Delineating self-referential processing from episodic memory retrieval: Common and dissociable networks

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ABSTRACT

Self-referential processing involves a complex set of cognitive functions, posing challenges to delineating its independent neural correlates. While self-referential processing has been considered functionally intertwined with episodic memory, the present study explores their overlap and dissociability.

Standard tasks for self-referential processing and episodic memory were combined into a single fMRI experiment. Contrasting the effects of self-relatedness and retrieval success allowed for the two processes to be delineated.

Stimuli judged as self-referential specifically activated the posterior cingulate/*anterior* precuneus, the medial prefrontal cortex, and an inferior division of the inferior parietal lobule. In contrast, episodic memory retrieval specifically involved the *posterior* precuneus, the right anterior prefrontal cortex, and a superior division of the inferior parietal lobule (extending into superior parietal lobule). Overlapping activations were found in intermediate zones in the precuneus and the inferior parietal lobule, but not in the prefrontal cortex.

While our data show common networks for both processes in the medial and lateral parietal cortex, three functional differentiations were also observed: (1) an anterior–posterior differentiation within the medial parietal cortex; (2) a medial–anterolateral differentiation within the prefrontal cortex; and, (3) an inferior–superior differentiation within the lateral parietal cortex for self-referential processing versus episodic memory retrieval.

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Introduction

Recently, self-referential processing (SRP) has received increasing interest in neuroimaging studies (Gillihan and Farah, 2005; Legrand and Ruby, 2009; Northoff and Bermpohl, 2004; Northoff et al., 2006). The heterogeneous nature of SRP, entailing a complex set of operations, poses significant challenges in identifying its specific neural correlates. Consistently, self-referential (relative to control) tasks induce increases in BOLD signals (hereafter, "activations") in the ventral (VMPFC) and dorsal medial prefrontal cortex (DMPFC) (extending into the anterior cingulate cortex (ACC)) as well as the medial and lateral parietal cortex (extending into temporal areas). Because this self-network is activated across different sensory modalities and cognitive domains (e.g., spatial, facial, emotional,

social) (Northoff et al., 2006), it could be assumed that distinct subregions within this network may correspond to specific processes involved in SRP. Investigators have recently started to disentangle these processes. For instance, they have studied SRP in relation to emotion processing (Moran et al., 2006; Northoff et al., 2009; Phan et al., 2004), theory of mind (Vogeley et al., 2001), inferential processing (Legrand and Ruby, 2009), reward processing (de Greck et al., 2008), realness (Summerfield et al., 2009) and sexual arousal (Heinzel et al., 2006).

Here we examine SRP in relation to episodic memory retrieval (EMR). There appears to be a theoretical consensus that SRP generally involves EMR; according to some authors, SRP and EMR are even intrinsically related (Conway and Pleydell-Pearce, 2000; Gardiner, 2001; James, 1892). Similar to EMR, SRP depends on the individual's life history and involves the recollection of past experiences. On the other hand, EMR seems to implicate reference to the self, as the retrieved episodic information is unique to an individual and is tied to a specific personal context (Craik et al., 1999; Ingvar, 1985; Tulving, 1983). Behaviorally, the link between SRP and EMR is reflected in the

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so-called self-reference effect of memory: encoding with reference to self yields superior memory performance relative to semantic or other-referential encoding (Rogers et al., 1977; Symons and Johnson, 1997). Further support for this link comes from neuroimaging investigations: EMR studies report activations in brain regions that are also identified by SRP tasks, again including the anterior and medial prefrontal cortex, as well as the medial and lateral parietal cortex (Donaldson et al., 2001; Fletcher et al., 1996; Henson et al., 2005; Konishi et al., 2000; McDermott et al., 2000) (for reviews see Cavanna and Trimble, 2006; Legrand and Ruby, 2009). Because these brain areas also show high neural activity during so-called rest conditions (i.e., conditions without externally focused tasks), both SRP and EMR have been considered components of the brain's default-mode network (Buckner et al., 2008).

Despite these commonalities, several lines of evidence indicate that SRP and EMR can be well distinguished: First, it is phenomenologically evident that besides retrieval, SRP requires reference to one's own person, i.e., reference to the person's self-concept (concerning physical and psychological traits), value system, motives, and internal goals among others (Zysset et al., 2002). Episodic memory processes, on the other hand, also concern the retrieval of events that are characterized by low self-relevance. Second, a series of priming experiments using trait adjectives as probes showed no impact of self-description (i.e., a form of SRP) on EMR and vice versa, indicating that one process does not automatically invoke the other (Kihlstrom and Klein, 1997). Third, some case studies in patients with retrograde amnesia following traumatic brain injury report a loss of EMR in combination with preserved self-description (Klein et al., 1996; Tulving, 1993), suggesting that both processes may, at least partially, be represented independently. Fourth, functional connectivity analyses of fMRI (functional magnetic resonance imaging) data suggest functional separation within the default-mode network, revealing two distinct subsystems, namely a medial temporal lobe subsystem associated with EMR and a medial prefrontal subsystem associated with SRP; both systems seem to converge on the medial and lateral parietal cortex (Buckner et al., 2008). Finally, functional neuroimaging studies suggest that functional specialization may exist within the medial parietal cortex: Cavanna and Trimble (2006) proposed a dissociation within the precuneus into an anterior region, involved in SRP and a posterior region, subserving EMR. Fig. 1 illustrates this dissociation based on studies reviewed by Cavanna and Trimble (2006).

Taken together, there is evidence for both functional overlap and dissociation between SRP and EMR. Because evidence provided so far is either indirect or relies on data from different imaging studies, the exact extent to which SRP and EMR depend on common and distinct brain regions remains unclear. The aim of the present study is to address this issue by combining standard tasks for both processes in one functional MRI (fMRI) experiment. Healthy volunteers were asked to perform both a self-referential and an episodic memory task in relation to each of 160 pictorial stimuli taken from the *International Affective Picture System* (IAPS) (Lang et al., 2005). The task demand thus remained the same, whereas self-relatedness and EMR varied across pictures. This allowed us to avoid confounds introduced by differences in task-related cues and task demands. For fMRI data analysis, picture trials were classified based on the participants' responses in the self-referential and episodic memory tasks, resulting in a 2×2 factorial design with the factors self-relatedness (self-referential, non-self-referential) and EMR (retrieved, non-retrieved). This allowed us to identify (1) the effect of SRP (self-referential > non-self-referential stimuli), (2) the effect of EMR (retrieved > non-retrieved stimuli), (3) common activations for SRP and EMR (conjunction of the two former contrasts), (4) SRP × EMR interaction effects, (5) activations specific for SRP relative to EMR (self-referential/non-retrieved > non-self-referential/retrieved), and (6) activations specific for EMR relative to SRP (retrieved/non-self-referential > non-retrieved/self-referential).
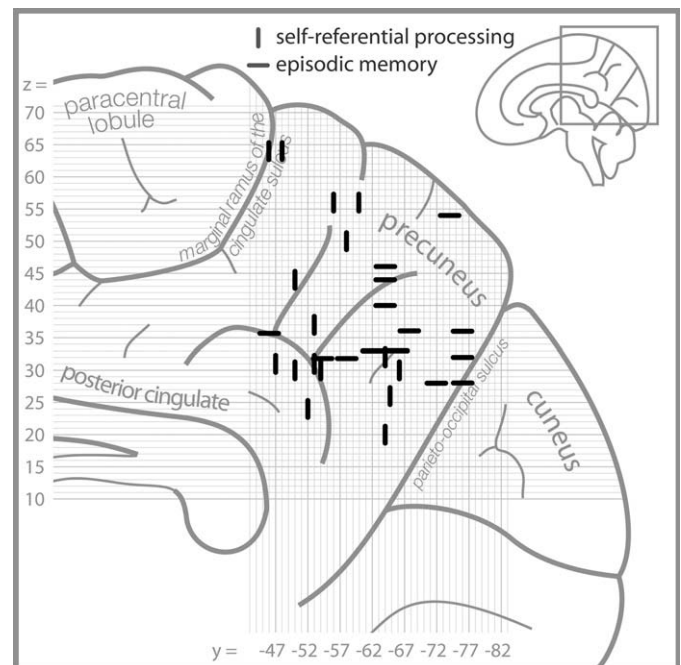

Fig. 1. Illustration of anterior–posterior functional differentiation within the precuneus. Talairach stereotactic coordinates reported by the studies listed in Cavanna and Trimble (2006) Table 3 (episodic memory) and Table 4 (self-referential processing) are depicted in horizontal and vertical bars, respectively.

