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Original Article

ORIGINAL ARTICLE

Reward-Driven Arousal Impacts Preparation to Perform a Task via Amygdala–Caudate Mechanisms

Noriya Watanabe[1,2,3,4], Jamil P. Bhanji[1], Hideki Ohira[3] and Mauricio R. Delgado[1]

[1]Department of Psychology, Rutgers University, 101 Warren Street, Newark, NJ 07102, USA, [2]Japan Society for Promotion of Science, Tokyo 102-0083, Japan, [3]Graduate School of Informatics, Nagoya University, Nagoya 464-8601, Japan and [4]Center for Information and Neural Networks, National Institute of Information and Communications Technology, Osaka 565-0871, Japan

Address correspondence to Noriya Watanabe (noriyawtnb@gmail.com); Mauricio R. Delgado (delgado@psychology.rutgers.edu)

Abstract

Preparing for a challenging task can increase physiological arousal, in particular when potential incentives are large (e.g., a solo musical performance in front of an audience). Here, we examine how potential reward and its influence on arousal, measured by pupil dynamics, are represented in the brain while preparing for a challenging task. We further ask how neural representations during preparation relate to actual performance. Trials resulting in performance failure were characterized by increased pupil dilation as a function of increasing reward magnitude during preparation. Such failure trials were also associated with activation of the right amygdala representing pupil dilation, and the left caudate representing reward magnitude. Notably, increases in functional connectivity between amygdala and caudate preceded performance failure. These findings highlight increased connectivity between neural regions representing reward and arousal in circumstances where reward-driven arousal impairs performance.

Key words: fMRI, physiological arousal, pupil dynamics, reward, task performance

Introduction

Imagine you are a musician in an orchestra and you are about to perform an important solo in a concert. The physiological arousal elicited by anticipating the solo performance along with the motivation to succeed can make it difficult to "keep calm and carry on" and perform at one's best. This example poses an intriguing question about how physiological arousal (i.e., individual autonomic response to stimulus or state in a situation) and the incentive associated with successful behavior (e.g., the potential positive evaluation from conductor and audience) interact to contribute to performance. While incentive magnitude is a factor that can generally benefit performance (Lazear 2000), the presence of incentives can also increase physiological arousal, which can negatively influence performance (Yerkes and Dodson 1908; Ariely et al. 2009). Indeed, a large literature describes a phenomenon known as "choking under pressure" (Beilock and Jackson 2007), which highlights individual differences in performance when the stakes are high and suggests involvement of the brain's reward circuit (Mobbs et al. 2009; Chib et al. 2012). In the current study, we characterize the unique contribution of physiological arousal as a function of incentive levels for successful task performance. Importantly, we investigate the brain mechanisms underlying the representation of arousal and incentive magnitude when participants are preparing to perform a task—that is, prior to the execution of any behavior. The goal is to better understand how momentary incentives and arousal responses relate to performance in a situation where preparation can determine success.

The regulation of physiological arousal is associated with the locus coeruleus (LC), a key noradrenergic center with anatomical connections to several structures involved in arousal, vigilance and salience such as the amygdala (Samuels and Szabadi 2008) and the dorsal anterior cingulate cortex (dACC) (Aston-Jones and Cohen 2005). In human neuroimaging studies, the amygdala and dACC are often linked with LC-driven physiological arousal responses, such as anticipation of fear or risk (for review see Critchley 2005; Phelps and LeDoux 2005; Delgado et al. 2006). And those responses can be measured by skin conductance or pupil dilation (Bradshaw 1967; Bradley et al. 2008; Delgado et al. 2009). Furthermore, physiological arousal and related amygdala or dACC activity are linked to measures of behavioral performance, such as decision making (Sokol-Hessner et al. 2013; Critchley et al. 2001). Taken together, these studies highlight the involvement of the human amygdala and dACC during arousing situations that may lead to behavioral changes, but leave open the question of how arousal may interact with incentive magnitude when preparing to execute a behavior.

Incentive processing is typically attributed to dopaminergic centers of the brain and their projections (Schultz et al. 1997; Haber and Knutson 2010). A common finding in human neuroimaging studies is involvement of the striatum in reward processing (for review see O'Doherty 2004; Knutson and Cooper 2005; Delgado 2007). A reward-related signal in the striatum tends to scale as a function of magnitude (Knutson et al. 2001; Delgado et al. 2003) and correlate with behavioral changes (Schonberg et al. 2007). Interestingly, striatum (Chib et al. 2012) and midbrain (Mobbs et al. 2009) activity during execution of sensory-motor tasks are associated with performance under high incentive situations, but the role of arousal during preparation is unexamined. Specifically, it is unclear how incentive-based brain signals interact with arousal levels to influence performance success during the key period of preparation, prior to any task execution. An interesting hypothesis is that incentive information, as processed by the striatum, integrates with arousal information, potentially represented by amygdala activation, to determine successful or unsuccessful performance. Indeed, striatal and amygdala functional interactions are commonly observed in highly arousing task-contexts, such as avoidance learning (Delgado et al. 2009). Enhanced learning is one potential outcome of increased functional connectivity (Watanabe et al. 2013, Watanabe and Haruno 2015; Stuber et al. 2011; Namburi et al. 2015). However, increased amygdala–striatal connectivity may not benefit performance in all situations. Such connectivity may have a detrimental outcome when reward-driven arousal can impair performance, for instance, when anticipating a solo performance in a concert.

In the current study, we examined neural activity underlying instances when reward-driven arousal during preparation, or anticipation of the actual behavior, leads to failure. We predicted that performance failure would be characterized by strong functional connectivity between neural representations of potential reward and physiological arousal during task preparation (Fig. 1A). In such trials, arousal level would be strongly affected by trial-wise potential reward (stakes). Further, increased interactions between arousal-related brain activity (e.g., amygdala or/and dACC) and reward-related activation (e.g., striatum) in trials would contribute to failures in performance. We tested these hypotheses with simultaneous measurements of functional magnetic resonance imaging (fMRI) and pupil dilation, which is an objective index of trial-based physiological arousal change (Bradshaw 1967; Partala and Surakka 2003; Bradley et al. 2008; O'Reilly et al. 2013; Preuschoff et al. 2011).

