Neurobiology of Value Integration: When Value Impacts Valuation

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Behavioral economics has investigated value integration mechanisms to predict choice behavior across a distribution of positive and negative values. Multiattribute utility theory suggests that the subjective value of multiattribute options equals the attributes’ weighted sum (Keeney and Raiffa, 1976; Wallenius et al., 2008). Although these models can predict choice behavior well (Huber, 1974; Wallenius et al., 2008), they require that the preference order of one attribute is independent of other attributes. However, human choice often violates this (Keeney and Raiffa, 1976); for example, when selecting a dinner menu with cheese, red wine has a higher value than white wine. But, with fish, white wine has a higher value. Here, an independent model fails to predict choice, whereas an interactive integration model would successfully predict choice by permitting an extra term for the dependence of attributes.

How the neural systems mediate the value integration is not well understood. The subgenual anterior cingulate cortex (sgACC) has been shown to encode both positive and negative values (Blood et al., 1999; Plassmann et al., 2010). Also, the amygdala represents values independent of valence (Breiter et al., 1996, 2001; Becerra et al., 2001; Gasic et al., 2009). Furthermore, these structures play a key role in both affect (Phelps et al., 2004) and pain regulation (Bingel et al., 2006; Wiech et al., 2008). Thus, the sgACC and the amygdala are ideally suited to facilitate interactive value integration.

In this study, we investigated how the brain integrates values across discrete stimuli into one subjective value to guide decision making. We hypothesized that (1) different values affect each other and (2) the sgACC and amygdala are critically involved. To test these hypotheses, we measured brain activity using fMRI while subjects accepted or rejected offers that were combinations of qualitatively different values of different valence (pain and money). The combination of values included a parametric variation in their intensities.

A well established approach to investigate cognitive processes underlying decision making is to compare cognitive models on behavioral data (O’Doherty et al., 2007; Mazur and Biondi, 2009; Talmi et al., 2009; Bhatt et al., 2010; Naalpakkam et al., 2010). However, if competing models predict the same pattern of choices, behavioral data are limited (Bruni and Sugden, 2007). In these cases, forcing the models to predict neural activity can provide decisive evidence (Glimcher and Rustichini, 2004; Hampton...
et al., 2006, 2008; Sanfey et al., 2006; Kable and Glimcher, 2007; Loewenstein et al., 2008). We tested four different subjective value models with either independent or interactive value integration mechanisms. We applied these models directly on behavioral and neural data, looking for decisive information about the implemented mechanism in the brain. Finally, we investigated how different brain regions interact when one attribute’s value affects another valuation process.

Materials and Methods

Subjects
Twenty-four healthy male subjects (age: 26.79 ± 0.66 years) were included in the study. Subjects reported no psychiatric or neurological disorder. Written informed consent was obtained from all participants after the procedure had been fully explained. The study was approved by the Ethics Committee of the Charité–Universitätsmedizin Berlin.

Task

Individual pain stimulus selection. Before the scanning session, subjects received 30 mild shocks of varying levels in randomized order and gave ratings on a visual analog scale (VAS) (Price et al., 1994; Brooks et al., 2010). The very left extreme of the VAS was labeled as 0 (not unpleasant at all); the very right extreme was labeled as 100 (worst imaginable unpleasantness) (Fig. 1A). For the tactile-stimulus application, we used a DS5 (Digitimer) stimulator controlled by a stimulation computer. A ring electrode was placed on the back of the left hand between thumb and index finger. For each subject, we fitted a power function to these ratings (Price et al., 1993) and defined five different pain stimuli with equal intervals in subjectively perceived unpleasantness (Fig. 1B). All visual and tactile stimuli as well as response recordings were controlled using Cogen2000 and MATLAB.