Based on the studies reported above, we hypothesized that both processes, SRP and EMR, would recruit a common neural network including (1) the medial parietal cortex, (2) the anterior and medial prefrontal cortex, and (3) the lateral parietal cortex. Besides overlapping activations, we also predicted an anterior–posterior gradient within the medial parietal cortex with SRP stronger activating the anterior division and EMR stronger activating the posterior division.

Materials and methods

Subjects

Twenty-nine right-handed healthy volunteers (14 men, 15 women, aged 30–50 years, mean ± standard deviation (SD) = 39 ± 5.5 years, mean IQ = 118 ± 13.5 measured with the Mehrfachwahl-Wortschatz-Intelligenztest (MWT-B) (Lehrl, 2005)), gave written informed consent to participate in the experiment. Exclusion criteria were left-handedness, current limiting general medical conditions, current neurological disorder and history of psychiatric axis I or II disorders in the subjects (assessed with SCID I and II screening) or axis I disorder in a first-degree relative according to DSM IV. The subjects were remunerated for their time at a rate of €10/h. The study was in compliance with the Declaration of Helsinki and was approved by the local ethics committee of the Charité-Universitätsmedizin Berlin.

Experimental design

The experimental paradigm comprised three blocks conducted over three subsequent days: An encoding procedure, the fMRI experiment and a post-scanning rating session.

Experimental stimuli

One hundred sixty standardized non-erotic pictures were selected from the IAPS (Lang et al., 2005) so that the normative valence scores of the presented pictures (9-point rating scale from 1, very negative over 5, neutral to 9, very positive) were neutral to positive and the variance of normative valence and arousal (9-point rating scale) scores

was reduced to a minimum $(\text{mean}_{\text{valence}} \pm \text{SD}_{\text{valence}} = 7.0 \pm 0.55;$ $\text{mean}_{\text{arousal}} \pm \text{SD}_{\text{arousal}} = 5.0 \pm 0.49).$ The selected photographs were arranged in two picture sets consisting of 80 photographs matched for valence and arousal according to the IAPS norm (Lang et al., 2005). We selected IAPS pictures as stimulus material, because they have produced robust effects in previous SRP tasks (Gusnard et al., 2001; Northoff et al., 2009; Phan et al., 2004). We chose pictures of neutral to positive valence because pilot experiments and a prior study (Northoff et al., 2009) indicated that this type of material would produce a sufficient number of trials for both levels of self-relatedness, i.e., rated as 'self-referential' or 'non-self-referential' by the study participants.

Encoding procedure

For encoding, participants were presented with pictures from one of the two picture sets in a randomized order. Each of the 80 pictures was shown for 4 s followed by fixation cross lasting 2.5 s. Participants were instructed to memorize the pictures for a memory test on the next day and to indicate in a forced-choice task during the presentation of each picture whether it depicted an indoor or outdoor situation to promote elaborate encoding. During the encoding procedure subjects were unaware of the SRP task on the second day.

fMRI experiment

Twenty-four hours $(\pm 4 \text{ h})$ after the encoding session $(24 \pm 4 \text{ h})$ subjects performed the following experimental task during fMRI acquisition (Fig. 2). Each trial started with a picture viewing phase (4 s). Subsequently, two forced choice judgments were obtained from the participants in a SRP and EMR task for each stimulus. Question screens were presented in randomized order each lasting for 3 s. After the two judgments a fixation-cross period (range: 13.65–19.5 s; mean: 15.99 s) was shown prior to the next trial. The SRP task was assessed with the question "Does this picture personally relate to you?" For the EMR task the question "Is this picture familiar to you?" was presented and it was explained to the participants that this question referred to the picture set encoded the day before.

Participants responded with a "yes" or "no" button press with the left or right index finger, respectively. Debriefing after fMRI revealed that study participants had started to carry out the tasks implicitly during the period of picture presentation, i.e., prior to presentation of the question screens. Because the same two tasks were performed in response to each picture stimulus, implicit task processing during the picture period should not have affected the comparison between experimental conditions in our study. The paradigm consisted of four runs each comprising 40 trials. All 160 pictures (80 old and 80 new) were presented in a pseudorandomized order. Prior to scanning participants were familiarized with the paradigm in a training session.

Post-scanning rating session

One day after the fMRI experiment subjects rated all 160 pictures with regard to self-relatedness ("How much does the picture relate to you?"), emotional valence and arousal on a 9-point scale ranging from 1 (low personal association/valence/arousal) over 5 (medium) to 9 (high). In addition, participants indicated for each picture whether it spontaneously elicited an autobiographic memory (defined as both temporally and spatially unique events (Conway and Pleydell-Pearce, 2000)). These trials were not used for data analysis to avoid interference of autobiographic memory with the episodic memory task.

Behavioral data analysis

To examine recognition memory performance the pattern of trial distribution (i.e., number of trials, classified based on SRP and EMR judgments given in the scanner) was assessed using a $2 \times 2 \times 2$ (old vs. new picture $\times$ familiar vs. non-familiar judged $\times$ self vs. non-self judged) repeated measures ANOVA. Furthermore d'-values were calculated for every participant.

Paired t-tests were calculated to compare response times of the SRP task (RTself) and EMR task (RTmem).

The analysis of post-scanning ratings focused on trials with correct memory decisions (i.e., hits (old pictures judged as familiar) and
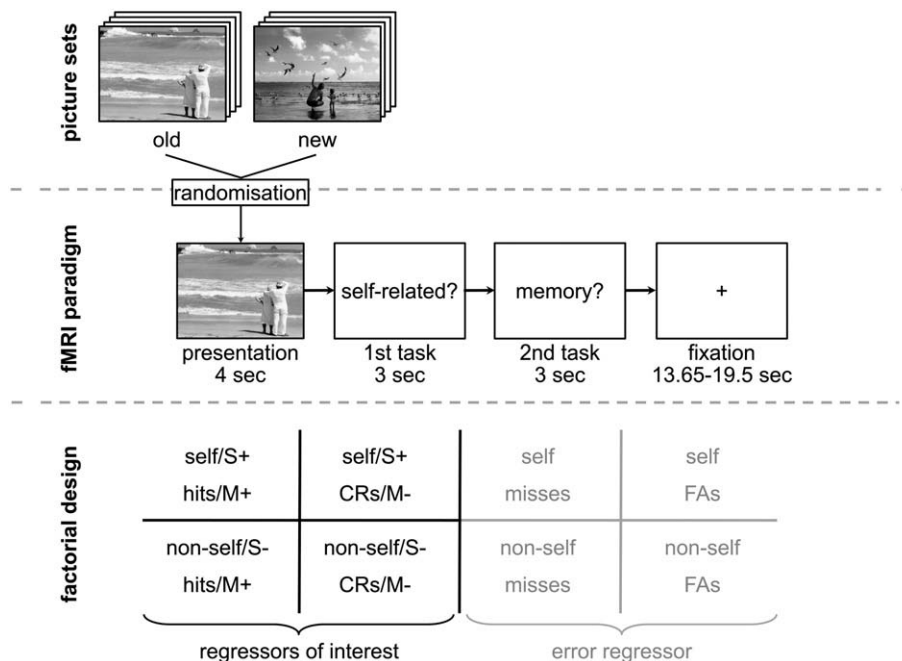

Fig. 2. Schematic of the fMRI paradigm: One day prior to MRI-scanning a set of 80 pictures was memorized by the participants (old pictures). During the fMRI paradigm 80 old and 80 new pictures were presented in pseudorandomized order followed by two forced choice tasks in randomized order: A self-task ("Does this picture relate to you?") and a memory task ("Is this picture familiar to you?") requiring a yes/no-button press. Each trial ended with a variable fixation period. Trials were classified based on the participants' responses resulting in a $2 \times 2 \times 2$ factorial design. fMRI and post-hoc rating data analysis focused on correct memory trials only. Hits (M+ = retrieved): old pictures judged as familiar; correct rejections (CRs = M− = non-retrieved): new pictures judged as non-familiar; misses: old pictures judged as non-familiar; false alarms (FAs): new pictures judged as familiar. Self = self-referential (S+); non-self = non-self-referential (S−).

