complete a similar task to that in experiment one but with two changes. First, instead of receiving a primary

reward (juice) participants received a secondary reward (money) on trials with reward predictive stimuli. Second, after making a dot-motion direction response, and prior to receiving outcome, participants had to explicitly rate the level of confidence they had that their dot-motion direction response was accurate. The major goals of this experiment were to see if the effect found in experiment one occurs when secondary rather than primary rewards are used, and to see if the neural processing of error in the MCC was related to continuous self-reports of decision confidence/uncertainty.

Experiment Two Materials and Methods

Ethics Statement

All participants were informed about the requirements of this study and completed written consent forms prior to initiation of the experiment. This study was approved by the ethics committee of Brain Science Institute of Tamagawa University.

Participants

The data of twenty-four participants were included in this experiment. These participants were all psychologically and neurologically healthy, right-handed, undergraduate students (12 female, 12 male, mean age 20.5 ± 1.3 years) with normal or corrected-to-normal vision. Data of seven of other participants were excluded from analyses due to excessive motion or low error rates. Participants were paid a baseline of ¥6000 yen for a two-hour session. This payment could be increased up to ¥7500 yen depending on the participant's performance.

Materials

Presentation of visual stimuli was controlled using the “psychophysics toolbox” (Brainard, 1997) running on Matlab 7.1 (Mathworks, Inc.). These stimuli were projected to an opaque screen inside the scanner via a mirror system and a (CP-SX1350, HITACHI; frame rate = 60 Hz) projector. MRI compatible response pads (HHSC-2x2, Current Designs, Inc., PA, USA) were used by participants to respond to stimuli.

Experimental Procedure

Practice Task

After watching a video about MRI and receiving instructions about the experiment, participants completed 20 practice trials out of the scanner. The sequence of events in this task was similar to that in the main task of experiment one. For the first 1 second a black screen with a red fixation point in the center was presented. Then for 0.5 seconds a cloud of small white dots appeared around this fixation point. These dots had the same parameters as those in experiment one and they similarly had a global motion direction of left or right. In this practice task dots moved with a coherence of 100% on every trial. After these dots disappeared, the red fixation point was left on the black screen for a further 4 seconds. Participants’ task was to indicate whether they thought the dots were moving to the right or to the left by pressing a button under their index finger on the response pad in their corresponding hand. They were able to respond at any time in the 4.5 second response period from the onset of the small white dots until the offset of the fixation point. When they pressed a button, the fixation point changed color to a darker red to indicate that the response had been registered. Unlike in experiment one, in all tasks in experiment two a white likert scale appeared on the black

screen after the response period. The numbers 1-7 were shown beneath the points on the scale from left to right. Participants had been instructed to select the number corresponding to the level of confidence that they had in their response about dot motion direction. They were told that 1 represented “absolutely no confidence, I chose a direction at random” (１は全く自信がなくて当てずっぽうの場合), that 4 represented “moderately confident in my response” (４はまあまあ自信がある場合), and that 7 represented complete confidence “I think I definitely chose the correct response” (７は絶対にあっていると思う場合). A white cursor randomly appeared above one of the numbers and participants were able to move this cursor to their selected level of confidence. They pressed the button under their index finger in their left hand to move the cursor leftwards and the button under their index finger in their right hand to move the cursor rightwards. When they had reached the number that corresponded to their level of confidence, they could press any other button in either hand to select it. This screen only terminated after participants selected a confidence level. Subsequently, the outcome of that trial was presented in white letters on a black screen for two seconds (¥30 or ¥0). Outcome was determined by dot direction (left or right) rather than by the participant’s response (correct or erroneous) so that if dots moved in a given direction (counterbalanced between subjects) then participants were rewarded (¥30) and if dots moved in the other direction then they received no reward (¥0). Finally, a black screen was presented for 1 second to provide an inter-trial interval. After completing these 20 practice trials, participants filled out a questionnaire about the experiment. It had questions to test their understanding of the task such as “what happens if the dots moved left but

you mistakenly respond that they moved right?" Participants were only allowed to move on once they had answered all questions correctly and therefore shown that they had a good understanding of the experiment.

Psychophysical measurement and training task:

This task (Figure 9 with 1s ITI) was completed in the scanner while participants' T1 scan was taken. The events in this task were identical to those in the practice task except for that the coherence was not 100% on all trials but rather 20 trials of each of the following coherences were used: 0, 5, 10, 15, 20, 40, 70, or 100%, 160 trials in total. The results of this experiment were used to determine each individual's "low coherence" (65% accuracy threshold) and "high coherence" (90% accuracy threshold).

On average, participants were found to respond with 90% accuracy when dots moved with a coherence of 24% (± 13%) and so this was the average high coherence. On average they were found to respond with 65% accuracy when dots moved with a coherence of 8% (± 5%) and so this was the average low coherence.

Figure 9.

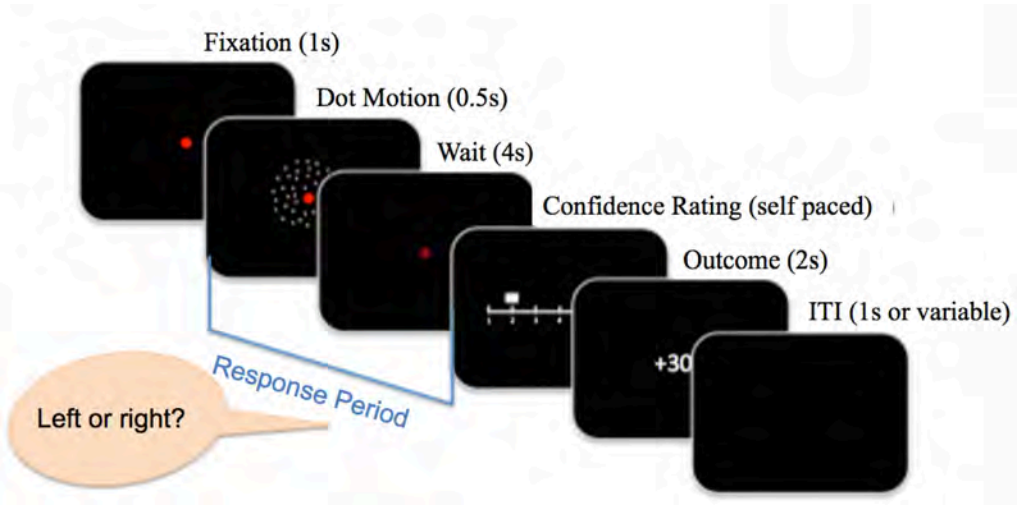

Figure 9. The sequence of events in each trial on the psychophysical testing and training task and on the main task from experiment two. After initial presentation of a red fixation point for 1 second, a cloud of moving dots was presented for 0.5 seconds. This cloud then disappeared leaving the fixation point on screen for another 4 seconds. Participants' task was to indicate whether the cloud of dots had a leftwards or rightwards global motion direction. They could respond any time from the onset of the dot motion until the fixation point disappeared. After the fixation dot disappeared a white likert scale appeared on the black screen. Participants' were told to then select the number corresponding to how much confidence they had that they had selected the correct dot motion direction (7 = most confident, 1 = least confident). Selection of a number terminated this screen after which the outcome of the current trial (¥30 or ¥0) was displayed in white letters on a black screen for 2 seconds. Finally a black screen was shown for 1 second as an inter-trial interval in the psychophysical testing and training task**/**for an amount of time that varied between trials on the main task.

Main task

This task was completed as BOLD signal was measured (Figure 9 with variable ITI). It was identical to the practice task except for the following. Participants completed as many sessions as was possible in their two-hour time slot. Each session contained 32 trials. The coherence on each trial was either the “low” or “high” coherence determined for the individual in the psychophysical testing phase. To be consistent with study one, a ratio of 22 low coherence trials: 78 high coherence trials was used. Inter-trial-intervals (ITI) were of variable lengths (0-23s, median = 3s, determined using Optseq2 (Greve, 2002)).

Participants were told that order of trials was random and that their payment was dependent on the sum of the trials that were randomly selected for their experiment (as well as the bonus if they earned it). In reality, while the order of trials was variable (determined using Optseq2 (Greve, 2002)), the experiment was designed so that if participants completed 10 sessions then the sum of the trials should be ¥6000. We paid this full amount even to participants who were unable to complete 10 sessions.

In experiment one, participants were not found to maintain 65% and 90% accuracy in “low” and “high” coherences trials during the main experiment. This could have been problematic, especially in the low coherence condition, if it meant that participants were simply responding at chance (which they were close to but still significantly above in experiment one, see the results section). Therefore, to avoid this potential problem in experiment two we implemented a further manipulation: Participants were told that they could

receive up to ¥1500 extra depending on their accuracy in the task. Participants who maintained the expected accuracy received ¥1000 and those who improved between sessions received the full bonus. This manipulation was included in the hope that it would motivate participants to try hard throughout the course of the whole experiment.

Imaging data acquisition

A Siemens Trio TIM 3T scanner with a 32-channel head coil was used for scanning acquisition. Anatomical images were acquired using a T1-weighted MP-RAGE protocol (TR = 2000 ms, TE = 1.98 ms, FA = 10°, FOV = 256 mm × 256 mm, resolution 1 × 1 × 1 mm^3). Subsequently, T2*-weighted images reflecting blood oxygen level-dependent (BOLD) signals were acquired using gradient-echo echo-planar imaging (EPI) (TR = 2000 ms, TE = 25 ms, 38 slices, FA = 90°, FOV = 192 mm × 192 mm, and resolution = 3.0 × 3.0 × 3.5 mm^3). Functional data were collected over a series of sessions, each of which took a minimum of 360 seconds and consisted of a minimum of 182 volumes (but were variable because the confidence ratings in this task were self-paced). The first two volumes taken in each session were discarded to ensure steady-state magnetization.

Behavioral data analyses

Using the same formula as in experiment one, we conducted a Signal Detection Theory (SDT; Green & Swets, 1966) analysis to estimate the sensitivity (*d'*) and bias (*c*) of each participant.

Imaging data analyses

SPM8 (Wellcome Trust Centre for Neuroimaging, University College London) was again used to pre-process and analyze the imaging data.

Standard pre-processing steps were identical to those in experiment one. Similarly, because we wished for results that could easily be compared to those in experiment one, we again performed separate general linear model analyses looking at the regressors of interest in the dot motion time period, at the response time, and at the outcome display time separately. In addition, we also performed two other general linear model analyses to investigate areas of the brain that increased in activity during stimulus presentation and at response time as self-reported confidence ratings increased or decreased.

The first of these analyses (EXPT2-GLM1, comparable to EXPT1-GLM1) was a whole-brain analysis with a factorial design that investigated brain activity that occurred during dot motion presentation time. This was split by coherence (high/low), stimulus (reward/non-reward predictive), and accuracy (correct/error) giving us eight conditions in total. For each subject, the general linear model was used to fit the fMRI time series. Each condition was modeled for the 500 ms from the onset of dot motion until the offset of dot motion. Four other trial-related regressors were included: left/right response (duration = 0s) and ¥30/¥0 outcome delivery (duration = 2s).

The second of these analyses (EXPT2-GLM2) was again a whole-brain analysis with a factorial design that investigated brain activity that occurred during dot motion presentation time, but in this analysis we were interested in the parametric modulation of this brain activity on each trial by the subsequently rated level of confidence. We found that splitting this activity into different conditions made no difference on results (except to diminish them somewhat due to reduced statistical power) and so we did not do so in the reported analysis. Normalized levels of confidence rating (z-scores) for each

participant on each trial were investigated as a modulatory parameter on neural activity at dot motion time. As in EXPT2-GLM1, four other trial-related regressors were included: left/right response (duration = 0s) and ¥30/¥0 outcome delivery (duration = 2s).

