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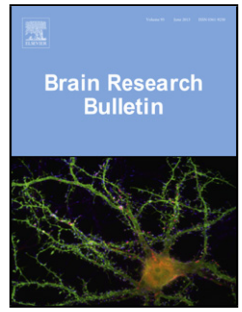

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Thinking about the past to shape the present: Neural activation during the recall of relationship episodes

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ABSTRACT

Reflecting on oneself and others in relationships is an ability that is central to our social existence. Specifically, considering formative autobiographical experiences in relationships may contribute to more flexibility in perceiving, as well as in shaping present relationships. Reflecting on such experiences mobilizes different social cognitive and affective processes. We aim to explore the neural basis of these processes. With a newly developed functional magnetic imaging (fMRI) task, we investigated brain activation in 35 healthy individuals during recall of relationship episodes involving themselves or others. We found that recalling formative episodes involving themselves modulated brain activity in the right parahippocampus, left precuneus, bilateral fusiform gyrus, bilateral insula, and left presupplementary motor area. These areas are involved in memory processes, self-generated thought, and affective experience. The recall of relationship episodes involving others led to similar activation patterns. Our results underscore the close link between self-reflection, understanding others, and memory processes and emphasize the role of affective dimensions for self-relevant experiences. They contribute to a growing body of research on neural mechanisms involved in complex social cognitive processes decisive for our capacity to navigate our social environment.

Keywords: relationship episodes; autobiographical recall; self- and other-referencing; functional magnetic resonance imaging

Total number of words incl. abstract, references, tables and figure legends: 8141.

1. INTRODUCTION

1.1. Interpersonal behavior is recurrent

It is a common experience to encounter the same constellations, conflicts and feelings in close relationships even though the significant others we meet throughout our lives may appear to be very different from one another (Downey, Freitas, Michaelis, & Khouri, 1998; Mikulincer & Shaver, 2007; Neff & Harter, 2003). Attachment theory provides a comprehensive theoretical framework to understand why this happens. Bowlby (1969) described how early interactions and formative experiences in our primary relationships are internalized in the form of "internal working models" that mold our expectations and perception of interpersonal experience. These "internal working models" shape our behavior and experiences in later relationships, sometimes in a dysfunctional manner. Recurrent and maladaptive interpersonal behavior has crucial relevance for many mental disorders (Gunderson, 2007; Sroufe, Duggal, Weinfield, & Carlson, 2000; Zlotnick, Kohn, Keitner, & Della Grotta, 2000). However, it is also significant to all of us, in health or disease, as satisfaction in relationships to our close ones has a powerful influence on our well-being over the lifespan (Waldinger, Cohen, Schulz, & Crowell, 2015). Thinking about formative experiences in relationships and internalized models of relationships can facilitate modifying the perception of others and, eventually, interpersonal behavior. Exploring these aspects of our own psychological functioning necessitates the mobilization of metacognitive abilities that have been described with the umbrella concept of mentalization (Allen & Fonagy, 2006).

1.2. Capacities of mentalization, self-reflection and social functioning are closely intertwined

Mentalization refers to the capacity to think about thinking or form cognitions about cognitions and affects (Allen & Fonagy, 2006). It is an umbrella concept capturing most meta-cognitive processes, such as self-reflection, mindfulness, empathy, and theory of mind. These processes can be characterized by different dimensional qualities including automatic and controlled, cognitive and affective, mentalizing about oneself and others and on internal or external features (Luyten & Fonagy, 2015). The imaginative mental activity that this requires is necessary not only to think about other people's minds but also to understand one's own psychic experiences and emotional states (Dimaggio, Lysaker, Carcione, Nicolò, & Semerari, 2008). Thinking about oneself and thinking about others are therefore capacities that are closely intertwined. Empirical research in developmental psychology has shown that these abilities have common developmental roots as the beginning of our mental life takes place in the context of dyadic interaction (Gergely & Watson, 1996; Tronick, 2007) and the human brain develops in interaction with significant others (Adolphs, 1999; Dunbar, 1998). Later in development, individuals who have difficulties experiencing and identifying their own emotional experiences, the so-called alexithymia, also show difficulties recognizing, understanding or empathizing with feelings of others (Guttman & Laporte, 2002; Moriguchi et al., 2006). Moreover, people with deficits in their mentalizing capacities also show difficulties in diverse areas of social functioning and psychopathology (Chung, Barch, & Strube, 2014; Cusi, Nazarov, Holshausen, MacQueen, & McKinnon, 2012; Ladegaard, Larsen, Videbech, & Lysaker, 2014).