Associating tactile stimuli with visual stimuli. The set of five different pain stimuli obtained for each individual was then associated with five visual cues via a classical conditioning procedure. In each trial, subjects saw an offer, which was a combination of a visual pain cue and an amount of money. After a variable delay, subjects either accepted or rejected the offer. Subjects were told that 15 trials would be randomly selected at the end of the experiment and both money and pain would be given in case the selected trial was an accepted offer and that they would receive nothing if it was a rejected offer. ISI, Interstimulus interval; ITI, intertrial interval.

Figure 1. Multiatribute decision-making task. A, Subjects rated tactile stimulations of different strengths on a VAS. B, To select five pain stimuli for each individual, we estimated individual power functions using the subjective unpleasantness ratings. C, The five selected pain stimuli were then associated with five different visual cues using a classical conditioning procedure. D, fMRI experiment. In each trial, subjects saw an offer, which was a combination of a visual pain cue and an amount of money. After a variable delay, subjects either accepted or rejected the offer. Several offers were selected at the end of the experiment and both money and pain would be given in case the selected trial was an accepted offer and that they would receive nothing if it was a rejected offer. ISI, Interstimulus interval; ITI, intertrial interval.

Subjective value models and behavioral analysis

The subjective value models integrated pain and money either independently or they additionally assumed an interaction between both attributes. The interactive term can be thought of as modulating the slope of the value of money as a function of pain. It quantifies by how much the increase in money (i.e., 1 to 99 cents) paired with low pain differs from the same monetary increase paired with high pain (Fig. 2A–D). Behavioral studies have suggested nonlinear value functions that allow concavity for positive values and convexity for negative values (Kahneman and Tversky, 1979). For completeness, we modeled the value functions for pain and money in both a linear and nonlinear manner. We refer to these models as (1) linear independent, (2) nonlinear independent, (3) linear interactive, and (4) nonlinear interactive (Fig. 2A–D). Mathematically, all models can be represented as a special case of the nonlinear interactive model, which defines the subjective value of a choice option $x$ by the subjective value of the monetary amount and the pain level of the option:

$$SV(x) = \beta_m m^x + \beta_p p^x + \beta_{mp} m^x p^x,$$

where $SV$ is the subjective value, $m$ is the monetary amount, $p$ is the pain level, and the $\beta$s represent the weights for money, pain, and the interaction, from left to right. The shape of the value functions for pain and money is modulated by an exponent $\alpha$ and $\beta$ such as used to deviate from linearity ($\alpha = 1$) to be concave ($\alpha < 1$) or convex ($\alpha > 1$). In case the exponent for the value functions is 1, Equation 1 represents the two linear models (Fig. 2A, B), and in case the exponent for the value functions is 1, Equation 1 represents the two nonlinear models (Fig. 2A, C). For all models, we assumed that the probability of accepting an option is a monotonic function of the options’ subjective value, as defined by the soft-max choice rule:

$$p(\text{accept } x) = \frac{1}{1 + e^{-\pi SV(x)}},$$

where $\pi$ is a sensitivity parameter defining the slope of the sigmoid function, that is, the choices’ stochasticity (the percentage of accepted offers plotted as a function of subjective value of the nonlinear independent model for demonstration; Fig. 2F).

Individual model parameters were estimated using a leave-one-out cross-validation procedure by minimizing the mean squared error (MSE: average squared difference between the model prediction and subjects’ actual choice behavior). Data from three runs were used to fit the free
model parameters, and their prediction accuracy was computed on the fourth independent test run. This procedure was repeated four times, each time using a different run as the independent test dataset. The prediction accuracy of a given model was defined as the average MSE in predicting the independent test data across all four cross-validation steps. This procedure allowed us to compare the MSE of four models against each other in predicting choice behavior, independent of the models’ complexities (i.e., number of free parameters) (Stone, 1974; Hampton et al., 2008). MSE scores did not significantly deviate from a normal distribution (Kolmogorov–Smirnov test, all \( p \) values < 0.7). We thus compared the models’ ability to predict choice behavior using a 2\( \times \)2 ANOVA (integration mechanism \( \times \) shape of value function).