Next we completed another a whole-brain analysis with a factorial design (EXPT2-GLM3, comparable to EXPT1-GLM2), this time investigating brain activity that occurred at response time. This was split by coherence (high/low), stimulus (reward/non-reward predictive), and accuracy (correct/error) giving us eight conditions in total. For each subject, the general linear model was used to fit the fMRI time series. Each condition was modeled from the onset of response as an event (duration = 0s). Four other trial-related regressors were included: left/right dot motion (duration = 500 ms) and ¥30/¥0 outcome delivery (duration = 2s).

We were interested in the parametric modulation of response time brain activity on each trial by the subsequently rated level of confidence and so we did another whole-brain analysis with a factorial design that investigated brain activity that occurred at response time (EXPT2-GLM4). Similar to EXPT2-GLM2, because we found that it made no difference on results but to reduce significance, we did not split activity by condition in the reported analysis of EXPT2-GLM4. Normalized levels of confidence rating (z-scores) for each participant on each trial were investigated as a modulatory parameter on neural activity at response time. Four other trial-related regressors were included: left/right dot motion (duration = 500 ms) and ¥30/¥0 outcome delivery (duration = 2s).

In EXPT2-GLM5, we redid the above analysis (EXPT2-GLM4) using only high coherence trials in which participants responded correctly. This is because we wished to see if parametric modulation of confidence ratings that might reflect uncertainty would hold even when participants made accurate responses. Because we did not want to confound effects of coherence, and because we had far more high than low coherence trials in our design, we therefore tested this effect on correct high coherence trials. Overall, with the exception that only high coherence correct trials were used, this analysis was identical to that of EXPT2-GLM4.

We completed a final whole-brain analysis with a factorial design (EXPT2-GLM6, comparable to EXPT1-GLM3) to investigate the brain activity that occurred at outcome time. This was split by coherence (high/low), stimulus (reward/non-reward), and accuracy (correct/error) giving us eight conditions in total. For each subject, the general linear model was used to fit the fMRI time series. Each condition was modeled from the onset of the outcome display screen as an event (i.e. duration = 0s). Two other trial-related regressors were included: dot motion leftwards and dot motion rightwards; these were modeled as starting at dot motion onset and lasting 500 ms until dot motion offset.

Identical to experiment one, in all GLMs random effect analyses at the group-level were conducted using an ANOVA design (Friston et al., 2002) that modeled the eight conditions of interest and the main effect of subjects. Significant clusters were identified using the voxel-level threshold of p-unc. = 0.001. The statistic threshold at cluster-level was set to p-FWE = 0.05 and the six motion regressors were included as effects of no interest.

Experiment Two Results

Behavioral Results

Response accuracy was investigated and participants were found to perform significantly better in high coherence trials (0.86 ± 0.10) than in low coherence trials (0.66 ± 0.11; $F(1,23)=109.91$, $P<0.001$; Figure 10a). Consistent with this finding, participants were found to have higher sensitivity in high ($d'= 2.43 \pm 0.72$) than in low ($d' =0.89 \pm 0.35$) coherence trials ($t(23)=10.28$, $P<0.001$; Figure 10b). Nevertheless, sensitivity in low coherence trials was still better than chance ($t(23)=12.49$, $P<0.001$). Additionally, participants showed no difference in bias between high and low coherence conditions ($t(23)=-1.45$, $P=0.16$; Figure 10c), and their overall bias did not differ significantly from chance ($t(23)=-1.21$, $P=0.24$ for high coherence trials, $t(23)=0.39$, $P=0.70$ for low coherence trials).

Figure 10.

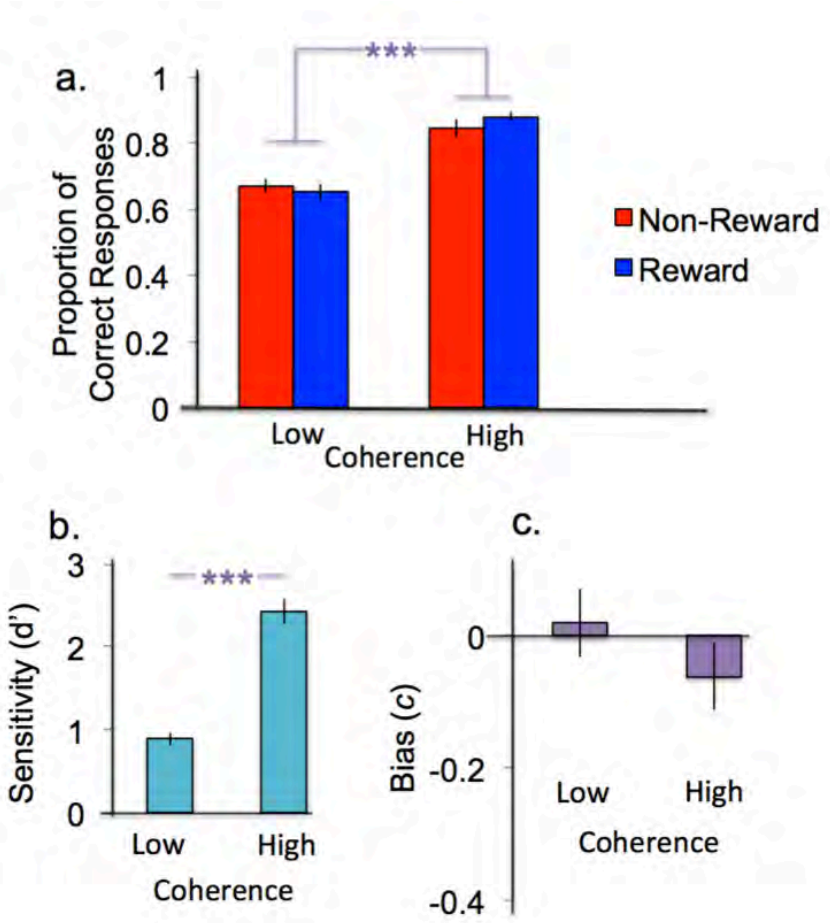

Figure 10. The accuracy and SDT results of the main task of experiment two. Asterisks indicate statistically significant differences. **a.** Accuracy: There was a main effect of coherence (high/low) on participants' dot motion direction discrimination performance. **b.** SDT Sensitivity: This (d') was significantly higher in high than in low coherence trials, and greater than chance in low coherence trials. **c.** SDT Bias (*c*): On average, participants had no response bias**.**

For behavioral data in this study “Response time” refers to the time period in each trial from dot motion onset until the time at which participants made a motion direction discrimination response. It does not refer to the time in which it took for participants to pick their level of confidence. When we investigated response time, a stimulus (reward/non-reward predictive) by accuracy (correct/error) interaction was found ($F(1,23)=5.28$, $P<0.05$; Figure 11a). Follow up paired-sample t-tests revealed that responses in correct trials were faster when stimuli were reward (0.93s ± 0.28s) compared to non-reward predictive (1.05s ± 0.34s; $t(23)=-2.70$, $P<0.05$, Bonferroni corrected), but that responses in error trials did not differ depending on the type of stimulus ($t(23)=1.70$, $P=0.10$). A coherence (high/low) by accuracy (correct/error) interaction was also found ($F(1,23)=8.33$, $P<0.01$). Follow up paired-sample t-tests revealed that responses in high coherence correct trials (0.90s ± 0.25s) were faster than responses in low coherence correct trials (1.09s ± 0.37s; $t(23)=-3.33$, $P<0.01$, Bonferroni corrected), but that responses in error trials did not differ depending on coherence ($t(23)=1.01$, $P=0.32$). Additionally, response times were faster in high coherence correct trials with reward (0.83s ± 0.18s) compared to non-reward predictive stimuli (0.97s ± 0.32s; $t(23)=2.57$, $P<0.05$, Bonferroni corrected). Overall, these results show that (a) response times were faster in correct reward trials than correct non-reward trials, (b) response times were faster in correct high coherence trials than correct low coherence trials, and therefore (c) similar to experiment one, response times in high coherence correct reward trials were faster than response times in high coherence correct non-reward trials. Therefore, like in experiment one, this finding means that when participants could easily see

which type of stimulus was at hand (high coherence correct trials), their speed in response discriminated between reward and non-reward conditions. This therefore provides evidence that participants had learned that stimuli with one direction of dot motion were associated with reward and that stimuli with the other direction of dot motion were associated with non-reward

Figure 11.

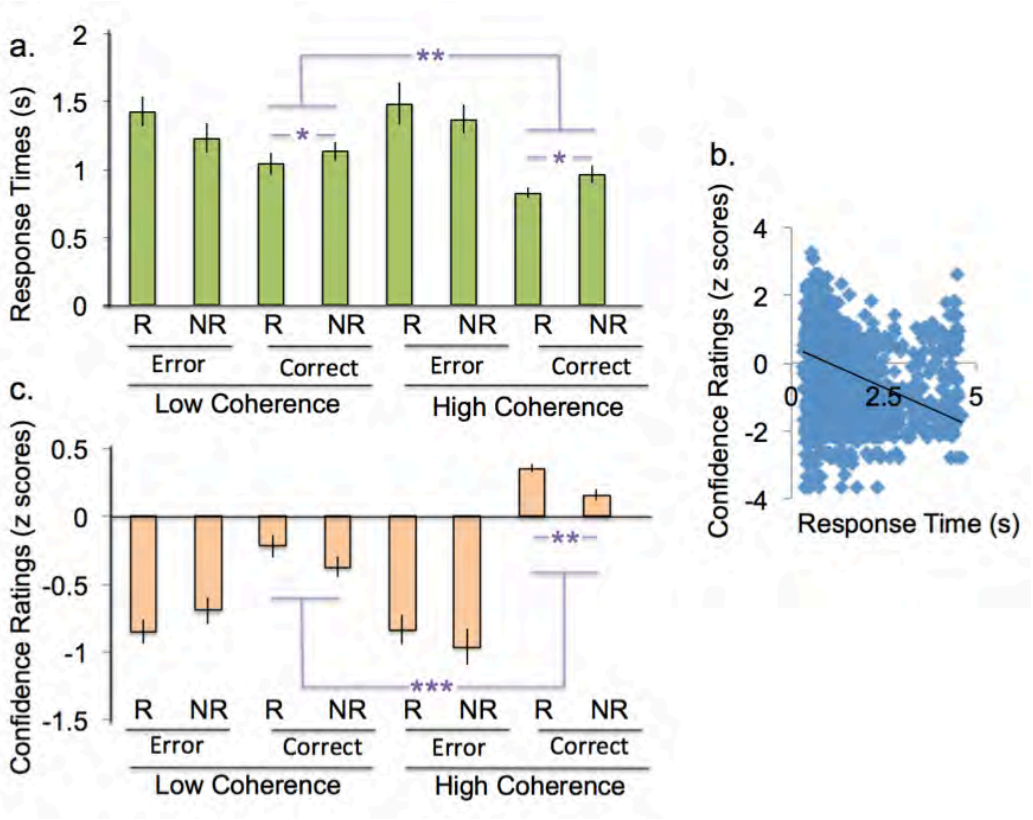

Figure 11. The response times and confidence ratings of the main task of experiment two. Asterisks indicate statistically significant differences. R = reward trials, NR = non-reward trials. **a.** Participants were faster to respond in correct high coherence reward trials than in any other trials. **b.** Participants had higher confidence in correct high coherence reward trials than in any other trials. **c.** The faster a participant responded on a given trial, the higher their self-reported confidence was.

