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Hedonic Hotspots Regulate Cingulate-driven Adaptation to Cognitive Demands

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Positive hedonic states are known to attenuate the impact of demanding events on our body and brain, supporting adaptive behavior in response to changes in the environment. We used functional magnetic resonance imaging to examine the neural mechanism of this hedonic regulation. The effect of hedonic state (as induced by funny vs. neutral cartoons) on flexible behavioral and neural adaptation to cognitive demands was assessed in a flanker task in female volunteers. Behavioral results showed that humor reduced the compensatory adjustments to cognitive demands, as observed in sequential adaptations. This modulation was also reflected in midcingulate cortex (MCC; also known as the dorsal anterior cingulate cortex, ACC) activation. Furthermore, hedonic context increased activation in ventral striatum (VS) and ventral pallidum (VP). These hedonic hotspots attenuated the medial prefrontal cortex response to the cognitive demands in the ACC (also known as the rostral ACC). Activity in the ACC proved predictive of subsequent behavioral adaptation. Moreover, psychophysiological interaction analyses revealed that the MCC and the ACC were functionally connected with VS and VP, respectively. These observations reveal how MCC–VS and VP–ACC interactions are involved in the detection and hedonic modulation of behavioral adaptations to cognitive demands, which supports behavioral flexibility.

Keywords: anterior cingulate cortex, basal ganglia, cognitive control, conflict adaptation, humor

Introduction

Positive emotions do not only feel good, they also soften the impact of adverse events on physical and mental health (Garland et al. 2010). More specifically, positive affect has been shown to modulate the impact of processing demands on the evaluation of its costs (cf. Botvinick 2007): positive hedonic states attenuate the perceived difficulty of demanding tasks and also reduce compensatory effort mobilization and behavior to such demands (for reviews, see Gendolla 2000; Dreisbach and Fischer 2012b). For example, when faced with a cognitive demand induced by a conflict-inducing stimulus, people typically upregulate cognitive resources, an adaptation that induces perseveration, which is maladaptive in situations that require flexible switching (Notebaert and Verguts 2008). Positive hedonic states have been shown to counter-regulate such adaptation and thus foster behavioral flexibility (Dreisbach and Goschke 2004; Dreisbach and Fischer 2012b).

Recent studies have identified hedonic hotspots in subcortical brain areas that are likely to play an important role in such adaptive attenuation of demand-related neural signaling. In particular, it has been shown that the ventral striatum (VS) and ventral pallidum (VP) encode and generate the hedonic response to pleasant events (Kringelbach and Berridge 2009; Haber and Knutson 2010). These regions are likely to interact with rostral cingulate areas known to process cognitive demands along with their affective evaluation, in particular the anterior cingulate cortex (ACC; also known as the "rostral" ACC) and the midcingulate cortex (MCC; also known as the "dorsal" ACC) (Bush et al. 2000; Botvinick et al. 2001; Holroyd and Coles 2002; Ridderinkhof et al. 2004; Botvinick 2007; Shackman et al. 2011; van Steenbergen, Band, et al. 2012; Shenhav et al. 2013). The integrated coding of cognitive demands and hedonic processing might operate via well-known anatomical connections that loop between these rostral cingulate regions and the basal ganglia (cf. Heimer et al. 1982; Botvinick et al. 2009; Haber and Knutson 2010).

We hypothesized that the counter-regulatory effect of positive hedonic states on demand-driven behavioral adjustments is driven by increased activity in subcortical hedonic hotspots, which might result in the dampened rostral cingulate response to demands observed when individuals experience positive affect (Luu et al. 2000; Wiswede et al. 2009; van Wouwe et al. 2011). In the present study, we used functional magnetic resonance imaging (fMRI) to measure rostral cingulate cortex activity as induced by an arrow-flanker conflict task. This task typically induces compensatory behavioral adaptations that can be observed in trials that follow demanding (conflict) trials (Gratton et al. 1992). These adaptations likely reflect the compensatory increases in cognitive effort or control often observed in response to cognitive demands (Botvinick et al. 2001; Egner 2007; cf. Hillgruber 1912; Ach 1935; Dreisbach and Fischer 2011). According to the conflict monitoring theory (Botvinick et al. 2001), the rostral cingulate cortex plays a central role in signaling the need for additional effort when cognitive demands increase. Previous studies indeed have shown that rostral cingulate cortex might drive these behavioral adaptations (Botvinick et al. 1999; Kerns et al. 2004; Horga et al. 2011; Sheth et al. 2012; Shenhav et al. 2013).

To study the hedonic regulation of this adaptation, we presented the conflict task in a positive or neutral context induced by funny and neutral cartoons, respectively (see Fig. 1). In order to ensure that the cartoon induced a lasting hedonic response, participants were instructed to keep enjoying the content of the cartoon presented. Prior studies have revealed that the hedonic aspect of humor increases pleasure-related processing in the basal ganglia (Mobbs et al. 2003; Franklin and Adams 2011). Based on previous studies reporting reduced behavioral adaptation to conflict following positive-mood induction (van Steenbergen et al. 2010; Kuhbandner and Zehetleitner 2011; for a review, cf. Dreisbach and Fischer 2012b), we expected that more short-lived positive affect induced by funny cartoons should likewise counter conflict-driven

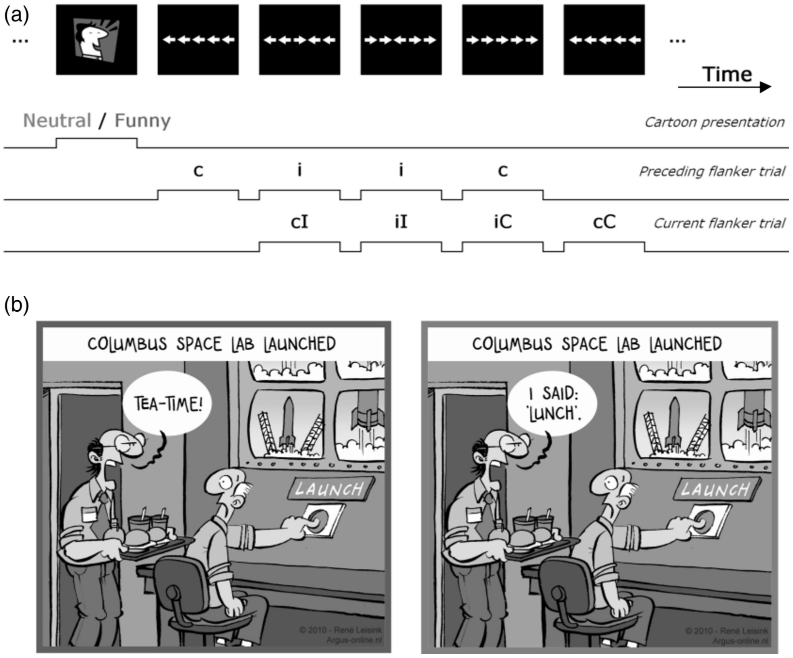

Figure 1. Experimental design. (*a*) Neutral and funny cartoons were presented in random order. Each cartoon was followed by a block of 5 randomly selected flanker trials being either compatible (C) or incompatible (I). Sequential behavioral analyses compared current compatibility (as indicated by upper-case letters C and I) as a function of the compatibility of the preceding trial (indicated by lower-case letters c and i). The neuroimaging analysis focused on the epochs related to the cartoons presentation (hedonic processing) and the preceding and current flanker trials (conflict processing). The brain–behavior analysis focused on whether neural activity during the preceding flanker trial is predictive of the behavioral adjustment observed in the current trial. (*b*) Example of a neutral (left) and funny (right) cartoon. Cartoons with funny cues omitted were presented as neutral cartoon (© 2010 René Leisink, reprinted with permission).

compensatory adjustments in behavior. This was confirmed by an independent behavioral pilot study (see Supplementary Material). In the current fMRI study, we investigated the role of the ventral basal ganglia and the rostral cingulate cortex in this hedonic regulation.