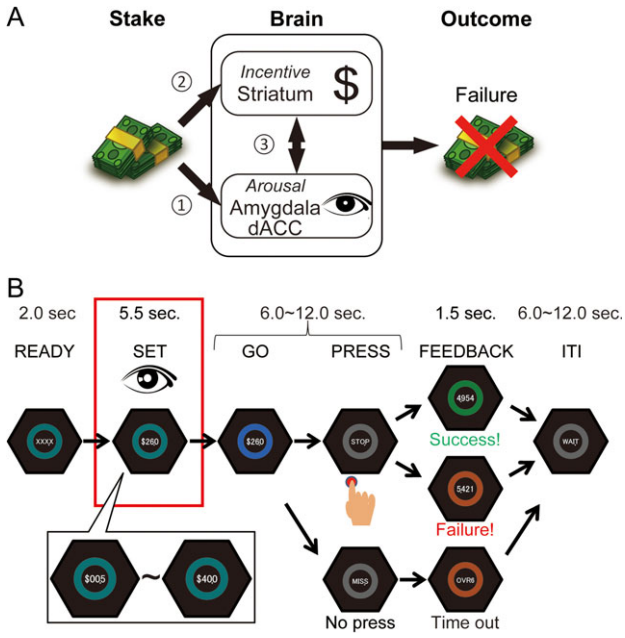

Figure 1. Experimental hypothesis and stop watch task procedure. (*A*) Hypothesized associations between representations of incentive and arousal during task preparation. The current study examined neural mechanisms underlying reward-driven arousal that leads to unsuccessful task performance. People may tend to fail when the potential reward strongly impacts subjective arousal level. This study examines hypotheses that 1) increasing potential reward (stake) leads to arousal-related amygdala and/or dACC activation, 2) increasing stakes lead to incentive-related striatum activation, and 3) interactions between arousal-related amygdala (or dACC) and incentive-related striatum activity during preparation of a behavior contributes to "failure" in performance. (*B*) Participants were required to stop the watch at exactly 5 s in this task. At READY phase, a lime-colored ring and 4 letters "XXXX" indicated the start of a trial. At the SET preparatory phase (red frame), a monetary offer was presented (e.g., $26.0) and pupil response was collected. The magnitude of the reward offer were changed every trial and varied between $0.50 and $40.00 (shown in inset). Participants counted 5 s in their heads from the GO signal (blue ring) and pressed the button to stop the watch (PRESS). Response time was shown at the FEEDBACK phase resulting in monetary reward for a press within an allowable margin around 5.0 s (Success), or no reward for presses outside the margin (Failure) and trials without a press within 6 s (Time out).

Materials and Methods

Participants

Participants were from the Rutgers University community with no history of psychiatric or neurological disorders. All experiments were conducted according to the principles in the Declaration of Helsinki and were approved by the Rutgers University Institutional Review Board. All 30 right-handed participants gave informed consent prior to the experiments on each day. However, we were unable to track pupil dynamics in the scanner for 8 people (over 15% pupil data unavailable). Therefore, we analyzed data from the remaining 22 participants (14 females, mean age 21.3, standard deviation [SD] = 2.4, range: 18–27 years old).

Equipment

Brain images were collected by a 3.0T Siemens TRIO scanner with a 12-channel head coil. For pupillometry, a SR search EyeLink 1000 Plus system was used. We tracked pupil diameter from the right eye with 500 Hz sampling rate with the centroid

mode to reduce the noise in the pupil data. For stimulus presentation and data analysis, we used MATLAB R2015a with Psychtoolbox 3.0.12 and Statistical Parametric Mapping 12 ver. 6685 (SPM12: Friston et al. 1995).

Stop Watch Task

During the experiment, participants were required to mentally estimate time and stop a watch at 5 s without a display of counting time. A successful stop close to 5 s led to the reward amount indicated during the preparation period. Trials consist of 5 phases (READY, SET, GO, PRESS and FEEDBACK: see Fig. 1*B*). First, a lime-colored ring and 4 letters "XXXX" indicate the start of a trial (READY phase, 2 s). Next, the letters changed to a dollar amount indicating the reward at stake for success for the trial. This amount changed every trial from $0.50 to $40.00 by pseudorandom order (preparatory SET phase, 5.5 s). During this preparatory phase, participants were instructed to prepare for the task and to keep their eyes open. Pupil amplitudes were recorded during this phase. Participants did not know the duration of the preparatory phase thus could not start counting early. The stop watch started when the color of the ring turned to blue (GO phase) then participants mentally estimated the time and pressed the button to try to stop the watch at exactly 5 s. The display showed "STOP" and the ring color changed to gray when the button was pressed. After 6.0–12.0 s from the GO signal, feedback was shown (FEEDBACK phase). Feedback was the actual response time (RT) with the ring color changed to indicate success (green) or failure (orange). If participants did not press within 6.0 s, the display showed "MISS", then "OVR6" (signifying a time over 6 s) during the FEEDBACK phase with no reward outcome. There was an intertrial interval after the FEEDBACK phase (ITI, 6–12 s). The order and distribution of trial-wise reward magnitude were counter balanced and luminance of each event display was controlled to minimize the light reflex of the pupil response.

This task includes several cognitive process, such as evaluation of potential reward, top-down attention to detect cue timing and time counting, and impulse (motor) control for button-press. All these cognitive processes can be affected by arousal change and influence performance. However, in the current study, we focused on the relationship between reward and arousal during the preparatory phase, when participants are anticipating the behavioral response necessary to attain the potential reward, and evaluated how these 2 factors interact in the brain.

Experimental Paradigm: Training, Execution and Manipulation Check

Training and performance of the task took place over 2 days in order to minimize learning effects during the fMRI session. On day 1, participants learned and trained on the Stop Watch (SW) task outside the MRI scanner. The goal of day 1 was to learn the task and determine the difficulty level (out of 4 possible levels) at which individuals' performance reached a plateau. Higher difficulty levels required participants to stop the watch within a smaller margin of error to be successful on a trial (level 1: 5 ± 0.250 s; level 2: 5 ± 0.200 s; level 3: 5 ± 0.150 s; level 4: 5 ± 0.100 s). The training difficulty level started at one and was upgraded when participants reached a minimum 60% success rate over the last 10 trials. For the task on day 2, the individualized difficulty level was set at the highest level attained on day 1. There was no trial-wise reward on day 1 (the display showed "$$$$" during the SET phase). Instead, we motivated participants to reach their highest level with a $1 bonus for every level increase. All participants met the 60% criterion for level 1 at a minimum, and no participants met criterion for level 4 within the 80 trials of day 1 training. Participants also learned not to blink their eyes during the preparatory SET phase in the training. Eye blinks during training were manually detected by means of a camera, and a feedback screen displayed "Don't blink at SET timing." Upon conclusion of day 1, all participants (1) learned to avoid blinking during the preparatory SET phase; (2) established difficulty level for day 2; and (3) were over-trained in task basics which minimized any learning for the MRI session.

On day 2, participants played 15 training trials to refresh their understanding of the trial sequence before entering the scanner. We then conducted simultaneous data acquisition of fMRI data and eye tracking while participants performed the task with variable real monetary rewards for success on each trial. Overall, 80 trials were distributed across 3 sessions (27 or 26 trials each). Eye tracking was calibrated before each session. Importantly, average performance across 3 sessions on day 2 was stable, as learning took place on day 1 (Supplementary Data 1 and Fig. S1). The SW task was "challenging" in the sense that the success rate was low (mean ± SD = 39.9 ± 10.1%) and perceived as subjectively difficult (ratings of difficulty were greater than zero [neutral]: one sample $t[21] = 4.915$, $P = 0.038$) in general.

As a manipulation check, participants rated subjective effort and fatigue levels after each session in the scanner to evaluate session-depend change of motivation (−50~+50 by moving slider starting at 0). The subjective effort level was significantly higher (S1: mean ± SD = 31.50 ± 14.36, S2: 29.50 ± 17.15, S3: 26.59 ± 20.19, $F[1,21] = 71.438$, $P < 0.001$) than zero and effort level did not significantly change across sessions ($F[2,42] = 1.640$, $P = 0.206$). However, fatigue increased gradually across sessions (S1: −15.05 ± 24.46, S2: −6.32 ± 26.00, S3: −2.27 ± 29.38, $F[2,42] = 4.273$, $P = 0.020$). Participants also rated their motivation, arousal, pressure, and difficulty experienced for trials of different reward magnitudes (5 levels: $0.50–$8.00, $8.50–$16.00, $16.50–$24.00, $24.50–$32.00, $32.50–$40.00) immediately after the experiment outside the scanner.