correct rejections (CRs: new pictures judged as non-familiar)). Corresponding to fMRI data analysis trials with misses (old pictures judged as non-familiar) and false alarms (FAs: new pictures judged as familiar) were excluded resulting in a 2×2 factorial design with the factors SRP (self-referential vs. non-self-referential) and EMR (hits = retrieved vs. CRs = non-retrieved) (Fig. 2). Two-way repeated measures ANOVAs were calculated to examine post-scanning ratings of valence, arousal and self-relatedness.

fMRI data acquisition and preprocessing

T2*-weighted echo planar images (EPIs) sensitive to blood oxygen level dependent (BOLD) contrast were acquired on a 1.5 T Siemens (Erlangen, Germany) Sonata scanner with a repetition time (TR) of 1950 ms, an echo time (TE) of 40 ms and a flip angel of 90°. Thirty-five oblique axial slices aligned to the plane connecting the anterior and posterior commissure were collected with a voxel dimension of $3 \times 3 \times 3.5$ mm³ providing full brain coverage.

fMRI data was analyzed using the Statistical Parametric Mapping (SPM 5) software (Wellcome Department of Imaging Neurosciences, London, UK). Preprocessing included slice time correction, realignment to the mean volume, spatial normalization to a standard MNI template and spatial smoothing using a Gaussian kernel of FWHM = 8 mm. A 128 s high-pass filter was applied to the time series in each voxel to remove low-frequency drifts.

fMRI data analysis

Preprocessed fMRI data of each subject were then submitted to a two-level procedure. First, condition and subject effects were estimated using the general linear model (GLM) approach. The fMRI data analysis focused on trials with correct responses in the EMR task. These trials were assigned to experimental conditions based on the online judgments in the SRP and EMR tasks, resulting in a 2×2 factorial design (Fig. 2) with the factors SRP (self-referential = S+ versus/non-self-referential = S−) and EMR (hits = retrieved = M+ versus/CRs = non-retrieved = M−). The picture onsets of the resulting four conditions (S+/M+, S+/M−, S−/M+, S−/M−) were modeled as regressors of interest. Picture valence as rated by the subjects in the post-scanning session was included as a parametric regressor. Regressors of no interest were movement parameters, a run constant, regressors for left-hand and right-hand button press during the task period and an error regressor containing error trials in the memory task (FAs, misses). The regressors were convolved with a hemodynamic response function (HRF) provided by SPM5. The regressors were simultaneously regressed against the BOLD signal in each voxel using the least squares criteria, and contrast images were computed from the resulting parameter estimates.

For second-level random-effects analysis, the single-subject contrasts were submitted to one-sample *t*-tests across the 29 subjects. Statistical parametric maps were estimated for the contrasts self-referential > non-self-referential [(S+M+/S+M−) > (S−M+/S−M−)], retrieved > non-retrieved [(S+M+/S−M+) > (S+M−/S−M−)], the conjunction of the two former contrasts testing the conjunction null hypothesis (Friston et al., 2005), the SRP × EMR interaction [(S+M+ > S−M+) > (S+M− > S−M−)], self-referential > retrieved (S+M− > S−M+) and retrieved > self-referential (S−M+ > S+M−). Significant activations were identified at a threshold of $p < 0.001$ with a cluster extend $k \geq 20$ voxels (Hayasaka and Nichols, 2004).

In relation to the ongoing debate on a potential anterior–posterior division of the precuneus (Cavanna and Trimble, 2006) we examined the context-dependent neural interplay of anterior and posterior precuneus activations specific for SRP and EMR, respectively. Specifically, an antero-superior precuneus cluster derived from the contrast self-referential > retrieved (S+M− > S−M+) ($p < 0.001$, $k \geq 20$) and a postero-inferior cluster derived from the contrast retrieved > self-referential (S−M+ > S+M−) ($p < 0.001$, $k \geq 20$) were used as seed regions of interest for a functional connectivity analysis employing the psychophysiological interaction (PPI) term (Cohen et al., 2005; Cohen et al., 2008; Friston et al., 1997; Kahnt et al., 2009; Pessoa et al., 2002). For each of the two models, the entire time series over the experiment was extracted from each subject in the two clusters mentioned above. Regressors for the antero-superior cluster (SRP-specific model) were created by multiplying the normalized time series with two condition vectors that contain ones for six TRs after presentation of each self-referential (S+/M+ and S+/M−) and non-self-referential (S−/M+ and S−/M−) picture, respectively and zeros otherwise. For the postero-inferior cluster (EMR-specific model) regressors were created by multiplying the time series with two condition vectors that contain ones for six TRs after presentation of each retrieved (S+/M+ and S−/M+) and non-retrieved (S+/M− and S−/M−) picture, respectively. After estimation, individual contrast images were computed for functional connectivity during self-referential > non-self-referential [(S+M+/S+M−) > (S−M+/S−M−)] and retrieved > non-retrieved [(S+M+/S−M+) > (S+M−/S−M−)] trials. Individual contrast images were then entered into second-level one-sample *t*-tests. To identify significant functional connectivity, *t*-maps were thresholded at $p > 0.001$ and a cluster extent of $k \geq 20$ voxels.

Results

Behavioral data

Trial distribution and familiarity task performance

Pictures presented during scanning were classified based on the participants' responses in the SRP and EMR tasks as well as the
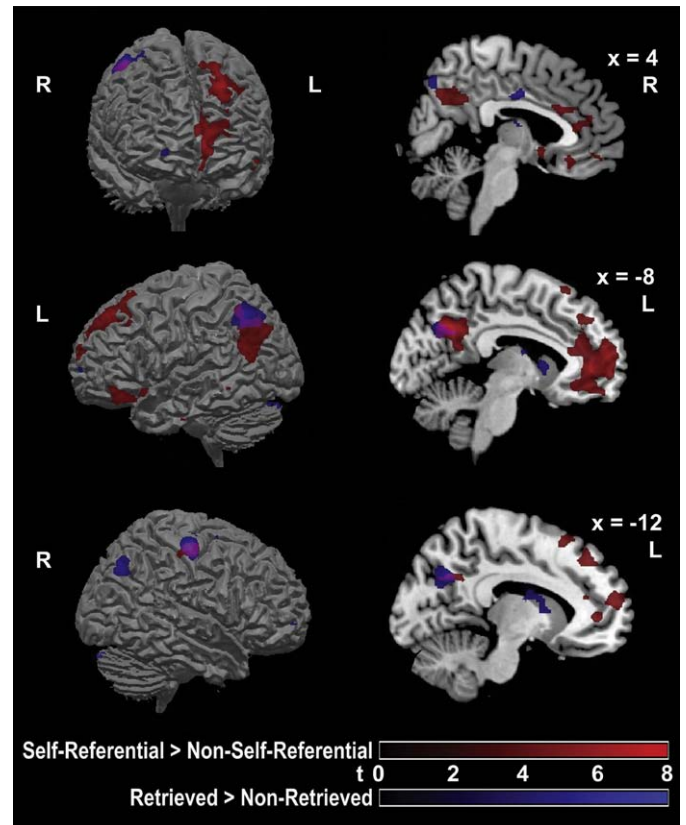
Fig. 3. Brain areas activated by the following contrasts: Red: 'self-referential > non-self-referential' [(S+M+/S+M−) > (S−M+/S−M−)]; blue: 'retrieved > non-retrieved' [(S+M+/S−M+) > (S+M−/S−M−)]; uncorrected p < 0.001, cluster size k ≥ 20. Overlapping areas are shown in violet. L = Left, R = Right, *t* = *t*-value. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

oldness of the pictures (Fig. 2). Analysis of the resulting number of trials per condition yielded a main effect for the factors SRP [$F(1,28) = 11.977$, $p = 0.002$] and familiarity [$F(1,28) = 13.016$, $p = 0.001$] with more pictures judged as non-self-referential and familiar, respectively [mean number of trials $\pm$ SD rated as self-referential: 67 ± 4; non-self-referential: 93 ± 20; familiar: 71 ± 13; non-familiar: 88 ± 13]. In addition, a strong oldness $\times$ familiarity interaction was found [$F(1,28) = 588.182$, $p < 0.001$] with old pictures predominantly judged as familiar, reflecting the participants' very good performance in the memory task [mean $d' \pm$ SD $= 2.07 \pm 0.6$]. We observed no main effect of oldness [$F(1,28) = 0.051$, $p = 0.823$], no SRP $\times$ familiarity interaction [$F(1,28) = 0.195$, $p = 0.662$], and no SRP $\times$ oldness interaction [$F(1,28) = 1.018$, $p = 0.322$].