1.3. Processes related to social cognition show a common neural basis

In the last decades, neuroimaging research investigating social cognition and internal mental processing has consistently grown. There is a considerable body of research exploring the neural basis of the various processes summarized under the concept of mentalization (Luyten & Fonagy, 2015). Regions identified in different studies commonly overlap. The temporo-parietal junction (TPJ) has been consistently shown to be implicated in theory-of-mind tasks such as perspective-taking but also the attribution of mental states (Saxe & Wexler, 2005; Schurz, Radua, Aichhorn, Richlan, & Perner, 2014; Van Overwalle, 2009). The medial prefrontal cortex (mPFC) seems to play a prominent role in self-reflection (Lieberman, 2006) and also in the retrieval of autobiographic memories (Gilboa, 2004). The posterior cingulate cortex (PCC) and the precuneus are typically involved in imaginary activity and have also been linked to self-referential processing (Cavanna & Trimble, 2006). The insula has been implicated in processes of self-awareness and introspection (Craig, 2009). Moreover, activity in the anterior insula and parts of the anterior cingulate cortex (ACC) has been associated with subjective experience and the experience of vicarious emotions (Bernhardt & Singer, 2012). Many of these regions are also involved in autobiographic memory processes (Spreng, Mar, & Kim, 2009) suggesting a close neurobiological link of experience and social cognitive abilities. Interestingly, the default mode network, which plays a key role in internally-directed mental activity and also self-generated thought (Andrews-Hanna, Smallwood, & Spreng, 2014; Axelrod, Rees, & Bar, 2017), overlaps with many regions identified as relevant for mentalizing (Spreng & Andrews-Hanna, 2015).

So far, little attention has been devoted to the neurobiological underpinnings of recalling specific autobiographic episodes of close relationships. Loughead and colleagues (2010) conducted semi-structured interviews with healthy participants to generate meaningful relationship episodes that participants had experienced with significant others. They then rated these narratives using the Core Conflictual Relationship Theme method (CCRT, Luborsky & Crits-Christoph, 1998) and used highly conflictual episodes that were connected to negative emotions as stimuli in the fMRI scanner. Confronting participants with written sentences of these episodes, Loughead and colleagues (2010) observed activation modulation in the ACC, the precuneus, inferior and middle frontal cortex and the inferior parietal cortex. The study presented several methodological shortcomings such as a small sample size (n = 11) and involving sentence reading during the scanning procedure.

1.4. An experimental procedure eliciting neural activation involved in the processing of relationship experiences: aim and hypotheses

The aim of this study was to investigate neural activation in healthy participants when they recall formative relationship episodes involving themselves or relationship episodes observed in others. After each episode recall, the participants rated emotional arousal and valence. We assumed that the recall of formative relationship episodes involving themselves would be emotionally more stimulating and connected to more difficult feelings than the recall of episodes involving others. In consequence, we expected higher subjective ratings of arousal and more negative ratings of valence in this condition. On the neural level, we hypothesized that the recall of formative experiences involving themselves would lead to modulation of activity in the mPFC, the PCC, the precuneus, the insula and the ACC. These regions are implicated in mentalizing processes and affective experience. We hypothesized that the recall of interpersonal relationship episodes observed in others would differentially lead to modulation of activity in particular in the TPJ.

Overall, our hypotheses aligned with findings of Loughhead and colleagues (2010). However, we did not expect to find similar modulation of areas in inferior and middle frontal cortex and inferior parietal cortex as these regions seem less specific with respect to our task and possibly in relation to language processing (Fedorenko, Hsieh, Nieto-Castañón, Whitfield-Gabrieli, & Kanwisher, 2010; Price, 2012) as sentences were used as experimental stimuli. We chose to avoid any reading during the fMRI task and used pictorial stimuli in order to stimulate an imaginative type of mental activity.