Finally, to determine their total compensation, participants pulled a slot machine simulator to select one of the 80 trial outcomes from the task they played in the scanner. They then received the outcome of the selected trial as a bonus in addition to an hourly payment and the level-up bonus from day 1.

Analysis of Behavioral Data

The performance in our SW task was calculated in a consistent manner with a previous study that used a similar task (Murayama et al. 2010). Specifically, the timing performance score was calculated by the following equation:

$$\text{Timing Performance Score} = 1 - (|5.00 - RT|/5.00)$$

Thus, the performance score is 1.0 when the response time (RT) is exactly 5 s and is lower the more RT deviates from 5 s. A trial was excluded from analysis when RT was <3 s (performance scores ranged from 0.6 to 1.0). One trial was excluded from 6 participants, 2 trials from 3 and 3 trials from 1 (mean ± SD exclusion = 0.681 ± 0.873 trials).

The threshold of success and failure during the experiment in the scanner was decided by individual performance during training in day 1. The timing threshold was upgraded when the

individual success rate reached to 60% in the last 10 trials during the training. Nine participants played at level 1 (5 ± 0.250 s), 8 at level 2 (5 ± 0.200 s), and 5 at level 3 (5 ± 0.150 s) (see Supplementary Data 1 for more detail).

Data Analysis of Pupil Dynamics

We tracked eye-pupil dynamics from the right eye during preparation to perform the task. Pupil amplitude as well as skin conductance responses are widely used for detection of trial-wise physiological arousal response (Bradshaw et al. 1967; Partala and Surakka 2003; Bradley et al. 2008; Preuschoff et al. 2011; O'Reilly et al. 2013). We used pupillometry, rather than skin conductance, as it is free from the effect of low humidity and temperature, and also free from potential reciprocal noise between MRI scanner and electrode in MRI environment as it was measured by an infrared camera through the mirror in the scanner. The pupil amplitude data were preprocessed and analyzed using a custom script that utilized MATLAB signal processing functions to remove the artifacts in the time series. First, eye blinks were removed by identifying times when the difference of the diameter changed over ±0.050 mm within 2 ms. Data ±25 ms from the detected blink points were removed. Removed data were interpolated with Piecewise Cubic Hermite Interpolating Polynomial (PCHIP) (Fritsch and Carlson 1980; Kahaner et al. 1988). Linear drift in each session was detrended, high pass filtered (125 s cutoff) and smoothed by Savitzky-Golay Filter with ±201 ms width to reduce the sampling noise (Orfanidis 1996). Then the data were z-normalized within each individual to further analyze at the group level. Data from the preparatory SET phase (5.5 s duration, 500 Hz sampling rate yielded 2750 samples per trial) were the outcome variable in a successive regression analysis, which is generally used in pupil data analysis (Preuschoff et al. 2011; O'Reilly et al. 2013). The pupil amplitudes were regressed on the log reward magnitude at each time point to identify incentive representations in pupil amplitudes for each participant. The estimated beta values were averaged by 500 ms windows (for success and failure trials separately) and evaluated by *T* tests by each time point with false discovery rate (FDR) corrections (11 time points) for group level analysis to examine incentive representations that varied by time during the preparatory phase.

Data Acquisition and Analysis of fMRI Data

Brain structural images were acquired with a T1-weighted MPRAGE sequence (256 × 256 matrix, FOV 256 mm, 176 1 mm sagittal slices). Blood oxygen level dependent (BOLD) functional images were acquired with an echo-planar imaging sequence (TR = 2000 ms, TE = 25 ms, FOV = 192 mm, flip angle 90°, bandwidth 2232 Hz/Px, echo spacing = 0.51, 35 oblique-axial slices aligned to the anterior commissure-posterior commissure line, voxel size 3 × 3 × 3 mm^3). We used SPM12 software for preprocessing and statistics (http://www.fil.ion.ucl.ac.uk/spm/software/spm12/). Preprocessing consisted of standard steps for each participant's functional data: slice timing correction, image realignment to the mean volume, spatial normalization to the Montreal Neurological Institute (MNI) standard (resampled at 2 mm^3), and spatial smoothing (8 mm Gaussian kernel).

Data for each participant were analyzed with a standard event-related general linear model. As our analysis focused on trial-by-trial BOLD changes, we modeled trial-wise pupil amplitude, reward magnitude and the interaction (pupil × reward) as parametric modulators during the preparatory SET phase. The pupil regressor was the mean pupil size during the preparatory phase (5.5 s) to represent trial-wise physiological arousal change. Although this is distinct from the behavioral analysis which focused on every 0.5 s, this transformation is necessary because temporal resolution of BOLD signal change is much slower than the pupil sampling rate. It is conceptually similar to skin conductance level which measures the trial-wise state of the autonomic response, rather than subsecond changes within a trial (Phelps et al. 2001; Nagai et al. 2004; Zhang et al. 2014). Importantly, the reward magnitude and pupil amplitude parametric regressors were not correlated in success trials (Fisher's Z: mean ± SEM = 0.001 ± 0.028, one sample $t[21] = 0.028$, $P = 0.978$) or in failure trials (mean ± SEM =–0.007 ± 0.036, one sample $t[21] = -0.184$, $P = 0.856$). The interaction regressor was calculated by multiplication of z normalized reward and pupil values. Additional regressors included onset of the PRESS and FEEDBACK phase with a parametric modulator representing feedback reward size. Regressors describing head motion (24 total) and eye movements (4 total) were included as regressors of no interest. We further used a "motion scrubbing" procedure to reduce the influence of head motion on results (Power et al. 2012; details in Supplementary Data 2).

Statistical Evaluation of fMRI Parameter Estimates

For voxel-level family-wise error (FWE) correction in fMRI group level analysis, we applied NonParametric Permutation Tests provided by the SnPM toolbox (http://warwick.ac.uk/snpm) to reduce false-positive rate associated with parametric statistics in SPM12 (Eklund et al. 2016). The number of the permutations was 10 000. We also applied Small Volume Correction (SVC) to identify effects of physiological arousal (amygdala and dACC), incentive magnitude (caudate nucleus, nucleus accumbens, and putamen), and their interaction (prefrontal cortex) in hypothesized brain regions. Detail of definitions for the SVC is shown in Supplementary Data 3.

For visualization of the absolute difference of each condition (success or failure) from baseline, estimated parameters for the pupil regressor in right amygdala (Fig. 3*B*) and the reward regressor in left caudate nucleus (Fig. 4*B*) were extracted based on the AAL template with MarsBaR (http://marsbar.sourceforge.net/). For the direct comparison of the parameter estimates between success and failure trials within the right IFG (Fig. 4*D*), which was identified by the interaction of pupil amplitude and reward across all trials (i.e., orthogonal to the success versus failure comparison), a 4 mm radius sphere was drawn around the peak and parameter estimates were entered into a paired t test between success and failure trials.

Group Level Correlation Analysis

Individual mean task performance was calculated by averaging the timing performance score of all trials with the same exclusion criteria as in the behavioral analysis. Mean beta values in each region were extracted from a 4 mm radius sphere drawn around individual activation peaks for the pupil amplitude regressor (failure versus success trials) in the right amygdala, bilateral dACC, the reward regressor (failure versus success trials) in the left caudate nucleus, and the interaction regressor (failure and success trials) in the right IFG.