Materials and Methods

Participants

Twenty-two healthy right-handed volunteers (age 18–29 years) with normal or corrected-to-normal vision participated in the study. In order to optimize the detection of humor-related subcortical activation, we tested only females; earlier studies have shown stronger mesolimbic responses to funny cartoons in females than in males (Azim et al. 2005). The volunteers gave written informed consent for participation in the study, and they were paid for participation in this experiment. The experiment was approved by the medical ethics committee of the Leiden University Medical Center.

Stimuli

Thirty-two funny cartoons were selected from a set of ~130 cartoons, on the basis of funniness ratings and simplicity ratings (i.e., how easy the jokes were to comprehend) provided by participants matched to the age and background of the experimental participants. Adopting the same approach as earlier studies (Mobbs et al. 2003; Azim et al. 2005), a closely matched set of 32 neutral cartoons was created by omitting funny cues of humor cartoons through visual and/or textual changes (see Fig. 1*b*). Both gray-scaled sets were matched on visual clarity, geometrical complexity, and mean luminosity. All cartoons were presented once during the experiment.

Task and Procedure

Before entering the MRI scanner, participants were informed about the task to be performed. They were encouraged to enjoy the content of the funny cartoons even during subsequent flanker trials. In addition, they were instructed to avoid head movements. Written instructions emphasized fast and accurate responses to the direction of the central target arrow of the flanker task. Optical response-button boxes (positioned on the upper leg) recorded index finger responses of the left and right hand. Participants performed 2 practice mini-blocks with performance feedback before the experiment started. Experimental data were then acquired in 2 consecutive runs of 32 mini-blocks.

All trials were presented against a black background (1024 × 768 pix). Each mini-block started with a funny or neutral cartoons (500 × 500 pix; presented in a quasi-random order) for 6 s. Each cartoon was only presented once during the task. Following each cartoon, a fixation cross (jittered duration between 2 and 6 s) and a block of 5 flanker trials were presented. Each trial in the block showed the imperative flanker stimulus (a row of 5 black arrows pointing either left or right; 100 × 7 pix) for 1 s, followed by a fixation cross (jittered, 3–5 s). The fixation cross following the final flanker stimulus of each mini-block was presented one second longer (jittered, 4–6 s). All flanker task stimuli contained moving flankers (for details, see Supplementary Material).

The same number of compatible (flankers in same direction as the central target) and incompatible (flankers opposite to central target) trials were used. A quasi-random trial sequence was created which ensured that all possible sequential combinations occurred equally often (32 repetitions for each combination) during the experiment. Data were collected in 1 test session that included 2 consecutive runs, each lasting about 20 min. In a final functional scan, a motion localizer task was presented (see Supplementary Material). After the scan session, participants rated the funniness of each cartoon they had seen in the scanner (9-points scale). Participants were fully debriefed at the end of the experiment.

Behavioral Data Analysis

Inspection of the postexperimental ratings revealed that a few cartoons were given funniness ratings that did not match the intended funny/neutral category. Cartoons with such extreme outlier ratings (more than 3 interquartile ranges below/above the 25/75th percentile; on average 1.8 cartoons per participants), and its subsequent block of flanker trials were marked as rating outliers and were excluded from all analyses. On initial inspection of the behavioral flanker task data, 2 participants turned out to have made more than 5% response omissions. These participants were excluded from further analyses, resulting in 20 participants (0.8% response omissions on average) included for the behavioral and fMRI analysis.

Correct reaction time (RT) and error rate were analyzed with repeated-measures ANOVAs and paired *t*-tests. The 8 conditions were derived from the factorial combination of current-trial compatibility (Compatible vs. Incompatible; abbreviation: C vs. I), previous-trial compatibility (compatible vs. incompatible; abbreviation: c vs. i), and humor context (funny vs. neutral cartoon). Each of the 8 conditions was presented for 32 times. The first trial of each block, trials following errors, trials following cartoons with outlying ratings, and behavioral outlier trials (RT > 2 SD from the condition-specific means, calculated for each participant separately) were excluded from all analyses (11.5% excluded; on average 28.3 trials per condition remained to be included for subsequent analyses).

After extracting mean RT and error rate for each condition, overall scores, interference effects and conflict-adjustment effects were calculated separately for both humor contexts. We report these measures in order to facilitate interpretation, as has been done in earlier work (cf. van Steenbergen et al. 2010; Kuhbandner and Zehetleitner 2011). More conventional repeated-measures ANOVAs showing the same pattern of results are reported in the Supplementary Material.

We used subtractions to obtain the following effects. Interference effects were calculated by subtracting the mean performance on compatible trials from the mean performance on incompatible trials, that is, interference effect = ((cI + iI) − (cC + iC))/2; Following Nieuwenhuis et al. (2006), standard conflict-adjustment effects were calculated by subtracting the interference effect (I − C) following a correct incompatible (conflict) trial (i) from the interference effect following a correct compatible (no-conflict) trial (c), that is, conflict-adjustment effect = (cI − cC) − (iI − iC). All analyses are reported with two-sided *P*-values. In one case, we additionally report the one-sided *P*-value because the hypothesis of reduced adaptation following humor was directional, that is *conflict-adjustment following humor cartoon < conflict-adjustment following neutral cartoon*.

fMRI Data Acquisition

Scanning was performed with a standard whole-head coil on a 3-T Philips Achieva MRI system (Best, The Netherlands) in the Leiden University Medical Center. For both task runs, 532 T_2*-weighted whole-brain EPIs were acquired, including 2 dummy scans preceding each scan to allow for equilibration of T_1 saturation effects (TR = 2.2 s; TE = 30 ms, flip angle = 80°, 38 transverse slices, 2.75 × 2.75 × 2.75 mm +10% interslice gap). During the motion localizer task, 141 of these EPIs were acquired. Visual stimuli were projected onto a screen that was viewed through a mirror at the head end of the scanner. After the functional runs, a high-resolution EPI scan and a T_1-weighted anatomical scan were obtained for registration purposes (EPI scan: TR = 2.2 ms; TE = 30 ms, flip angle = 80°, 84 transverse slices, 1.964 × 1.964 × 2 mm; 3D T_1-weighted scan: TR = 9.717 ms; TE = 4.59 ms, flip angle = 8°, 140 slices, 0.875 × 0.875 × 1.2 mm, FOV = 224.000 × 168.000 × 177.333).

fMRI Data Analysis

Data analysis was carried out using FEAT (FMRI Expert Analysis Tool) Version 5.98, part of FSL (FMRIB's Software Library, www.fmrib.ox.ac.uk/fsl) (Smith et al. 2004). The following prestatistics processing was applied: motion correction, nonbrain removal, spatial smoothing using a Gaussian kernel of FWHM 8.0 mm, grand-mean intensity normalization of the entire 4D dataset by a single multiplicative factor, high-pass temporal filtering (Gaussian-weighted least-squares straight line fitting, with sigma = 100.0 s). Functional scans were registered to high-resolution EPI images, which were registered to T_1 images, which were registered to the standard space of the MNI (Montreal Neurological Institute) with 2 mm resolution using FLIRT.