fMRI acquisition and preprocessing

Functional imaging was conducted on a 3 tesla Siemens Trio scanner with 12-channel head coil. In each of the four runs, 465 T2*-weighted gradient-echo EPIs containing 33 slices (3 mm thick) separated by a gap of 0.75 mm were acquired. Imaging parameters were as follows: TR = 2000 ms, TE = 30 ms, flip angle = 90°, matrix size = 64 \( \times \) 64, and FOV = 192 mm, voxel size = 3 \( \times \) 3 \( \times \) 3.75 mm.

Functional data were analyzed using SPM5 (Wellcome Department of Imaging Neuroscience). The first three volumes of each run were...
discarded to allow for magnetic saturation effects. Images were slice time corrected, re-aligned, spatially normalized to a standard T2* template of MNI, resampled to 3 mm isotropic voxels, and spatially smoothed using an 8 mm FWHM Gaussian kernel. All included subjects moved less than the size of a single voxel (3 mm; maximal between-scan movement in mm, mean ± SEM, x = 0.15 ± 0.02; y = 0.36 ± 0.04; z = 0.61 ± 0.1; in radians, mean ± SEM, pitch = 0.0087 ± 0.0025; roll = 0.0031 ± 0.0004; yaw = 0.0025 ± 0.0003).

Model-based fMRI data analysis
To test the four models against each other at the neural level, for each subject, we set up a GLM with a parametric design (Buchel et al., 1998) for each subjective value model, resulting in four GLMs per subject. Each GLM had three regressors of interest: (1) onset of the offer, (2) the trial-wise subjective value of the offer, and (3) response onset. The subjective value regressor was created by parametrically modulating the stimulus function of the offer value regressor was created by parametrically

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Onset by the standardized (mean modulating the stimulus function of the offer value regressor was created by parametrically

fer, and (3) response onset. The subjective value regressor was created by parametrically modulating the stimulus function of the offer.

between pain and money actually modulates the effective connectivity of the sgACC as a seed region. After having shown that the sgACC is involved in interactive value integration, we aimed to investigate how the interaction between pain and money affects valuation. We first created regressors for each of the three pain levels. Within each of these three regressors, we coded the three money levels: that is, six TRs following the onset of high money trials were coded as 1, whereas six TRs following the onset of low money trials were coded as 0.

Task-dependent changes in connectivity with the sgACC
We performed a whole-brain psychophysiological interaction (PPI) analysis (Friston et al., 1997; Kahnt et al., 2009; Park et al., 2010) with the sgACC as a seed region. After having shown that the sgACC is involved in interactive value integration, we aimed to investigate how the interaction between pain and money actually modulates the effective connectivity of the sgACC with any other brain region. In contrast to the standard PPI analysis with only one psychological factor, we set up a PPI using two psychological factors (pain and money). We then searched for changes in effective connectivity with the interaction of pain and money. We first sorted all trials according to their pain and money levels into nine classes (3 money [low, middle, and high] × 3 pain [low (levels 1 and 2), middle (level 3), and high (levels 4 and 5)]). We extracted the entire time series from each subject in the cluster of the sgACC, in which activity showed significantly higher correlation with subjective values of the interactive models compared with that of the independent models (see Results, Neural representation of different subjective values). We then created regressors for each of the three pain levels. Within each of these three regressors, we coded the three money levels: that is, six TRs following the onset of high money trials were coded as 1, whereas six TRs following the onset of low money trials were coded as 0.

Error bars indicate SEM.

Figure 5. sgACC is involved when value affects valuation. A, sgACC (0, 27, −15) showing significantly larger effect sizes for the subjective values (SV) of the interactive compared with the independent models in a direct whole-brain model comparison. Slice represents the sagittal view of structural brain image with superimposed statistical map. B, This difference was also significant when testing the linear and nonlinear models separately. Error bars indicate SEM.

