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Is our self based on reward? Self-relatedness recruits neural activity in the reward system

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Every organism has to evaluate incoming stimuli according to their current and future significance. The immediate value of stimuli is coded by the reward system, but the processing of their long-term relevance implements a valuation system that implicates self-relatedness. The neuronal relationship between reward and self-relatedness remains unclear though. Using event-related functional MRI, we investigated whether self-relatedness induces neural activity in the reward system. Self-relatedness induced signal changes in the same regions that were recruited during reward including the bilateral nucleus accumbens (NACC), ventral tegmental area (VTA) and ventromedial prefrontal cortex (VMPFC). The fMRI signal time courses revealed no differences in early BOLD signals between reward and self-relatedness. In contrast, both conditions differed in late BOLD signals with self-relatedness showing higher signal intensity. In sum, our findings indicate sustained recruitment of the reward system during self-relatedness. These findings may contribute to a better understanding of the reward-based nature of our self.

Introduction

Value is a central dimension of biological life which is crucial in constituting and shaping the organisms' behavior within its environment. The determination of sensory stimuli's value for an organism is a central component of reward which has been called reward value (Berridge and Robinson, 2003; Knutson et al., 2005; Montague and Berns, 2002; Montague et al, 2006; O'Doherty et al., 2006; Schultz, 2004). Reward value has been associated with neural activity in specific brain regions like the nucleus accumbens (NACC), the ventromedial prefrontal cortex (VMPFC), and the midbrain with the ventral tegmental area (VTA) (Breiter et al., 2001; Montague and Berns, 2002; Knutson et al., 2001, 2003, 2005; Montague et al., 2006; O'Doherty, 2004; Schultz, 2006). The very same regions have also been associated with salience (Zink et al., 2003, 2004, 2006) and product preference (Erk et al., 2002; Deppe et al., 2005; Knutson et al., 2007; McClure et al., 2004; Paulus and Frank, 2003). This resulted in some authors associating the neural activity in the NACC, the VMPFC and the VTA with a so-called "valuation system" (Montague and Berns, 2002; Montague et al., 2006). Such "valuation system" does not only code the stimuli's immediate relevance, the reward value, but also their long-term value for the organism. The long-term value mirrors the importance and meaning of the stimulus for the organism which recently has been associated with self-relatedness (Johnson et al., 2002; Keenan et al., 2001; Kelley et al., 2002; Mitchell et al., 2005, 2006; Northoff et al., 2006; Northoff and Bermpohl, 2004; Ochsner et al., 2004, 2005; Wicker et al., 2003). This association suggests that self-relatedness may be considered a more stable and continuous long-term valuation system of the organism when compared to reward.

Neuroanatomically, self-relatedness has been shown to be associated with a variety of subcortical and cortical regions, including the NACC, the VMPFC and the VTA, among others (Kelley et al., 2002; Moran et al., 2006; Northoff et al., 2006; Phan et al., 2004). Since the latter regions represent the reward system, these findings raise the question for possible neuroanatomical overlap and differentiation between reward and self-relatedness. The goal of our study was to investigate whether self-relatedness induces neural activity in the same regions that are recruited during reward. Using event-related fMRI, subjects had to perform two tasks with the identical stimulus set: a reward task and a self-

Abbreviations: AC–PC, anterior commissure–posterior commissure; BOLD, blood oxygenation level-dependant; EPI, echo planar imaging; fMRI, functional magnetic resonance imaging; FoV, field of view; IAPS, international affective picture system; NACC, nucleus accumbens; NAPS, normative appetitive picture system; PERL, practical data extraction language; SPM2, statistical parametric mapping 2; TE, time to echo; TR, time to repeat; VMPFC, ventromedial prefrontal cortex; VTA, ventral tegmental area.

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evaluation task. The reward task consisted of a win–lose event that has previously been demonstrated to successfully engage the reward system (Reuter et al., 2005). Whereas the self-evaluation task, based on publications by Kelley et al. (2002) and Schmitz et al. (2004), concerned the mere judgment (without any reward component) of whether stimuli were high or low self-related. This allowed us first to identify the regions sensitive to reward and second to investigate signal intensities in these regions during self-relatedness while our focus was not on the interaction between reward and self.

Based on this design, we hypothesized that self-relatedness induces neural activity in reward-related regions. However, self-relatedness implicates a higher information load than reward since the actual stimulus must be integrated with the person's past and possible future. We therefore assumed that self-relatedness shows longer reaction times and sustained neural processing when compared to reward. In order to differentiate the time course of neural activity, we reconstructed the post stimulus BOLD response and distinguished between early and late BOLD signal changes for reward and self-relatedness respectively.

Materials and methods

Subjects

We investigated 15 healthy and right handed subjects (7 women, 8 men; mean age = 31.8 ± 7.9 SD) without any psychiatric, neurological, or medical illness. After a detailed explanation of the study design and any potential risks, all subjects gave their written informed consent. The study was approved by the institutional review board of the University of Magdeburg, Germany.

Experimental design

The experiment contained three different types of tasks. During reward trials subjects had to perform a gambling situation, where they could win and lose. During self-evaluation trials subjects were supposed to gauge a stimulus whether it was high or low self-related. The third task was a control task, in which subjects had to assess the orientation of a presented stimulus. The sequence of all trial types was designed as similarly as possible to allow comparisons (see Fig. 1).

All trials began with the presentation of a decision phase (2 s duration), in which subjects had to perform a button press with either their left or right hand. During this phase a picture was displayed in the center of the screen and two little triangles at the bottom symbolized the task that had to be performed. The decision phase was directly followed by a feedback phase (2 s duration), where subjects got a short symbolized feedback. The display contained a symbol on the site of the response and a state bar in the center. Every location on the screen where pictures or symbols could appear was surrounded by a thin frame. Before every next trial a short inter trial interval (ITI, duration 1 or 2 s) was presented in which only the four empty location frames were presented.