In native space, the fMRI time series were analyzed using an event-related approach in the context of the general linear model with local autocorrelation correction. Models were high-pass-filtered (Gaussian-weighted least-squares straight-line fitting, with sigma = 100.0 s). All regressors used square-wave functions to represent stimulus duration and were convolved with a canonical HRF and its temporal derivative. After confirming that individual runs were registered correctly and did not indicate excessive motion, the relevant contrasts were combined across the 2 runs on a subject-by-subject basis using fixed-effects analyses. Second-level contrast images were submitted to third-level mixed-effects group analyses.

For whole-brain analyses, we report regions with a height threshold of $Z > 2.3$ and a cluster probability of $P < 0.05$, thereby correcting for whole-brain multiple comparisons [using Gaussian random field theory (GRFT)] (Worsley 2001). Given our a priori hypotheses about conflict-related rostral cingulate cortex activation triggered by incompatible flanker stimuli, analyses for these contrasts were constrained to a mask/small volume of interest defining this region (using the anterior division of the cingulate cortex as defined by the Harvard–Oxford structural atlas, 70%-likelihood threshold; volume = 803 voxels/6424 mm^3). For these analyses, we report regions with a height threshold of $Z > 2.3$ and a cluster probability of $P < 0.05$, using a correction for multiple comparisons (GRFT) across this volume of interest (Worsley et al. 1996). All figures showing contrasts used this cluster-corrected threshold. For visualization purposes, the contrasts were overlaid on a MNI template with 0.5-mm resolution.

When reporting analyses based on a functional ROI, individual mean *z*-scores were extracted with Featquery from second-level analyses.

Analytic Strategy

Different models were constructed in order to identify the *concurrent neural correlates* as well as the neural *antecedents* of the hedonic regulation of performance as measured in the conflict task. In order to do so, analyses focused on neural activity during the *current* flanker trial (focusing on concurrent brain activity which might mirror behavioral adaptation), the *preceding* flanker trial (focusing on antecedent brain activity which might have "caused" adaptation), and the *cartoon* preceding the block of flanker trials. See Figure 1*a* and note that separate models for activation related to current and previous trials were necessary because current versus previous flanker trials were not completely overlapping: The flanker task was presented in blocks of 5 consecutive trials, so the first trial versus the fifth trial of each block were not to be included for the current-trial versus the preceding-trial analysis, respectively. The different types of model we used are specified below.

Concurrent Neural Activity Reflecting Adaptation

Paralleling the behavioral (RT) analysis, a first model analyzed sequential adaptation in conflict-related rostral cingulate activation. These analyses focused on comparing iI and cI trials following neutral and funny cartoons. The model included all 8 possible combinations of current-trial compatibility (Compatible vs. Incompatible), previous-trial compatibility (compatible vs. incompatible), and humor context (trials following neutral cartoons vs. following funny cartoons) as separate regressors. Additional regressors included funny cartoon and neutral cartoon presentation, as well as events representing the first flanker trial of each block, errors, trials following errors, and outliers (i.e., exactly equivalent to the behavioral analysis). This model was used to visualize the adjustment effects for the neutral and humor context. A separate analysis modeled the interaction between humor context and previous conflict on current incompatible trials, that is, $[cI > iI]_{Neutral} > [cI > iI]_{Funny}$ (and all remaining events) as a regressor.

Neural Activity Before Adaptation

In order to reveal modulating neural effects of humor during the trials that preceded the adaptation observed in the subsequent trial, we ran a second model. These regressors were exactly the same trials as those included for the first model, except that we now modeled the associated brain activity at the time point that the preceding trial was presented. Given that the trial compatibility is not predictive of the subsequent trial presented, we pooled iC and iI resulting in a single regressor for incompatible trials (iX); we also pooled cC and cI trials resulting in a single regressor for compatible trials (cX). These events were modeled separately for both humor contexts. The moment of cartoon presentation was also modeled. In addition, separate confound regressors included the remaining events including the fifth flanker trial of each block, errors, trials before errors, and trials before outliers.

A variant of this model examined whether rostral cingulate activity during conflict trials predicts intra-individual sequential adjustments in the subsequent conflict trial. This model included all 8 possible combinations of current-trial compatibility (Compatible vs. Incompatible), *subsequent*-trial compatibility (compatible vs. incompatible), and humor context (neutral vs. funny cartoons). These events were added as two series of 8 regressors. The first series used standard fixed weights to account for invariant BOLD responses to stimulus presentation. The second series of regressors used a weighting vector. The amplitude of this vector was determined by condition-specific standardized RT values of the subsequent trial. This allowed us to reveal any conflict-related BOLD responses in the rostral cingulate that predicts subsequent adaptation in iI trials. All remaining events were modeled as confound regressors.

Functional Connectivity

Another variant of the model described above modeled interactions in functional connectivity between subcortical reward areas and rostral cingulate cortex during conflict trials, which might have driven the behavioral adaptation. Please note that psychophysiological interaction (PPI) analyses do not carry information about the direction of flow of information between brain regions, so anatomical evidence is needed to constrain directionality inferences. Two PPI analyses (Friston et al. 1997) were run separately for the two hedonic hotspots identified in the earlier analysis (see Results), that is the VS seed and the VP seed. Physiological regressors used the extracted time-course information, based on a sphere of radius 4 mm that fitted in the VS (center of sphere: 6, 20, −4) and VP (center of sphere: 14, −10, −8), and which included the peak-activation voxel in the respective region from the funny versus neutral cartoon contrast. The convolved psychological regressor represented the contrast *incompatible trials after funny cartoons* (iX_{Funny}) – *incompatible trials after neutral cartoons* ($\text{iX}_{\text{Neutral}}$). In order to partition out shared variance, an $\text{iX}_{\text{Funny}} + \text{iX}_{\text{Neutral}}$ regressor was also added. Compatible trials following funny and neutral cartoons were modeled separately. The PPI regressor was computed as the product of the demeaned physiological time course and the centered psychological regressor. Again, all remaining events were modeled as confound regressors. Note that PPI models implemented in FSL convolve the psychological regressor, rather than deconvolving the physiological regressor as usually done in SPM. Although similar PPI models have been applied in related studies (Harsay et al. 2011), it has been argued that the implementation of this PPI analysis might be biased toward areas with a similar shaped HRF (Gitelman et al. 2003). Because block designs are substantially less susceptible to this confound, we also considered modeling the psychological regressor as a block encompassing all consecutive trials following each cartoon. Note, however, that, by nature of this strategy, the design would be less sensitive to conflict-related fluctuations in BOLD response because half of the trials included in the blocks are compatible (no-conflict) trials. Nevertheless, the block-design PPI produced similar activations in MCC and ACC regions, although it needed a more lenient threshold (i.e., analysis were based on functional ROIs derived from the contrasts depicted in Figures 2*c* and 3*a*, respectively, data not shown).