Table 1. Average effects of subjective values (p < 0.001, k = 10)

<table>
<thead>
<tr>
<th>Region name</th>
<th>BA</th>
<th>MNI</th>
<th>x</th>
<th>y</th>
<th>z</th>
<th>t value</th>
</tr>
</thead>
<tbody>
<tr>
<td>OFC</td>
<td>11</td>
<td>L</td>
<td>−21</td>
<td>33</td>
<td>−15</td>
<td>3.83</td>
</tr>
<tr>
<td>Medial OFC</td>
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<td>L</td>
<td>0</td>
<td>39</td>
<td>−3</td>
<td>3.69</td>
</tr>
<tr>
<td>Central OFC</td>
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<td>L</td>
<td>−36</td>
<td>48</td>
<td>−6</td>
<td>4.39</td>
</tr>
<tr>
<td>dIPFC</td>
<td>8</td>
<td>R</td>
<td>42</td>
<td>30</td>
<td>51</td>
<td>4.09</td>
</tr>
<tr>
<td>dIPFC</td>
<td>8</td>
<td>L</td>
<td>−24</td>
<td>36</td>
<td>54</td>
<td>3.67</td>
</tr>
<tr>
<td>Parietal cortex</td>
<td>7</td>
<td>L</td>
<td>−24</td>
<td>−63</td>
<td>54</td>
<td>3.67</td>
</tr>
<tr>
<td>Parietal cortex</td>
<td>40</td>
<td>R</td>
<td>−51</td>
<td>−42</td>
<td>57</td>
<td>3.43</td>
</tr>
<tr>
<td>Occipital lobe</td>
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<td>L</td>
<td>−12</td>
<td>96</td>
<td>6</td>
<td>7.70</td>
</tr>
<tr>
<td>Occipital lobe</td>
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<td>R</td>
<td>−27</td>
<td>−99</td>
<td>−6</td>
<td>4.39</td>
</tr>
<tr>
<td>Cerebellum</td>
<td>−27</td>
<td>L</td>
<td>−81</td>
<td>−48</td>
<td>−33</td>
<td>3.65</td>
</tr>
<tr>
<td>Cerebellum</td>
<td>−42</td>
<td>R</td>
<td>−81</td>
<td>−33</td>
<td>4.18</td>
<td></td>
</tr>
</tbody>
</table>

Figure 4. Brain regions encoding the subjective value of the four models. A, Linear independent; B, nonlinear independent; C, linear interactive; D, nonlinear interactive. Slices represent coronal (left) and sagittal (right) views of structural brain images with superimposed statistical maps.
Table 2. Comparison between interactive and independent models (collapsed across the curvature of value function; \( p < 0.005, \kappa = 5 \), masked with the average map of subjective values (\( p < 0.05 \))