While the ITI was identical in all three tasks, the specific content of the two phases was different for every task. In the decision phase of gambling trials subjects were asked to bet by deciding for the left or right site of the display. Subjects were instructed to imagine that they were gambling about the content that was shown on the picture. In the following feedback phase they were informed whether they had won or lost. This was symbolized by the presentation of a plus or minus sign on the chosen site. Additionally the state bar, that reflected the actual amount of the subject's salary raised or shrunk. Subjects were made believe that their luck during the gambling trials had direct influence on the amount of their salary. Indeed the course of wins and losses was predefined.

During the decision phase of self-evaluation trials subjects had to evaluate the presented picture whether it was high or low self-related. In the feedback phase of these trials an equality sign was presented when the button press was delivered in time. In contrast to both of the other tasks the minus sign has been only presented when no response occurred. We decided to present an equality sign instead of the plus sign to make sure that this task had no rewarding component. The state bar was presented in these trials as well for consistency reasons. Subjects though were instructed that it had no meaning and the actual value fluctuated around the midline.

In control trials it was the subject's task to identify the alignment of the presented picture during the decision phase. All stimuli had the shape of a rectangle, half of the stimuli were horizontally aligned and half of them vertically. When subjects gave the right answer a plus sign was presented in the decision phase and a minus sign in false trials, respectively. As described above the feedback display contained the fluctuating state bar that was irrelevant in these trials, too.

A total of 120 stimuli were presented four times during the experiment, once during self-evaluation and control trials and twice during gambling trials. The 120 stimuli were composed of each 40 food stimuli, alcohol stimuli and gambling stimuli. The selection of stimuli was driven by our question which kind of stimuli might be best suited to investigate the relationship between reward and self-relatedness. Based on previous imaging experiments we decided to take stimuli that show a strong reward value like natural reinforcers, e.g. food stimuli (Killgore et al., 2003; Wang et al., 2004). For the selection of further stimuli, we turned our attention towards addictive disorders. Addictive disorders can either be substance-related like alcoholism and non-substance-related like pathological gambling where the respective stimuli, e.g., alcoholic and gambling stimuli, can develop high degrees of self-relatedness. In addition to the natural reinforcers, this makes these types of stimuli particularly suitable to test the relationship between reward and self-relatedness. The food pictures were taken from the InternationaI Affective Picture System (IAPS, Lang et al., 1999) and slightly resized. As alcohol stimuli served pictures from the Normative Appetitive Picture System (NAPS, Stritzke et al., 2004) which were modified as well. The gambling stimuli comprised typical gambling scenes and were developed especially for this study. Likewise the state bar presented in the feedback phase had three different colors reflecting the actual stimulus category.

Trials were presented in rows of ten stimuli of the same category. Hereafter a baseline event occurred that lasted for 4, 5 or 6 s. The experiment was divided in 8 sessions with the same task, i.e., four gambling sessions, two sessions with self-evaluation and two control sessions. Sessions and trials were presented in a pseudo-randomized order.

At the end of each session a short evaluation period was presented, in which subjects were asked to state their actual situation. They had to describe their hungriness, craving for alcohol, and craving for gambling as well as their general contentment by virtually moving a bar on a visual analogue scale. The experiment was executed on a ordinary desktop personal