Online response times

Response times were significantly longer in the SRP task (mean$_{RTself} \pm$ SD $= 1197 \pm 242$ ms) compared to the EMR task (1106 ± 218 ms; $t_{paired} = -4.96$, $p_{two-sided} < 0.001$).

Post-scanning self-relatedness ratings

Self-referential (according to SRP task) and retrieved pictures received clearly higher post-scanning self-relatedness ratings than non-self-referential and non-retrieved pictures, respectively [main effect for SRP: $F(1,28) = 234.919$, $p < 0.001$; EMR: $F(1,28) = 20.442$, $p < 0.001$; mean post-scanning self-relatedness rating $\pm$ SD for pictures judged as self-referential during fMRI: 5.5 ± 1.3; non-self-

referential: 2.7 ± 0.9; retrieved: 3.9 ± 1.0; non-retrieved: 3.6 ± 1.0]. The interaction [SRP $\times$ EMR: $F(1,28) = 0.159$, $p = 0.693$] was not significant.

Post-scanning valence ratings

Self-referential and retrieved pictures received higher post-scanning valence ratings than non-self-referential and non-retrieved pictures, respectively [main effect for SRP: $F(1,28) = 155.124$, $p < 0.001$; EMR: $F(1,28) = 31.398$, $p < 0.001$; mean valence rating $\pm$ SD for pictures judged as self-referential: 6.8 ± 0.8; non-self-referential: 5.4 ± 0.7; retrieved: 6.1 ± 0.7; non-retrieved: 5.8 ± 0.7]. The interaction [SRP $\times$ EMR: $F(1,28) = 0.119$, $p = 0.732$] was not significant.

Post-scanning arousal ratings

Post-scanning arousal ratings showed no significant main effects [SRP: $F(1,28) = 0.796$, $p = 0.38$; EMR: $F(1,28) = 1.984$, $p = 0.17$] nor an interaction [SRP $\times$ EMR: $F(1,28) = 3.038$, $p = 0.092$].

fMRI data

Self-referential > non-self-referential

To assess the main effect of SRP, we contrasted self-referential with non-self-referential trials [(S+M+/S+M−) > (S−M+/S−M−)]. This contrast revealed clusters of activation in the medial prefrontal cortex (DMPFC and VMPFC extending into ACC and lateral prefrontal cortex), the medial parietal cortex (posterior cingulate cortex (PCC)/retrosplenial cortex and precuneus), the inferior parietal lobule extending

Table 1
Contrasts 'self-referential > non-self-referential' and 'retrieved > non-retrieved'.

Anatomical region	BA	k	T	Peak (x, y, z)		
Self-referential > non-self-referential:						
(S+M+/S+M−) > (S−M+/S−M−)						
L>R DMPFC, VMPFC: medial frontal gyrus, ACC	10, 9, 32, 24, 33	2033	6.53*	−6	46	2
R subgenual ACC	25	28	4.47	4	8	−8
L DLPFC: superior frontal gyrus, middle frontal gyrus	8, 9	1351	7.58*	−22	34	44
L DLPFC: middle frontal gyrus, inferior frontal gyrus	9	24	3.93	−40	10	38
L VLPFC: inferior frontal gyrus	47	405	5.32*	−44	32	−14
R precentral gyrus, postcentral gyrus	4, 3	290	5.88*	44	−16	56
L>R precuneus, PCC	31, 7, 23, 30	1237	7.58*	−4	−60	34
L inferior parietal lobule, superior temporal gyrus, middle temporal gyrus	39, 40, 22, 21	1020	5.45*	−52	−58	26
L inferior temporal gyrus	20	29	4.13	−62	−14	−30
L middle temporal gyrus	21	20	3.75	−60	−48	−6
R caudate head and body		44	4.41	14	16	4
Retrieved > non-retrieved:						
(S+M+/S−M+) > (S+M−/S−M−)						
R aPFC: superior frontal gyrus	10	47	4.41	28	58	0
L aPFC: superior frontal gyrus, middle frontal gyrus	10	22	3.77	−28	62	4
L DLPFC: middle frontal gyrus	46	20	3.65	−42	40	18
R mid-cingulate cortex	24	78	5.46*	6	−8	36
L precentral gyrus, middle frontal gyrus	4, 6	36	3.70	−34	10	48
R precentral gyrus, postcentral gyrus,	4, 3, 6	549	7.18*	42	−18	56
R postcentral gyrus, precentral gyrus	3, 4	33	4.00	32	−36	62
R premotor cortex: middle frontal gyrus	6	47	4.49	36	2	64
R precuneus	7, 31	559	6.62*	18	−62	28
L precuneus	7, 31	263	5.13	−10	−64	32
R inferior parietal lobule, superior parietal lobule	7, 19, 39, 40	267	5.34*	38	−70	44
L inferior parietal lobule, superior parietal lobule	40, 7, 39	856	6.33*	−42	−60	44
R cerebellum: tuber, uvula, declive		67	4.70	34	−68	−34
R cerebellum: declive, uvula		193	5.98*	12	−80	−26
L cerebellum: culmen, declive		121	4.48	−22	−54	−30
L caudate head and body		305	4.86	−12	−2	20
R caudate head and body		302	5.76*	12	10	8
L putamen		45	5.05	−16	6	−12

Maximum t-values and peak voxel coordinates for activation clusters, uncorrected $p = 0.001$, $k \geq 20$; * activations with asterisked t-values survive FWE-correction at 0.05. Anatomical regions and BAs sorted in descending order according to their proportion of the cluster. Following Van Hoesen et al. (1993) we regard BA 31 as a transition zone that belongs to both PCC and precuneus.
BA = Brodmann area, k = cluster size, t = t-value, L = Left, R = Right, ACC = anterior cingulate cortex, aPFC = anterior prefrontal cortex, DLPFC = dorsolateral prefrontal cortex, DMPFC = dorsomedial prefrontal cortex, PCC = posterior cingulate cortex, VMPFC = ventromedial prefrontal cortex, VLPFC = ventrolateral prefrontal cortex.
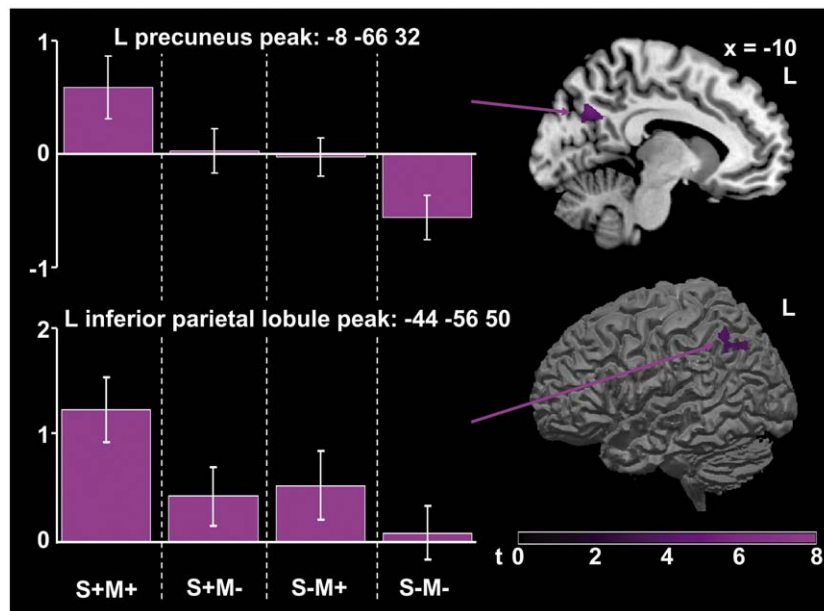
Fig. 4. Brain areas detected by the conjunction analysis testing the conjunction null hypothesis of the contrasts 'self-referential > non-self-referential' [(S+M+/S+M−) > (S−M+/S−M−)] and 'retrieved > non-retrieved' [(S+M+/S−M+) > (S+M−/S−M−)]; uncorrected p<0.001. Bar graphs illustrate parameter estimates (±standard error of the mean) of each condition averaged for the 29 subjects in arbitrary units for the peak voxels indicated. L=Left, R=Right, t=t-value.

into superior and middle temporal gyrus and further regions (Fig. 3 and Table 1).