Psychophysiological Interaction Analysis

As explained in the introduction, the incentive-correlated pupil representation on failure trials could be potentially explained by excessive interaction between amygdala and striatum. In another words, we hypothesized that the amygdala activity is

facilitating incentive representation in striatum, and this modulation should be stronger in failure than success trials. This hypothesis was tested with psychophysiological interaction (PPI) analysis. For the physiological factor, right amygdala seed regions for each participant were defined by a 4 mm radius sphere around the pupil amplitude parametric contrast individual peak voxel, which was masked by the AAL amygdala template. For each participant the principal eigenvariate was extracted, adjusted for all contrasts at cue timing. For the psychological factor, trial-wise parametric reward magnitude was used to test whether neural incentive representation was selectively modulated by the seed activation. Therefore, a brain region identified by this analysis represents the interaction of amygdala and reward modulation. We tested whether these interaction parameter estimates were different between success and failure trials (Amygdala × Reward [Failure > Success]).

Results

Reward Magnitude Modulated Subjective Motivation but not Performance

To evaluate effects of monetary reward magnitude, participants provided subjective ratings of motivation, arousal, pressure, and difficulty for trials of different reward magnitude levels immediately after fMRI scanning. All measures of subjective experience were influenced by higher levels of reward magnitude (Fig. 2A: Motivation: $F[4,84] = 42.596$, $P < 0.001$, Arousal: $F[4,84] = 62.499$, $P < 0.001$, Pressure: $F[4,84] = 50.666$, $P < 0.001$, Difficulty: $F[4,84] = 6.367$, $P < 0.001$). Next, we investigated whether displayed reward magnitude impaired or improved performance (linear effect: Lazear 2000) or whether the direction of the effect differed at high magnitudes (i.e., a "choking" curvilinear effect: Ariely et al. 2009; Chib et al. 2012; Lee and Grafton 2015). "Timing performance score" was calculated based on the absolute temporal distance from 5 s on each trial and regressions were conducted at the level of trial-wise data for each participant to examine effects of reward magnitude on performance (Fig. 2B). Reward magnitude was not related to timing performance linearly (Beta mean ± SEM = 0.039 ± 0.030, one sample $t[21] = 1.273$, $P = 0.217$) nor quadratically (0.035 ± 0.029, one sample $t[21] = 1.198$, $P = 0.244$). Also this magnitude could not explain performance even after accounting for subjective ratings of effort and fatigue change (linear: 0.039 ± 0.030, one sample $t[21] = 1.302$, $P = 0.207$, quadratic: 0.037 ± 0.030, one sample $t[21] = 1.229$, $P = 0.233$). Response time (RT) also was not explained by reward magnitude (Supplementary Data 4 and Fig. S2). These results show that although subjective motivation

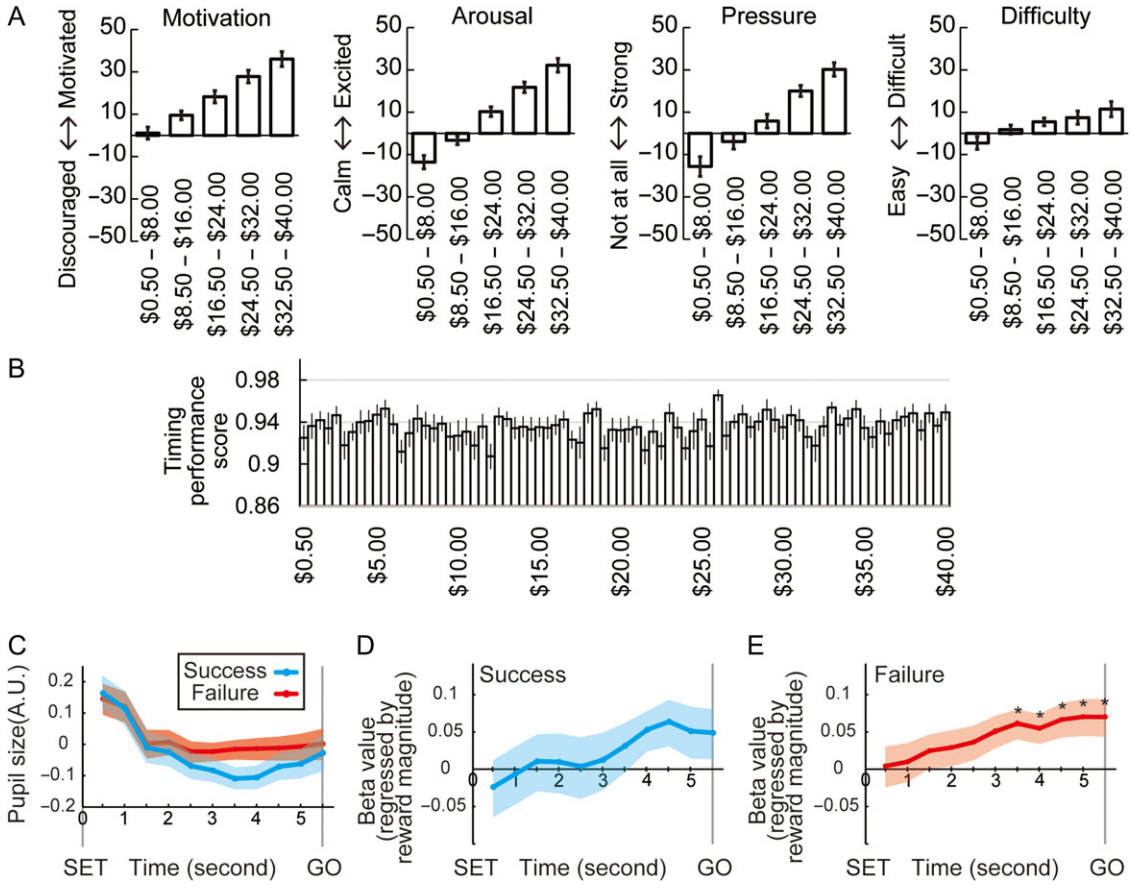

Figure 2. Relationship among reward magnitude, motivation, performance, and pupil dynamics. (*A*) Mean subjective ratings sorted by 5 levels of monetary magnitude. Immediately after the fMRI scan, participants ($n = 22$) answered questions about their motivation, arousal, pressure, and difficulty associated with the reward magnitude presented in the preparatory SET phase immediately after the fMRI scan. All 4 ratings increased as a function of reward magnitude. (*B*) Actual mean timing performance score during the fMRI scan by reward magnitude. Performance was not simply explained by linear nor quadratic function of reward magnitudes. (*C*) Averaged pupil dynamics of all participants. Points represent pupil size over successive 500 ms windows of the preparatory phase. The shaded areas show standard error of the mean (SEM). (*D* and *E*) Representation of reward magnitude in pupil size during the preparatory SET phase in success trials (*D*) and failure trials (*E*). *Reward representation from 3.5 to 5.5 s was greater than zero in failure trials ($P < 0.05$) FDR corrected.

increased with reward magnitude, actual timing performance score was not directly related to reward magnitude. Thereupon, we analyzed pupil dynamics to investigate whether reward magnitude influenced physiological arousal level in trials resulting in success or failure.