Results

Behavioral Data

Data from 20 healthy female volunteers were analyzed (see Table 1 and Supplementary Material for more details). The flanker task produced standard interference effects in reaction time, both following funny, $t_{(19)} = 7.9$, $P < 0.001$, and following neutral cartoons, $t_{(19)} = 9.8$, $P < 0.001$, confirming that conflict trials were more demanding than no-conflict trials. Neither the interference effect nor the overall RT was modulated by humor context, $t_{(19)} = 1.6$, $P = 0.123$ and $t_{(19)} = 1.7$, $P = 0.114$, showing that humor did not induce reliable differences in base-levels of control/distractedness or response speed.

In order to test the hypothesized reduction of *adaptation* by humor, a planned comparison tested whether the behavioral

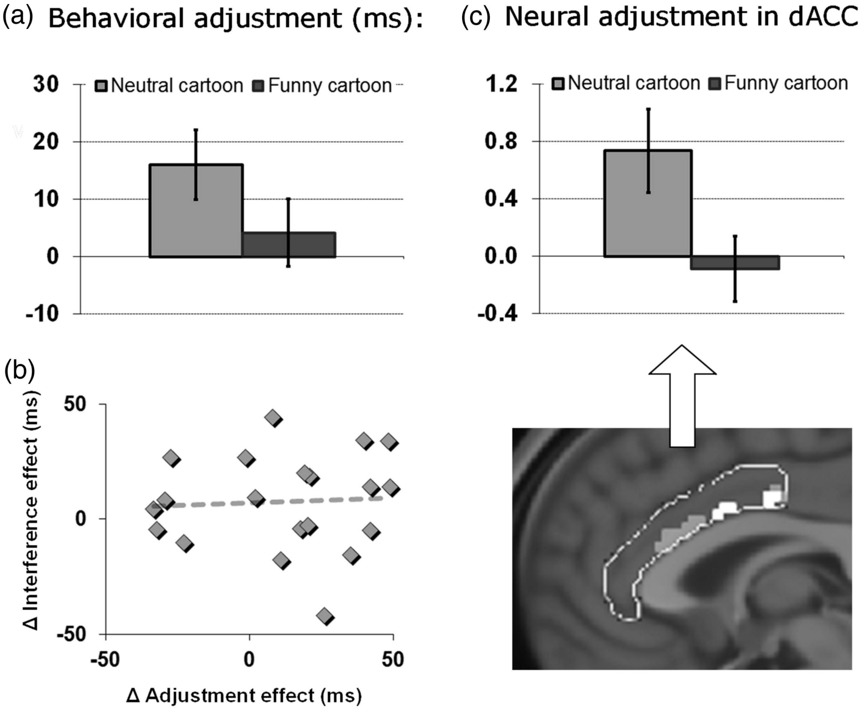

Figure 2. Effects of humor on behavior and brain in current flanker trials. (*a*) The behavioral conflict-adjustment effect in the flanker task was reduced in the context of a funny (vs. neutral) cartoon. See Table 1 for more details. (*b*) Individual effects of humor context ($\Delta =$ neutral minus funny) on the behavioral adjustment effect (*X*-axis) and the behavioral interference effect (*Y*-axis) were uncorrelated. (*c*) Gray: Neural sequential adaptation (for the contrast cI > iI) in the context of a neutral cartoon in MCC (peak voxel in MNI coordinates: 2, 22, 20; $z = 2.90$). White: Paralleling the reduced conflict-adjustment effect in behavior, neural sequential adaptation (for the contrast cI > iI) in current conflict processing was significantly reduced by funny (vs. neutral) cartoons in MCC cortex (peak voxels in MNI coordinates: 0, −8, 34; $z = 2.37$ and −2, 6, 30; $z = 2.41$). The bar graph shows the interaction extracted from this contrast. The figure only shows activation within the rostral cingulate cortex mask.

adaptation (as measured by the conflict-adjustment effect, see Materials and Methods) was reduced after funny in comparison to neutral cartoons. Indeed, as predicted, the positive hedonic context reduced behavioral adjustments to conflict, $t_{(19)} = 1.9$, $P = 0.07$, $P_{1-\text{sided}} = 0.038$ (see Fig. 2*a*). Follow-up tests showed standard compensatory behavioral adaptation after neutral cartoons, $t_{(19)} = 2.6$, $P = 0.016$, but not after funny cartoons, $t_{(19)} = 0.71$, $P = 0.487$. Note that the findings reported here showed a behavioral pattern that is similar to results from an independent behavioral experiment that was carried out earlier as a pilot study (see Supplementary Material).

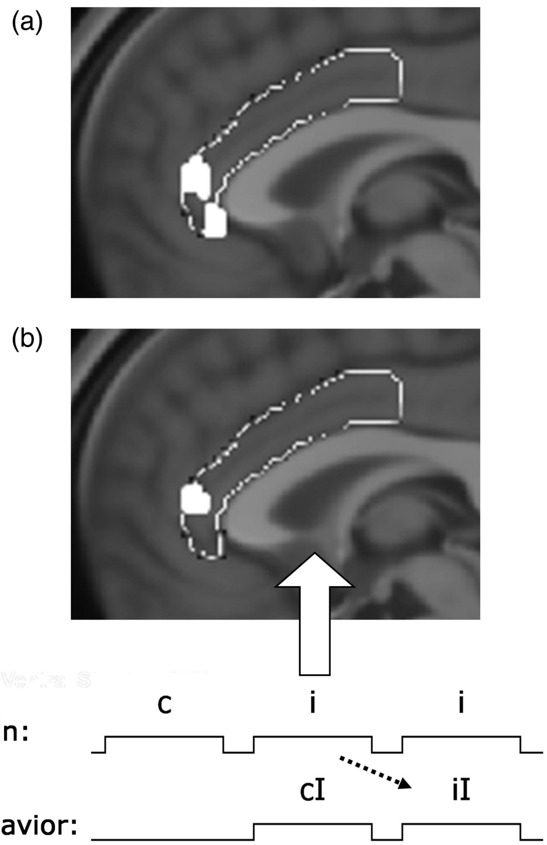

Figure 3. Effects of humor on neural activity in preceding flanker trials. (*a*) Attenuated conflict processing by hedonic context: deactivation in ACC (peak voxel in MNI coordinates: 2, 42, 12; $z = 2.94$) for preceding conflict (iX) trials presented in the context of funny (vs. neutral) cartoons. The figure only shows activation within the rostral cingulate cortex mask. (*b*) The brain–behavior analyses focused on brain activity that was predictive of subsequent performance adaptation in 2 consecutive conflict (iI) trials in the hedonically neutral context. Activity in ACC (peak voxel in MNI coordinates: −4, 40, 10; $z = 2.73$) was observed to predict behavioral speeding (RT) for subsequent iI flanker trials in the neutral context. The figure only shows activation within the rostral cingulate cortex mask.