Retrieved > non-retrieved

The contrast 'retrieved > non-retrieved' [(S+M+/S−M+) > (S+M−/S−M−)] identified the main effect of EMR success. Clusters of activation included among others the bilateral anterior prefrontal cortex (aPFC), the precuneus and the superior and inferior parietal lobule (Fig. 3 and Table 1). Fig. 3 illustrates that the main effects of SRP and successful EMR revealed partly overlapping and partly dissociable activations in the medial and lateral parietal cortex.

Conjunction analysis

To further explore the overlap between SRP and EMR success, we conducted a conjunction analysis testing the conjunction null hypothesis of the contrasts 'self-referential > non-self-referential' [(S+M+/S+M−) > (S−M+/S−M−)] and 'retrieved > non-retrieved' [(S+M+/S−M+) > (S+M−/S−M−)]. This analysis revealed activations in the left precuneus and the left inferior parietal lobule (Fig. 4 and Table 2). Effects observed in right sensorimotor areas were most likely related to the preparation of the button response given by the participants during the experiment (left hand responded to both self-related and familiar pictures; right hand responded to non-self-related and non-familiar pictures).

Interaction effect

We found no significant SRP × EMR interaction effect [(S+M+ > S−M+) > (S+M− > S−M−)].

Self-referential > retrieved

To dissociate SRP from EMR and identify specific effects of SRP, we contrasted self-referential with retrieved trials (S+M− > S−M+). Among other regions, this contrast revealed significant activations in the medial prefrontal cortex (DMPFC/VMPFC extending into ACC and lateral prefrontal cortex), the medial parietal cortex (PCC, anterior superior portion of the precuneus) and the inferior division of the inferior parietal lobule extending into the superior and middle temporal gyrus (Fig. 5 and Table 3).

The contrast 'self-referential > retrieved' (S+M− > S−M+) may reveal both activation related to SRP and deactivation related to EMR. To determine the contribution of each of the two processes to the observed differential effect, each condition was separately compared to baseline (bar graphs in Fig. 5). This analysis showed that differential effects were mainly related to increased signal intensities during SRP rather than decreased signal intensities during EMR. In the MPFC, both effects seem to contribute to the differential effect observed.

Retrieved > self-referential

To dissociate EMR from SRP and to identify specific effects of EMR, we contrasted retrieved with self-referential (S−M+ > S+M−) trials. This contrast revealed activations in the right aPFC, the posterior inferior portion of the right precuneus, the superior parietal lobule and the superior division of the inferior parietal lobule (Fig. 5 and Table 3).

Baseline comparisons showed that these differential effects were mainly related to increased signal intensities during EMR rather than decreased signal intensities during SRP (bar graphs in Fig. 5).

Table 2
Conjunction: self-referential > non-self-referential ∩ retrieved > non-retrieved: (S+M+/S+M−) > (S−M+/S−M−) ∩ (S+M+/S−M+) > (S+M−/S−M−).

Anatomical region	BA	k	t	Peak (x, y, z)		
R precentral gyrus, postcentral gyrus	4, 3	239	5.88*	44	−16	56
L precuneus	7, 31	151	5.08	−8	−66	32
L inferior parietal lobule	40, 39	198	4.11	−44	−56	50
R caudate head and body		26	4.25	14	16	4

Maximum t-values and peak voxel coordinates for activation clusters, uncorrected p=0.001, k≥20; * activations with asterisked t-values survive FWE-correction at 0.05. Anatomical regions and BAs sorted in descending order according to their proportion of the cluster. BA=Brodmann area, k=cluster size, t=t-value, L=Left, R=Right.
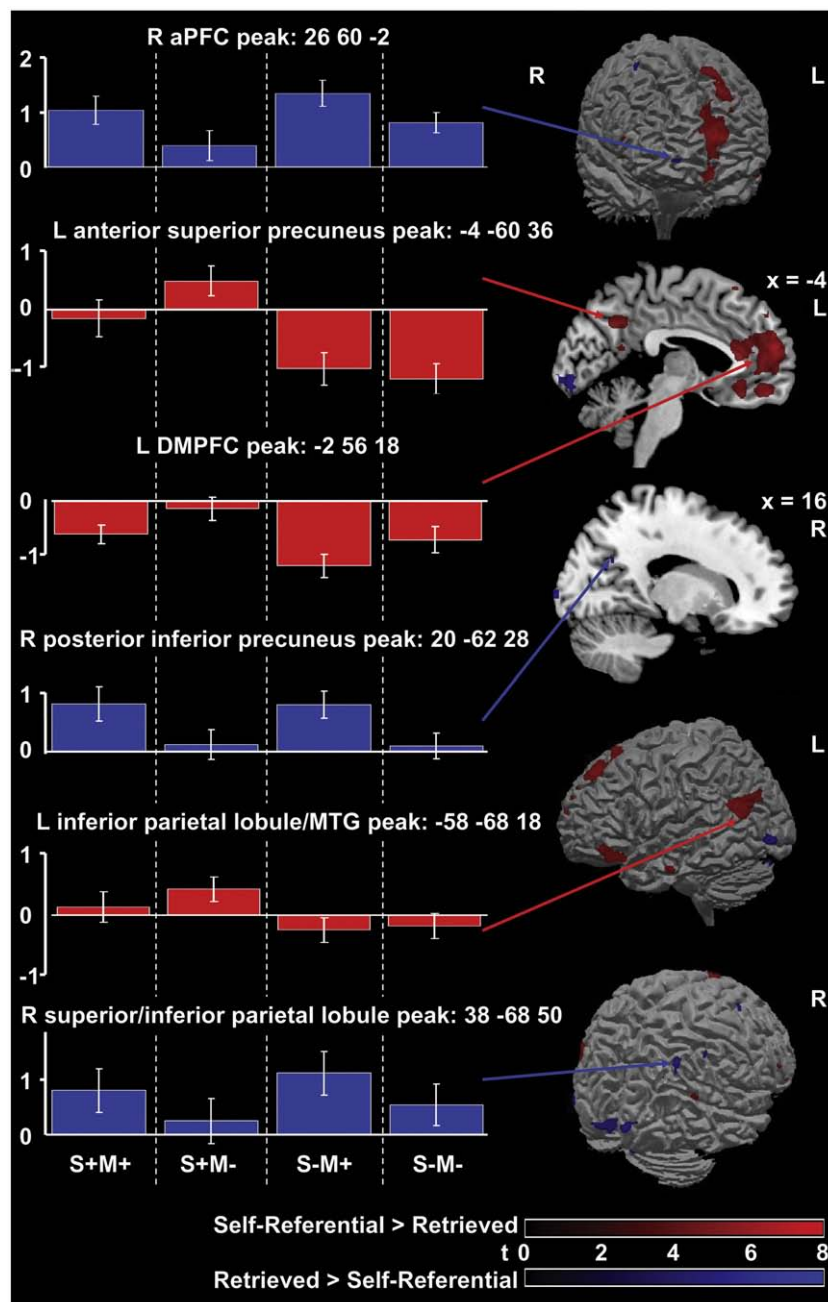
Fig. 5. Brain areas activated by the following contrasts: Red: 'self-referential > retrieved' (S+M− > S−M+); blue: 'retrieved > self-referential' (S−M+ > S+M−); uncorrected $p < 0.001$, cluster size k ≥ 20. Bar graphs illustrate parameter estimates (± standard error of the mean) of each condition averaged for the 29 subjects in arbitrary units for the peak voxels indicated. aPFC = anterior prefrontal cortex, DMPFC = dorsomedial prefrontal cortex, MTG = middle temporal gyrus, L = Left, R = Right, t = t-value. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

Functional connectivity analyses (PPI)

SRP and EMR produced partly dissociable (Fig. 5) activations in the precuneus. If regional dissociation reflects functional dissociation, functional connectivity should differ between precuneus portions specifically associated with SRP and EMR. We performed a PPI analysis using the precuneus clusters identified in the contrasts 'self-referential > retrieved' (hereafter self cluster) and 'retrieved > self-referential' (hereafter memory cluster) as seed regions. Activity in the self cluster correlated with activations in the medial premotor cortex (BA 6), left dorsal ACC (BA 33), fusiform gyrus (BA 37), and superior parietal lobule (BA 7) during self-referential > non-self-referential stimulus processing (Fig. 6 and Table 4). In contrast, activity in the memory cluster was associated with the responsiveness in a distinct region in the left dorsal anterior paracingulate cortex (BA 32, 6) during successful EMR (Fig. 6 and Table 4).