2. MATERIALS AND METHODS

2.1. Participants

Participants were recruited via a university mailing list, a local Internet platform, and the distribution of flyers in a nearby orthopedic hospital and the university campus. Two participants had to be excluded post-hoc due to excessive head movement (>6mm) during the scanning procedure, one because of an incorrectly conducted preparation task, and three due to a technical failure of the recording device during the preparation task. This resulted in a final sample of 35. Sociodemographic characteristics are described in table 1. None of the participants presented a mental disorder as assessed in a diagnostic short interview for mental disorders (mini-DIPS [Diagnostisches Kurz-Interview bei psychischen Störungen], Margraf, 1994).

The ethics committee of the canton of Zurich approved the study, and all participants gave their written informed consent.

2.2. Instruments

2.2.1. Mini-DIPS

The mini-DIPS (Margraf, 1994) is a structured clinical interview based on the diagnostic criteria of DSM IV and ICD, allowing to diagnose anxiety, obsessive-compulsive, affective (depressive and bipolar), somatoform, and eating disorders and problematic alcohol and substance use. It also includes a psychosis screening. For each disorder, the mini-DIPS comprises general screening questions as well as more detailed questions exploring specific symptoms. Its reliability and validity have been repeatedly tested (Margraf, Cwik, Pflug, & Schneider, 2017).

2.2.2. MIPQS and IRPS

The Maladaptive Interpersonal Patterns Q-Sort (MIPQS [Beziehungsmuster-Q-Sort, BQS], Zimmermann, Stasch, Grande, Schauenburg, & Cierpka, 2014) is a self-rating instrument to identify recurrent interpersonal behavior. This instrument uses a card-sorting procedure: Participants rate 32 items describing interpersonal behavior as relevant for them or not. It enables the construction of a scaled profile of interpersonal behavior, ranging from very relevant to non-relevant. While the MIPQS was originally developed to assess dysfunctional interpersonal behavior in clinical populations, it can also be used to assess recurrent interpersonal behavior that is not dysfunctional. Its items are theoretically based on the Structural Analysis of Social Behavior (SASB) describing the whole range of interpersonal behavior (Benjamin, Rothweiler, & Critchfield, 2006). For this description, it uses two axes: affiliation and interdependence. The SASB is a common model of the interpersonal circumplex and has been used in a wide range of research with healthy and clinical populations (Fournier, David, & Zuroff, 2012).

The Interpersonal Relations Picture System (IRPS, http://www.u65.ch/wissenschaftliche-arbeit/irps, figure 1) is a stimuli set that graphically illustrates the 32 MIPQS items of interpersonal behavior patterns. It was validated in a large healthy population (Fuchs et al., 2018).

2.3. Procedures

Before fMRI scanning, a psychologist conducted the mini-DIPS and the MIPQS illustrated with the IRPS pictures with the participants. The participants were then instructed to develop three narratives concerning their most relevant interpersonal behavior patterns. They were asked to identify key episodes in a relationship to a significant other in which these specific behavior patterns occurred. Additionally, they were instructed to develop narratives based on three items, which they had rated as non-relevant. For these non-relevant items, the participants were asked to recall a relationship episode in which they had observed these types of behavior displayed by other people. They were instructed to pick a situation in which they were not involved themselves. Participants were then invited to memorize which episode corresponded to the respective IRPS picture. The IRPS pictures then served as stimuli in the fMRI experiment.

Before scanning, participants read a written instruction and performed a test trial. In the scanner, their task was to recall the relationship episode when the corresponding IRPS item was shown and put themselves back into that specific situation. When control items were shown, participants were asked to look at these without imagining anything specific. After each item, participants rated their arousal and the valence referring to their feelings when re-experiencing the autobiographic situation.

----------------INSERT FIGURE 1 (black and white)------------------

Figure 1. Example of IRPS items: a. idealizing, b. harmonizing, c. accusing, d. neutral control picture, e. neutral control picture.