In line with recent studies suggesting independent modulatory effects on conflict-driven adjustments versus base levels of cognitive control (van Steenbergen et al. 2010; Kuhbandner and Zehetleitner 2011), humor context effects on the interference effect and the adjustment effect were uncorrelated ($r = 0.06$, $P = 0.81$; Fig. 2*b*). There were no modulating effects of humor on error rate, indicating that the effects observed in reaction time could not be attributed to a speed-accuracy tradeoff. Postexperimental cartoon ratings (9-points scale) outside the scanner confirmed that humor cartoons were funnier than their neutral counterparts ($M = 6.1$ vs. $M = 2.3$, $t_{(19)} = 13.0$, $P < 0.001$). Note that the conflict-adjustment effect in the neutral condition showed the standard sequential effects in reaction times, consistent with the hypothesis that a preceding conflict trial evokes compensatory increases in cognitive effort or control, affecting subsequent performance (Botvinick et al. 2001; Egner 2007). Specifically, incompatible trials preceded by incompatible trials (iI) were faster than incompatible trials preceded by compatible trials (cI), effect = 11 ms, $t_{(19)} = 2.2$, $P = 0.041$ (see Table 1). Additionally, compatible trials preceded by incompatible trials (iC) were numerically, but not significantly, slower than compatible trials preceded by compatible trials (cC), effect = 5 ms, $t_{(19)} = 1.3$, $P = 0.215$.

Because it is somewhat controversial to what extent the conflict-adjustment effect reflects conflict-driven control processes (Botvinick et al. 2001), feature binding processes (Mayr et al. 2003; Hommel et al. 2004), or a combination of both (Verguts and Notebaert 2009), some authors have recommended excluding stimulus repetitions from the analyses (Mayr et al. 2003). In order to test whether excluding these trials would significantly impact the modulatory effect of humor context on the conflict adjustment, we compared the result of the analyses including and excluding stimulus repetitions. We did not observe an influence of type of analysis on the effect humor context on conflict-adjustment in RT, $P = 0.915$. Moreover, a more powerful analysis that combined the pilot and scanner data showed that the modulatory effect of humor context on conflict adjustment was present in the analysis that excluded stimulus repetitions ($P = 0.021$, for details, see the Supplementary Material). Thus, there is no evidence that lower order priming significantly contributed to the modulatory effect of humor we report here (cf. Trübutschek and Egner 2012).

Table 1
Behavioral data

	Humor context							
	After neutral carton				After funny cartoon			
	RT (ms)		Error rate		RT (ms)		Error rate	
	Mean	SD	Mean (%)	SD (%)	Mean (%)	SD (%)	Mean (%)	SD (%)
cC	527	67	0.2	0.7	528	68	0.5	1.2
cI	576	72	2.2	3.5	563	75	2.9	3.8
iC	532	69	0.8	2.1	527	67	0.5	1.3
iI	565	65	1.3	2.1	558	66	1.2	1.7
Interference effect = ((cI + iI) − (cC + iC))/2	40	18	1.3	2.4	33	18	1.5	1.7
Conflict-adjustment effect = (cI − cC) − (iI − iC)	16	27	1.5	2.6	4	26	1.7	4.5

Note: The table reports mean response times (RTs), error rates, and the corresponding interference effects and conflict-adjustment effects. cC, compatible trials following compatible trials; cI, incompatible trials following compatible trials; iC, compatible trials following incompatible; iI, incompatible trials following incompatible trials.

Neuroimaging Data

The neuroimaging analysis aimed to investigate the neural correlates and antecedents of the hedonic regulation in behavior (see also Materials and Methods). In order to do so, we first identified regions in rostral cingulate cortex that mirrored the adaptation observed in behavior and thus carry information about the current changes in task demands produced by the adaptation. Second, we probed neural rostral cingulate cortex activity in the preceding trial, which might have caused the hedonic counter-regulation in the adaptation. This analysis allowed us to test the hypothesis that positive hedonic processing attenuates rostral cingulate cortex activity, resulting in reduced adaptation to be observed in the subsequent trial. In addition, brain-behavior correlations were used to test whether preceding rostral cingulate cortex activity predicts subsequent behavioral adaptation. Third, we investigated neural activity to the humor versus neutral cartoons which preceded the block of flanker trials. This analysis aimed to identify the subcortical hedonic hotspots involved in positive affect. Finally, PPI analyses were applied to investigate conflict-related functional connectivity between rostral cingulate cortex and the hedonic hotspots identified in the earlier analysis.

Concurrent Neural Activity Reflecting Adaptation

In keeping with conflict monitoring theory (Botvinick et al. 2001) and previous observations (e.g., Botvinick et al. 1999; Kerns et al. 2004), we predicted that behavioral adjustment to conflict on a given trial should concur with reduced conflict registered in rostral cingulate cortex on the subsequent trial. This sequential adaptation effect should not be observed following a funny cartoon, in which behavioral conflict adjustment was cancelled out. Confirming predictions, we found that MCC showed the typical reduction in activity for iI when compared with cI trials ($[\mathrm{cI} > \mathrm{iI}]_{\mathrm{Neutral}}$) following neutral cartoons, see gray cluster in Figure 2*c*, (Botvinick et al. 1999; Kerns et al. 2004), whereas no rostral cingulate cortex modulation was observed following funny cartoons. Explorative analyses outside the rostral cingulate cortex mask did not reveal activation indicative of top-down control (e.g., Kerns et al. 2004; Egner and Hirsch 2005) when looking for reversed activation (i.e., [iI > cI]).

Critically, an interaction between humor context and preceding trial on current conflict processing (i.e., $[\mathrm{cI} > \mathrm{iI}]_{\mathrm{Neutral}} > [\mathrm{cI} > \mathrm{iI}]_{\mathrm{Funny}}$) was also evident in closely adjacent clusters in MCC (see white cluster and bar graphs in Fig. 2*c*). This analysis confirmed that pleasure eliminates not only the behavioral adjustment to conflict but also the detection of this adaptation in MCC. However, ROI analyses failed to detect a correlation with behavioral adaptation.

Neural Activity Before Adaptation: Preceding Conflict

To test the hypothesis that pleasure-driven reduction of conflict adaptation is mediated by an attenuated rostral cingulate cortex response to previously encountered conflict, we compared rostral cingulate cortex activity elicited by preceding conflict trials (see Fig. 1*a*) in the neutral and humor context ($\mathrm{iX}_{\mathrm{Neutral}} > \mathrm{iX}_{\mathrm{Humor}}$). Pleasure-related deactivation to conflict was observed in the anterior part of the cingulate cortex (ACC; Fig. 3*a*). In order to rule out the explanation that this deactivation simply reflects a general reduction in conflict processing (due to the slight reduction observed in the RT interference effect after humor, see Table 1 and Fig. 1*b*), we reran the analysis and regressed out the individual effects of humor on the interference effect. This adjusted model revealed a similar cluster of activation in ACC.