Discussion

The present data suggest common and dissociable networks for SRP and EMR. Three main findings concern (1) the medial parietal cortex (PCC, precuneus), (2) the prefrontal cortex, and (3) the lateral parietal cortex (Fig. 7). More specifically, self-referential stimuli specifically activate the PCC/*anterior* precuneus, the ventral and dorsal medial prefrontal cortex (extending into the ACC), and an inferior division of the inferior parietal lobule extending into the superior and middle temporal gyrus. In contrast, EMR success specifically involves the *posterior* precuneus, the aPFC, and a superior division of the inferior parietal lobule extending into the intraparietal sulcus and the superior parietal lobule. Overlapping activations can be found in intermediate zones in the precuneus and the inferior parietal lobule, but not in the prefrontal cortex.

Table 3
Contrasts 'self-referential > retrieved' and 'retrieved > self-referential'.

Anatomical region	BA	k	t	Peak (x, y, z)		
Self-referential > retrieved: (S+/M−) > (S−/M+)						
L > R DMPFC, VMPFC: medial frontal gyrus, ACC, superior frontal gyrus	10, 32, 9, 24, 33	2275	7.01*	−2	56	18
bilateral subgenual ACC	25	55	4.57	2	10	−12
L DLPFC: middle frontal gyrus	9	117	5.22	−28	28	36
L VLPFC: inferior frontal gyrus, middle frontal gyrus	47	230	4.86	−48	30	−16
R VLPFC: inferior frontal gyrus	47	29	3.78	44	32	−16
R VLPFC extending into DLPFC: inferior frontal gyrus	45, 46	31	4.15	54	26	12
R VLPFC: inferior frontal gyrus	47, 45	21	4.27	58	32	0
L FEF, premotor cortex: superior frontal gyrus	8, 6	574	5.97*	−16	42	48
L PCC	23, 30	25	4.28	−6	−54	18
L>R anterior superior precuneus	7, 31	199	4.91	−4	−60	36
L inferior division of inferior parietal lobule, superior temporal gyrus, middle temporal gyrus	39, 22, 40, 21	448	5.56*	−58	−68	18
R inferior division of inferior parietal lobule, superior temporal gyrus	39, 22	46	3.97	48	−62	24
L middle temporal gyrus, inferior temporal gyrus	21, 20	48	4.32	−60	−10	−22
R parahippocampal gyrus, fusiform gyrus	37, 36	38	3.76	34	−42	−12
L substantia nigra, red nucleus		24	3.84	−8	−20	−12
Retrieved > self-referential (S−/M+) > (S+/M−)						
R aPFC: superior frontal gyrus	10	29	4.35	26	60	−2
L precentral gyrus, middle frontal gyrus	6, 4	21	3.85	−24	−18	56
R premotor cortex: middle frontal gyrus	6	31	4.27	36	2	64
R posterior inferior precuneus	31	46	4.38	20	−62	28
R superior parietal lobule, superior division of inferior parietal lobule	7, 19, 39	75	4.42	38	−68	50
R inferior parietal lobule	40	29	4.06	36	−50	40
R superior division inferior parietal lobule	40	31	3.90	48	−50	52
bilateral lingual gyrus, cuneus	17, 18	288	4.72	−4	−92	−6
L middle occipital gyrus, inferior occipital gyrus	19, 18	81	4.74	−44	−88	−4
R cuneus, middle occipital gyrus	18	71	4.87	18	−102	4
R cerebellum: declive		44	4.53	10	−82	−26

Maximum t-values and peak voxel coordinates for activation clusters, uncorrected p = 0.001, k ≥ 20; * activations with asterisked t-values survive FWE-correction at 0.05. Anatomical regions and BAs sorted in descending order according to their proportion of the cluster.
BA = Brodmann area, k = cluster size, t = t-value, L = Left, R = Right, ACC = anterior cingulate cortex, aPFC = anterior prefrontal cortex, DLPFC = dorsolateral prefrontal cortex, DMPFC = dorsomedial prefrontal cortex, FEF = frontal eye field, PCC = posterior cingulate cortex, VLPFC = ventrolateral prefrontal cortex, VMPFC = ventromedial prefrontal cortex.

Extending earlier work on SRP and EMR, the present fMRI study combines standard tasks for both domains in one experiment. This approach permits reference to one study population, matching of task demands between conditions, and fMRI data processing in one and the same analysis (guaranteeing identical preprocessing steps, templates, statistical tests, and thresholds). As a result, this allows a more direct and detailed identification of common and dissociable activations for both processes. Most notably, besides the conventional comparisons ('self-referential versus non-self-referential', retrieval success contrast), our study design allows the contrast 'self-referential/non-retrieved versus non-self-referential/successfully retrieved'. Thus subtracting the effects of EMR from SRP (and vice versa), we are able to delineate the neural correlates of SRP from EMR (and vice versa).

The finding of shared activations confirms our hypothesis of commonalities between SRP and EMR which was proposed based on theoretical considerations (Conway and Pleydell-Pearce, 2000; Gardiner, 2001; James, 1892), behavioral experiments (self reference effect; Rogers et al., 1977; Symons and Johnson, 1997), functional connectivity MRI (Buckner et al., 2008), and review of functional neuroimaging studies investigating each domain separately (Cavanna and Trimble, 2006; Gillihan and Farah, 2005; Legrand and Ruby, 2009; Northoff and Bermpohl, 2004; Northoff et al., 2006). The identified areas in the medial parietal cortex (precuneus) and inferior parietal lobule are anatomically and functionally connected and are both considered components of the default-mode network (Buckner et al., 2008).

Medial parietal cortex

Extending previous work, our study suggests a functional segregation within the PCC/precuneus for SRP and EMR, respectively:

SRP induces significantly larger activations relative to EMR in the PCC and anterior (and superior) precuneus, whereas EMR is associated with significantly larger activations relative to SRP in the posterior (and inferior) precuneus. Further support for such functional dissociation comes from our functional connectivity analysis using precuneal portions specific for SRP and EMR, respectively, as seed regions: Activity in the SRP-related seed in the PCC/anterior precuneus correlates with the medial premotor cortex (BA 6), dorsal ACC (BA 33), fusiform gyrus (BA 37), and superior parietal lobule (BA 7) during SRP. In contrast, activity in the EMR-related seed in the posterior precuneus is associated with the responsiveness in a distinct region in the dorsal anterior paracingulate cortex (BA 32, 6) during EMR. The observed dissociation within the PCC/precuneus confirms the hypothesis derived from functional neuroimaging studies investigating SRP and EMR in separate experiments (Fig. 1 and Cavanna and Trimble, 2006).