2.4. fMRI stimuli

The participants viewed the black-and-white IRPS pictures during scanning on a video mask. All stimuli were presented using Presentation® software (Neurobehavioral Systems, Inc., Berkeley, CA, www.neurobs.com). Out of the 32 IRPS pictures, we individually presented the three most relevant (self-relevant condition) and three non-relevant items (other condition) that the participants had selected in the MIPQS and had memorized with reference to their narratives. We also used the control pictures of the IRPS (control condition). These are pictures depicting the same stick figures in a neutral position with no interaction being illustrated (cf. figure 1).

2.5. fMRI experimental Design

The experimental design is illustrated in figure 2. Stimuli were presented in a pseudo-randomized “mixed block design”: Relevant with reference to self, non-relevant with reference to others and control stimuli were arranged in blocks in a pseudo-randomized sequence. After each stimulus, the participants rated arousal and valence on the Self-Assessment-Manikin (SAM, Bradley & Lang, 1994). The SAM is a visual rating scale using emotional figures depicting arousal and valence on a scale from 1 to 9. Blocks with relevant and non-relevant pictures were each repeated six, those with control pictures four times. This led to the presentation of 6 x 3 relevant and 6 x 3 non-relevant pictures and 4 x 3 control pictures. Blocks were arranged in two sessions. In between sessions, the participants were able to take a break while staying in the scanner. The experiment took approximately 32 minutes in total without the break.

----------------INSERT FIGURE 2 (color online, black-and-white in print possible)------------------

Figure 2. Illustration of the experimental design of the fMRI task. a. The three chosen relevant (cues to own formative relationship episodes) and non-relevant (cues to relationship episodes observed in others) chosen by the participants as well as control stimuli were pseudo-randomized in blocks (Self-Relevant Block, Other Block, Control Block). b. A block consisted of three stimuli shown for 16 seconds followed by rating scales of arousal and valence shown for 8 seconds each. At the end of one block we showed a fixed cross for 20 seconds. c. Self-Relevant Blocks, Other Blocks, Control Blocks were pseudo-randomized and arranged in two sessions.

2.6. fMRI Data Acquisition

Data acquisition was performed on a Philips Intera 3T whole-body MR unit equipped with a 32-channel Philips SENSE head coil. Functional time series were acquired with a sensitivity-encoded single-shot echo-planar sequence (SENSE-sshEPI) (Pruessmann, Weiger, Scheidegger, & Boesiger, 1999). The following acquisition parameters were used in the fMRI protocol: echo time = 35 ms, field of view = 220mm x 220mm x 128mm, acquisition matrix = 80 x 80, voxel size: 2.75 mm x 2.75 mm x 4 mm, SENSE acceleration factor R = 2.0. Using a mid-sagittal scout image, 32 contiguous axial slices were placed along the anterior-posterior commissure plane covering the entire brain with a TR of 2000 ms (θ=80°). The first five acquisitions were discarded to eliminate the influence of T1 saturation effects.

2.7. fMRI Data Analyses

Functional MRI data was analyzed using Matlab version 2015a (The MathWorks, Inc. 2015) and SPM 12 (Statistical Parametric Mapping, Welcome Department of Cognitive Neurology, 2014). We used sweetView for visualization (http://www.sweetneuron.at/wp/sweetview/) of neuroimaging results.

Functional images were corrected for head motion using the realign functions of SPM12. We performed realignment and spatial normalization. Images were smoothed using a Gaussian kernel of 6 mm full width at half maximum. The data was linearly detrended and filtered by a band pass filter (0.01-0.08 Hz) to suppress cardiac and respiratory motion induced effects. None of the participants had to be excluded due to signal drop out.

At the single-subject level, we computed a general linear model to obtain parameter estimates of event-related activity at each voxel, for each condition and each subject and statistical parametric maps of the *t* statistic resulting from linear contrasts between different conditions. We modeled the conditions self-relevant, other, and control. Six movement parameters extracted from realignment were entered as regressors. We convolved all explanatory variables with the canonical hemodynamic response function. Our contrasts of interest were A) self-relevant > control, B) other > control, C) self-relevant > other, D) other > self-relevant.