A negative correlation between confidence and response time was found so that the more confident a person was on a given trial, the quicker their response time was, n=5632 trials, r=-0.34, *P* <0.001 (Figure 11b).

Confidence ratings that had been normalized (z-scores) for each participant were put into a coherence (high/low) x stimulus (reward/ non-reward predictive) x accuracy (correct/error) ANOVA (Figure 11c). A stimulus (reward/non-reward predictive) by accuracy (correct/error) interaction approached significance ($F(1,23)=3.95$, $P<0.059$). An accuracy x coherence interaction was found ($F(1,23)=54.28$, $P<0.001$). Similar to the accuracy by coherence interaction found with response times, confidence in high coherence correct trials (z-scores = 0.26 ± 0.08) was found to be higher than confidence in low coherence correct trials (z-scores = -0.30 ± 0.34; $t(23)=6.77$, $P<0.001$, Bonferroni corrected), but confidence in error trials was not found to significantly differ depending on coherence ($t(23)=-1.95$, $P=0.063$). Finally, comparable with response times, confidence was significantly higher in high coherence correct trials (z-scores = 0.35 ± 0.14) with reward compared to non-reward predictive stimuli (z-scores = 0.16 ± 0.22; $t(23)=2.93$, $P<0.01$, Bonferroni corrected). No differences were found between conditions in the time that participants took to rate their level of confidence.

Response times and confidence ratings in low coherence conditions did not significantly correlate with response bias (*c*) in low coherence conditions. Likewise, response times and confidence ratings in high coherence conditions did not significantly correlate with response bias in high coherence conditions.

In high coherence trials with non-reward predictive stimuli, as participants sensitivity (*d'*) increased they were faster (n=24, r =-0.54, *P* <0.01) and more confident (n=24, r =0.42, *P* <0.05) when they made the correct responses, and slower (n=24, r =0.38, *P* =0.064) and less confidence (n=24, r =-0.73, *P* <0.001) when they made erroneous responses. Sensitivity was not found to correlate with response times or confidence in any other conditions.

fMRI Results

Dot Motion Duration BOLD Contrasts: EXPT2-GLM1

Brain activation that occurred during the stimulus presentation time was investigated. Similar to the findings of experiment one, significantly increased activity in trials where participants would subsequently make a correct compared to an erroneous response (correct > error) was seen in the visual areas, including the putative MT area, which is associated with visual motion perception (Krug et al., 2013; Table 4; Figure 12). Similar activity was also found in the IFG and putamen. No areas were found to be significantly active in trials where participants were subsequently to make an erroneous compared to a correct response. Similar to experiment one, the significant activity that was found did not differ depending on whether stimuli were reward or non-reward predictive. No activity was found to significantly differentiate between trials with reward and non-reward predictive stimuli at this time.

Table 4. Summary of brain activation found in EXPT2-GLM1.

Contrast / Region	Peak in MNI coordinates			Hemisphere	*z*-score (peak)	Cluster size
	x	*y*	*z*			
Correct > Error						
Visual areas	−26	−94	−6	Left	6.16	5231
	22	−98	−4	Right	5.95	
	46	68	2	Right	5.39	
IFG	40	8	26	Right	5.39	368
Putamen	−26	10	2	Left	4.78	659
	−40	0	30	Left	4.19	
	−38	14	10	Left	3.74	

IFG = inferior frontal gyrus.

Figure 12.

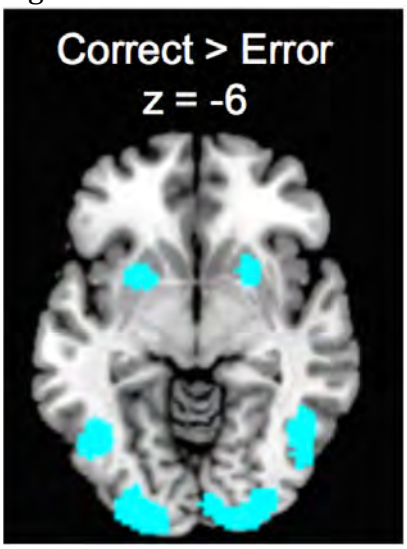

Figure 12. The results of EXPT2-GLM1, i.e. activity during the dot motion period, rendered on the template of SPM with *P* <0.001, uncorrected. The correct > error contrast revealed significant activation in the visual cortex including the MT.

Dot Motion Duration Parametric Modulation Analysis: EXPT2-GLM2

Brain activation during the stimulus presentation time that varied with the subsequently selected level of confidence (z-scores) was investigated (Table 5, Figure 13). It was found that as the level of activation increased in the IFG, the right MCC, and the left insula at stimulus presentation time, the subsequently selected level of confidence decreased. On the contrary it was found that as the level of activation increased in the PCC, SFG, IPL, and MFC at stimulus presentation time, the subsequently selected level of confidence also increased.

Table 5. Summary of brain activation at dot motion time that correlated with confidence ratings found in EXPT2-GLM2.

Contrast / Region	Peak in MNI coordinates			Hemisphere	z-score (peak)	Cluster size
	x	*y*	*z*			
Negative Correlations						
IFG	34	24	−2	Right	4.92	1310
	42	22	−8	Right	4.72	
MCC	8	26	40	Right	4.90	2365
	14	14	70	Right	4.74	
	−10	24	38	Left	4.04	
Insula	−30	24	4	Left	4.15	368
	−34	20	−8	Left	3.95	
	−40	12	0	Left	3.26	
IFG	−52	4	30	Left	3.53	345
	−52	8	18	Left	3.45	
	−54	14	2	Left	3.34	
Positive Correlations						
PCC	−6	−48	30	Left	5.62	5704
	8	−52	22	Right	4.63	
	12	−44	66	Right	4.58	
SFG	−14	56	34	Left	4.69	3973
	−16	42	46	Left	4.63	
	−22	34	46	Left	4.53	
IPL	−42	−70	30	Left	4.43	523
	−40	−74	38	Left	4.25	
MFC	20	36	12	Right	3.91	256
	22	26	24	Right	3.86	
	26	38	4	Right	3.63	

IFG= inferior frontal gyrus, MCC = midcingulate cortex, PCC = posterior cingulate cortex, SFG = superior frontal gyrus, IPL = inferior parietal lobe, MFC = middle frontal cortex.

Figure 13.

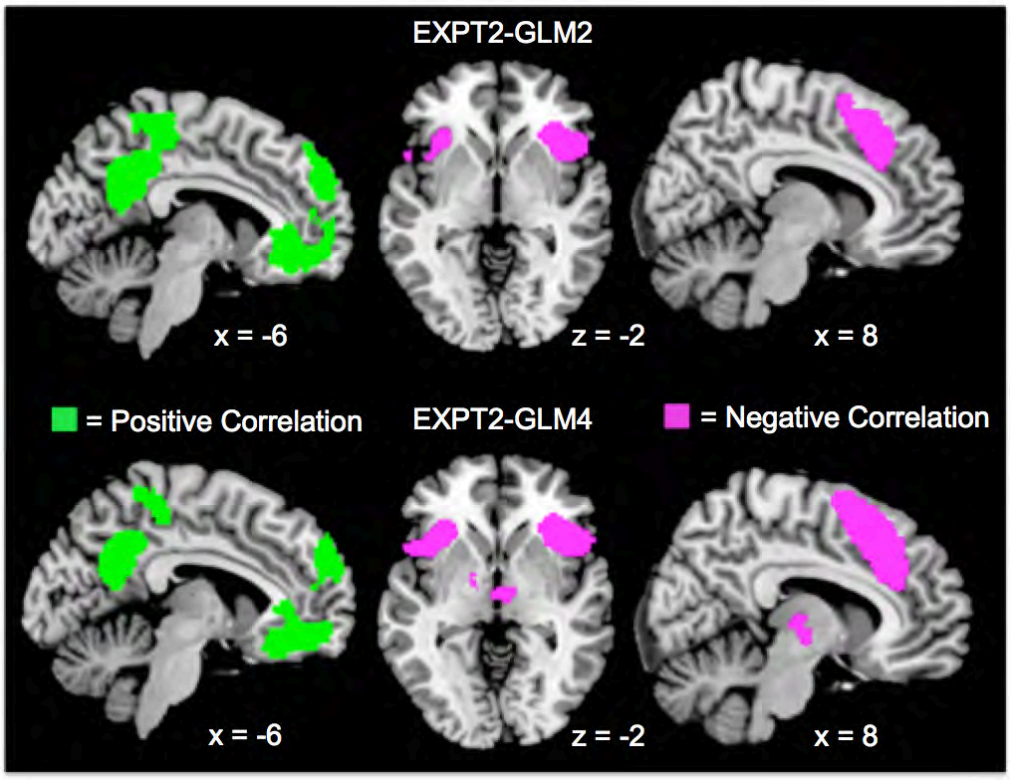

Figure 13. The results of EXPT2-GLM2 and EXPT2-GLM4 , i.e. activity during the dot motion and response periods that correlated positively and negatively with subsequently rated confidence, rendered on the template of SPM with *P* <0.001, uncorrected.

Response Time BOLD Contrasts: EXPT2-GLM3

We examined neural activation that occurred when participants responded whether the dots were moving to the left or to the right. Similar to the results of experiment one, the bilateral precentral gryus/IFG, an array of visual areas, and the right insula had increased activity at this time when participants selected the erroneous compared to the correct response (Table 6, Figure 14). We split these trials by stimulus type (reward/non-reward predictive). Re-doing the same contrast but using only trials with reward predictive stimuli (reward error > correct) we found that activity in the bilateral precentral gryus/IFG, an array of visual areas, and right PMFC was significantly increased at this time when participants selected the erroneous compared to the correct response. Doing the same contrast using only trials with non-reward predictive stimuli (non-reward error > correct) only showed activation in visual areas. These results showed that error-related activity was much broader and significantly more active in reward compared to non-reward trials. No areas were more active at this time when participants selected the correct compared to the erroneous response.

Table 6. Summary of brain activation found in EXPT2-GLM3.

Contrast / Region	Peak in MNI coordinates			Hemisphere	z-score (peak)	Cluster size
	x	*y*	*z*			
Error > Correct						
Precentral Gyrus/IFG	50	0	48	Right	5.66	945
	44	6	30	Right	4.81	
	42	18	24	Right	3.60	
Visual Areas	12	−96	16	Right	5.54	4945
	−20	−88	22	Left	5.20	
	10	−76	2	Right	4.89	
Precentral Gyrus/IFG	−46	−6	48	Left	5.07	529
	−38	4	28	Left	4.19	
Insula	38	26	0	Right	4.67	433
Reward Error > Reward Correct						
PMFC	12	2	66	Right	6.31	1011
	−12	−6	62	Left	4.44	
	−10	2	64	Left	4.10	
Visual areas	14	−96	16	Right	5.26	4624
	−6	−80	0	Left	4.87	
	6	−80	2	Right	4.75	
Precentral Gyrus/IFG	50	0	46	Right	4.98	877
	40	6	26	Right	4.51	
	42	18	26	Right	3.86	
Precentral Gyrus/IFG	−42	−6	50	Left	4.65	635
	−40	4	28	Left	4.08	
	−34	−24	48	Left	3.53	
Non-Reward Error > Non-Reward Correct						
Visual areas	−18	−88	20	Left	4.20	315
Visual areas	10	−96	14	Right	4.02	617
	12	−78	0	Right	3.69	
	4	−92	10	Right	3.64	
Center of ROIs that revealed interaction between reward and accuracy						
MCC	−10	6	52	Left		
	14	10	52	Right		

IFG = inferior frontal gyrus, PMFC = posterior medial frontal cortex, MCC = midcingulate cortex.