Recently, anterior–posterior differentiation within the PCC/precuneus has also been suggested based on studies not related to SRP: First, cytoarchitectonic maps demonstrate a distinction between PCC and precuneus as well as subdivisions within the precuneus (Economo and Koskinas, 1925; Scheperjans et al., 2008). Second, tract tracing studies in the macaque (Kobayashi and Amaral, 2007; Leichnetz, 2001) show that these cytoarchitectonic differences reflect differences in anatomical connectivity. While the PCC has strong reciprocal connections with the medial temporal lobe, the medial and lateral prefrontal cortex, the superior parietal cortex (BA 7), and the precuneus, the precuneus has strong reciprocal connections with occipital and parietal areas linked to visual processing and frontal areas associated with motor planning. Third, based on resting state studies and functional connectivity results, it has been suggested that
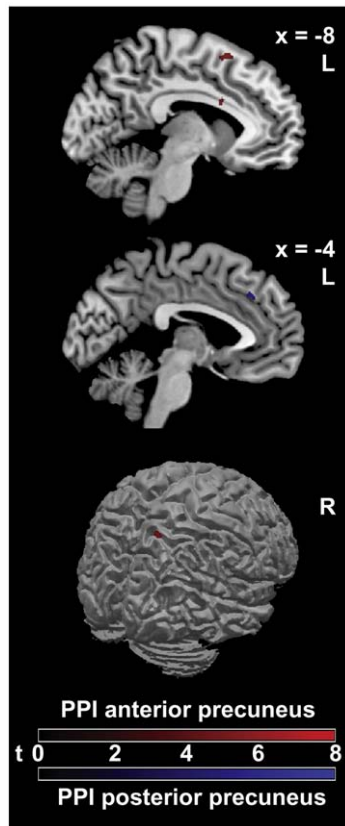
Fig. 6. Brain areas detected by two connectivity analyses (psychophysiological interaction, PPI): Red: activity in the contrast 'self-referential > non-self-referential' [(S+M+/S+M−) > (S−M+/S−M−)] correlated with the SRP-specific seed cluster in the anterior precuneus (peak −4 −60 36); blue: activity in the contrast 'retrieved > non-retrieved' [(S+M+/S−M+) > (S+M−/S−M−)] correlated with the EMR-specific seed cluster in the posterior precuneus (peak 20 −62 28); uncorrected p<0.001, cluster size k≥20. L=left, t=t-value. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

the posterior precuneus is not part of the default-mode network, whereas the PCC is (Buckner et al., 2008). Fourth, neuroimaging studies show that different aspects of EMR are represented in distinct regions within the PCC/precuneus: The posterior precuneus is associated with EMR success in general (independent of imageable characteristics (Schmidt et al., 2002) or contextual detail (Henson et al., 1999; Yonelinas et al., 2005)) and, in particular, with mnemonic visual information processing (Cavanna and Trimble, 2006), which is consistent with the co-activation of visual areas during EMR success in our study. In contrast, the PCC/anterior precuneus is linked to specific aspects of EMR, including memory-related imagery (Fletcher et al., 1995), recollection of contextual details (Henson et al., 1999; Yonelinas et al., 2005), retrieval of previous self-referential judgments

(Lou et al., 2004), and autobiographical memory (Burianova and Grady, 2007). Our findings may help to qualify the function of the PCC/ anterior precuneus in these tasks.

Medial and anterior prefrontal cortex

Our data also reveal a functional segregation between the medial and anterior prefrontal cortex: SRP induces significantly larger activations in the medial prefrontal cortex relative to EMR, whereas EMR is associated with significantly larger activations in the lateral aPFC relative the SRP. These findings are consistent with earlier neuroimaging studies examining both processes in separate paradigms: The VMPFC has been linked to emotional and representational aspects and the DMPFC to cognitive and evaluational aspects of self-referential stimulus processing (Amodio and Frith, 2006; Northoff and Bermpohl, 2004; Zysset et al., 2002), whereas the bilateral aPFC has been associated with EMR success (McDermott et al., 2000), control processes related to EMR (King et al., 2005), and retrieval mode (Velanova et al., 2003). Combining both processes in one experiment, our data extend these earlier studies: First, both conjunction analysis and overlay of main contrasts for SRP and EMR suggest that there is no functional overlap between the prefrontal clusters engaged in SRP and EMR, respectively. Second, specification of BOLD effects (baseline comparisons, Fig. 5) indicates that involvement of EMR does not enhance (but rather attenuates) SRP-related signals in the medial prefrontal cortex; and involvement of SRP does not enhance (but rather attenuates) EMR-related signals in the aPFC. Consequently, we find no interaction between SRP and EMR in the prefrontal cortex.

The observed functional dissociation is consistent with data from functional connectivity MRI studies suggesting that the medial prefrontal cortex and the bilateral aPFC belong to separate networks, associated with internally directed (i.e., self-referential) cognitive processes and cognitive control processes (e.g., tracking performance on detection tasks like our EM task), respectively (Vincent et al., 2008). Our finding is also of interest in light of earlier studies associating the medial prefrontal cortex with autobiographical memory retrieval (Gilboa, 2004; Svoboda et al., 2006), retrieval of self-referential episodes (Zysset et al., 2002), retrieval of self-generated versus externally presented words (Vinogradov et al., 2008), and the self-reference effect of memory (Macrae et al., 2004). These processes have in common that they involve self-referential and memory components at the same time. Our data seem to suggest that the self-referential component particularly contributes to medial prefrontal activations observed in these studies.

Lateral parietal cortex

We find lateral parietal activations during both SRP and EMR. This is in accordance with earlier studies, linking the lateral parietal and adjacent temporal cortex to SRP (in particular, first-person perspective

Table 4
PPI: activations correlated with self-referential and retrieved seed region in the precuneus.

Anatomical region	BA	k	t	Peak (x, y, z)		
PPI self-referential seed region in anterior precuneus (peak: −4 −60 36)						
L dorsal ACC	33	20	4.46	−8	12	26
L premotor cortex: superior frontal gyrus	6	60	4.76	−10	14	60
L premotor cortex: medial frontal gyrus	6	36	5.10	−14	−8	58
R superior parietal lobule	7	46	6.03	14	−66	56
R fusiform gyrus	37	36	4.41	40	−54	−16
PPI retrieved seed region in posterior precuneus (peak: 20 −62 28)						
L dorsal anterior paracingulate	32, 6	43	4.94	−4	34	36

Maximum t-values and peak voxel coordinates for activation clusters, uncorrected p=0.001, k≥20. BA=Brodmann Area, k=cluster size, t=t-value, L=Left, R=Right, ACC=anterior cingulate cortex.
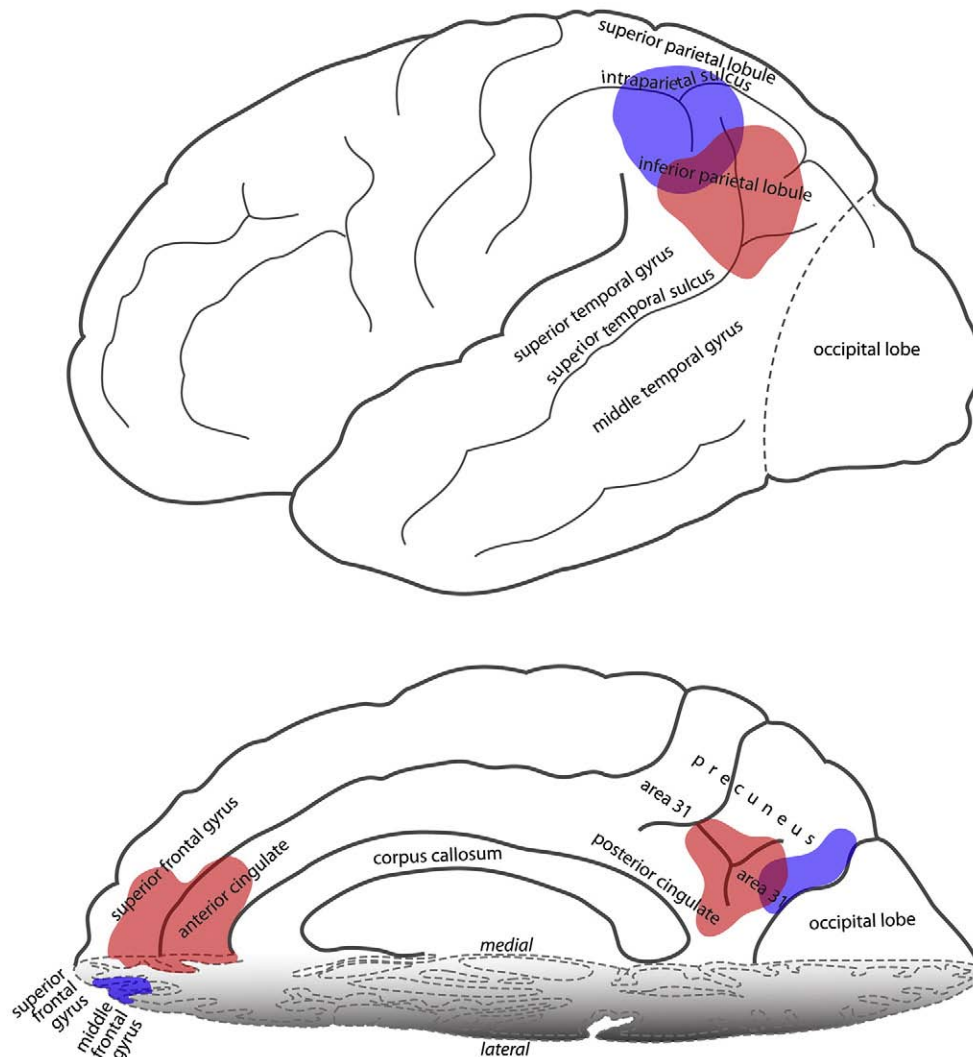
Fig. 7. Schematic illustration of the three main dissociable findings in: (1) the medial parietal cortex, (2) the prefrontal cortex, and (3) the lateral parietal cortex. *Top*: Lateral surface of the brain. *Bottom*: Mesial sagittal surface and axial slice at approximately $z = 0$ in MNI standard space. Networks associated with self-referential processing are depicted in red, networks associated with episodic memory retrieval in blue, and overlapping networks in violet. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of the article.)