We used intraindividual brain–behavior correlations to test whether cingulate cortex activity is correlated with subsequent behavioral adjustments—a necessary (although not sufficient) condition to show that the rostral cingulate cortex plays a causal role in adjusting behavior. Since behavioral adaptation measured in the current trial is thought to be contingent on conflict registration by rostral cingulate cortex on the previous trial (cf. Botvinick et al. 1999; Horga et al. 2011; Kerns et al. 2004), the observed cingulate cortex activity might be predictive of subsequent behavioral adjustments in the neutral context. Thus, we used intraindividual fluctuations in behavior adaptation in RT during iI trials as a regressor to model predictive brain activity originating from the preceding conflict trial (see Fig. 3*b*). We found that conflict-related BOLD response increases in ACC were a successful predictor of subsequent speeded behavioral adaptations following neutral cartoons only (Fig. 3*b*). In order to be sensitive to possible effects in MCC, the same analysis was repeated while restraining it to a functional ROI that was derived from the previous contrast showing the interaction between humor context and preceding trial on current conflict processing in MCC (i.e., the contrast $[\mathrm{cI} > \mathrm{iI}]_{\mathrm{Neutral}} > [\mathrm{cI} > \mathrm{iI}]_{\mathrm{Funny}}$). No predictive brain activation was observed for this MCC ROI ($|t|s < 0.5$).

Neural Activity Before Adaptation: Effect of Hedonic Context

In order to determine a possible neural origin of the conflict-related rostral cingulate cortex attenuation by hedonic context, we further compared brain activation elicited by the cartoons, which preceded the flanker trials. Previous neuroimaging studies have found that humor increases pleasure-related processing in the basal ganglia (Mobbs et al. 2003, 2005; Azim et al. 2005; Franklin and Adams 2011), whereas the initial cognitive processes related to the reintegration of the unexpected information introduced by the joke (Suls 1972) instead recruit cortical areas (Mobbs et al. 2003; Franklin and Adams 2011). In line with these findings, funny cartoons recruited a large network of brain areas involved in the representation of language, semantic, and motor aspects of humor (see Supplementary Table 2). More importantly, the analysis also revealed the involvement of an affective network, that not only includes the amygdala, midbrain, insula, and medial prefrontal cortex, but that also encompasses the mesolimbic circuitry involved in positive hedonic processing. Confirming our hypothesis, funny cartoons elicited more activation than neutral cartoons both in VS and in VP, as shown in Figure 4*a*. Although early stimulation studies identified other regions, such as the hypothalamus, as possible generators of “pleasure” (e.g., Heath 1972), more recent accounts suggest that only the VS and VP can cause proper hedonic “liking” reactions (Kringelbach and Berridge 2009; Smith et al. 2010). Consequently, the seeds of the subsequent functional connectivity analysis were constrained to these regions.

Functional Connectivity

To investigate how activity in VS and VP might be related to changes in connectivity with rostral cingulate cortex-related conflict processing, we carried out a PPI analysis. PPI provides a measure of condition-specific functional connectivity between 2 brain regions (Friston et al. 1997). This approach

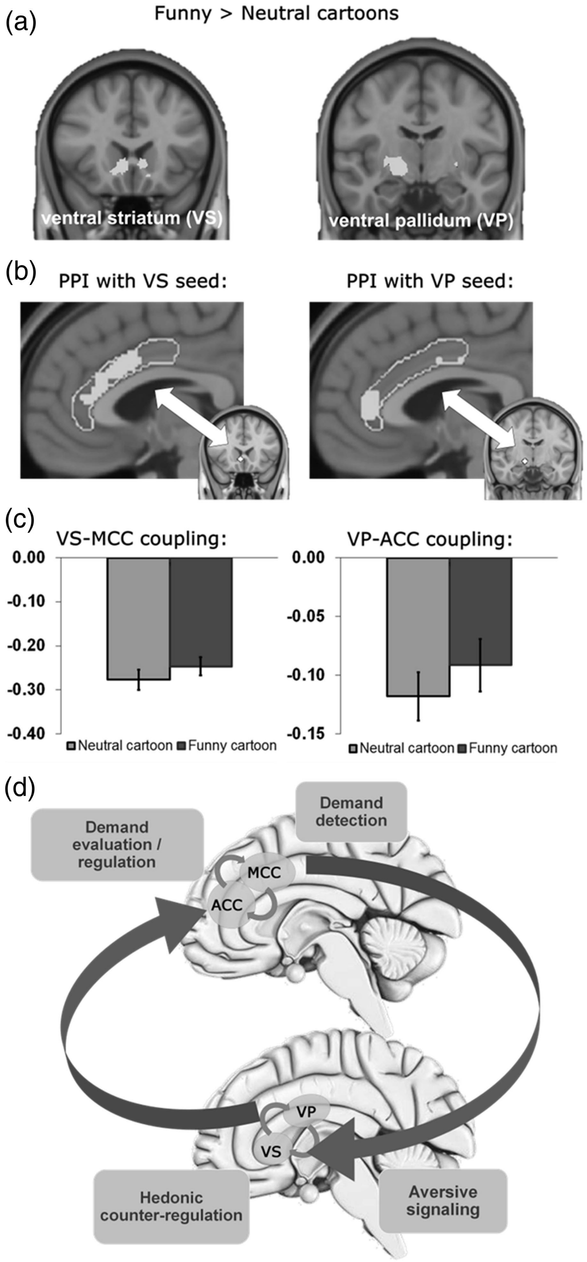

Figure 4. Effects of humor on neural interactions. (*a*) In comparison to neutral cartoons, funny cartoons increased neural activation in the ventral striatum (left; peak voxel in MNI coordinates: 4, 20, −6; $z = 3.66$) and right posterior ventral pallidum (right, peak voxel in MNI coordinates: 14, −10, −8; $z = 3.68$). Images are in radiological convention (left hemisphere to viewer's right) and only show activation within the accumbens and pallidum masks (using the Harvard–Oxford atlas). Activations in other regions for the contrast Funny > Neutral are reported in Supplementary Table 2. (*b*) Results from the PPI analyses that focused on a pleasure-driven attenuated anti-correlation between regions within the ventral basal ganglia and rostral cingulate cortex. PPI analyses were based on seed regions in the VS and VP using a sphere of radius 4 mm (centered at 6, 20, −4 and 14, −10, −8) that fitted in the respective area and included the peak-activation voxel found in the contrast depicted in (*a*). Dorsal rostral cingulate cortex (peak voxel in MNI coordinates: 4, 22, 26; $z = 2.92$) was observed to be functionally connected with the ventral striatum, whereas ACC (peak voxel in MNI coordinates: 0, 40, 8; $z = 2.85$) was found to be functionally connected with the ventral pallidum (right). Figures only show activation within the rostral cingulate cortex mask. (*c*) Hedonic context reduced the anti-correlated interactions between VS and MCC (left) and between VP and ACC (right). (*d*) Summary depicting the observed interactions between basal ganglia and rostral cingulate cortex that support hedonic counter-regulation. Labels indicate the proposed function of the respective areas (see Discussion).