Figure 14.

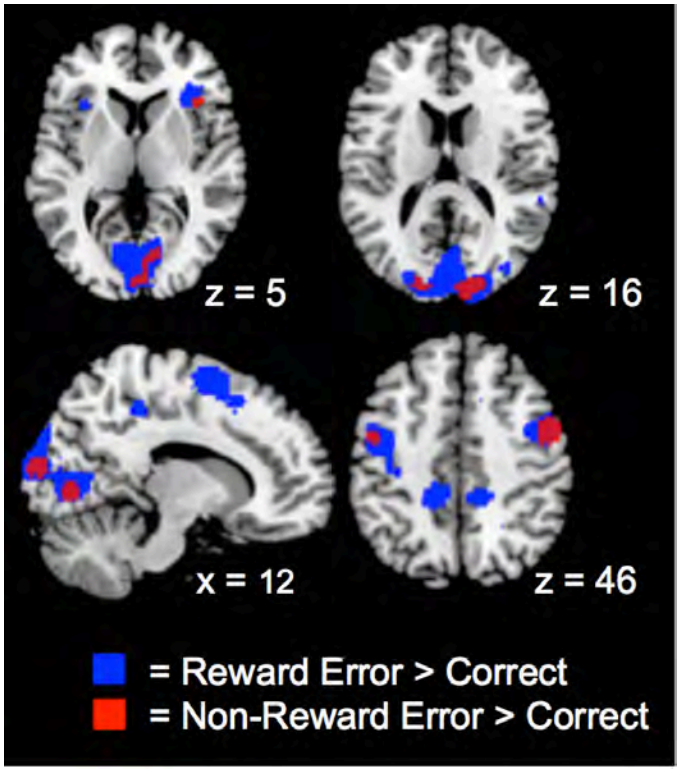

Figure 14. The results of EXPT1-GLM3, i.e. activity at the time of response, rendered on the template of SPM with *P* <0.001, uncorrected. Error-related activity in the precentral gyrus/IFG, PMFC, insula, and visual areas was more significant and broad in reward trials (reward error > correct; blue) than in non-reward trials (non-reward error > correct; red).

However, the areas from the error > correct contrast did not survive when an interaction between stimulus (reward/non-reward predictive) and accuracy (correct/error) was calculated. We then examined the averaged beta values from three 4mm spherical regions of interest (ROIs) in the MCC. These ROIs were the three parts of the MCC found to be significant for this interaction in experiment one (Table 2, Figure 7). Specifically averaged beta values from 4mm around the peak voxels in these areas were used in this ROI analysis. These ROIs were selected because we hypothesized that the interaction found in experiment one in these regions might also occur in experiment two, despite the use of different rewards and participants, and despite a slight change in task. The interaction in two of these ROI was found to be significant in experiment two (P <0.01 and P <0.05) and to follow the same pattern of results as in experiment one (Figure 15). Activity in the third ROI followed the same pattern of results but did not reach statistical significance. Specifically, error-related activity (activity in error trials minus activity in correct trials) in these ROIs was greatest in trials with reward compared to non-reward predictive stimuli. The fact that this interaction was significant in the MCC at the whole brain level in experiment one, but only at the ROI level in experiment two, perhaps shows differences in the strength of this effect for stimuli associated with primary compared to secondary rewards.

Figure 15.

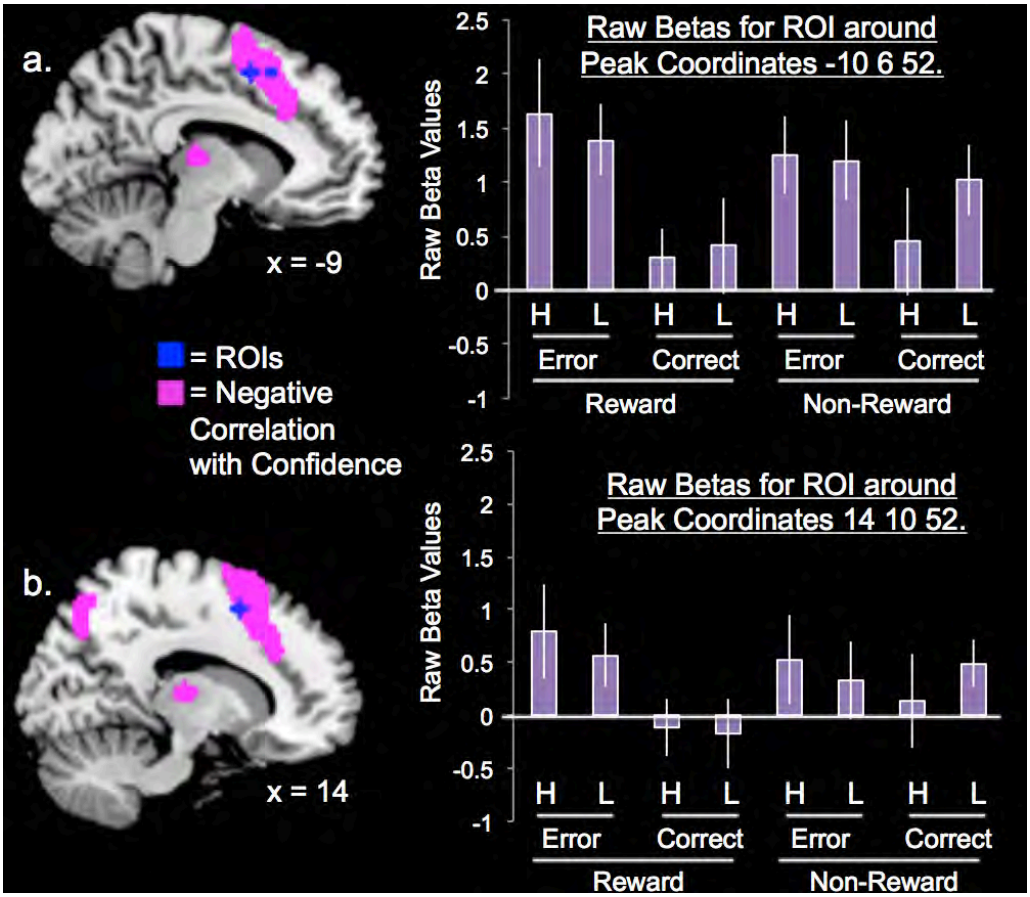

Figure 15. The MCC ROIs in EXPT2-GLM5, and the activity at response time that was found to negatively correlate with reported confidence, rendered on the template of SPM with *P* <0.001, uncorrected. **a.** The two ROIs in the left hemisphere. **b**. The one ROI in the right hemisphere. An interaction, indicating increased error-related activity in reward compared to non-reward trials, was significant in two of these ROIs (one in the left hemisphere, centered around peak coordinates -10, 6, 52, and one in the right hemisphere centered around peak coordinates 14, 10, 52). Raw beta values from these two ROIs are shown. All ROIs (blue) overlapped with activity at response time that was found to negatively correlate with reported confidence (magenta). H = high coherence, L = low coherence.

As in experiment one, we got beta values from each of these MCC ROIs for each participant for each of the 8 conditions. We correlated the betas from high coherence conditions with participants' response bias in the high coherence trials and we correlated the betas from low coherence conditions with participants' response bias in the low coherence trials. No correlations were found to reach significance.

Response Time Parametric Modulation Analysis: EXPT2-GLM4

Brain activation that occurred at response time and which varied with the subsequently selected level of confidence (normalized) was investigated (Table 7, Figure 13). This was found to occur in very similar areas to that in EXPT2-GLM2 and therefore, for the sake of brevity, only the results of EXPT2-GLM4 will be further discussed in this thesis. Specifically, as activation in the right MCC, the left inferior parietal lobe (IPL), the right superior parietal lobe, and the right intraparietal sulcus (IPS) increased at response time, the level of subsequently rated confidence decreased. Interestingly, this activation overlapped with all of the ROIs used in EXPT2-GLM3 showing that activity in these ROIs significantly increased as subsequent confidence ratings decreased (Figure 15). Finally, as activation in the posterior cingulate cortex (PCC), middle temporal gyrus (MTG), prenuceous, orbitofrontal cortex (OFC), IPL, post-central gyrus, and superior frontal gyrus (SFG) increased at response time, the level of subsequently rated confidence also increased. Activity in none of these areas overlapped with the ROIs or any other error-related activity.

Table 7. Summary of brain activation at response time that correlated with confidence ratings found in EXPT2-GLM4 and EXPT2-GLM5.

Contrast / Region	Peak in MNI coordinates			Hemisphere	z-score (peak)	Cluster size
EXPT2-GLM4						
	x	*y*	*z*			
Negative Correlations						
MCC	8	26	40	Right	5.31	9904
	8	22	50	Right	5.24	
	34	22	4	Right	5.20	
IPL	−46	−36	44	Left	4.24	1115
	−28	−48	42	Left	4.22	
	−22	−68	32	Left	3.83	
Precuneus	18	70	54	Right	3.95	418
	30	−72	30	Right	3.87	
	14	−70	44	Right	3.68	
IPL	42	−44	46	Right	3.85	544
	52	−40	42	Right	3.76	
	32	−46	42	Right	3.67	
Positive Correlations						
PCC	−4	−46	38	Left	5.24	1506
	−6	−50	28	Left	5.12	
	8	−54	28	Right	5.04	
MTG	−58	−6	−22	Left	5.18	429
	−64	−18	−18	Left	3.18	
Precuneus	−14	−46	70	Left	5.05	504
	−18	−38	64	Left	4.14	
	−6	−38	58	Left	3.82	
OFC	−8	50	−12	Left	4.95	1660
	0	46	−12		4.93	
	−8	30	−16	Left	4.11	
IPL	−42	−70	30	Left	4.84	583
	−48	−70	36	Left	4.79	
Postcentral Gyrus	16	−42	70	Right	4.80	580
	10	30	62	Right	4.33	
	20	38	62	Right	4.03	
SFG	−20	34	46	Left	4.73	1421
	−12	56	32	Left	4.69	
	−16	44	46	Left	4.52	
EXPT2-GLM5						
	x	*y*	*z*			
Negative Correlations						
MCC	8	24	44	Right	4.70	483
	−4	14	50	Right	3.88	
Positive Correlations						
SMG	−10	52	36	Left	4.47	1019
	−10	48	44	Left	4.15	
	−22	40	46	Left	3.90	

IPL	−48	−72	36	Left	4.28	615
	−42	−66	26	Left	4.08	
	−38	−80	42	Left	3.68	
PCC	8	−48	28	Right	4.04	529
	−2	−58	28	Left	3.90	

MCC = midcingulate cortex, IPL = inferior parietal lobe, PCC = posterior cingulate cortex, MTG = middle temporal gyrus, OFC = orbitofrontal cortex, SFG = superior frontal gyrus, SMG = superior medial gyrus.