taking (Vogeley and Fink, 2003)) and EMR success (Donaldson et al., 2001; Konishi et al., 2000). Extending these findings, the present data suggest functional dissociation within the lateral parietal and adjacent temporal cortex: SRP is associated with activations in a postero-inferior division of the inferior parietal lobule and the adjacent superior and middle temporal gyrus (temporo-parietal junction). In contrast, EMR induces activations in an antero-superior division of the inferior parietal lobule extending into the intraparietal sulcus and the superior parietal lobule. This dissociation is, again, compatible with data from functional connectivity studies (Vincent et al., 2008), linking the posterior inferior parietal lobule to internally directed (i.e., self-referential) cognitive processes, while associating the superior parietal lobule and anterior inferior parietal lobule with attentional and cognitive control processes, such as detecting targets and tracking performance in our EMR task.

Our findings are also compatible with studies reporting dissociation of memory-related functions within the lateral parietal and adjacent temporal cortex (Henson et al., 2005; Maguire and Mummery, 1999; Skinner and Fernandes, 2007; Vilberg and Rugg, 2009; Wagner et al., 2005): the superior parietal lobule has been associated with the relative salience of retrieval cues in memory tasks and the intraparietal sulcus with retrieval success, consistent with our findings during EMR success. The inferior parietal lobule, on the other hand, has

been implicated with the recollection of contextual information. Although neither task in our study explicitly required such recollection, we cannot exclude that this accounts for the overlapping activation observed in the inferior parietal lobule for SRP and EMR. Independent of this interpretation, our findings suggest that the postero-inferior division of the inferior parietal cortex and the adjacent superior and middle temporal gyrus are particularly involved in self-referential processes, possibly the retrieval of personally relevant (contextual or non-contextual, cf. Maguire and Mummery, 1999) information.

Methodological considerations

Response times were longer for the SRP relative to the EMR task, which may indicate that the SRP task was more demanding. However, differences in task difficulty and related attentional processes should not have affected the results reported here: The comparisons of our experiments did not concern tasks (e.g., SRP task versus EMR task) but stimulus qualities (e.g., self-referential/not retrieved versus non-self-referential/successfully retrieved stimuli). Because subjects had to perform both tasks in relation to each stimulus, we can assume that the attention level during the picture perception period was similar among conditions.

We cannot exclude that the emotional valence of our pictorial stimuli has influenced both SRP (cf. Northoff et al., 2009) and EMR (cf. Kensinger, 2004). Although one may consider valence an intrinsic element of self-referential processing (Moran et al., 2006; Phan et al., 2004), we attempted to reduce valence effects on SRP and EMR findings in our experiment: we kept the variance of the normative valence scores across the picture set to a minimum when we selected IAPS pictures for our study. In addition, we included the individual valence ratings as a covariate in our fMRI data analysis.

It is acknowledged that different tasks could have been chosen to address our research question: Instead of episodic memory, we could have used semantic or autobiographical memory tasks as control conditions. Instead of self-referential picture judgment, we could have used a self-referential trait (Kelley et al., 2002) or color (Johnson et al., 2005) judgment task. At this point, one can only speculate on how different task demands would have influenced our findings. In general, potential alternative tasks could have increased the functional overlap (e.g., autobiographical memory task introducing a stronger self-referential component in the memory task) or the functional dissociation (e.g., self-referential task in relation to colors minimizing the memory component) between SRP and memory retrieval. Our results demonstrate that the standard tasks chosen here were able to explore both functional overlap and dissociation for both processes. Notably, the implicit involvement of SRP in the EMR condition and of EMR in the SRP condition did not affect our search for specific networks, because the direct comparison between self-referential/not retrieved versus non-self-referential/successfully retrieved stimuli was used to cancel out the potentially confounding processes.

Behavioral studies on trait judgments have suggested that self-referential processing may involve semantic besides episodic memory retrieval (Klein et al., 1996; Tulving, 1989, 1993; Klein et al., 2002). Semantic personal memories can be regarded as summary representations of the personal past that have been generalized from episodic memories. It has been proposed that semantic and episodic memory systems function independently for some tasks but not others (Kihlstrom and Klein, 1997; Klein et al., 2002). Because self-referential trait and picture judgments involve similar brain regions (Northoff et al., 2006), it seems plausible that the present self-referential task also involved both memory systems: Subjects may have made self-referential picture judgments based on general knowledge of the circumstances of their lives in some cases and on episodic (or both semantic and episodic) memories in others. Semantic memory retrieval could be reflected in left middle temporal gyrus (BA 21) activation during SRP (Svoboda et al., 2006). However, the present study does not allow directly examining the relation between semantic memory retrieval and SRP, because we did not include a semantic memory task as a control.

Based on resting state (Greicius and Menon, 2004), tract tracing studies in the macaque (e.g., Kobayashi and Amaral, 2007), functional connectivity MRI studies (Vincent et al., 2006), and functional neuroimaging studies in EMR (Skinner and Fernandes, 2007), one might have expected to find EMR-related activations also in the hippocampus. Such effect was not observed in our study, possibly because the hippocampus also activates to novel items (implicit encoding, Stark and Okado, 2003) and is more engaged in explicit contextual information processing than simple recognition (Dobbins et al., 2003; Yonelinas et al., 2005). An alternative explanation is that medial temporal activation is more linked to retrieval mode (retrieval efforts) than to retrieval success (Donaldson et al., 2001).

Conclusion

SRP and EMR engage both overlapping and segregated activations in a neural network including the medial parietal cortex, medial and anterior prefrontal cortex, and lateral parietal cortex. In large parts this network corresponds to the so-called default-mode network.

While the present study helps to qualify the function of this network in SRP and EMR, further processes from different domains have been associated with this network. They include resting state, inductive and deductive reasoning, navigation, envisioning the future, evaluation of rewards (Montague et al., 2006), social cognition, moral decision making, imagery, and autobiographical memory (Buckner and Carroll, 2007; Buckner et al., 2008; Legrand and Ruby, 2009; Schilbach et al., 2008; Spreng et al., 2009). Although these processes are often studied as distinct and interpreted within their own domain, it has been speculated that they rely on a common set of internally directed processes by which past experiences are used adaptively to imagine self-referential events beyond those that are perceived in the immediate external environment. The present study demonstrates that combining two of these processes in one fMRI paradigm can be a useful approach to explore the functional relevance, subdivisions, and specificity of the default-mode network. Further work is needed to understand how SRP and EMR relate to other processes associated with this network.

Conflict of interest

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