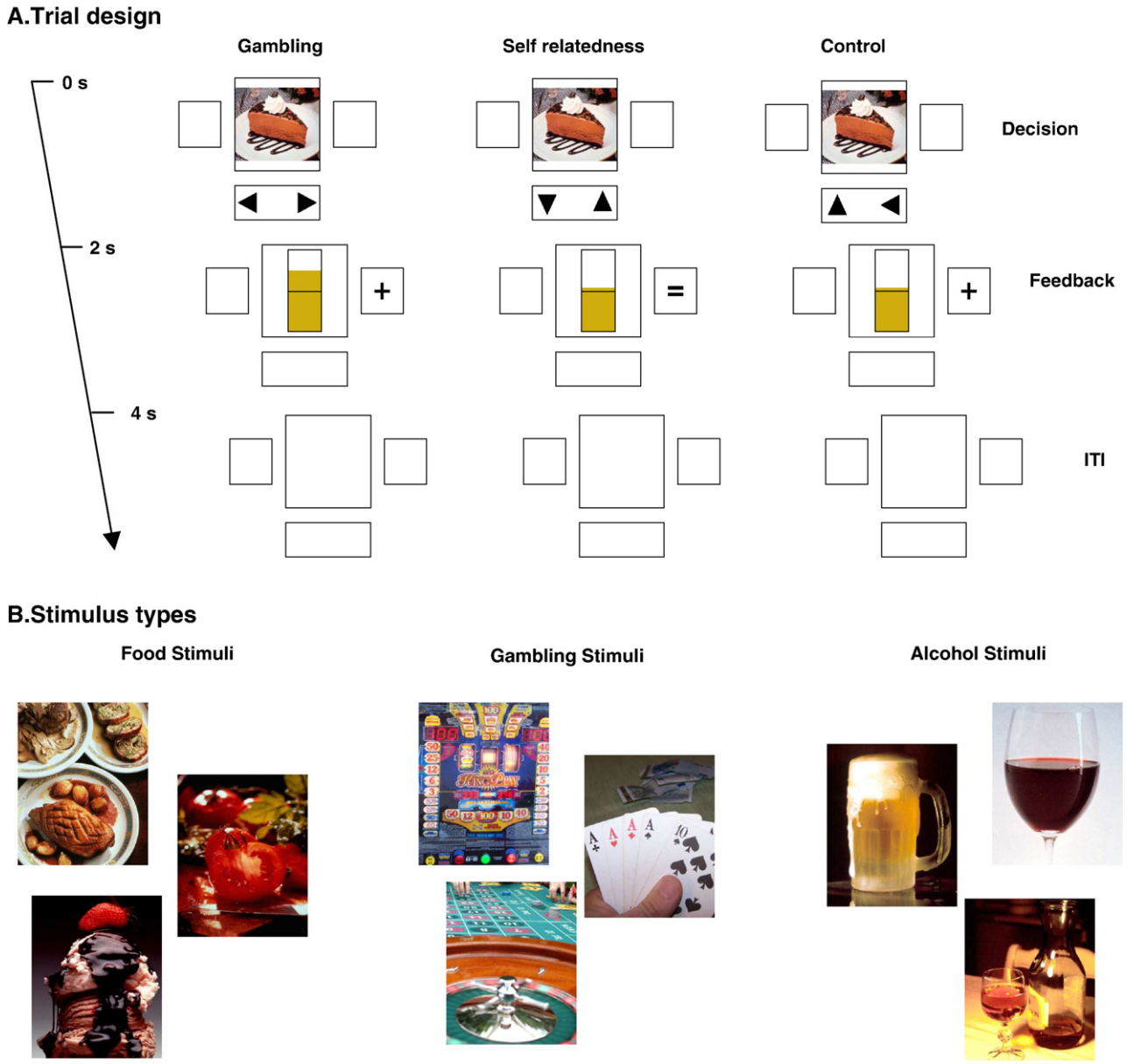

Fig. 1. Study design. (A) Trial design: the experiment contained three types of trials with a similar structure but different tasks. Each trial began with a decision phase (2 s duration) followed by a feedback phase (2 s duration). Before the next trial occurred a short inter trial interval (ITI, 1 or 2 s duration) was presented. Gambling trials: subjects had to bet for either the left or right side in the decision phase. Whether they had won or lost was symbolized by the presentation of plus or minus sign on the chosen side in the feedback phase; win or loose were indicated by the bar and +/− signs. Self-evaluation trials: subjects were asked to assess the presented picture during the decision phase. In the feedback phase the answer was represented by an equal sign in order to avoid confusion with the other two feedback tasks. For consistency purposes the state bar was also presented showing two alternating values. Subjects were instructed that the presentation of the state bar is irrelevant during self-evaluation trials. Control trials: subjects had to evaluate the alignment of the stimulus whether it had a horizontal or a vertical orientation. The correct and incorrect answers were symbolized by the presentation of a plus or minus sign in the feedback period. The state bar was as well presented in the feedback phase with an alternating irrelevant value. (B) Stimulus types: three different types of stimuli were used in each of the three tasks. Food stimuli were taken from the International Affective Picture System (IAPS). These stimuli contained different types of food. The gambling stimuli contained slot machines, card playing situations or roulette scenes. These stimuli were designed especially for this study. Alcohol stimuli were taken from the Normative Appetitive Picture System (NAPS), they showed different kinds of alcohol liquids. In total, we used 40 different stimuli of each stimulus type in the experiment.

computer using the software package “presentation” (http://www.neurobs.com/presentation). Subjects were lying inside the scanner and were watching the projected experiment on a matt screen through a mirror attached on the head coil.

Prior to the experimental session, subjects were familiarized with the paradigm by completing a test run. Subsequent to the fMRI session all subject performed a postscanning experiment in which they evaluated all presented stimuli with respect to their self-relatedness and the craving that was induced by the stimulus. After the 2 s presentation of the stimulus subjects had to assess whether they could consent to two displayed statements (self-relatedness: “The content has a lot to do with me”; craving: “I have a strong

craving for the content") by virtually moving a bar on the screen. The postscanning paradigm was displayed on an ordinary desktop personal computer using as well the experimentation software package "presentation."

Behavioral data analysis

Intrascanner reaction times from all subjects underwent a statistical analysis using repeated measurements analysis of variance and paired *t*-tests. Intrascanning and postscanning data for self-relatedness were correlated with those for craving using a Pearson correlation. The subject values were Fisher's *Z*-transformed and averaged, before retransforming the means using the inverse Fisher's *Z*-transformation.

fMRI data acquisition and analysis

Functional measurements were performed on a 3-T whole-body MRI system (Siemens Magnetom Trio, Erlangen, Germany) with echo planar imaging (EPI) using an eight-channel head coil. The slices were acquired parallel to the AC–PC plane in an odd–even interleaved direction. 32 T2*-weighted echo planar images per volume with blood oxygenation level-dependent (BOLD) contrast were obtained (matrix 64×64; 32 slices per volume; FoV 224×224 mm; spatial resolution, 3.35×3.35×4 mm; TE=30 ms; TR=2000 ms; flip angle=80°). Functional data were acquired in eight scanning sessions containing 210 volumes per session for each subject.

The first four volumes were discarded. The fMRI data were preprocessed and statistically analyzed by the general linear model approach (Friston et al., 1995) using the SPM2 software package (Wellcome Department of Cognitive Neuroscience, University College, London, UK) and MATLAB 6.5 (The Mathwork Inc.). All functional images were slicetime corrected with reference to the first slice acquired, corrected for motion artefacts by realignment to the last volume, and spatially normalized to a standard T2-weighted SPM template (Ashburner and Friston, 1999). The normalization was realized by warping the subjects' last functional image to the SPM template and applying these parameters to the other functional images. The images were resampled to 2×2×2 mm and smoothed with an isotropic 6-mm full-width half-maximum Gaussian kernel.

The time-series fMRI data were filtered using a high pass filter and cut-off of 128 s. A statistical model for each subject was computed by applying a canonical response function (Friston et al., 1998). Regionally specific condition effects were tested by employing linear contrasts for each subject and different conditions. The resulting contrast images were submitted to a second-level random-effects analysis. Here, one-sample *t*-tests were used on images obtained for each subjects' volume set and different conditions. To control for the multiple testing problem we performed a false discovery rate correction (Nichols and Hayasaka, 2003). The anatomical localization of significant activations outside of the midbrain was assessed with reference to the standard stereotactic atlas by superimposition of the SPM maps on a standard brain template (Montreal Neurological Institute) provided by SPM2.

In a second step we analyzed the fMRI raw data using the Marseille Region of Interest Toolbox software package (MarsBaR 1.86, http://www.sourceforge.net/projects/marsbar). Using a sphere-shaped region of interest (ROI, radius 5 mm), we extracted the raw data from those significant coordinates that were observed in second-level analysis. This resulted in 1680 raw fMRI signal values for each condition and subject, that underwent a linear interpolation, onset adapting and normalizing procedure using the software package Practical Data Extraction and Reporting Language (PERL, http://www.perl.org) to account for intersubject differences. Mean normalized fMRI signal values from the three following time steps in the early phase (4 s, 6 s and 8 s after feedback onset) and late phase (10 s, 12 s and 14 s after feedback onset) of the BOLD were included in the statistical analysis using repeated measurements analysis of variance (ANOVA) and paired *t*-tests (Dreher et al., 2006; Yarkoni et al., 2005).