Because certain models of confidence/uncertainty (e.g. Kepecs et al., 2008) predict that neural confidence/uncertainty processes should be related to decision boundaries, we investigated how activity in the areas found in EXPT2-GLM4 (in both areas that correlated positively and negatively with self-reported confidence) correlated with the response bias of participants. Specifically, we took the peaks from EXPT2-GLM4 and investigated betas averaged over a 4 mm sphere around them in EXPT2-GLM3 (because this activity was also at response time and had the same regressors of no interest but was split by condition). Correlations were calculated between betas from high coherence trials and response bias in high coherence trials, and between betas from low coherence trials and response bias in low coherence trials. No correlations were found to reach significance.

Response Time Parametric Modulation Analysis in Correct High Coherence Trials: EXPT2-GLM5

For EXPT2-GLM5 we redid EXPT2-GLM4 but using only correct high coherence trials. We essentially found activity in the same regions to have negative and positive correlations with self-reported confidence as in EXPT2-GLM4. Only the MCC reached significance for the negative correlation, and only the superior medial gyrus (SMG), IPL, and PCC reached significance for the positive correlation, but when a more liberal p-value threshold was applied, activity in the same regions as in EXPT2-GLM4 was found. The difference in statistic power difference is likely just because there are fewer trials included in EXPT2-GLM5 than in EXPT2-GLM4.

Outcome Time BOLD Contrasts: EXPT2-GLM6

Brain activation that occurred when participants were presented with an outcome (reward/non-reward) was examined (Table 8, Figure 16). When participants' outcome was inconsistent with their response (e.g. they had responded that dots were moving in the reward associated direction but then they were presented with the non-reward outcome) there was significant activation in part of the MFC, the right SMG, compared to when participants' outcome was consistent with their response. In the analogous analysis in experiment one (EXPT1-GLM3) we only found significant error-related activity when non-reward trials were exclusively put into the analysis. Therefore, we split these trials by stimulus type (reward/non-reward predictive) in EXPT2-GLM6. Re-doing the same contrast but using only trials with reward predictive stimuli we found no areas to be significantly active. Doing the same contrast using only trials with non-reward predictive stimuli again showed significant activation in the same region, supporting the finding in experiment one that this effect in the MFC is strongest in non-reward trials.

Table 8. Summary of brain activation found in EXPT2-GLM6.

Contrast / Region	Peak in MNI coordinates			Hemisphere	z-score (peak)	Cluster size
	x	*y*	*z*			
Error> Correct						
SMG	6	22	56	Right	5.08	1493
	4	48	40	Right	4.19	
	6	34	44	Right	4.04	
Error Non-Reward > Correct Non-Reward						
SMG	2	22	56	Right	4.55	1212
	4	40	38	Right	4.10	

SMG= superior medial gyrus.

Figure 16.

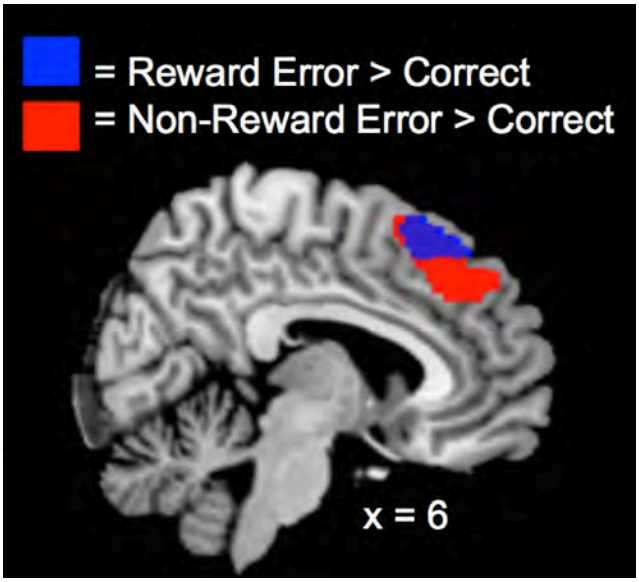

Figure 16. The results of EXPT2-GLM6, i.e. activity at outcome time, rendered on the template of SPM with *P* <0.001, uncorrected. The superior medial gyrus was found to be activated in an error > correct contrast. This activity was broader and more significant when exclusively non-reward trials were investigated (red) compared with when exclusively reward trials (blue) were investigated.

Experiment Two Discussion

In experiment two the behavioral results and neural activity that occurred prior to response, at response time, and outcome time were found to be comparable to those found in experiment one. These findings persisted despite the fact that the reward, the participants, and to a certain extent the task, were different between experiments. In addition, in experiment two we found activity in a range of neural regions to correlate with self-reports of decision confidence. Therefore, we managed to both confirm and extend the results of experiment one.

Compared to in experiment one, in experiment two the participants' accuracy and sensitivity were slightly higher overall and therefore the bias for the response associated with reward predictive stimuli found in experiment one was reduced to non-significance in experiment two. Nevertheless, as in experiment one, response times in experiment two were significantly faster for correct trials where stimuli were reward predictive compared to when they were non-reward predictive. A correlation analysis found that as response times were faster, self-reports of confidence were higher (see Figure 11). Similar to the effect found for response times, an effect of reward value was found on self-reported confidence. Specifically, participant's self-reported confidence was significantly higher in reward compared to non-reward correct trials. The effects of reward value on response time and confidence ratings in correct trials only reached significance in high coherence trials. This furthers the idea that these effects occurred due to evidence related to reward value because this should have been more available in high than in low coherence trials. These behavioral results show that even when participants do not have

response biases and even when reward/non-reward outcome and response accuracy are unrelated, if perceptual evidence is high then the reward value of a stimulus can have an effect on the speed and confidence with which participants respond correctly to it.

The main neural finding from experiment one was replicated in experiment two. We created three 4mm sphere ROIs around the peak coordinates of the interaction in the MCC found in experiment one. In experiment two, the same interaction was found to be significant for BOLD activity in two of these ROIs at the time of response. Specifically, error-processing (defined as activity in erroneous responses minus activity in correct responses) in these parts of the MCC was again found to be enhanced in reward compared to non-reward trials. The replication of the effect found in experiment one where we used a primary reward, in experiment two where we used a secondary reward, shows that this effect is robust to reward type. Therefore, the effect of stimulus reward value on the processing of error after a decision has been made might occur in a variety of different rewarding situations ranging from when you see a stimulus associated with primary reward (e.g. an apple tree) to when you see a stimulus associated with a secondary reward (e.g. a slot machine).

Importantly, a parametric analysis in experiment two showed that BOLD activity at response time in these MCC ROIs had a significant negative correlation with normalized levels of subsequently self-reported decision confidence. This negative correlation still held even when only correct high coherence trials were included in the parametric analysis. This indicates that, even in correct trials with high coherence, this MCC activity was higher when

confidence was rated as low. This result therefore fits with the idea that this MCC processing reflects decision uncertainty rather than the simple processing of errors. Because binary analysis of this activity (error > correct contrasts) shows what appears to be effects of error-processing, and a more continuous analysis (parametric modulation of activity) shows what appears to be effects of uncertainty, these results provide support to several recent papers that suggest that the “error-processing” and “confidence/uncertainty” literatures might actually be investigating similar neural mechanisms via different strategies (Boldt & Yeung, 2015; Yeung & Summerfield, 2012). If this is true, then because these literatures remain largely distinct, this is very relevant and shows that they could potentially learn a lot from one another.

Activities in the bilateral insula and bilateral IFG were found in the overall error > correct contrast at response time. Similar to experiment one, these activities were found to still survive this contrast when it was re-calculated with only reward trials (reward error > correct) but not when it was re-calculated with only non-reward trials (non-reward error > correct). Nevertheless, again comparable to experiment one, due to small non-significant amounts of activity in non-reward trials (seen in Figure 14 where the significance threshold is reduced), activity in the bilateral insula and bilateral IFG did not survive the interaction between accuracy (error/correct) and stimulus (reward/non-reward predictive). Importantly, these regions were found to have a significant negative correlation with normalized levels of subsequently self-reported decision confidence. They did not however, survive this correlation when only high coherence correct trials were included in analysis (although they were visibly active when the p-value was set to 0.001 uncorrected).

Overall, activities in these regions needs to be further examined because, while they appeared very similar to that in the MCC in all contrasts, they did not always reach significance threshold. Therefore, while error (or potentially uncertainty) activity in these regions may be affected by the reward value associated with stimuli, this remains yet to be definitively proven.

In experiment two we found a range of areas (see Table 7 and Figure 13) to have increases in activity at response time as subsequently self-reported confidence also increased. The function of these activities is more difficult to determine because none of these regions were activated more in correct than erroneous trials (or vice versa), nor were they more active in reward than non-reward trials (or vice versa). This indicates that while activity in these regions was related to self-reports of accuracy monitoring they were not in any way related to actual accuracy. Therefore, further investigation is required to see why activity in these areas are related to increases in confidence.

Finally, in experiment two we were unable to replicate our finding of increased neural activity in the IFG and MFC prior to erroneous compared to correct responses. Whether this was due to differences in task, reward, or participant strategies (e.g. bias) remains to be further examined.

Overall, in experiment two using a secondary reward we replicated the main result of experiment one showing that reward value enhances error-processing in the MCC at response time. In addition, we found that activity in this same region is negatively correlated with self-reports of decision confidence. This was true even when only high coherence correct trials were included in analysis, which indicates that this region might signal decision uncertainty.

General Discussion

Brief summary of results

In this study, over two experiments, we used fMRI measures to investigate the independent effect of reward value on neural monitoring of response accuracy. To do this we used a task in both experiments in which participants made a perceptual decision about visual stimuli; On each trial it was the stimulus presented rather than the accuracy of the participants' response that was predictive of whether or not the participant would then receive a reward. In our second experiment, participants also self-reported how confidant they felt that their responses on each trial were correct. We found that participants responded faster and with more self-reported confidence in high coherence correct trials with stimuli predictive of reward than in all other trials, even when compared to high coherence correct trials with stimuli predictive of non-reward. In both experiments we found a significant interaction indicating that at the time that a response was made, error-related activity (activity in error trials minus activity in correct trials) in the MCC was significantly greater in trials with reward compared to non-reward predictive stimuli. Similarly, a variety of other classic error-processing regions (bilateral IFG/precentral gyrus, bilateral insula, and bilateral posterior middle frontal gyrus/MCC) had significant error-related activity when reward trials were investigated but not when non-reward trials were investigated (for evidence that these areas are commonly found to be active after errors see Garavan et al., 2002; Klein et al., 2007; Menon et al., 2001). Admittedly, a low, non-significant level of error-related activity occurred in these areas even

in non-reward trials (see Figures 6 and 14), and this is why they did not survive the interaction. Nevertheless, the fact that in both experiments the size and significance in error-processing found in these regions differed between these reward and non-reward conditions at least suggests that further examination could be interesting. In our second experiment we further found that activity in the same region of the MCC, as well as in the other classic error-related regions reported above, correlated negatively with the level of confidence a participant reported having about the accuracy of their response. This activity in the MCC was found to correlate negatively with self-reports of confidence even when *only correct* high coherence trials were examined showing that this activity is more likely to reflect increased perceived likelihood of error (uncertainty) rather than just the processing of error. Finally, after participants were given their outcome (reward or non-reward), error-related activity in the MFC was then increased in non-reward but not in reward trials. Overall, these results show that, even when the value of an outcome is not related to the accuracy of a decision, the reward value associated with stimuli can influence response times, self-reports of decision confidence, and neural performance monitoring. The fact that these effects were found in both experiments is remarkable given that (a) in the first experiment we used juice, which is a primary reward, but that in experiment two we used money, which is a secondary reward, (b) different participants were used in these experiments, and (c) the experimental procedures were somewhat different between experiments.