Effects of Reward Magnitude on Physiological Arousal Precede Performance Failure

The pupil data was initially preprocessed, averaged by 0.5 s windows, and sorted by success and failure trials to test relationships between reward magnitude and arousal over the duration of the preparatory phase on trials resulting in success or failure. The first test was a simple comparison of success versus failure during the preparatory phase, which did not yield a significant difference (Fig. 2C: main effect of success/failure: $F[1,21] = 1.162$, $P = 0.293$; interaction with time: $F[10\,210] = 1.163$, $P = 0.105$). Although pupil size itself did not differ between success and failure trials, we conjectured that one reason might be because participants fail when pupil size is overly influenced by reward magnitude. That is, people may fail if they are overly aroused by expected reward during task preparation. We examined this possibility with successive regression analyses at each time point with reward magnitude as a predictor of pupil size. These regressions were conducted separately for success and failure trials, then estimated beta coefficients were averaged across participants at each time window (Fig. 2D,E). We tested whether representation of reward magnitude increased over the preparatory phase. One sample t test at each time point with FDR correction showed that reward magnitude beta values were significantly positive toward the end of the preparatory SET phase for failure trials (Fig. 2E: from 3.5 to 5.5 s: $2.727 \leq t[21] \leq 3.017$, $P = 0.0278$; from 0.5 to 3.0 s: $0.167 \leq t[21] \leq 2.344$, $0.0531 \leq P \leq 0.8692$) However, the reward regression beta values in success trials from 0.5 to 5.5 s were not different from zero (= no correlation) (Fig. 2D: $-0.582 \leq t[21] \leq 2.059$, $0.335 \leq P \leq 0.906$). We also tested the beta values between success and failure trials, but there was no significant difference ($-0.841 \leq t[21] \leq -0.027$, $0.410 \leq P \leq 0.979$). We also conducted an additional behavioral experiment with different participants ($n = 24$) to evaluate the reproducibility of our observation (Supplementary Data 5 and Fig. S3). All results about potential reward, pupil dynamics and performance were reproduced.

Furthermore, we tested the effect of arousal level on time perception (Supplementary Data 6 and Fig. S4) as previous research has shown that higher arousal makes people estimate a unit of time as passing more quickly (Droit-Volet et al. 2004; Mella et al. 2011; Lake et al. 2016). Consistent with those reports, we found that pupil amplitude was larger when participants failed by pressing before 5 s ("TooEarly" trials) compared with when pressing after 5 s ("TooLate" trials) (Supplementary Fig. S4B). However, reward magnitude was not significantly related to pupil amplitude when failure trials were sorted separately into TooEarly and TooLate trials (Supplementary Fig. S4C). Thus, high arousal during preparation may be associated with accelerated time perception, but time perception did not impact the relation between reward magnitude and pupil amplitude.

Taken together, these observations with pupil dynamics in failure trials partially support the idea that excessive reward-driven arousal during preparation is associated with performance failure. However, we did not observe a clear difference between success and failure trials in the incentive representation in pupil amplitude. Next we investigated brain dynamics during the preparatory SET phase to characterize neural representations of arousal level and incentive magnitude as a function of success or failure trials.

Neural Representation of Mean Pupil Amplitude in Amygdala was Attenuated for Success Trials

We investigated BOLD signal correlated with physiological arousal and examined differences between success and failure trials during the preparatory SET phase. Here, we focused on mean value of trial-by-trial pupil amplitude in amygdala and dACC as previous literature supports the representation of physiological arousal in these regions (Delgado et al. 2006; Phelps and LeDoux 2005; Critchley 2005).

Consistent with our hypothesis, right amygdala (Fig. 3A,B) representation of arousal differed in the contrast of failure versus success trials (peak voxel: x = 22, y = 6, z = −16, t = 3.62, $P = 0.026$ FWE corrected). Exploratory whole brain analysis identified other regions including fusiform area, calcarine sulcus, posterior hippocampus, and cuneus by the same contrast (Supplementary Table S1: $t \geq 3.31$, $P < 0.001$ uncorrected) but these regions did not survive FWE correction in the whole brain ($ts \leq 4.27$, $P > 0.173$). Activity in the dACC, which was an a priori region of interest, did not survive correction. Instead, it was only identified showing differences between failure and success trials at a more liberal threshold ($P < 0.005$, uncorrected: Supplementary Data 7 and Fig. S5).

Finally, we compared arousal-related brain activity between TooEarly and TooLate trials in the right amygdala to examine a possible effect of time perception. No significant difference was observed between the 2 types of failure trials for representation of arousal in the amygdala (TooEarly; mean ± SD = −0.171 ± 0.354, TooLate; mean ± SD = −0.025 ± 0.345, paired $t[19] = -1.254$, $P = 0.225$).

Preparatory Amygdala Activity is Negatively Correlated With Timing Performance Score

We additionally examined whether individual differences in the right amygdala representation of arousal were related to individual differences in performance. Specifically, we tested whether better performance related to weaker neural (i.e., amygdala) representations of arousal. Right amygdala individual representations of arousal were measured as parameter estimates for the pupil amplitude regressor in the region identified by the contrast of failure versus success. Right amygdala arousal representation in success trials negatively correlated with individual timing performance scores (Fig. 3C: $r = -0.525$, $P = 0.012$), but the relationship was not significant in failure trials (Fig. 3D: $r = 0.022$, $P = 0.922$). These results suggest that participants performed better when amygdala activity during preparation to execute a behavior was negatively related to their arousal level.

Neural Representation of Incentive Value in the Caudate Nucleus was Attenuated in Success Trials

Next, we investigated BOLD signal related to reward magnitude during the preparatory phase and compared this incentive representation between success and failure trials. As the pupil changed correlated with reward magnitude only during trials resulting in failure, we predicted that the incentive representation in striatum would be increased in failure trials. Consistent with the prediction, the contrast of failure versus success trials