Methodologically, one should consider that specifically the late BOLD phase might be confounded by the signal changes associated with the subsequent trial. We developed a balanced evaluation design to make it nevertheless possible to reason about this period. The group of onsets that underwent the raw data analysis consisted of an equal number of oppositional trial pairs (e.g., the group of reward win onsets contained as many onsets for reward win events that were followed by reward win events as reward win events that were followed by reward lose events).

Results

Behavioral data

Reaction times in the decision phase were included in the statistical analysis. The repeated measurements ANOVA showed a significant main effect ($F(1.154)=30.731$; $p<0.001$). Paired *t*-tests revealed significant higher reaction times during high self trials when compared to low self trials ($t(14)=5.201$; $p<0.001$). In addition, we observed that reaction times for both high and low self were significantly higher than those for win and lose ($t(14)=6.382$; $p<0.001$, $t(14)=6.731$; $p<0.001$, $t(14)=4.910$; $p<0.001$, $t(14)=5.233$; $p<0.001$, see Fig. 2A for further details).

Based on the subjects' intrascanner response patterns, we analyzed the number of performed trials using a repeated measurements ANOVA with nine levels of the factor condition (gambling win, gambling lose, gambling no response, high self, low self, self trials with no response, control correct, control incorrect, control trial with no response) and found a significant main effect ($F(8)=231.808$; $p<0.001$). As expected by our a priori determination of win versus lose trials, post hoc analysis with paired *t*-test showed significant more gambling win trials (mean: 31.7 trials per session±2.1 trials SD) than gambling lose trials (mean: 26.0 trials per session±2.3 trials SD; $t(14)=38.028$; $p<0.001$). Subjects rated the stimuli rather as low self (mean: 39.1 events per session±28.4 events SD) than as high self (mean: 18.4 events per session±8.5 events SD; $t(14)=4.827$; $p<0.001$). Similarly, subjects performed more control events with correct responses (mean: 56.9 events per session±3.9 events SD) than with incorrect responses (mean: 1.7 events per session±2.7 events SD; $t(14)=33.638$; $p<0.001$). We did not find any significant differences between the number of trials with no response between the conditions.

We also examined the win and lose stimuli with regard to the subjects' self-relatedness, e.g., whether, for instance, win stimuli were associated with high rather than low self-relatedness. Using a two-factorial repeated measurements ANOVA with two levels of the factor reward task (win and lose) and two levels of the factor self value (high self, low self), we found a main effect for the factor

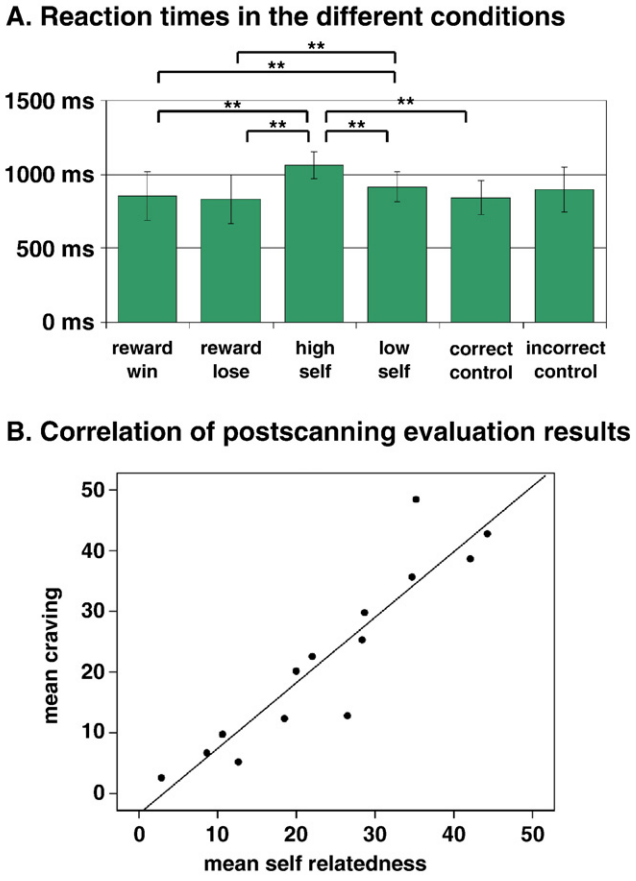

Fig. 2. Behavioral findings. (A) Reaction times in the different conditions. Reaction times in milliseconds of five conditions (reward win, reward lose, high self, low self and correct control) underwent a statistical analysis. The repeated measurements ANOVA showed a significant main effect. Paired *t*-tests revealed significant higher reaction times during high self trials when compared to low self trials. In addition, we observed that reaction times for both high and low self were significantly higher than those for win and lose. (B) Correlation of postscanning evaluation results. We here correlated subjective postscanning ratings of self-relatedness with those for craving. Each of the 15 subjects is represented by a dot. The mean self-relatedness value of all stimuli is reflected by each subject's value on the *x*-axis, the subject's mean craving value is pictured by its height on the *y*-axis. We found a strong correlation of self-relatedness with craving indicating the tight association between reward and self-relatedness on a subjective level. $^{**}p<0.001$.

self value ($F(14)=22.979$; $p<0.001$) but no interaction between both factors. This indicates no specific association of either win or lose with either high self or low self evaluation.