The individual contrast images of all participants were entered into a random-effects model and within-group activation was assessed using one sample t-tests. Whole-brain cluster inference was completed using false discovery rate (FDR) corrected for multiple comparisons with a threshold of $p = 0.05$. The cluster-forming height threshold was set to $p = 0.001$ uncorrected.

In a post-hoc analysis we built 10mm region-of-interest (ROI) spheres around the peak-voxel of the significant clusters of the contrasts self-relevant > control and other > control using the WFU PickAtlas toolbox (Maldjian, Laurienti, Kraft, & Burdette, 2003). We extracted the BOLD (Blood Oxygenation

Level Dependent) - signal in these ROIs using the toolkit rex (https://www.nitrc.org/projects/rex/) for the contrasts self-relevant > control and other > control. We correlated the extracted parameters with the subjective ratings of arousal and valence. For these, we calculated the difference in ratings for the self-relevant versus control as well as other versus control conditions.

2.8. Behavioral Data Analyses

Statistical analysis of behavioral data and correlation analyses of the BOLD-signal with behavioral data were performed using IBM SPSS Statistics 22 (IBM Corp. Released 2013. IBM SPSS Statistics for Macintosh, Version 22.0. Armonk, NY: IBM Corp). Differences in ratings of arousal and valence were assessed using paired t-tests. Effect sizes for the t-statistics were calculated using an online tool (https://www.psychometrica.de/effektstaerke.html#dep) based on Borenstein (2009). We employed Pearson's product-moment correlation as correlation measures investigating associations of the BOLD-signal and behavioral data.

3. RESULTS

3.1. Behavioral Data: Arousal and valence ratings

Subjective ratings during the fMRI experiment indicated that the participants found the self-relevant condition more arousing ($M = 5.29$, $SD = 1.43$) than the other condition ($M = 4.44$, $SD = 1.41$; $t(34) = -4.12$, $p < 0.001$, $d = 0.6$). Control stimuli were less arousing ($M = 2.41$, $SD = 1.33$) than the self-relevant condition ($t(34) = 9.94$, $p < 0.001$, $d = 2.09$) and the other condition ($t(34) = 8.91$, $p < 0.001$, $d = 1.48$) (cf. figure 3).

Mean ratings in valence for the self-relevant and the other condition did not differ significantly ($t(34) = 0.60$, $p = 0.55$). The participants reported more negative feelings for the self-relevant ($M = 3.62$, $SD = 1.18$; $t(34) = 6.68$, $p < 0.001$, $d = 1.47$), and the other condition ($M = 3.77$, $SD = 1.10$; $t(34) = -7.36$, $p < 0.001$, $d = -1.4$) than for the control condition ($M = 5.53$, $SD = 1.40$) (cf. figure 3).

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Figure 3. a. Means of subjective arousal and valence ratings for the self-relevant, the other, and the control condition. b. Means of subjective valence ratings for the self-relevant, the other, and the control condition.

3.2. Neuroimaging Data

In the contrast self-relevant > control, we found modulation of brain activation in the right parahippocampus, the insula bilaterally, the left precuneus, bilaterally in the fusiform gyrus, and the left presupplementary motor areal (pre-SMA) (table 2, figure 4). In the contrast other > control we found modulation of brain activation in the left precuneus, in the fusiform gyrus bilaterally, two motor regions, and the left dentate (table 3, figure 4). We did not find any significant activation differences in the contrasts self-relevant > other / other > self-relevant.

Using post-hoc ROI-analyses, we explored the association of cluster activations in the contrast self-relevant > control and other > control with subjective ratings of arousal and valence. Activation in the precuneus in the contrast self-relevant > control correlated with subjective arousal ratings (*r* (33) = .37 p = .027). None of the other correlations were significant.

Table 3.

Results for the contrast other > control.