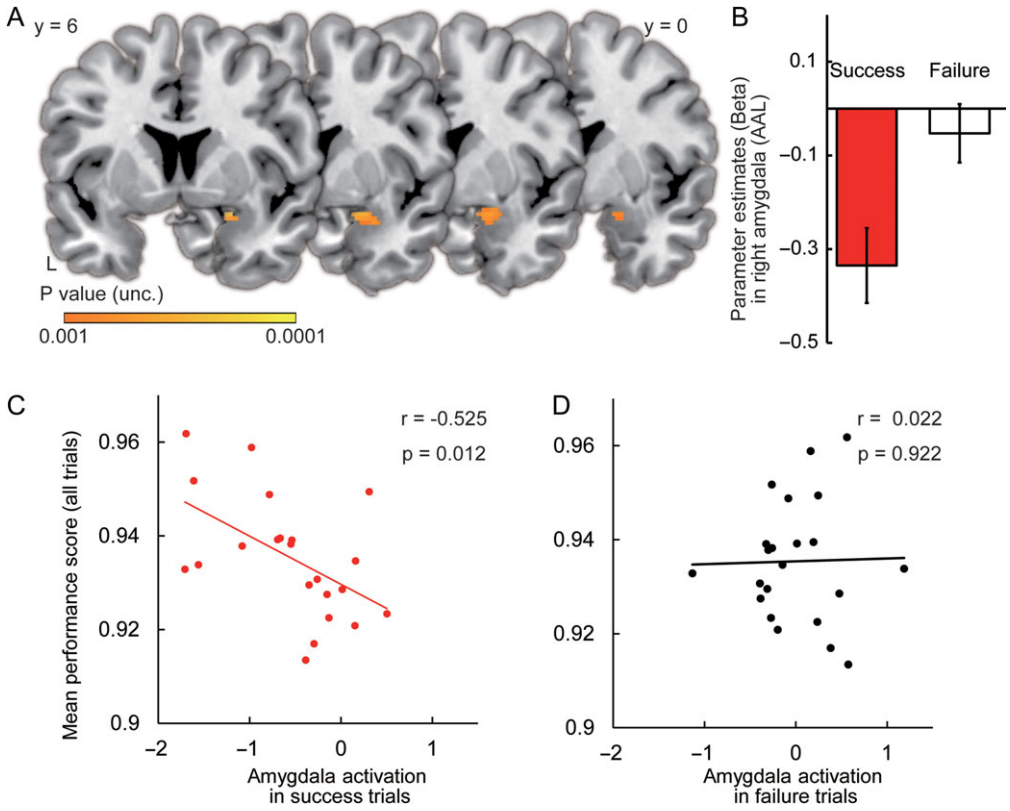

Figure 3. Brain activity correlated with pupil amplitude in failure compared with success trials, and correlation of individual amygdala activation and mean performance during SW task. (*A*) Physiological arousal representation showed greater activation in failure trials than success trials in right amygdala. Presented threshold is $P < 0.001$ uncorrected, cluster size ≥20 and masked by the anatomically defined amygdala and dACC (peak voxel is $t = 3.62$, $P = 0.026$ FWE corrected). (*B*) Parameter estimates of the mean pupil regressor extracted from anatomically defined right amygdala (for visualization only). (*C* and *D*) Individuals with negative representations of arousal in right amygdala showed better performance.

showed significantly greater parametric modulation by reward magnitude in the left caudate nucleus (Fig. 4*A*,*B*, peak voxel: $x = -6$, $y = 18$, $z = 0$, $t = 4.26$, $P = 0.031$ FWE corrected). We did not find any other significant voxels in the contrast of success versus failure trials with respect to incentive representation in whole-brain analysis (Supplementary Table S2). We also explored the representation of reward magnitude irrespective of performance, that is, across success and failure trials. Several clusters including middle frontal gyrus and anterior cingulate cortex showed positive representations of reward magnitude (Supplementary Table S2: $t \geq 3.65$, $P \leq 0.001$, uncorrected), but did not survive FWE correction. Parameter estimates in these regions were also not different for failure versus success trials (paired $t[21] \leq 1.587$, $P \geq 0.127$). Therefore, the caudate nucleus was the only region where incentive representation differed by performance, showing a more positive representation of reward magnitude during preparation on trials resulting in failure compared with success. We also investigated the relationship between individual timing performance score and brain activation in this left caudate nucleus. However, no correlation was observed in success ($r = 0.248$, $P = 0.267$), or in failure ($r = -0.021$, $P = 0.926$) trials.

Interaction of Mean Pupil Size and Reward Magnitude was Represented in Inferior Frontal Gyrus

We also tested the interaction term of the trial-wise pupil size regressor and trial-wise reward magnitude regressor during the preparatory SET phase, and compared this representation between success and failure trials. The purpose of this analysis was to investigate potential sites involved in computing the integration of arousal level and reward magnitude information to influence performance. Given the characteristic involvement of the prefrontal cortex in the integration of emotion and cognition (Ochsner and Gross 2008; Pessoa 2009; Salzman and Fusi 2010), we explored whether the interaction of arousal and reward magnitude information engaged prefrontal regions during trials that resulted in successful performance. One unique cluster in right inferior frontal gyrus (IFG) was identified across all trials (Fig. 4*C*, peak voxel: $x = 50$, $y = 40$, $z = 16$, $t = 5.27$, $P = 0.021$ FWE corrected, also see Supplementary Table S3). Further region of interest (ROI) analysis showed that the parameter estimates in IFG were greater in success trials than failure trials (Fig. 4*D*, paired $t[21] = 2.312$, $P = 0.031$). This result suggests that right IFG represented the interaction of arousal and incentive information in both success and failure trials but the contribution was greater in success trials. This stronger activation in success trials suggests a potential role of the IFG for controlling arousal to succeed, as well as integrating the arousal and reward information. However, this is tempered by the observation that the IFG activation did not relate to the mean timing performance score (success trials: $r = 0.066$, $P = 0.769$; failure trials: $r = 0.224$, $P = 0.316$).

Amygdala Modulates Incentive Value Representation in Striatum, but Decreased Modulation is Associated With Success

In this experiment, trials resulting in failure were marked by increased amygdala activity related to arousal and increased

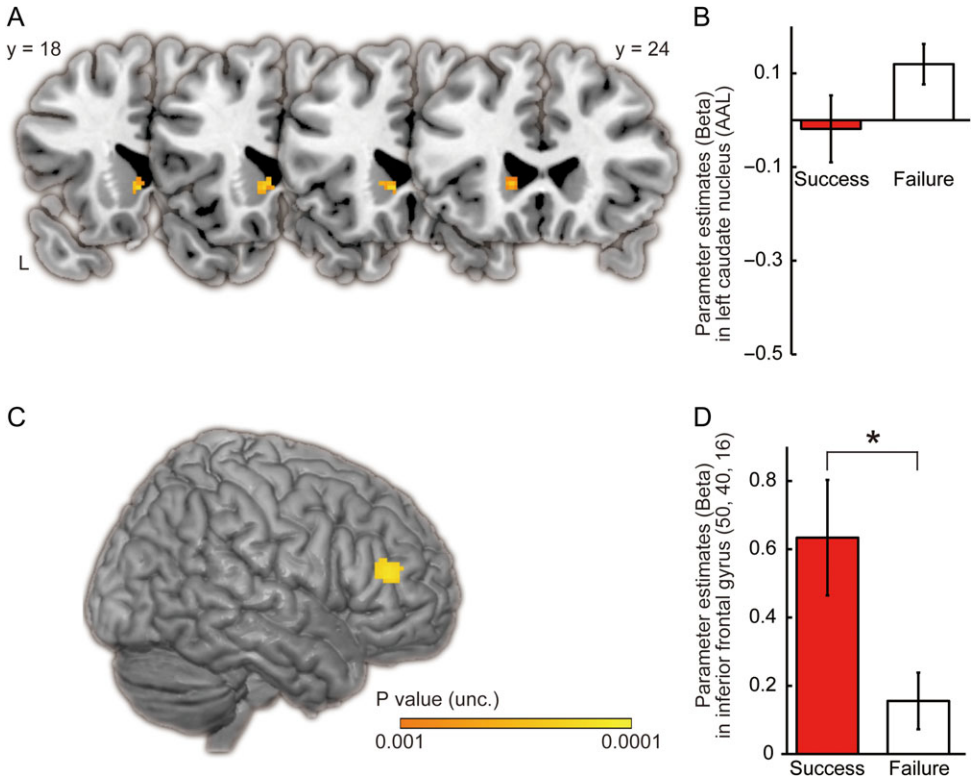

Figure 4. Brain activity correlations with reward magnitude in failure compared with success trials, and during the interaction of reward and pupil size. (*A*) Incentive representation in the left caudate nucleus was greater in failure trials than success trials. (*B*) Parameter estimates of the reward magnitude regressor extracted from anatomically defined left caudate nucleus (for visualization only). (*C*) Right IFG was positively correlated with the interaction of pupil amplitude and reward magnitude across success and failure trials. (*D*) Direct comparison of parameter estimates in success versus failure trials within the IFG (4 mm radius sphere from center coordinate) showed significantly higher value in success trials. *$P < 0.05$. Presented threshold in *A* and *C* is $P < 0.001$ uncorrected, cluster size ≥20 and masked by the anatomically defined bilateral caudate nucleus (peak voxel is $t = 4.26$, $P = 0.031$ FWE corrected), or prefrontal cortex respectively (peak voxel is $t = 5.27$, $P = 0.021$ FWE corrected).

caudate nucleus activity related to incentive representation. Previous studies have reported that interactions between amygdala and striatum can facilitate arousal and value-related representations to enhance learning and memory (McGaugh 2004; Delgado et al. 2009; Li et al. 2011; Watanabe et al. 2013). However, increased amygdala–striatal interaction can also be problematic for behavioral performance if it is due to increases in arousal (given excessive incentive representation). We reasoned that this interaction would be decreased in trials where performance was successful. We tested this hypothesis with a PPI analysis in which the seed region was the right amygdala and the psychological factor was the reward magnitude (Figs 1A and 5A). We identified a significant cluster in the contrast of failure versus success in the right caudate nucleus (Fig. 5B; peak voxel: $x = 16$, $y = 20$, $z = 6$, $t = 4.06$, $P = 0.042$ FWE corrected). This analysis highlights that amygdala–caudate incentive related interaction was relatively increased on failure trials compared with success trials. Other clusters and contrasts are shown in Supplementary Table S4. This analysis supported the hypothesis that the amygdala is an important region for the modulation of incentive representation in the striatum.