The intrascanner self-evaluation values were compared with the postscanning ratings for self-relatedness and craving. Spearmen correlation coefficients for the correlation of the intrascanner self-relatedness values with postscanning self-relatedness values were highly significant positive ($r=0.630$; $t(14)=3.765$; $p<0.01$) as well as the coefficients for the correlation with postscanning craving values ($r=0.616$ SD; $t(14)=3.574$; $p<0.01$). The correlation of postscanning self-relatedness values with postscanning craving values revealed a significant result, too ($r=0.848$; $t(14)=10.918$; $p<0.01$). Additionally, we correlated the mean postscanning values for self-relatedness and craving of each subject. Mean scores in craving correlated with mean scores in self-relatedness (Pearson correlation, $r=0.925$; $p<0.001$): the higher the scores in craving, the higher subjects scored the very stimuli with regard to self-relatedness (see Fig. 2B).

fMRI data

Recruitment of the reward system by self-relatedness

We first investigated the contrast reward win > reward lose and obtained significant signal changes in the right (16, 14, −8; $Z=4.00$, pFDR = 0.029) and left NACC (−24, 12, −12; $Z=3.67$, pFDR = 0.032), the left VMPFC (−2, 54, 14; $Z=3.61$, pFDR = 0.034) and the right VTA (14, −18, −16; $Z=3.74$, pFDR −0.032; see images on the left in Fig. 3) as well as in other regions, e.g., insula, temporal cortex, parietal cortex (see Table 1). In a second step, we plotted the fMRI signals in exactly these regions for four conditions, reward win, reward lose, high self and low self (see curves of the fMRI signal in the middle part of Fig. 3), and calculated their differences between conditions (see bar diagrams on the very right in Fig. 3). fMRI time courses did not only show significant differences between win and lose but also between high self and low self in the very same regions. Using a repeated measurements ANOVA with four levels of the factor task (reward win, reward lose, high self, low self) and three levels of the factor stimulus category we also checked whether signal changes in these regions were dependent on the stimulus type and did not obtain any significant result (i.e., no significant main effect and interaction). In order to demonstrate that our reward-based signal changes during self-relatedness were not due to non-specific cognitive–evaluative confounds, we directly compared fMRI signal changes from the ascertained reward regions during self-relatedness with those during the control condition. The exact results concerning the control task are presented in our Supplementary Fig. 1.

Distinction between early and late signal changes in the reward system

In order to further compare reward and self-relatedness, we analyzed the fMRI signal in reward-related regions with respect to two different time periods. Strength differences between conditions separately for early (4–8 s) and late (10–14 s) periods underwent a statistical analysis. We observed no significant differences between win–lose and high self–low self in the early period (4–8 s) in all four regions (right and left NACC, VMPFC, VTA). Whereas a significant difference was obtained in the late period (10–14 s) in the VTA as well as (being marginally significant) in the NACC and the VMPFC (see Fig. 4). The contrast high self > low self induced stronger signal strength differences in the late period in these regions when compared to the contrast win > lose.

Discussion

The central result of our study is that self-relatedness induces neural activity in exactly those regional foci, the NACC, the VMPFC and the VTA, that were recruited during reward. There was no difference between self-relatedness and reward in early signal changes whereas both conditions differed in late signal changes. This is the first study that investigates how self-relatedness modulates activity in reward structures and it therefore contributes to a better understanding of the reward-based nature of our self.

The NACC, the VMPFC and the VTA have been demonstrated to be crucially involved in coding the immediate value of stimuli,