Brain Region	Hemis-phere	BA	Coordinates			Cluster size	Cluster P (FDR-corr)
			x	*y*	*z*		
Precuneus	L	31	-8	-56	34	418	**<0.001
Fusiform Gyrus	R	37	50	-68	2	318	**<0.001
Fusiform Gyrus	L	37	-52	-52	14	690	**<0.001
Pre-SMA	L	6	-4	8	56	262	*0.001
Somatosensory Cortex	L	3	-46	-22	56	918	**<0.001
Dentate Left Cerebellum	L		14	-52	-26	120	*0.026

Note. Pre-SMA = Presupplementary Motor Area, L = left, R = right, BA = Brodman Area, FDR = False Discovery Rate, * = p < 0.05, ** = p < 0.001.

---------------INSERT FIGURE 4 (color online and in print preferable)------------------

Figure 4. Significant cluster activations (FDR-corrected) for the contrast self-relevant > control in red-orange, and for the contrast other > control in green.

4. DISCUSSION

Reflecting on oneself and others in relationships is a key aspect of the ability to navigate the social environment. We developed an experimental procedure to investigate the neurobiological underpinnings of this reflective ability. To our knowledge, this is the first study to explore these mechanisms in a substantial sample of healthy participants.

Behavioral ratings on arousal and valence suggested that our experimental set-up enabled the participants to put themselves back into formative relationship experiences during scanning. Recalling relationship episodes involving oneself and others both led to activation in a set of brain areas linked to memory processes and self-generated thought. These findings underscore the close link between self-reflection, the understanding of others, and autobiographic memory.

4.1. Behavioral results

Subjective ratings in the scanner on arousal and valence indicated that recalling relationship episodes involving oneself (self-relevant condition) was more arousing and connected to more negative feelings for the participants than looking at the neutral control pictures (control condition). Higher ratings on arousal for the self-relevant condition compared to recalling relationship episodes involving others (other condition) indicated that these episodes were emotionally more strongly engaging for the participants and that our experimental procedure worked the way that we expected. First, our preparation task allowed identifying emotionally relevant episodes experienced in relationships. Second, in the scanner, the participants were able to put themselves back into these experiences in a way that this was emotionally arousing for them. We found no difference in the valence of emotions rated for the self-relevant and other condition. However, both conditions were rated as being linked to more negative emotions than the control condition. There can be at least two reasons for this. First, when describing relationship experiences relevant for recurrent interpersonal behavior patterns, there may be a tendency to identify difficult experiences connected to more intensive and negative emotions rather than positive experiences that are well integrated in self-perception. Second, the instruction for the MIPQS begins with a statement that certain behavior patterns often reoccur in interpersonal relationships and that these can be experienced as difficult or problematic. In our experimental set-up, this instruction may have encouraged the exploration of relationship episodes connected to rather negative feelings.

Research on memory and emotion has established how both dimensions, arousal and valence, play an important role in the encoding and the retrieval of autobiographic events (Mather, 2015).

Emotionally arousing autobiographic events are more likely to be well remembered than emotionally neutral events (Hamann, 2001). Regarding our experimental procedure, this fact likely contributed to the choice of relationship episodes by the participants. The role of valence for the encoding and retrieval of memories is less straightforward. Some findings suggest that negative memories are better remembered than positive ones (Baumeister, Bratslavsky, Finkenauer, & Vohs, 2001); however, some studies also found that there is a bias towards remembering emotionally positive events (Rubin & Berntsen, 2003). It would be interesting to study this question in a more specific context: how does emotional valence influence remembering events that specifically have an impact on the present? This is the case in our study where we explored formative relationship experiences that are linked to present recurrent interpersonal behavior patterns.

4.2. Neuroimaging results

When the participants recalled a formative episode in a relationship involving themselves (self-relevant condition) compared to looking at control pictures (control condition), neural activation was modulated in a first set of regions that are involved in memory-processes such as the parahippocampus and self-generated thought such as the precuneus. Activation in the precuneus correlated with subjective arousal ratings. A second set of regions showed modulated activity that is implicated in affective processing such as the insula and the pre-SMA. When participants recalled a relationship episode that they had observed in other people (other condition), they showed modulation of brain activity that was similar to the one we observed in the self-relevant condition. Comparing the self-referential and other condition directly, we did not find any significant differences.