Relation of our results to "evidence accumulation" models of error-processing and uncertainty

In the introduction to experiment one we introduced the “votes in a committee” analogy used by Rabbitt et al. (1978) to describe the processing of error. This analogy has been formalized in several “evidence accumulation” models of both error-processing and confidence/uncertainty (e.g. Resulaj, Kiani, Wolpert & Shadlen, 2009). Although naturally there are differences in these models, the overall general predictions of them were summed up nicely by Yeung and Summerfield (2012; see Appendix A). Importantly, according to these models error-processing and uncertainty depend on continued accumulation of evidence after a decision has been made.

One explanation for our results, consistent with “evidence accumulation” models of error-processing and uncertainty, is that evidence in our study was accumulated better, or faster, in trials with reward predictive stimuli compared to in trials with non-reward predictive stimuli. Our finding that response times were fastest in high coherence correct reward trials, even when compared to high coherence correct non-reward trials, fits well with faster evidence accumulation in reward than non-reward trials. If evidence accumulation continued to be faster or greater in reward than non-reward trial after decision as well, then according to “evidence accumulation” models, this should either confirm or cause uncertainty about the accuracy of the response. Consistent with this, we found MCC activity at response time (after committing to a decision but prior to receiving feedback about its accuracy) to discriminate between correct and error trials at response time in reward but not non-reward trials.

In non-reward error trials, consistent with insufficient processing of stimuli after decision, MCC activity did not discriminate between correct and error

trials at response time. However, at outcome time error was processed in these trials. This may be because at this time explicit evidence from an external source (i.e. the outcome) proved that the selected response was incorrect, and so the “generic error processing system” (discussed in the introduction to experiment one) was finally able to process error at this point

If it is true that evidence is better accumulated after decisions have been made in response to reward predictive stimuli then this has various implications. For example, better accumulation of evidence is thought to lead to more changes of mind (e.g. Resulaj et al., 2009) and to higher rates of error correction (e.g. Rabbitt & Vyas, 1981). It has also been suggested to lead to better preparation for impending outcomes (Yu & Zhou, 2009), although whether or not this holds when the outcomes are unrelated to response remains uninvestigated. Therefore, our results may imply that the reward value associated with stimuli affects post-decision behavior, a topic that might be interesting for future studies,

One finding of ours, found in a parametric analysis, did not fit so neatly with an explanation of current “evidence accumulation” models. As the reader may recall, even though the MCC was significantly more active in erroneous than in correct trials, this activity correlated negatively with self-reported confidence even when only correct trials were included in analysis. These results may reflect the fact that confidence was lower in error than in correct trials overall, but that it still varied within correct trials. This finding has implications for “evidence accumulation” models. This is because these models presume that stimulus evidence will begin to regress to its real mean over time. However, if this is the case then decision uncertainty should never

be found in correct trials and thus we should not have found this correlation in correct trials. Instead, still consistent with an "evidence accumulation" approach, perhaps in correct trials with decision uncertainty, continuation of accumulation of evidence after the making of a decision can actually sometimes cause less support for the correct response when the evidence is noisy enough. For example, in our experiments if the participant was not looking at the screen when the dots were moving, and then by chance still happened to make a correct response, continuation of processing should not lead to increased evidence for the correct decision since no evidence was perceived to begin with. In such a case, noise could even push the stimulus evidence back below a decision threshold that had originally been crossed, leading to decision uncertainty despite the fact that the response was correct. This needs to be considered by future "evidence accumulation" models.

How might the reward value associated with stimuli affect processing after committing to a decision?

If it is true that that evidence continues to be accumulated more in erroneous trials after decisions made in response to reward predictive compared to non-reward predictive stimuli, then one needs to consider why this might be. In a task where participants were rewarded for correct but not incorrect responses, Hajcak et al. (2005) found that the ERN was increased in errors when a higher reward was at stake than when a lower reward was at stake. This finding indicates that error-processing is affected by the amount of reward missed out on as a consequence of one's actions. Hajcak et al. (2005) termed this an effect of the "motivational significance" of errors. In line with this, several other studies have found evidence that such "motivational

significance" of errors might affect error-processing (Gehring & Willoughby, 2002; Ridderinkhof, Ramautar, & Wijnen 2009) and this has commonly been accepted as the reason for effects of reward value on error-procesing. However, our study showed that a difference in error-processing between trials with reward and non-reward predictive stimuli occurs even when participants don't need to respond correctly to obtain reward. It also showed that enhanced error-processing actually occurred in error trials where participants were still able to receive reward (i.e. when, despite making an error, they did not miss on reward). Therefore, while our results do not rule out effects of the "motivational significance" of errors, they do show that this is not the exclusive way in which error-processing is affected by reward.

Increased evidence accumulation in reward compared to non-reward trials in our task might be explained by the fact that the reward value associated with stimuli has an effect on their "attentional priority" (Anderson, 2013). Specifically, stimuli associated with higher reward value have been shown to capture attention more than stimuli associated with lower or no reward value (Anderson, 2013; Marx & Einhauser, 2015; Stormer, et al., 2014). This effect has been found to robustly occur even when increased attention to stimuli associated with reward proves disadvantageous to participants' performance (Anderson et al., 2011a, Anderson et al., 2011b; Hickey, et al., 2010; Sali, et al., 2014; Vaidya & Fellows, 2015). Similarly, the monitoring of response conflict that often occurs in error trials has been proposed to cause increases in attention (Botvinick, Braver, Barch, Carter, & Cohen, 2001). Therefore it follows that stimuli associated with increased reward value to which errors are made should capture the most attention

overall.

Of course it is noted that no specific measures of attention (such as pupil diameter, e.g. Hoeks & Levelt, 1993) were taken in this experiment, and that this should therefore be examined further in future studies. However, consistent with effects of attention, the areas that we found to be active in error trials, and which correlated negatively with self-reported confidence, are the same areas that are proposed to form the Salience Network (Figure 18). This is thought to function to focus a “spotlight of attention” (Menon, 2015). These areas were particularly or exclusively active for error-processing to reward predictive stimuli (see Figures 6, 7, 14, & 15). This makes sense because, consistent with increases in attention, activity in the Salience Network is proposed to increase in response to infrequent events (such as errors) or to biologically important stimuli (such as reward; Menon, 2015; Menon & Uddin, 2010; Seeley et al., 2007) and so could be expected to be more active for errors in trials with reward predictive stimuli. Therefore, our finding that enhanced error-processing occurred in reward compared to non-reward trials at response time might be explained by the reward predictive stimuli in these erroneous trials capturing more attention, as evidenced by activation in the salience network, and thereby leading to more evidence accumulation. If this is true then this should lead to more uncertainty-related neural activity in erroneous reward compared to correct reward trials than in erroneous non-reward compared to correct non-reward trials, which is exactly what we found.

If the above is true, then to know which stimuli required more attention at response time the brain must have, at some level, distinguished between

reward and non-reward predictive stimuli prior to response. Consistent with this idea, activity prior to response (at stimulus presentation time) was found to be different in trials with reward and non-reward predictive stimuli. This activity did not differ according to subsequent response accuracy, and therefore this processing was likely not explicit enough to be used to make the correct response. Nevertheless this activity may have provided sufficient information for the brain to determine whether or not, or how much, to continue evidence monitoring after committing to a response. No activity was found to distinguish between non-reward and reward trials at stimulus presentation time in experiment two, and so this idea needs to be further explored in future studies

Figure 17.

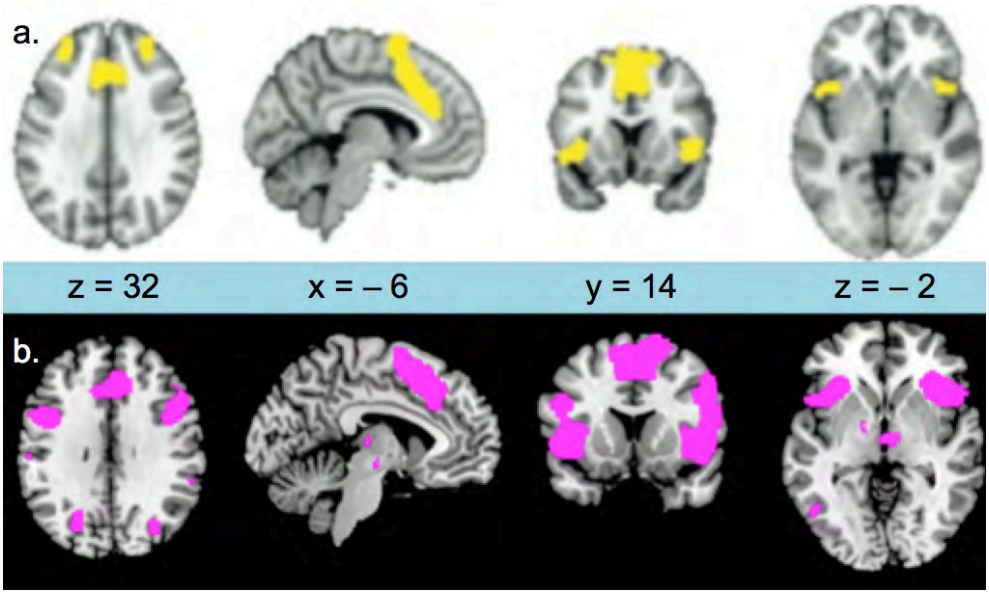

Figure 17. The Salience Network. x, y, z coordinates from the top and bottom images are the same and these are shown in the center of this figure. (a) This is taken from a figure by Menon (2015) showing the Salience Network. (b) This is activity that we found in our study to correlate negatively with confidence ratings- this activity appears to be in the same regions as the Salience Network shown above.

How does neural activity in the MCC relate to actual self-reports of confidence?

We found activity in the MCC to have greater error-processing in trials with reward predictive compared to non-reward predictive stimuli, and we found that this activity correlated negatively with self-reports of confidence. However, surprisingly, although this activity appeared to be related to uncertainty we found no effect of the reward value associated with stimuli on the actual self-reports of confidence in *error* trials. We did, however, find that when there was much stimulus evidence available (high coherence trials), there was an effect of the reward value associated with stimuli on the actual self-reports of confidence in *correct* trials. In high coherence correct reward trials self-reports of confidence were highest and response times were fastest, even when compared to high coherence correct non-reward trials.

This surprising effect can perhaps be understood when considering the valance of the beta values of neural activity in the MCC in experiment two. These were positive compared to baseline for all trials except for correct reward trials (see Figure 15) and this contributed to why error-processing (activity in error minus correct trials) was found to be greatest overall in these reward trials at this time. This result indicates that correct reward trials were the only trials in which uncertainty-related neural behavior did not occur. Therefore, because uncertainty-related neural behavior was found to occur to some degree in erroneous reward, erroneous non-reward, and correct non-reward trials, this may have caused enough uncertainty for self-reports of confidence to be low in all of these. On the contrary, because uncertainty-related neural behavior was not found to occur at all on reward correct trials,

this may explain why self-reports of perceived accuracy were highest (i.e. decreased uncertainty) on these trials.

A system for the monitoring of uncertainty

Holroyd and Coles (2002) proposed that a generic error-processing system exists in the cingulate cortex that signals error either at response time or at feedback time, essentially when it first realizes that "the consequences of an action are worse than expected" (p. 694). They proposed that this system functions to signal negative prediction errors for negative reinforcement learning, and that as reinforcement learning proceeds, due to learning, these prediction errors stop being signaled after feedback and begin to be signaled soon after response instead.