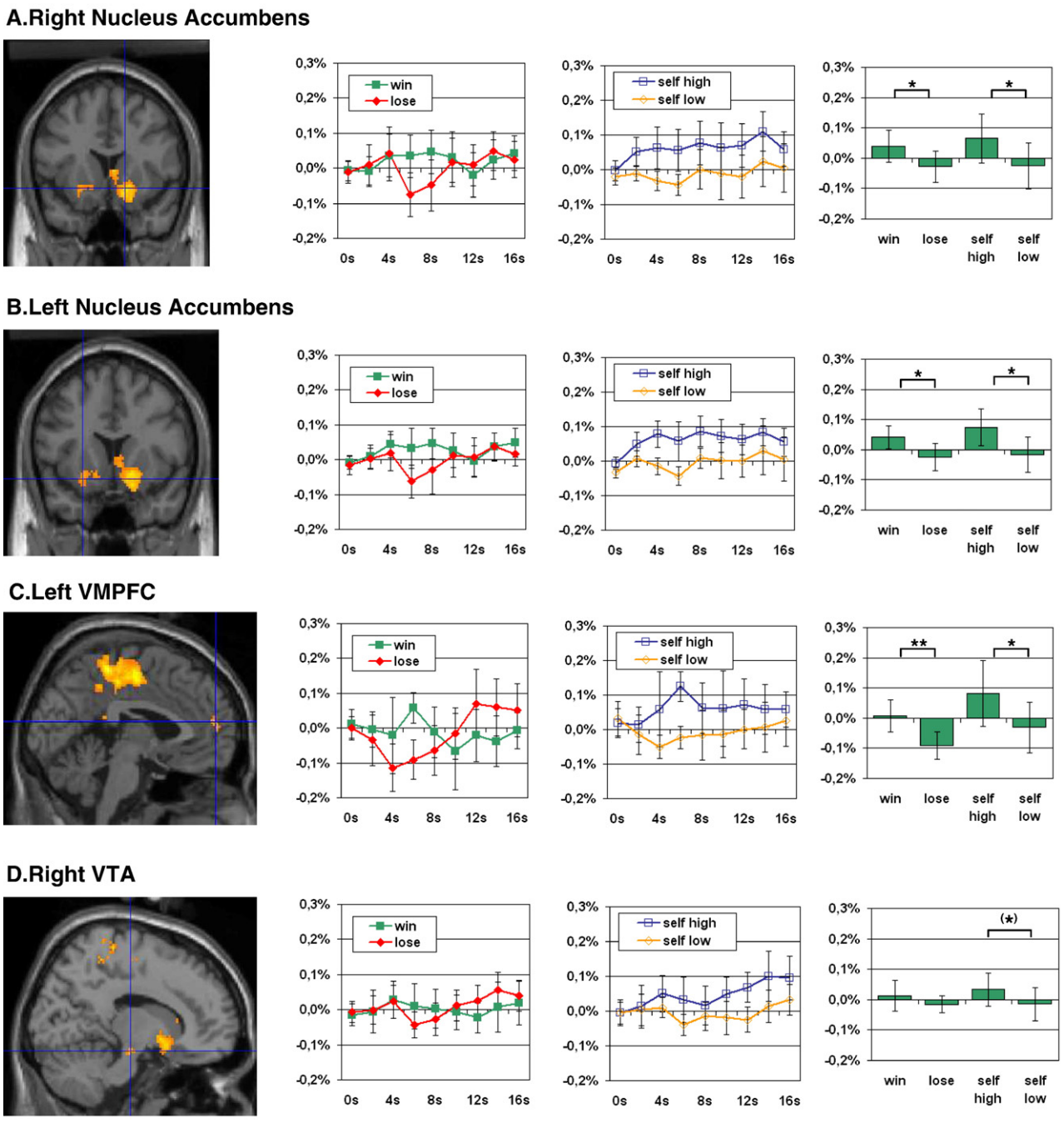

Fig. 3. Activation in reward regions during win, lose, high self and low self events. The second-level group statistic for the contrast reward win > reward lose revealed activations in the right and left nucleus accumbens, the left ventromedial prefrontal cortex (VMPFC) and the ventral tegmental area (VTA). The left picture of each line shows the t contrast calculated with SPM2. The two diagrams in the middle of each line show the mean normalized fMRI signal changes (y-axis) for the conditions gambling win, gambling lose, high self and low self (error bar: standard deviation) with $t=0$ for the start of the feedback phase. The box diagram on the right pictures the mean normalized fMRI values (y-axis) for the timepoints 4–8 s. (A) Right nucleus accumbens (16, 14, −8). We found a higher mean fMRI signal for reward win compared with reward lose ($t(14)=3.092$; $p=0.008$) and a higher mean fMRI signal for high self events compared with low self events ($t(14)=2.664$; $p=0.019$). (B) Left nucleus accumbens (−24, 12, −12). We found greater mean fMRI signals for reward win compared with reward lose ($t(14)=3.449$; $p=0.004$) and for high self compared with low self events ($t(14)=3.770$; $p=0.002$). (C) Left VMPFC (−2, 54, 14). Reward win events compared with reward lose event caused highly significant greater fMRI signal ($t(14)=5.320$; $p<0.001$). The comparison of high self compared with low self events was significant, too ($t(14)=2.724$; $p=0.016$). (D) Right VTA (14, −18, −16). The contrast of reward win and reward lose failed significance ($t(14)=1.669$; $p<0.112$). The comparison of high self compared with low self events revealed a statistical trend ($t(14)=1.941$; $p=0.073$) for a higher mean fMRI signal during high self events. Abbreviations: VTA = ventral tegmental area, VMPFC = ventromedial prefrontal cortex, *$p<0.05$, (*)$p<0.1$.

Table 1
Activations for the contrast [reward win] > [reward lose]

Region	x, y, z [mm][a]			Z	p (FDR)
Right nucleus accumbens	16	14	−8	4.00	0.029
Left nucleus accumbens	−24	12	−12	3.67	0.032
Left ventromedial prefrontal cortex	−2	54	14	3.61	0.034
Right ventral tegmental area	14	−18	−16	3.74	0.032
Right nucleus caudatus	10	18	8	4.01	0.029
Left nucleus caudatus	−22	26	8	3.93	0.030
Right insula	42	2	6	3.48	0.036
Left insula	−30	−30	14	3.55	0.035
Right superior temporal gyrus	54	−24	6	3.76	0.032
Right middle temporal gyrus	60	4	−12	3.63	0.033
Left superior temporal gyrus	−60	−6	−4	3.99	0.029
Right temporoparietal junction	56	−40	26	3.52	0.035
Left temporoparietal junction	−54	−40	20	3.90	0.030
Right medial parietal cortex	6	−32	60	5.08	0.027
Right lateral parietal cortex	62	−34	28	3.39	0.039
Right precentral gyrus	34	−18	48	4.67	0.027
Left posterior cingulate cortex	−6	−26	46	4.66	0.027
Right cerebellum	42	−72	−46	4.36	0.027
Left postcentral gyrus	−38	−30	38	3.98	0.029
Left thalamus	−14	−28	12	3.48	0.036

[a] Coordinates refer to the MNI stereotactic space.

the reward value (Berridge and Robinson, 2003; Breiter et al., 2001, Knutson et al., 2005, Knutson et al., 2001, 2003, 2005; Montague et al., 2006; Montague and Berns, 2002; Schultz, 2004; O'Doherty, 2004; O'Doherty et al., 2006; Schultz, 2006). Since we obtained signal changes during reward, e.g., the win–lose task, in exactly these regions, our results are well in accordance with these observation and an earlier study that employed a similar paradigm (Reuter et al., 2005). Most importantly, we demonstrated that self-relatedness induced neural activity in the reward system including the NACC, the VTA and the VMPFC. This is in accordance with previous studies on self-relatedness. The VMPFC has been associated with self-relatedness in numerous studies (Kelley et al., 2002; Northoff and Bermpohl, 2004; Phan et al., 2004, see Northoff et al., 2006 for an overview). One study also observed modulation of signal changes in the NACC and the VTA/Tectum by self-relatedness (Phan et al., 2004). Our results complement and extend these findings in that they demonstrate the involvement of those regional foci in self-relatedness that were recruited during reward. This indicates close relationship between reward and self which needs to be discussed in further detail.

In addition to reward, the NACC, the VTA and the VMPFC have also been demonstrated to be activated during salience (Zink et al., 2003, 2004, 2006) and product preference (Erk et al., 2002; Knutson et al., 2007; McClure et al., 2004; Paulus and Frank, 2003; Deppe et al., 2005). Similar to reward, salience and product preference implicate the value of the stimulus for the organism. The three regions have subsequently been considered to form what Montague et al. (2002, 2006) call a "valuation system". Such "valuation system" does not only code the stimulus immediate value, as in reward, but also its long-term value for the organism. The long-term value implicates self-relatedness since stimuli with high long-term value may show a higher degree of self-relatedness than those with low long-term value. One would consequently expect that self-relatedness induces neural activity in those regions that subserve the "valuation system". Our observation of activation in the NACC, the VTA, and the VMPFC suggests involvement of the "valuation system" in processing self-relatedness. This is further supported by the fact that self-relatedness induced neural activity in exactly those regional foci that were recruited during reward. However, future studies that compare self-relatedness with salience and product preference as well as investigation of the direct interaction between self-relatedness and reward are necessary to lend further support to the assumed involvement of the "valuation system" in self-relatedness.