Regarding our initial hypotheses, we found some of the expected results such as the modulated activation in the precuneus and the insula (in the self-referential condition). Some other expectations were not confirmed such as the implication of the mPFC or the differential activation in the TPJ for the recall of relationship episodes involving others versus oneself.

Our instruction to “put yourself back into that situation” when recalling a formative relationship episode very likely involved a type of mental activity that has previously been associated with the precuneus, a region structurally and functionally strongly related to the posterior cingulate cortex and core part of the default mode network (Fransson & Marrelec, 2008; Utevsky, Smith, & Huettel, 2014). It plays a role in many tasks of self-generated thought and imagery such as self-processing, spatial navigation, mind wandering, and memory processes (Freton et al., 2014; Mason et al., 2007; Spreng, Mar, & Kim, 2008). Freton and colleagues (2014) proposed that the precuneus takes a specific role in egocentric navigation, as it is the case for example when retrieving autobiographical memories and first-person perspective. Precuneus activation correlated with subjective ratings of arousal. This may be linked to a more vivid mental navigation for those relationship episodes that were emotionally arousing.

We also found modulated activation in the parahippocampus. Its role in memory processes is well established. Specifically, Martinelli, Sperduti and Piolino (2013) demonstrated the importance of the parahippocampus for the processing of episodic autobiographic memories in their meta-analysis on what they called a “self-memory-system”. Our findings fit well into this literature as our task mobilizes the processing of self-referential autobiographic memories.

The modulated activation in the insula during the recall of self-relevant episodes can be linked to the emotional experience stimulated during our fMRI task. The insula plays an important role for interoceptive awareness and the perception of bodily states (Craig, 2009). Both of these perceptive dimensions are closely intertwined with the processing and subjective experience of feelings (Critchley, Wiens, Rotshtein, Öhman, & Dolan, 2004; Pollatos, Gramann, & Schandry, 2007).

We also found modulated activation in the pre-SMA and the fusiform gyrus - findings that we had not expected. The pre-SMA is a region associated with motor inhibition, but also language processing and memory (Hertrich, Dietrich, & Ackermann, 2016; Nachev, Kennard, & Husain, 2008). However, it also appears to be implicated in different aspects of emotion regulation. In their meta-analysis on cognitive emotion regulation, Kohn and colleagues (2014) describe the involvement of the pre-SMA in executive and cognitive aspects of emotion regulation. It is very plausible that this kind of regulatory process is also mobilized by our fMRI task. The fusiform gyrus is a region identified as typically being implicated in face recognition (Fusar-Poli et al., 2009; Haxby, Hoffman, & Gobbini, 2000). However, it has also been shown that the fusiform gyrus is linked to visual mental imagery (Knauff, Mulack, Kassubek, Salih, & Greenlee, 2002), to visual memory recognition (Schacter & Slotnick, 2004), and more generally to successful recognition in specific and general memory processes (Garoff, Slotnick, & Schacter, 2005). The modulation in this region may be linked to the fact that participants in our fMRI paradigm have to remember which IRPS stimulus belongs to which autobiographic memory during the scanning procedure.

Most intriguingly, we did not find modulation of brain activity in the mPFC as we expected. Overall, a number of questions remain open concerning the functions of different parts of the mPFC involved in social cognition (Bzdok et al., 2013). Qin and Northoff (2011) performed a meta-analysis on self-referential processes. They presume that the mPFC plays an important role in "meta-representing" self-referential stimuli. It may be that the mPFC is in fact involved in a more cognitively driven processing of self-referential stimuli (Brewer, Garrison, & Whitfield-Gabrieli, 2013). In contrast, our fMRI task clearly mobilizes a complex holistic type of affective-cognitive self-referential processing.

We had also hypothesized that the recall of interpersonal relationship episodes observed in others versus oneself would differentially lead to modulation of activation in the TPJ based on previous findings (Rabin, Gilboa, Stuss, Mar, & Rosenbaum, 2009). This expectation was not met. Instead, we found modulated activation in mostly overlapping regions for these two conditions.