allowed us to test whether there is a negative coupling (i.e., anticorrelation) between regions within the ventral basal ganglia and rostral cingulate cortex during conflict processing (Holroyd and Coles 2002; Münte et al. 2008) that is attenuated in the context of funny cartoons. A PPI analysis that used VS as a seed region revealed connectivity with a dorsal portion of the cingulate cortex that is the MCC (Fig. 4*b*; left). This cluster overlaps the region we identified as being involved in the monitoring of conflict-related adjustments in behavior (cf. Fig. 2*c*; see also Supplementary Fig. 1). Instead, a PPI analysis that used VP as a seed region revealed connectivity with a rostral portion of the cingulate cortex, that is the ACC (Fig. 4*b*; right) This cluster overlaps the conflict region we identified as being attenuated by the hedonic context and as being predictive of subsequent behavioral adjustments (cf. Fig. 3; see also Supplementary Fig. 2). Additional models that analyzed the functional connectivity separately for the funny and neutral context confirmed that both the BOLD activity in the VS–MCC network and the VP–ACC network were functionally anti-correlated, and that humor reduced their negative coupling (see Fig. 4*c*).

Discussion

Replicating previous behavioral findings of hedonic regulation (van Steenbergen et al. 2010; Kuhbandner and Zehetleitner 2011), we observed that positive affect induced by humor reduces compensatory adjustments in a conflict task. The present study reveals for the first time the neural underpinnings of this effect. It was shown that hedonic context activated VS and VP, regions in the basal ganglia well known for their role in pleasure causation. Those regions interacted with rostral cingulate cortex activity during the flanker task.

In the last decade, considerable research effort has been directed to the role of the rostral cingulate cortex and the basal ganglia in value-based decision making and cognitive control (Holroyd and Coles 2002; Frank 2005; Botvinick 2007; Rangel et al. 2008; Haber and Knutson 2010; Shackman et al. 2011). Extending these lines of research, the present findings show that reciprocal loops connecting the prefrontal cortex with the basal ganglia are also central to the hedonic regulation of compensatory behavioral adjustments to conflict (Dreisbach and Fischer 2012b). In line with earlier findings (Mobbs et al. 2003, 2005; Azim et al. 2005; Franklin and Adams 2011), humor was shown to activate regions implied in affective and hedonic processing, such as the amygdala, midbrain, insula, and medial prefrontal cortex. More importantly, humor was also shown to activate VS and VP. Recent studies have indicated that these regions lie at the heart of a hedonic network that generates the experience of pleasure and happiness (Kringelbach and Berridge 2009; Smith et al. 2010).

The PPI analyses provide the first evidence that these hedonic hotspots interact with demand-related processing in rostral cingulate cortex. Given anatomical evidence (Heimer et al. 1982; Haber and Knutson 2010), it is most likely that VS receives signals from MCC whereas VP feeds information back to rostral cingulate cortex via the thalamus. By activating the ventral basal ganglia, hedonic states attenuated the negative (anticorrelated) functional coupling of this loop, which presumably produced the reduced conflict-driven adjustments observed in behavior. Based on these different patterns of connectivity, we propose that MCC and ACC are both important for the detection and regulation of demands, but that they play distinctive roles. See also the summary in Figure 4*d*.

MCC and Interactions with VS

In line with earlier theories, our findings show that MCC is most likely involved in the detection of behavioral demands. The observation of sequential adjustments in MCC that co-vary with the behavioral adaptations to conflict replicate previous studies showing similar effects (Botvinick et al. 1999; Kerns et al. 2004). According to the conflict monitoring theory, compensatory adjustments in cognitive effort are triggered by such signals from MCC (Botvinick et al. 2001). Consistent with this account, a recent study has indeed shown that behavioral adjustments diminish following a MCC lesion (Sheth et al. 2012; but see also Fellows and Farah 2005).

It is likely that projections from MCC to other brain regions support its regulatory function (Shenhav et al. 2013). For example, given recent evidence that the aversive quality of cognitive demands might drive behavioral adjustment (van Steenbergen et al. 2009; van Steenbergen, Band, et al. 2012; Dreisbach and Fischer 2012b; see also Kool et al. 2010; Schouppe et al. 2012, 2013; Lindström et al. 2013; Riesel et al. 2013; van Steenbergen and Band 2013), it is likely that activity from MCC acts as a general aversive (Botvinick 2007; Dreisbach and Fischer 2012a; Shenhav et al. 2013) or error signal (Alexander and Brown 2011; Proulx et al. 2012) that inhibits positive hedonic processing in VS (Leknes and Tracey 2008). The observed anticorrelation between MCC and VS supports this conjecture. Convergent evidence for the integration of MCC and VS signals has been provided by studies investigating action monitoring (Münte et al. 2008; Cohen et al. 2009) and effort-based cost–benefit valuation (Botvinick et al. 2009; Croxson et al. 2009).

It is likely that dopamine signaling in the midbrain supports frontostriatal interactions (Holroyd and Coles 2002; Frank 2005; Aarts et al. 2012). MCC provides feedback signals that may be conveyed down to the midbrain, resulting in inhibited dopamine neurons (Frank 2005), which subsequently could modulate activity in VS (Jocham and Ullsperger 2009). Pharmacological manipulations targeting the dopamine system indeed have been shown to change conflict-related rostral cingulate cortex activation (Jocham and Ullsperger 2009), although the effect on behavioral adjustments needs further research (Chiew and Braver 2011b; Aarts et al. 2012). Future studies might use high-resolution imaging techniques to uncover the role of these brainstem nuclei (D'Ardenne et al. 2008).

ACC and Interactions with VP

The analyses focusing on preceding neural activity provide several clues for possibly different roles of MCC and ACC. Unlike MCC, conflict-related ACC activity was both predictive of subsequent behavioral adaptation (cf. Horga et al. 2011) and it was attenuated by the positive hedonic context. This suggests that ACC plays an important role in regulating the adaptation to demands, perhaps informed by signals that originate from MCC. Those signals might convey through the BG, where they become integrated with and modulated by hedonic state information. In line with such an explanation, other studies have suggested that ACC supports conflict resolution in the context of affective conflict or aversive conflict tasks (Etkin et al. 2006; Egner et al. 2008; Kanske and Kotz 2011a, 2011b).

Alternatively, it is also possible that ACC codes the negative evaluation of demand-related signals in the environment as well as the subjective need to allocate more effort (cf. Gendolla 2000). Such signals are likely to be dampened by positive affect whereas negative affect amplifies them (cf. van Steenbergen, Booij, et al. 2012). Dampened conflict-driven rostral cingulate cortex responses and performance adjustments to errors have not only been shown in studies that induced positive affect (Luu et al. 2000; Wiswede et al. 2009; van Wouwe et al. 2011). Substances with anxiolytic effects such as benzodiazepines (e.g., de Bruijn et al. 2004) and alcohol (Ridderinkhof et al. 2002; Bartholow et al. 2012) have similar effects, likely because they reduce negative affect (Bartholow et al. 2012).