Self-relatedness overlapped with reward in early signal changes in all three regions whereas both conditions differed in late signal changes. Self-relatedness induced higher signal changes in the late time course in the very same regions when compared to reward. These findings indicate that self-relatedness may be distinguished from reward by sustained neural activity. Sustained neural activity has been associated with increased requirements of temporal integration that reflects the need to process higher loads of information (McClure et al., 2004; Yarkoni et al., 2005; Dreher et al., 2006). Self-relatedness mirrors the stimulus' long-term value which, unlike their immediate value as in reward, requires integration with past information and possible future goal orientation implying higher information load. The assumption of higher information load is supported by our observation of longer reaction times in self-relatedness when compared to reward. What remains unclear however is whether the herein observed sustained neural activity can be reduced to this higher information load in self-relatedness. For that future studies that compare the effects of different information loads during both reward and self-relatedness on late signal changes would be necessary. The overlap of both conditions in early signal suggests that reward as mediated by the NACC may be implicated in early processing of self-relatedness. In contrast to early signal changes, reward and self-relatedness seem to dissociate in late signal changes. We found a stronger self contrast (i.e., high self–low self) in comparison with the reward contrast (i.e., win–lose) for the late phase of the fMRI signal, while there were no differences for the early phase. Since we however did not include an explicit temporal dimension in our paradigm, this assumption remains speculative. Future studies employing MEG/EEG and different fMRI designs are needed to lend further support to the presumed early involvement of reward in self-relatedness.

Our results should however be interpreted cautiously considering several methodological limitations. One could doubt the validity and reliability of our self-relatedness task and its distinction from reward. We tested for intrasubject reliability of self-relatedness by comparing intra- and postscanning measurements and observed a correlation that indicates high intrasubject reliability. However, similar to reward that contains distinct aspects like anticipation, omission etc., self-relatedness may include distinct components (representation, monitoring, evaluation, integration; see Northoff et al., 2006) which need to be tested and compared with reward in future studies.

Another issue concerns the fact that we did not test for the interaction between reward and self-relatedness in our paradigm. Our paradigm was designed to focus on clearly identifying reward-associated regions without any active self-evaluation component. Conversely, we aimed to introduce a self-evaluation task without any traces of a reward component. While both tasks concerned the same stimuli in order to exclude any potential pictorial confounds. This design allowed us best to test the hypothesis whether self-evaluation recruits neural activity in those regions that are involved in reward. Whereas this design did not allow us to test for any interaction effects between self-relatedness and reward. For that a