Discussion

How does reward-driven arousal influence our preparation for performance? That is, when the size of potential rewards influences our arousal level, does it affect our ability to effectively prepare for a task? The present study used simultaneous fMRI and pupil dilation data collection to investigate neural representations of physiological arousal and potential reward respectively, while preparing to perform a challenging task. During the preparation phase, when participants were presented with incentive information about the value of the upcoming trial, we observed that the amygdala representation of arousal and caudate representation of reward were decreased for trials that resulted in success compared with failure. Performance differences across participants were also explained by deactivation of the amygdala in success trials. Further, a PPI analysis revealed an increase in functional connectivity between amygdala and caudate nucleus as a function of reward magnitude during trials that resulted in failure compared with success. These results highlight how reward-driven arousal prior to the execution of a behavior can negatively impact performance via interactions between amygdala and striatum.

Neural Representations of Physiological Arousal and Potential Reward Relate to Subsequent Performance

The current results add a new layer to our understanding of how neural representations of arousal and incentives during preparation relate to subsequent behavioral performance. Arousal representation in the right amygdala increased relatively in failure compared with success trials. In fact, the amygdala was negatively related to arousal in success trials. Furthermore, the group level correlation analysis suggested that the negative relation between amygdala and arousal

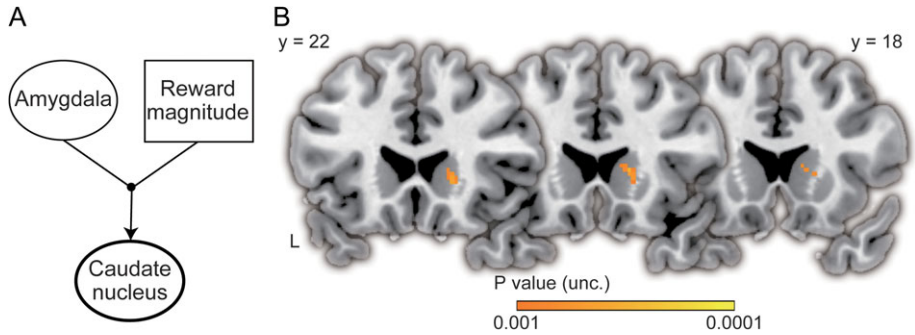

Figure 5. Model for psychophysiological interaction analyses identified brain activity in right caudate nucleus. (A) Schematic of the psychophysiological interaction between the amygdala and reward magnitude. Square box represents psychological modulators, the ellipse represents the physiological seed and bold ellipse is brain activation identified by the analyses. (B) Activity in the right caudate nucleus as identified by the psychophysiological interaction (failure versus success contrast, $P < 0.001$ uncorrected, cluster size ≥20 and masked by the anatomically defined bilateral caudate nucleus). Peak voxel is $t = 4.06$, $P = 0.042$ FWE corrected.

during success trials explained individual differences in task performance at the group level in addition to trial-wise performance. The inverse relation between amygdala and arousal suggests the existence of suppressive control over amygdala activation. Although further research is necessary, a recent study has reported that amygdala activation negatively correlated with pupil amplitude during fear conditioning (Leuchs et al. 2017). The current findings highlight how the relation between amygdala and arousal, particularly during preparation may be significant for understanding how people control arousal to effectively prepare to perform.

Previous literature has highlighted the relationship between pupil change and activity in dACC (Ebitz and Platt 2015; Critchley et al. 2005). In the current experiment, we observed activity in the dACC that was similar to the pattern to right amygdala, however, this cluster did not survive correction. One important difference in our study was the focus on neural activity during task preparation rather than execution.

Consistent with the association between physiological arousal and performance failure, representation of the potential reward in the left caudate nucleus was increased only in failure trials. Importantly, the caudate nucleus was a unique cluster in the contrast of failure versus success trials. Although we identified potential reward related positive activation also in ACC, anterior insula and other regions, these other clusters did not distinguish between success or failure trials.

The observation of relatively decreased caudate reward representation for success trials is interesting in the context of emotion regulation, where cognitive strategies have been used to dampen both the physiological response measured by SCR (Delgado et al. 2008) and neural responses in the caudate nucleus (Delgado et al. 2008; Staudinger et al. 2009; Martin and Delgado 2011) associated with expected value of a reward. Specifically, the current finding helps to explain how this suppression of an incentive representation in the caudate nucleus can contribute to actual performance. The current study provides a novel and important example of this system for better performance in a challenging task and emphasize the importance of regulation of value-related activation of the caudate nucleus during preparation for successful performance.

Amygdala–Caudate Connectivity During Preparation is Associated With Performance Failure

The findings show that communication between neural regions representing arousal and potential reward can be important to understand performance. We demonstrated that the interaction of preparatory amygdala activity and potential reward magnitude was represented in caudate nucleus more strongly in failure compared with success trials. This suggests that the amygdala plays a role in modulating incentive representation in the striatum (Friston et al. 1997), at least during preparation to perform a behavior. Although it is difficult to conclude the direction of causality by PPI (Horwitz et al. 2005; McIntosh 2010), direct anatomical projections are unidirectional from amygdala to striatum (Russchen et al. 1985; Fudge et al. 2002) and animal studies demonstrate the importance of amygdala influencing reward representation in the striatum (Namburi et al. 2015; Stuber et al. 2011).

A critical contribution of the current study is that it demonstrates amygdala–striatum connectivity is not always beneficial to performance. Previous human studies have reported that the amygdala–striatum functional interaction enhances learning and memory consolidation (Camara et al. 2008; Delgado et al. 2009; Li et al. 2011; Watanabe et al. 2013; McGaugh 2004). In contrast to these studies, the current study reported a negative aspect of amygdala–striatum interaction during preparation to perform a challenging task. Indeed, a possible key difference between the current study and prior ones is the period in which the activity is measured. Interestingly, this negative contribution of amygdala–striatum connectivity during task preparation can improve understanding of amygdala–striatum connectivity reported in pathological studies such as gamblers and heroin users (Liu et al. 2009; Peters et al. 2013). One possibility is that excessive interaction may relate to impulsive behavior driven by high sensitivity to incentives. However, complete elimination of modulation from amygdala to striatum may also deteriorate goal-directed behavior severely (Stuber et al. 2011). Therefore, the current findings highlight the importance of optimizing, that is, increasing or decreasing, the amygdala–striatum interaction depending on the performance context.