<table>
<thead>
<tr>
<th>Region name</th>
<th>BA</th>
<th>x</th>
<th>y</th>
<th>z</th>
<th>t value</th>
</tr>
</thead>
<tbody>
<tr>
<td>sgACC</td>
<td>25</td>
<td>0</td>
<td>27</td>
<td>-15</td>
<td>2.87</td>
</tr>
<tr>
<td>R dIPFC</td>
<td>8</td>
<td>42</td>
<td>33</td>
<td>42</td>
<td>3.43</td>
</tr>
<tr>
<td>R OFC</td>
<td>11</td>
<td>12</td>
<td>39</td>
<td>-21</td>
<td>3.23</td>
</tr>
<tr>
<td>L Inferior parietal cortex</td>
<td>40</td>
<td>-42</td>
<td>-42</td>
<td>48</td>
<td>2.82</td>
</tr>
<tr>
<td>R Inferior parietal cortex</td>
<td>40</td>
<td>45</td>
<td>-42</td>
<td>57</td>
<td>2.82</td>
</tr>
<tr>
<td>L Cerebellum</td>
<td>11</td>
<td>-36</td>
<td>-48</td>
<td>-30</td>
<td>3.16</td>
</tr>
<tr>
<td>R Thalamus</td>
<td>6</td>
<td>-15</td>
<td>9</td>
<td>3.12</td>
<td></td>
</tr>
<tr>
<td>Periaqueductal grey</td>
<td>3</td>
<td>-33</td>
<td>-6</td>
<td>3.45</td>
<td></td>
</tr>
<tr>
<td>R Precentral cortex</td>
<td>6</td>
<td>54</td>
<td>-6</td>
<td>54</td>
<td>2.89</td>
</tr>
<tr>
<td>L Angular gyrus</td>
<td>7</td>
<td>36</td>
<td>-63</td>
<td>48</td>
<td>2.80</td>
</tr>
<tr>
<td>L Middle occipital gyrus</td>
<td>37</td>
<td>-51</td>
<td>-63</td>
<td>20</td>
<td>3.31</td>
</tr>
<tr>
<td>L Occipital lobe</td>
<td>19</td>
<td>-27</td>
<td>-66</td>
<td>42</td>
<td>3.10</td>
</tr>
<tr>
<td>R Occipital lobe</td>
<td>19</td>
<td>36</td>
<td>-81</td>
<td>21</td>
<td>2.89</td>
</tr>
</tbody>
</table>

Figure 6. Whole-brain direct comparison between nonlinear interactive versus nonlinear independent models (A, B) and the whole-brain effective connectivity of sgACC (C). A, B, Brain regions showing significantly larger effect sizes for the nonlinear interactive model compared with the nonlinear independent model. Slices represent sagittal (left) and transversal (right) views of structural brain images with superimposed statistical maps. The circled areas indicate anterior vmPFC (BA 11 [6, 48, -9], \( t_{(92)} = 3.18, p < 0.001 \)) (A) and dIPFC (BA 9 [30, 45, 42], \( t_{(92)} = 3.78, p < 0.001 \)) (B). C, Functional connectivity between sgACC and left amygdala is enhanced as a function of money offers within the high-pain compared with the low-pain condition (\( t_{(92)} = 4.14, p < 0.001 \); coronal view of structural brain image with superimposed statistical map).

Table 3. Nonlinear interactive > nonlinear independent (\( p < 0.001, \kappa = 10 \))

<table>
<thead>
<tr>
<th>Region name</th>
<th>BA</th>
<th>x</th>
<th>y</th>
<th>z</th>
<th>t value</th>
</tr>
</thead>
<tbody>
<tr>
<td>R OFC</td>
<td>10/11</td>
<td>6</td>
<td>48</td>
<td>-9</td>
<td>3.18</td>
</tr>
<tr>
<td>R dIPFC</td>
<td>8</td>
<td>30</td>
<td>45</td>
<td>42</td>
<td>3.78</td>
</tr>
<tr>
<td>R Posterior cingulate cortex</td>
<td>6</td>
<td>3</td>
<td>-30</td>
<td>57</td>
<td>3.81</td>
</tr>
<tr>
<td>L Posterior cingulate cortex</td>
<td>6</td>
<td>-3</td>
<td>-30</td>
<td>72</td>
<td>3.42</td>
</tr>
<tr>
<td>R Occipital lobe</td>
<td>19</td>
<td>-33</td>
<td>-78</td>
<td>27</td>
<td>3.77</td>
</tr>
<tr>
<td>R Thalamus</td>
<td>12</td>
<td>12</td>
<td>12</td>
<td>3.57</td>
<td></td>
</tr>
<tr>
<td>L Cerebellum</td>
<td>-36</td>
<td>-48</td>
<td>-30</td>
<td>3.48</td>
<td></td>
</tr>
<tr>
<td>R Midbrain</td>
<td>-12</td>
<td>-12</td>
<td>-27</td>
<td>3.37</td>
<td></td>
</tr>
<tr>
<td>L Parietal cortex</td>
<td>7</td>
<td>-27</td>
<td>-78</td>
<td>45</td>
<td>3.33</td>
</tr>
<tr>
<td>R Temporal cortex</td>
<td>37</td>
<td>51</td>
<td>-63</td>
<td>-18</td>
<td>3.32</td>
</tr>
<tr>
<td>R Medial orbitofrontal cortex</td>
<td>6</td>
<td>36</td>
<td>6</td>
<td>3.30</td>
<td></td>
</tr>
<tr>
<td>L Precentral gyrus</td>
<td>56</td>
<td>-30</td>
<td>-9</td>
<td>60</td>
<td>3.47</td>
</tr>
<tr>
<td>L Parahippocampal gyrus</td>
<td>30</td>
<td>-22</td>
<td>-36</td>
<td>-15</td>
<td>3.25</td>
</tr>
<tr>
<td>R Parahippocampal gyrus</td>
<td>30</td>
<td>21</td>
<td>-24</td>
<td>-18</td>
<td>3.23</td>
</tr>
</tbody>
</table>