Affective signaling from the ACC might be used by other brain regions to recruit additional resources at a later moment in time. However, recent evidence suggests that compensatory adjustments in control can occur very rapidly, i.e., within the same trial (Scherbaum et al. 2011). This makes it difficult to dissociate neural time courses of conflict/cost processing versus control adjustments. In order to further understand the temporal dynamics of these interactions, future studies thus need to use imaging techniques with higher temporal resolution. In any case, ACC possibly plays a causal role in behavioral adaptation since lesioning this region has been shown to eliminate behavioral adjustments, at least in some tasks (di Pellegrino et al. 2007; Maier and di Pellegrino 2012; but see also Fellows and Farah 2005). However, further research is warranted because many fMRI studies focusing on behavioral adaptation without an affective context have not reported ACC activation.

Interestingly, our data suggest that the hedonic modulation of ACC might be driven by the VP. Although the pallidum has often been mainly conceived of as the motor output structure of the basal ganglia, accumulating recent findings indeed have revealed its important role for the causation of hedonic responses to pleasant stimulation (Kringelbach and Berridge 2009; Smith et al. 2010). In addition, lesion studies have shown that rostral cingulate cortex activity indeed depends on intact pallidal structures (Ullsperger and von Cramon 2006).

It is striking that ACC and VP have also been implicated in many studies investigating the impact of hedonic experience and opioid modulation on pain processing. Opioid receptors are densely distributed in these areas (cf. Luu et al. 2000) and increased opioid function has been linked to positive emotional states such as relief of pain and feelings of euphoria, well-being, and relaxation (Zubieta et al. 2003; Leknes and Tracey 2008; Kringelbach and Berridge 2009). One essential topic for future research is to investigate the shared neural mechanisms of demand and pain processing (Shackman et al. 2011) and to study whether opioid signaling also mediates the hedonic impact on behavioral adjustment to conflict, as shown in this study.

Affective Versus Motivational Mechanisms

It is important to note that the recent work on the effects of hedonic valence and positive affect reviewed here diverge from other lines of research that have studied the motivational effects on cognitive control (Chiew and Braver 2011b; Dreisbach and Fischer 2012b). To investigate the effect of motivational states, those studies often use performance-contingent incentives (Harsay et al. 2011; Padmala and Pessoa 2011; Sturmer et al. 2011; Braem et al. 2012, 2013). Although neuroimaging studies using incentive manipulations usually also imply frontostriatal interactions (Harsay et al. 2011; Padmala and Pessoa 2011), those rewards have been shown to either improve or impair control-related functions (Krebs et al. 2010, 2011), the effects depending on the specific design and pay-off scheme used (Chiew and Braver 2011a; Braem et al. 2013).

In contrast, the effects of humor described here are probably due to the difference in hedonic valence or "liking" of the affective context. Our results suggest that earlier identified neural interactions between motivational and cognitive networks (e.g., Engelmann et al. 2009; Pessoa and Engelmann 2010), thus might also be involved when affect is incidental and not directly relevant to the task at hand. However, although motivational and hedonic aspects of reward might be coded in similar regions of the ventral basal ganglia, they likely serve different functions and involve a different neurochemical transmission, for example, dopamine versus opioid neuromodulation (Barbano and Cador 2007; Kringelbach and Berridge 2009). As neither overall reaction time nor interference effects were reliably modulated by hedonic context, we consider it unlikely that tonic motivational effects contributed strongly to the effects reported (see also Dreisbach and Fischer 2012b). More importantly, our behavioral findings are in line with earlier studies using mood induction, which have reported similar observations, while manipulations in tonic arousal level did not effectively change the conflict-adjustment effect (van Steenbergen et al. 2010; Kuhbandner and Zehetleitner 2011).

Limitations

Although we consider it likely that the effects observed here are determined by a lasting affective or hedonic state, we acknowledge that our study did not provide direct evidence for this assumption from an independent measure of affect (cf. Shackman et al. 2006). Although retrospective ratings of the cartoons confirmed that humor cartoons were funnier than neutral cartoons and even though instructions emphasized to keep enjoying the content of the preceding cartoon during the flanker task, we did not directly measure the hedonic response to the cartoons in the experiment itself. Considering the multidimensional nature of humor, even if such measures were included one could not exclude the possibility that other factors, such as the more cognitive processing of the stimulus, might have driven or contributed to the effects observed on behavior. We think, however, that it is unlikely that the effects on adaptation are due to attentional distraction in our design (cf. Strick et al. 2010), since humor context did not affect general reaction time and interference scores. Nevertheless, it is possible that factors such as cognitive appraisal might have contributed to the effects observed on behavioral adaptation (cf. Abel and Maxwell 2002).

Two other limitations concerning the sample should also be acknowledged. First, we tested only females because earlier studies demonstrated stronger VS responses to funny cartoons in females than in males (Azim et al. 2005). Given our a priori hypothesis that the rostral cingulate cortex might depend on subcortical hedonic processing, and since we aimed to maximize such effects, we only included females in our sample. On the other hand, studies have shown that the subjective evaluation of humor typically is not different for males (Azim et al. 2005; Waugh and Gotlib 2008). Moreover, increased neural responses to positive stimuli have also been observed in males, so the direction of modulation might depend on the specific type of stimulus used (Whittle et al. 2011).

Second, our study used a modest sample size because piloting work suggested that this would be sufficient to observe the behavioral effect of hedonic context on behavioral adaptation (see Supplementary Material). Additionally, the analyses described here were based on a priori hypotheses and built on and replicated solid effects reported earlier. Nevertheless, given recent concerns and discussions about the power of neuroimaging work (Barch and Yarkoni in press; Button et al. 2013), it is advisable that future studies use bigger sample sizes (but see also Friston 2012; Ashton 2013).

Conclusions

The present study yielded evidence for a neural mechanism that produced hedonic regulation serving behavioral flexibility. Humor-induced pleasure was shown to counter-regulate demand-driven behavior by activating the ventral basal ganglia, which dampened the conflict response in different portions of the rostral cingulate cortex through reciprocal interactions between both regions. Our results provide new evidence that MCC and ACC both play a central role in the monitoring of and responding to situational demands, and that hedonic processing in VS and VP interacts with those regions. Viewed from a broader perspective, these results may also provide valuable insights into how positive affect and humor provide an antidote to stressful responses to demanding events in everyday life (Lefcourt and Martin 1986; Garland et al. 2010). Ultimately, a better understanding of the neural basis of these interactions between hedonic processing and stress might aid the prevention and treatment of anhedonia and stress-related neuropsychiatric disorders (Der-Avakian and Markou 2012).

Supplementary Material

Supplementary material can be found at: http://www.cercor.oxfordjournals.org/

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Notes

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