IFG Represents Interaction of Arousal and Incentive Information

We also investigated the interaction of physiological arousal and incentive value in the prefrontal cortex. Broadly, the prefrontal cortex plays an important role in executive control (Miller 2000; Miller and Cohen 2001), being involved in integrating and regulating emotional and cognitive information (Ochsner and Gross 2008; Pessoa 2009; Salzman and Fusi 2010). We identified one unique right IFG activation, roughly corresponding to

Brodmann area (BA) 45, across all trials associated with the interaction of arousal and reward magnitude. This activation suggests that the IFG was increased when both reward and arousal levels were high or both levels were low. BA45 as well as BA44 are thought to be involved in affective evaluation (Kohn et al. 2014), in particular being one of several prefrontal regions involved in emotion regulation (Buhle et al. 2014). Another explanation for this characteristic activation is that the IFG is not only evaluating affect but also regulating a network including amygdala and caudate to optimize the mental state (e.g., keep calm). In support of this idea, the activation in IFG showed stronger activation during success compared with failure trials, which suggests a potential role in suppressing physiological arousal to promote better performance. Indeed, some reports suggest that inhibition of right lateral PFC (ventrolateral PFC: Jay et al. 2014, or dorsolateral PFC: Berger et al. 2017) by repetitive transcranial magnetic stimulation increases physiological arousal measured by skin conductance response. Although there are differences in precise localization within the PFC, highlighting the need for multiple-region network analysis, these findings and the current IFG observation suggest a potential role of PFC regions in evaluating and regulating the sensitivity to arousal and incentive during preparation for a task.

Significance of Physiological Arousal During Task Preparation

Compared with previous studies of the relationship between performance and reward magnitude (e.g., performance under pressure) during task-execution (Mobbs et al. 2009; Chib et al. 2012; Lee and Grafton 2015), the current study focused on the relationship between performance and arousal level during task-preparation. This focus on preparation is important as the striatum contributes both reward expectancy (Schultz et al. 1992; Knutson et al. 2001) and motor execution (Graybiel et al. 1994; Groenewegen et al. 2003). The current findings demonstrated novel relationships among arousal, reward and performance. This study also differs from findings that pupil size represents error detection, for example, in a Stroop task (Critchley et al. 2005), because pupil represented potential reward during preparation (before a failed execution), suggesting a possible influence on performance rather than detection of performance errors.

A feature of this study was the dynamic measure of arousal during preparation using pupil size, which is widely used as a measurement of physiological emotional response, expectation of value, and other cognitive functions (Hess and Polt. 1960; Bradshaw 1967; O'Doherty et al. 2006; Bradley et al. 2008; O'Reilly et al. 2013; Preuschoff et al. 2011). The current findings showed that pupil amplitudes after the potential reward onset corresponded to reward magnitude in failure trials. Whereas in success trials, the potential reward did not significantly change the pupil size. This result can be interpreted as people tended to fail when the reward strongly impacted trial-wise subjective arousal level. On the other hand, although it is difficult to identify why there was no correlation in success trials, the reward might not have sufficiently impacted individual arousal, or top-down suppression system of reward-driven arousal may reduce the impact of reward stakes on success trials.

A second feature is that, in our behavioral task, we did not observe linear (Lazear 2000) or quadratic (Ariely et al. 2009; Chib et al. 2012; Lee and Grafton 2015) effects of reward magnitude on performance. The contrast between reward levels is one possible reason for differences from prior work. These previous experiments have high contrast in step-wise reward stakes (e.g., in Ariely et al. 2009, the incentive changed from the lowest level to 10 or 100 times the size). Our experiment used a gradual change of reward stakes ($0.50–$40.00 with $0.50 steps). This successive change is useful to detect trial-wise brain activation correlated with reward magnitude, but may dampen the impact of contrasts between levels of incentives.

Limitations

One limitation in this experiment is that the relationship of reward-driven physiological arousal to behavioral performance is not fully clear. Although, neural analyses revealed differences between success and failure trials, the direct comparison of representations of reward magnitude in pupil amplitude between success and failure trials did not significantly differ in any experiment. We found a significant increase of reward representation in preparatory pupil amplitude only in failure trials in the scanner and supplementary behavioral experiment (Supplementary Data 5). Therefore, reward-driven arousal is one of many factors influencing performance and was not sufficient to predict future success and failure. Future examination of the relation between reward, physiological arousal, and behavioral performance will be beneficial.

A second limitation is the interpretation of current observation of pupil change. Although we used pupil dynamics as a measurement of physiological arousal change, we could not exclude the possibility that pupil amplitude also represents different factors such as a preference to specific cues (Hess and Polt 1960; O'Doherty et al. 2006; Rieger and Savin-Williams 2012) and fatigue level (Hopstaken et al. 2015). Additionally, according to subjective ratings after the experiment, the potential reward magnitude also increased subjective motivation, pressure and difficulty as well as subjective arousal (Fig. 2A). However, it is also true that all these alternative interpretations strongly relate to arousal change. For example, when people see the preferred reward cue and it drives individual motivation to gain it, individual arousal must be increased at the same time. Therefore, our behavioral findings at least partially represent subjective arousal response to each potential reward stake.

In the current analyses, although we concluded that increased incentive representation in the caudate by amygdala modulation leads to performance failure, this conclusion does not exclude the effect of arousal on other cognitive factors, such as, evaluation of potential reward, top-down attention to detect cue timing and time counting, and impulse (motor) control for button-press. Especially the influence of arousal on time perception may have played a role in performance that could not be detected. In our SW task, participants were required to count in their head. Previous research has shown that higher arousal makes people estimate a unit of time as passing more quickly (Droit-Volet et al. 2004; Mella et al. 2011; Lake et al. 2016). We found that pupil-related arousal was associated with accelerated time perception in failure trials. However, we also found time perception did not significantly impact the relation between reward magnitude and pupil amplitude. Additional analyses focusing the time perception effect in fMRI data did not show any overlap with the activation we reported in main results (Supplementary Data 6). Therefore, there was no evidence in the current dataset that findings could be explained by altered time perception instead of physiological arousal.

Future Directions

In this study, we investigated the physiological and neural basis of the preparation mechanism for optimal task-execution. Our results demonstrated that physiological arousal differences during preparation relate to future performance and that an increased interaction between the amygdala and caudate leads to failure in performance. An important question derived from our current observations is how such interaction might be controlled to improve performance. The IFG is one candidate which we identified as representing the interaction of arousal and reward. Other regions that may be important for controlling amygdala–striatum interaction are ventromedial prefrontal cortex, orbitofrontal cortex, and anterior cingulate cortex, given direct anatomical connection with the subcortical regions (Aggleton et al. 1980; Carmichael and Price 1995; Ferry et al. 2000) and links to emotion regulation (Banks et al. 2007; Ochsner and Gross 2008), monitoring mental state (Salzman and Fusi 2010) and sustaining task control (Seeley et al. 2007, Neta et al. 2014, Gratton et al. 2018). Understanding how a potential brain network may interact during task preparation to control arousal can contribute to identifying and developing new targets to treat individuals who have difficulty managing high arousal, such as in social anxiety disorder (Etkin and Wager 2007). For example, pupil amplitude can be useful for biofeedback training for controlling arousal (Nagai et al. 2004), while amygdala–striatum synchronization has the potential to reduce reward-driven arousal by using neurofeedback training (Zhao et al. 2018 in BioRxiv).

Supplementary Material

Supplementary material is available at *Cerebral Cortex* online.

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Notes

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