Our results are consistent with a generic system in the cingulate cortex that has error-related activity that occurs either at response time or after error feedback. However, they are not consistent with the circumstances under which Holroyd and Coles (2002) purported this system to run. First, although we cannot fully rule out the possibility that associations were formed between response accuracy and outcome in our task, there was no consistent reinforcement to bolster such associations, and in our second experiment participants explicitly confirmed on a questionnaire prior to beginning that they understood this design. Therefore, as mentioned repeatedly, because we found error-related activity to occur in our task despite the fact that there was no consequence to erroneous or correct responses, our results indicate that this error-processing occurs even when there is no benefit in learning. Thus this activity may not need to be dependent on the "consequences of an action" as Holroyd and Coles (2002) claimed.

Second, unlike previous studies, we investigated both rewarded and non-rewarded error conditions. This means that like previous studies we investigated errors where the outcome was “worse than expected” (where participants responded that dots were moving in the reward associated direction but they were not and so non-reward was delivered), but it also means that unlike previous studies we also investigated errors where the outcome was “better than expected” (where participants responded that dots were moving in the non-reward associated direction but they were not and so reward was delivered). We found both of these types of errors to be signaled in the cingulate cortex showing that Holroyd and Cole’s claim that the cingulate signals errors when the outcome is realized to be “worse than expected” is not the full story. The function of signaling errors even when the outcome is to be “better than expected” needs to be further investigated. It may be the case that the realization of error itself functioned as a somewhat negative outcome.

Finally, consistent with some recent research (e.g. Boldt & Yeung, 2015) we found activity in these “error-related” regions to occur even in correct trials as a negative function of self-reported confidence. Therefore, rather than simply signaling that an error has been made, this system might be better described as signaling the subjectively perceived likelihood that an error has been made. Therefore, it fits better with definitions of “uncertainty” than “error-processing” and so might be better called an uncertainty-processing system.

Correct/Error-processing and Confidence/Uncertainty

As described earlier, ERP components that were originally thought to reflect the processing of error have since been shown to have more graded

activity that can be found even in correct trials when uncertainty is high (Boldt & Yeung, 2015; Scheffers & Coles, 2000). Consistent with these findings, our fMRI experiment showed that activity in the cingulate was greater after errors than after correct responses, but that this activity correlated negatively with confidence ratings even when only correct trials were included in the analysis. Therefore, because by nature “error-processing” should not occur in correct trials, our results fit with the idea that, despite often being found after errors have been made, this type of cingulate activity might reflect the neural processing of uncertainty rather than the processing of error per se (e.g. Boldt & Yeung, 2015). This implies that there is lot that the confidence/uncertainty literature could learn from the largely independent error-processing literature. For example, because the results of our and several other studies imply that activity in the cingulate is graded depending on perceived likeliness of response accuracy, the confidence/uncertainty literature, which has until now largely focused on areas such as the OFC (e.g. (e.g. Kepecs, et al., 2008; Kepecs & Mainen, 2012) and the lateral intraparietal cortex (e.g. Kiani & Shadlen, 2009) should consider a greater role of the cingulate cortex. Additionally, this literature might benefit from further manipulations of traditional measures of error-processing (such as the ERN and feedback ERN and corresponding fMRI activations).

Because activity in the visual cortex is thought to indicate accumulation of perceptual evidence for making a perceptual decision (Fetsch et al., 2014), our finding that the visual cortex was more active in correct compared to error trials at stimulus time might simply show that more perceptual evidence was gathered in correct than in error trials (no regions were found to have an

increase in activity in correct compared to error trials at response time). Interestingly, while we found the PCC, MTG, prenuceous, OFC, IPL, post-central gyrus, and SFG found to have positive correlations with self-reported confidence at both stimulus time and response time, these regions did not overlap with the visual regions that were more active in correct than erroneous trials. Therefore, increases in decision confidence may not be simply explained by the increases in perceived stimulus evidence that appear to occur more often in correct than erroneous trials. Lak et al. (2014) found that inactivation of the OFC causes a decrease in confidence, as measured by the amount of time that rats wait for reward. This implies that this region is important for the processing of confidence. Interestingly, they found that this occurs without having any effect on accuracy. Therefore, both that study and our own indicate that activity in the OFC is related to confidence but not to accuracy. Because the OFC is thought to be part of the "emotional network" (e.g. Ochsner & Gross, 2005), the function of the OFC in confidence may therefore be related to more subjective feelings of competence. This obviously needs to be much further examined. Future studies that decode the contribution of different regions of the brain to decision confidence/uncertainty might prove useful in clarifying their functions.

Relation of our results to "distance to decision boundary" models of error-processing and uncertainty

While "evidence accumulation" models of error-processing/uncertainty have been much discussed in this thesis, there is in fact one other famous type of model often used to explain results in these fields (e.g. Kepecs et al., 2008; Steinhauser & Yeung, 2010). This is the "distance to decision

boundary" type of model (described in Appendix B). This type of model uses Signal Detection Theory (SDT; briefly described in the method section of experiment one) and essentially predicts that error-processing/uncertainty depends on how far away the evidence for a given stimulus falls from a person's decision boundary when they make a decision. A decision boundary refers to the level of evidence needed for a certain decision before you make it (Green & Swets, 1966). Within the SDT framework It is measured as *c,* or "response bias".

Distance to decision boundary" models predict that participants with different response biases should have different levels of error-processing/uncertainty to the same level of stimulus evidence. These models propose that this is the case because (a) people with different levels of response bias have decision boundaries in different positions, (b) the distance between a given level of stimulus evidence and the decision boundary differs depending on the position of the decision boundary (see Appendix C for an example), and (c) error-processing/uncertainty for a stimulus differs depends on the distance between the evidence for it and the participant's decision boundary. If this is true, then in our task, correlations should be found between uncertainty (behavioral and neural correlates) and participants' decision boundaries (as measured using SDT *c*). Importantly, these correlations should have *opposite* signs for reward correct and reward error trials and opposite signs for non-reward correct and non-reward error trials. This is because as the average evidence for a reward correct trial gets closer to the decision boundary and thereby averaged uncertainty increases, the average evidence for a reward error trial should get further away from the

decision boundary and thereby averaged uncertainty should decrease (and vice versa). The same should apply for non-reward correct and non-reward error trials (again, see Appendix C for an example).

In our experiments we measured response boundaries of participants by calculating *c* using SDT. Because response time is supposed to be informative about a person's level of confidence/uncertainty (e.g. see Kiani, Corthell, & Shadlen, 2014) we calculated correlations between response times and *c*. In experiment one, while a correlation between *c* and response time was found in high coherence reward erroneous trials, problematic for "distance to decision boundary" models, no correlation was found in high coherence reward correct trials. On low coherence trials a positive correlation was found between *c* and response time in both reward erroneous and correct trials, but again problematic for "distance to decision boundary" models, both of these correlations had the same sign (positive). The positive sign of these three correlations indicates that the greater a bias a person had for the response associated with reward predictive stimuli (the more negative their *c*), the faster they responded in these conditions (the shorter their response times). On experiment two of our study, where participants had a smaller range of response bias (see Figures 3 and 10), no significant correlations were found between *c* and response times at all. Similarly, participants' self-reported level of confidence did not correlate with *c* in any conditions. Overall, these behavioral results do not fit with the predictions of "distance to decision boundary" models. The sign of all correlations in experiment one, including those that did not reach significance, were all positive. Therefore, a more parsimonious explanation for these results is that as experiment one's

participants' response biases for the response associated with reward predictive stimuli increased, their response times were simply faster. Because nearly all participants were biased for the reward-associated direction and only a few were biased for the non-reward associated direction, this therefore means that participants with more bias overall responded more quickly overall.

To test the predictions of "distance to decision boundary" models at a neural level, we took beta values for all conditions from the areas in the MCC in which the interaction was found and correlated these with participants' *c* (separately for high and low coherence conditions). In the first experiment the only significant correlation was found to occur between high coherence *c* and betas from the MCC in high coherence reward error trials; these betas increased as participant's biases for the response associated with reward predictive increased. In the second experiment no significant correlations were found at all. Again, these results are not sufficient to support predictions made based on "distance to decision boundary" models. Importantly, when other areas that significantly decreased with subsequent confidence ratings were investigated (bilateral IFG/precentral gyrus, bilateral insula, and bilateral posterior middle frontal gyrus/MCC), activity in none of these regions was found to significantly differ with participants' response bias (*c)* either. Likewise, activity in the regions that were more active as subsequent confidence ratings got higher (PCC, MTG, prenuceous, OFC, IPL, post-central gyrus, and SFG) did not correlate with *c*.

Therefore, there was a lack of support for "distance to decision boundary" models found in both behavioral and neural measures of our study. "Distance

to boundary" models have been critiqued for not being able to explain findings of "changes of mind" and error correction due to the fact that these models do not consider potential changes in activity after a decision is made (Resulaj et al., 2009). Although we acknowledge that our task design may have been the reason for these non-results, our findings potentially add to previous critique by showing that "Distance to boundary" models were unable to explain response times, explicit confidence ratings, and uncertainty-related neural activity that occurred at response time.

We note that predictions based on decision boundaries could also be made in "evidence accumulation" models, and that our results do not support these. However, "evidence accumulation" models *also* allow for an alternate explanation of our results based on a difference in the continuation of evidence accumulation after response between reward and non-reward conditions. Our results do fit with this type of explanation.

Implication for pathological gambling disorder

Atypical error-related neural activity in the cingulate cortex has been found to occur in several groups of people with mental health illnesses including people with major depressive disorder (e.g. Schoenberg, 2014), generalized anxiety disorder (e.g. Weinberg, Olvet, & Hajcak, 2010), and obsessive compulsive disorder (e.g. Endrass, Klawohn, Schuster, & Kathman, 2008). The results of the current study imply that reward value can influence error-related neural activity. Therefore, it is possible that people who have mental health illnesses associated with atypical processing of reward, such as those with pathological gambling disorder (e.g. see Potenza, 2008), might also have atypical processing of error.

While various gambling tasks have been utilized in the error-processing literature, healthy participants have tended to be used as subjects (e.g. Dunning & Hajcak, 2007; Gehring, & Willoughby, 2002; Marco-Pallares, Cucurell, Munte, Strien, & Rodriguez-Fornells, 2011) and so little is known about error-processing in people with pathological gambling disorder. Nevertheless, because slot machines are specifically designed so that people cannot manipulate their outcome with their behavior, similar to our experiment, people who gamble on slot machines can only learn to make associations between stimuli and outcome, not between response and outcome. These associations are likely stronger for people who pathologically gamble than for healthy people. For example, neural activation in response to gambling-related stimuli is stronger in participants with pathological gambling than in healthy controls (e.g. see Crockford, Goodyear, Edwards, Quickfall, & el-Guebaly, 2005). Our finding that confidence was highest in correct trials with reward predictive stimuli might therefore be one explanation for why people continue to gamble after they have learned to make associations between gambling-related stimuli and outcome. In line with the current results, the presence of gambling-related stimuli that have been associated with reward in the past may lead to increases in confidence levels/decreases in uncertainty levels in individuals with pathological gambling disorder, even when they know that their gambling behavior is unrelated to the value of gambling outcomes. This increase in confidence/decrease in uncertainty might be associated with continued gambling. Further investigation into the error and confidence/uncertainty processing of people with pathological gambling disorder might prove fruitful, therefore, in obtaining a better

understanding of this disorder.