onset of low money trials were coded as -1, and the middle money trials were coded with zeros. The time window of six TRs was selected to capture the entire hemodynamic response function (Kahn et al., 2009; Park et al., 2010). These regressors were then multiplied by the normalized time series of sgACC. Thus, for each pain level, the resulting regressor represents the interaction between sgACC activity and money for one pain level. The middle regressors of pain and money were included in the single-subject model, but were not used to compute the group contrasts because of the smaller number of trials in these classes. Importantly, the created PPI regressors were used as covariates in a separate regression, which also included all the psychological regressors [three onset regressors for three pain levels, each regressor coding the onset of high money (as +1), middle money (as -1, 0), and low money (as -1), convolved with an HRF] and the physiological regressor (the entire time series of sgACC). Because the seed region is defined (the contrast interactive vs independent) in a similar way as the psychological factor of the PPI regressors (interaction between pain and money), the psychological, PPI, and physiological regressors may be correlated. Note that this deviates from the standard PPI approach, in which the seed ROI definition is usually orthogonal to the psychological factor. However, because we entered all regressors simultaneously into the model, the shared variance would not be attributed to any of the regressors. According to this, the PPI regressor explains the incremental variance that is neither explained by the psychological regressors nor by the physiological regressor. Individual contrast images for sgACC connectivity modulated by money for high-pain and low-pain levels were then entered into second-level \( t \) tests.

Results

Model predictions on choice behavior

The Khiing et al. (2011) reported that all MSEs did not differ from normal distributions (\( p \) values for MSE linear independent = 0.996; linear interactive = 0.877; nonlinear independent = 0.993; nonlinear interactive = 0.734). A 2 \( \times \) 2 ANOVA (integration mechanism \( \times \) shape of value function) with the four models revealed that the nonlinear models had higher predictive power compared with the linear models (\( F_{(1,23)} = 17.17, p < 0.001 \)). However, we found a significant interaction effect (\( F_{(1,23)} = 21.35, p < 0.001 \)) demonstrating the superiority of the interactive model over the independent model only when the value functions were modeled linearly. Within the nonlinear value functions, the predictive power of both integration mechanisms did not differ substantially (\( t_{(23)} = 1.28, p = 0.21 \)) (Fig. 2E; Fig. 3A–D shows choice behavior of a single subject as a function of the subjective values derived from the four models). Thus, we conclude that, on the basis of choice behavior, it is not possible to identify the integration mechanism. Therefore, we further compared the predictive power of the models directly on neural data to gain insight into the underlying cognitive integration mechanism.