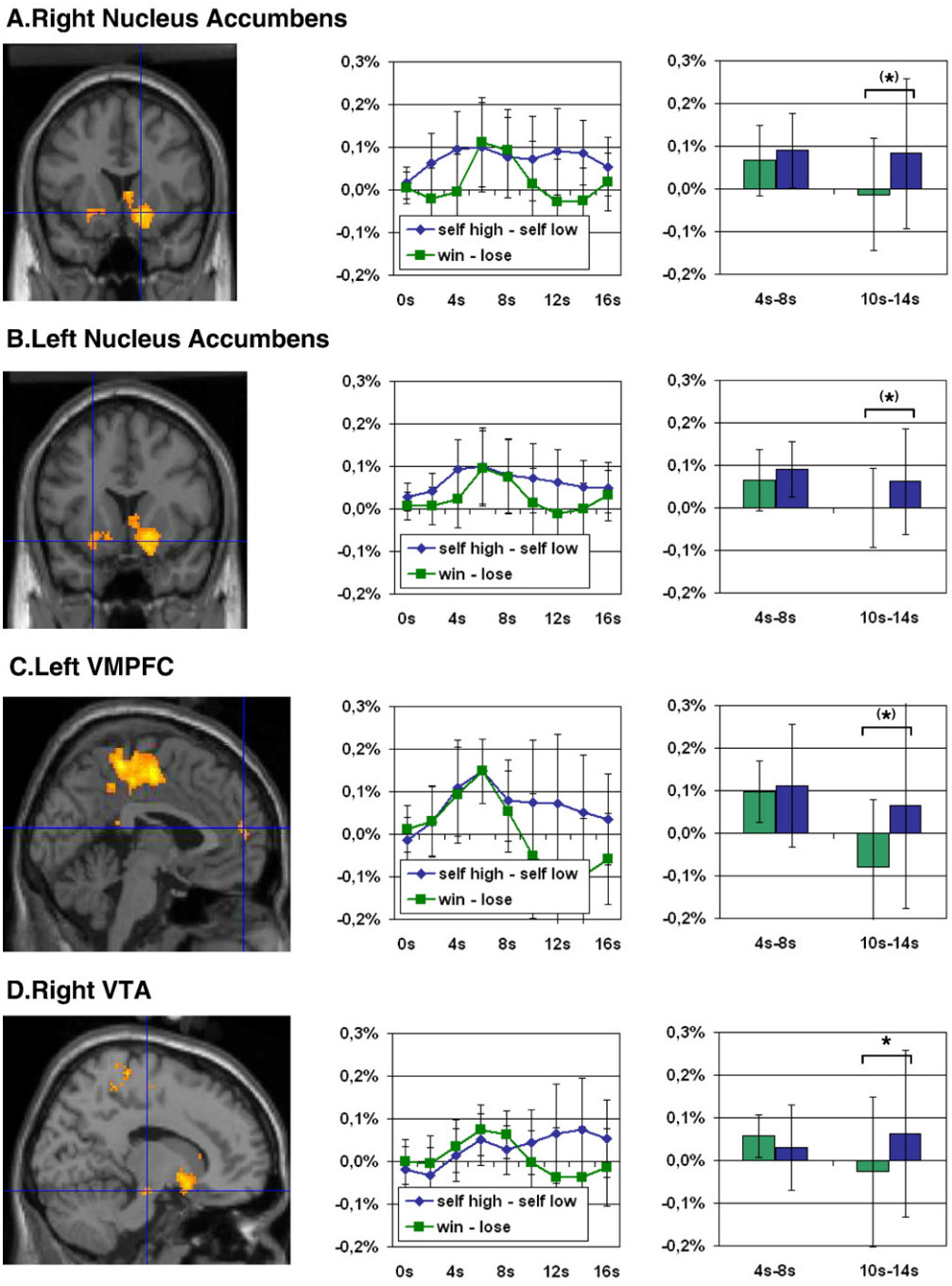

Fig. 4. Early and late fMRI signal changes in reward regions during reward and self events. The same regions introduced in Fig. 2 underwent a more detailed analysis with respect to different fMRI signal phases. Early (4 s to 8 s after feedback onset) and late (10 s to 14 s after feedback onset) differences of the mean normalized fMRI signal (*y*-axis) for the contrasts reward win–reward lose and high self –low self were examined with paired *t*-tests. (A) Right nucleus accumbens (16, 14, −8). While there was no significant difference between both contrasts in the early phase ($t(14)=0.903$; $p=0.382$), there was a statistical trend for a higher self contrast compared with the reward contrast ($t(14)=1.947$; $p=0.072$). (B) Left nucleus accumbens (−24, 12, −12). The comparison of the reward contrast and the self contrast failed significance for the early phase ($t(14)=1.158$; $p=0.266$). Again there was a statistical trend for a higher self contrast in the late phase ($t(14)=1.863$; $p=0.084$). (C) Left VMPFC (−2, 54, 14). We found the same pattern for this region. The comparison of the reward and self contrast revealed no significant result for the early period ($t(14)=0.319$; $p=0.754$) but there was statistical trend for a higher self contrast in the late phase ($t(14)=1.865$; $p=0.083$). (D) Right VTA (14, −18, −16). Again the comparison of both contrasts revealed no significant result for the early phase ($t(14)=0.534$: $p=0.602$). There were significant higher signal intensities in the self contrast when compared with the reward contrast ($t(14)=2.186$; $p=0.046$). Abbreviations: VTA = ventral tegmental area, VMPFC = ventromedial prefrontal cortex, *$p<0.05$, (*)$p<0.1$.

different design that includes a high and low reward component within the self-evaluation task would be needed.

One might criticize that reward and self-relatedness may differ in psychological regard. Our reward task implicated a decision phase and a subsequent feedback phase. While the decision phase was held identical for win and lose trials the feedback period differed significantly since the subjects were informed about win or lose. Our analysis with regard to the reward task hence focused on the feedback phase. Self-relatedness might in contrast already be induced in the anticipation phase when subjects are first confronted with the stimulus. While this does not affect the herein observed neuroanatomical overlap, one might argue that temporal differences between reward and self-relatedness might be due to such psychological differences. However, we did not directly compare means in the late BOLD effect between reward and self-relatedness but only within each task between win and lose as well as between high and low self-relatedness. Thus our study might be considered a starting point for future and more detailed investigation of differences in early and late BOLD effects in relation to the abovementioned psychological differences between reward and self-relatedness.

Another point to consider is that we cannot completely exclude some impact of reward even during the self-relatedness task because we used primary reinforcers, i.e., food, which subjects had to evaluate with regard to self-relatedness. Though we cannot exclude such reward–self interaction completely, our observation that neural effects of self-relatedness occurred in all three stimulus categories argues against this interpretation. However, to completely exclude reward–self interaction, a design using non-primary reinforcers would be needed.

Finally one might criticize that our concept of reward needs to be parsed into distinct aspects of reward as proposed by Berridge and Robinson (2003). Unfortunately our design does not allow us to clearly distinguish between the appetitive pre-consummatory aspects (what Berridge and Robinson (2003) call "wanting") on the one hand and hedonic consummatory aspects (what Berridge and Robinson (2003) call "liking") on the other for three reasons. First, since we indicated in the decision phase that subjects could either win or lose, the decision phase does not reflect exclusively appetitive pre-consummatory aspects but may also include anticipation of possible aversion or punishment. In other terms, our decision phase cannot be associated exclusively with appetitive pre-consummatory aspects ("wanting") because it may possibly be confounded by punishment. Second, we did not include temporal spacing between the decision and the feedback phases which makes it impossible to properly separate the respective signal changes from each other in fMRI analysis. Third, another confound consists in the fact that we included the picture (e.g., pictures with alcohol, food and gambling stimuli) in the decision phase. Since the picture itself might induce some potentially appetitive state, our decision phase might also be confounded by craving. Taken together, these confounds made it rather difficult to clearly assign a specific reward component to the decision phase. Due to these possible confounds in the decision phase, our focus was on the feedback phase where subjects were informed about possible reward (or punishment). The feedback phase implicates predominant hedonic consummatory aspects of reward which, similar to Reuter et al. (2005), were the main focus of our study. Future studies are necessary to better distinguish between appetitive pre-consummatory and hedonic consummatory aspects of reward and their possible implication in self-relatedness. On the one hand, one might for instance apply the monetary incentive delay task, as developed by the group around Knutson et al. (2001), in order to better account for appetitive pre-consummatory aspects and consequently for what has also been associated with seeking (Alcaro et al., 2007), while on the other hand, one might include temporal spacing between decision and feedback phases to better delineate appetitive pre-consummatory and hedonic consummatory aspects of reward. Accordingly, our study and its results set the stage for a more specific and refined analysis of reward processes and their possible involvement in self-relatedness.

In conclusion, we demonstrate that self-relatedness induces neural activity in exactly those regional foci, the NACC, VTA and VMPFC, that were recruited during reward. Self-relatedness overlapped with reward in early signal changes whereas self-relatedness differed from reward in late signal changes which might be interpreted as sustained neural activity. Taken together, our findings indicate regional involvement of reward in early processing of self-relatedness and thus, more generally, possible reward-based nature of our self as the organism's "valuation system."

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.neuroimage.2007.11.006.

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