Conclusions

In this study we examined how the reward value associated with stimuli affects the monitoring of response accuracy in perceptual decisions. We found that behaviorally, when much perceptual evidence was provided and participants were able to correctly identify the provided stimulus, they were quicker and self-reportedly more confident in doing so when this stimulus was associated with reward compared to when it was associated with non-reward. Due to the design of our task, this finding shows that the reward value associated with stimuli can influence behavior even when accurate behavior is not required to receive reward. At a neural level, at a time when participants had committed to a response but not yet received feedback about its accuracy, enhanced error-related processes in the MCC (and to a lesser degree other classic error-processing regions) was found in conditions where stimuli were associated with reward compared to non-reward. This activity was shown to significantly increase as self-reported ratings of decision confidence decreased. This finding held even when only high coherence correct trials were examined and so activity here likely reflects the processing of decision uncertainty rather than the processing of actual errors, per se. These results therefore indicate that the reward value associated with stimuli can affect neural processes at response time related to decision confidence/uncertainty, even when accurate behavior is not required to receive reward. In non-reward trials error was not significantly processed at this time, but it was instead found to be significantly processed later when explicit feedback was provided.

Based on these results and current models of error-processing/uncertainty, we speculate that in our experiment the reward value associated with stimuli might have influenced how much evidence was continued to be gathered after a decision had been made. Specifically, because error-processing and confidence/uncertainty are thought to depend on evidence accumulation after decision, better or faster processing of evidence in reward compared to non-reward trials after committing to a decision may explain why error-processing at response time was better in reward compared to non-reward trials. This finding may have occurred due to effects of attention, since the areas we found to have active error-processing in reward compared to non-reward trials at this time make up the salience network, which is said to function to focus attention. These results have various implications for theories and models of error-monitoring, decision confidence/uncertainty, cingulate cortex function, and gambling disorder.

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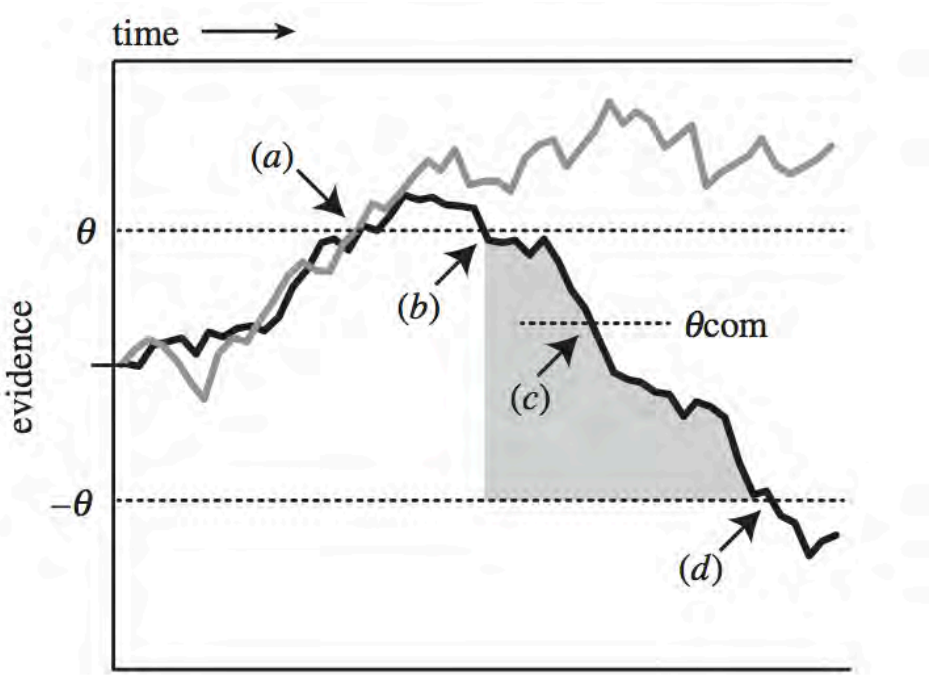
Appendix A.

Predictions from "Evidence accumulation" models of error-processing and uncertainty.

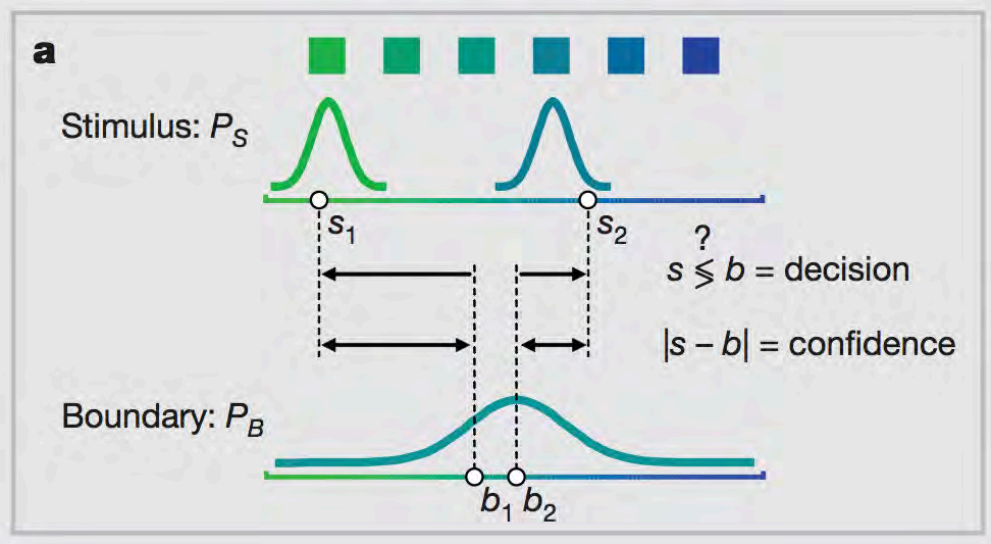


The above figure was taken from Yeung and Summerfield (2012). This figure shows predictions from "evidence accumulation" theories, which are as follows. In a two-choice decision the brain accumulates evidence for both potential responses (e.g. *θ* or - *θ*). (a) Once the accumulated decision evidence for one of these responses reaches a certain level (e.g. the *θ* boundary indicated by the top dotted line), the corresponding response will be made (e.g. the *θ* response). However, even after the response has been made, evidence can continue to accumulate. If you have made the correct response (grey line) then accumulated evidence should continue gathering beyond the decision boundary that you selected and thus continue to support the response that you selected. (b) However if, for example due to random fluctuations in noise, you have made an erroneous response (black line) then

continued accumulation of evidence should eventually cause this evidence to regress to its true mean and therefore to cross back under the (e.g. θ) decision boundary it first crossed. (c) Over time this evidence should continue regressing towards its true mean and eventually reaches a “change of mind” boundary. (d) Finally, after enough evidence has been further accumulated, it should reach boundary for the other (correct) decision (e.g. the $-\theta$ boundary indicated by the bottom dotted line). Error-processing and uncertainty (the shaded section in the above figure) is considered to begin when the evidence first crosses back under the original (e.g. θ) decision boundary and to increase until it crosses the other (e.g. $-\theta$ boundary) where error detection occurs. Therefore, according to these models, error-processing and uncertainty depend on continued accumulation of evidence after response.

Appendix B

Predictions from "distance to decision boundary" models of error-processing and uncertainty.



This above figure shows a typical "distance to decision boundary" model, taken from Kepecs et al., (2008). It essentially shows that if stimulus evidence (*s*) is greater than a remembered decision boundary (*b*), then the corresponding decision will be made and if it is less than the remembered boundary then the corresponding decision will not be made. Confidence (defined in this paper as the opposite of uncertainty) depends on how far over or below the decision boundary this stimulus evidence falls. The further from the boundary (either above or below) the stimulus evidence falls on a given trial, the greater the confidence and the lower the uncertainty in making (or nor making) that decision. This can be seen in the instance of $s_{1,}$ which is relatively far from the boundary b_1. Greater confidence/lower uncertainty makes inherent sense in this instance because there is *far more* evidence to make (or not make) the decision. On the contrary, the closer to the boundary (either above or below) the stimulus evidence falls on a certain trial, the lower

the confidence and the greater the uncertainty in making (or nor making) that decision. This can be seen in the instance of $s_{2,}$ which is relatively close to the boundary b_2. Higher error-processing/uncertainty in this instance makes inherent sense, because this amount of evidence is only *just enough* to make (or not make) the decision.

Appendix C

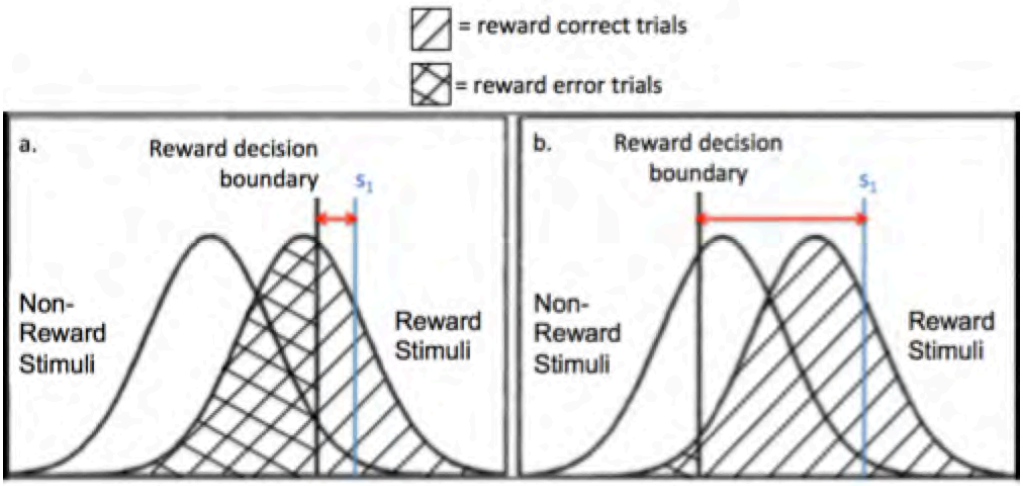


Figure 20. This shows a simple example of (a) a person who is biased to judge stimuli as “non-reward”, and (b) a person who is biased to judge stimuli as “reward”, as determined by the different positions of their “reward decision boundaries”. When a stimulus with a given amount of evidence is provided to these people (e.g. s_1), the distance between this and the “Reward decision boundary” of each person differs (shown by the length of the red arrows). Therefore, according to “distance to decision boundary” models, because the distance between stimulus evidence (s_1) and reward decision boundary is shorter for the participant in (a) than for the person in (b), error-processing/uncertainty in response to this stimulus should be higher for the participant in (a). This demonstrates how error-processing/uncertainty in response to stimuli should differ dependent on the position of decision boundaries and therefore why error-processing/uncertainty should correlate with decision bias (which is a measure of decision boundary).

Note that these correlations should have *opposite* signs for correct and error trials. In the above example, as decision boundaries move left (it is further left for the person in b than the person in a), the average evidence for

correct reward trials becomes farther away from this boundary (it is further away for the person in b than the person in a) and so the average uncertainty on *correct* reward trials should decrease. But at the same time, the average evidence for error reward trials becomes closer to this boundary (it is closer for the person in b than the person in a) and so the average uncertainty on *error* reward trials should increase. In this example as the decision boundaries of participants move left, the average uncertainty should decrease on correct reward trials but increase on error reward trials. Therefore, one can see that that correlations between uncertainty and decision boundaries should have opposite signs in correct and error trials.