Model-based fMRI data analysis

Neural representation of different subjective values

The four models showed similar patterns of correlation with BOLD responses (Fig. 4). On average, the subjective values of the four models showed significant correlation in the medial prefrontal cortex [mPFC (0, 39, -3), \( t_{(92)} = 3.69, p < 0.001 \)], the central orbitofrontal cortex [cOFC (-36, 48, -6), \( t_{(92)} = 4.39, p < 0.001 \)], and the dorsolateral prefrontal cortex [dIPFC (-24, 36, 54), \( t_{(92)} = 3.67, p < 0.001 \)] (see Table 1 for whole-brain results).
Next, we performed a whole-brain model comparison by statistically testing the effect sizes of the different models. The interactive models showed significantly larger effect sizes in sgACC [BA 25 (0, 27, −15), $t_{(92)} = 2.87$, $p < 0.005$] compared with the independent models (collapsed across linear and nonlinear models) (Fig. 5A, see Table 2 for whole-brain results). In contrast, there were no voxels in which BOLD responses were better predicted by the subjective values of the independent models. Furthermore, we did not find any voxels in which BOLD responses were significantly better predicted by the subjective values of the nonlinear compared with the linear models or vice versa.

A post hoc ROI analysis revealed that in the sgACC, the effect sizes of the interactive models were larger than those of the independent models in both linear and nonlinear models separately ($t_{(253)} = 2.47$, $p < 0.05$; $t_{(253)} = 2.87$, $p < 0.05$, respectively) (Fig. 5B). Thus, we conclude that values are integrated by means of an interactive integration mechanism and that sgACC plays a crucial role in this function.

Identifying the neural integration mechanism

We have shown that both nonlinear models made better behavioral predictions than the two linear models. However, within the nonlinear models, both integration mechanisms (interactive and independent) predicted choice behavior equally well (see above). Therefore, we used the brain data to identify which of the nonlinear integration mechanisms is superior in predicting the BOLD signal in value-sensitive brain regions. Thus, this analysis can serve as a tiebreaker between competing models of brain processes underlying decision making. The nonlinear interactive model revealed voxels with higher effect sizes than the nonlinear independent model in the medial OFC [(6, 48, −9), $t_{(92)} = 3.18$, $p < 0.001$] and the dlPFC [(30, 45, 42), $t_{(92)} = 3.78$, $p < 0.001$] as well as other regions (Fig. 5, A, B, Table 3). In contrast, we did not find any voxel in which BOLD changes were significantly better predicted by the nonlinear independent model compared with the nonlinear interactive model. Hence, we conclude that the nonlinear interactive model provides the better description of the neural processes underlying choice behavior among multiattributive options.

Effective connectivity of sgACC

Finally, the whole-brain PPI analysis with the sgACC as seed region revealed a significant difference in the money-dependent connectivity modulation when contrasting high versus low pain in the amygdala/sublenticular extended amygdala (SLEA) [$|−12, −3, −12|$, $t_{(60)} = 4.14$, $p < 0.001$] (Fig. 6C).

Discussion

In the present study, we showed that value affects valuation when advantages and disadvantages are integrated into an overall subjective value. This study provides a concrete example of how neuroimaging directly allows one to test between computational models of decision making and facilitates the evaluation of cognitive computations. Thus, our study supports the promise of neuroeconomics that neuroimaging can significantly contribute to the evaluation of economic questions.

Although independent and interactive subjective value models rely on different assumptions, both models make very similar predictions about the choice behavior. Indeed, in our case, the interactive and independent models performed equally well in predicting subjects’ behavior when the value functions were modeled nonlinearly. Thus, behavioral data alone were insufficient to conclude which integration mechanism (interactive vs independent) best describes the cognitive process of integrating the attributes’ values into the subjective value of multiattribute options. Therefore, we went on to compare the predictive power of the models on the neural data. This revealed that interactive models are superior to the independent models in predicting neural activity in the sgACC, independent of the curvature of the value functions. Thus, this analysis of neural activation provides a potential solution for the computational mechanisms of value integration, for which behavioral measures in this study were not informative. Only a few studies so far have compared different models directly on neural data (Hampton et al., 2006, 2008; Montague et al., 2006; Kable and Glimcher, 2007; Rangel et al., 2008). This approach is related to some model-based fMRI studies (Breiter et al., 2001; O’Doherty et al., 2004; Seymour et al., 2004; Kim et al., 2006; Talmi et al., 2009) and provides a concrete example of using neural signals with modeling to identify integration computations that cannot be easily identified by behavioral measures. The identification of the better describing model is essential, even if the two models may yield similar patterns of prediction for choice behavior on one dataset, because this does not imply that this will be the case in other decision situations. Specifically, it is important to identify more accurate descriptions of the underlying process because such models will make new and more precise predictions in future and alternative situations (see also Camerer, 2007). In line with this, future studies should create decision situations in which those models make diverging predictions and compare the models’ accuracy in predictions.

Finally, we showed that the connectivity between the sgACC and the amygdala/SLEA was modulated as a function of money only during high-pain conditions. This suggests that interactive value integration relies on the interplay between the sgACC and the amygdala/SLEA.

Subjective values of all four models showed significant correlations with the BOLD signal in medial PFC and OFC. This is in line with evidence suggesting that the ventral part of the medial PFC and OFC encodes the reward value of choice options (Aharony et al., 2001; Daw et al., 2006; Kim et al., 2006; Plassmann et al., 2008; Gasic et al., 2009; Hare et al., 2009; Kahnt et al., 2010, 2011; Philiastides et al., 2010; Smith et al., 2010). Talmi and colleagues (2009) have demonstrated that activity in this region increases with rewards and is attenuated by the prospect of pain. Furthermore, our result that sgACC, together with the amygdala/SLEA, is involved in interactively modulating hedonic experience is consistent with a large body of evidence from cognitive neuroscience. In studies investigating monetary gains and losses, Breiter et al. (2001) have reported that SLEA activity is modulated not only by the prospect of monetary gains and losses but also by their outcomes. In monkeys and rats, analogous regions are involved in regulating fear by exerting inhibitory control over amygdala activity (Sotres-Bayon et al., 2004; Quirk and Beer, 2006; Milad and Rauch, 2007). Studies on fear extinction in rats have shown that stimulating this PFC region modulates amygdala responses, thereby affecting the expression of conditioned responding (Quirk et al., 2003; Rosenkranz et al., 2003). In humans, during extinction and the regulation of learned negative values, the sgACC is actively engaged together with the amygdala independent of the modulation strategy (Plebus et al., 2004; Etkin et al., 2006; Delgado et al., 2008; Schiller and Delgado, 2010). Similarly, sgACC–amygdala coupling is involved in pain regulation such as placebo analgesia and pain habituation (Mayberg et al., 2002; Bingel et al., 2006, 2007). An interesting question is whether our results can be generalized to other types of cost–benefit integra-
tion. Recent evidence suggests distinct valuation subsystems for different types of costs and benefits. For example, Prévost et al. (2010) have shown that delay and effort discounting engage different neural circuits (see also Croxson et al., 2009). Also, besides sgACC and amygdala, ventromedial PFC, and striatum have been shown to play a key role in initial acquisition and modulation of the fear response (Schiller and Delgado, 2010).

In summary, the present study compared different subjective value models with independent and interactive value integration mechanisms directly on fMRI data. This procedure provided neural evidence that an interactive rather than an independent integration mechanism is implemented in the brain. Furthermore, it suggests that the sgACC, in concert with the amygdala, is critically involved in this process. By demonstrating how different values are integrated in the brain, our results substantially extend our knowledge about the neurobiological underpinnings of human choice behavior. Moreover, they contribute to the field of neuroeconomics by showing that direct model comparisons on brain data can be used to uncover cognitive processes and thereby to decide among competing models of decision making.

References