Interestingly, there seems to be growing evidence on the overlap of brain networks involved in self-referential and other-referential processing (Lombardo et al., 2009; Oosterwijk, Snoek, Rotteveel, Barrett, & Scholte, 2017; Uddin, Iacoboni, Lange, & Keenan, 2007) although there is also evidence for distinct activation patterns (Herold, Spengler, Sajonz, Usnich, & Bermpohl, 2016; Rabin et al., 2009; van Veluw & Chance, 2014). Considering that thinking about oneself and others are developmental achievements that are closely intertwined, the fact that similar areas in the brain are involved in these types of mental activity seems less surprising. This is consistent with Simulation Theory (ST) stating that mental activities of others are represented by mental simulation (Gordon, 1992). Therefore, individuals perceive mental states of others through the knowledge about their own mental states and processes. Different authors have pointed out the important interdependence between self-reflection, theory of mind and autobiographic memory (Corcoran & Frith, 2003; Dimaggio et al., 2008; Saxe, Moran, Scholz, & Gabrieli, 2006). Awareness of one's own thoughts and perceptions enables the understanding of mental states of others but is also closely connected to one's own experience: we make reference to our own experience in order to understand others. This aligns with neuroimaging findings that point out the involvement of similar regions in these mental activities (Spreng et al., 2009). This combination of mentalization and memory processes is stressed in our experiment where the retrieval of relationship episodes is at the core of the task.

4.3. Limitations

Our study is not without limitations. First, the task used in our study is a very complex one and involves a multitude of cognitive-affective processes. Our aim was to develop an experimental design with ecological validity. We wanted to study the neural basis of a mental activity that is central to our existence as social beings: reflecting upon formative relationship experiences and others in relationships. However, this implies that many different processes are mobilized such as mental imagery, episodic memory retrieval, self- and other referencing, and, to a certain extent, emotion processing. Therefore, a dissociation of brain regions involved with these different processes is impossible. This is a common finding with these types of tasks, and other efforts to dissociate processes involved in internal mental imagery have been made (Axelrod et al., 2017). Second, we compared our two active conditions (self-relevant and other) to a control condition that involved viewing control pictures. Therefore, no episodic memory retrieval or instruction-led mental imagery was mobilized. Third, we chose a whole-brain-level of analysis because of the exploratory approach of our experiment. This presents the disadvantage that differences in brain modulation (e.g. between the self-relevant versus other condition) need to be strong in order to reach statistical significance. Fourth and associated with the previous aspect, our study might be underpowered. We performed a post-hoc power analysis using NeuroPower (neuropowertools.org, Durnez et al., in press) for our data. According to this analysis, we would have needed a sample size of 44 to achieve sufficient power of 0.8. Even though our sample size of 35 is quite large compared to the majority of studies in the field, our results therefore need to be interpreted with care. Underpowered studies are a common problem in fMRI research (Poldrack et al., 2017), with a median sample size of 28.5 for single group fMRI studies. In the future, our results should be replicated in a larger sample. Fifth, we did not model habituation effects in our fMRI analyses. We tried to reduce habituation by including three different stimuli per condition. Still, habituation to the presented stimuli may occur overall. However, we assume that habituation effects will occur in all three conditions (self-referential, other, control). As we were interested in the comparison of these conditions, habituation effects may mostly be accounted for by their presence in all three conditions. Sixth, our sample is mostly female (27 female, 8 male). We conducted separate analyses of behavioral and neuroimaging data for women only. The patterns of results remained overall unchanged with a few minor differences in the neuroimaging data. In consequence, we chose to include the male participants into the analyses in order to augment the sample size and power of the analyses. However, our findings should be replicated in a larger sample size with participants balanced in gender in future.

4.4. Future directions

We presented results of an fMRI study investigating the neurobiological underpinnings of reflecting on oneself and others in relationships. This is an ability that is central to our navigation of the social world. Our findings underscore the close link of self-reflection, understanding others, and memory processes in healthy participants. It will be of great interest to use our experimental procedure with other populations, for example with participants showing difficulties in their social insertion, serious interpersonal problems or mental disorders. It may also be of interest to study effects of interventions, such as the specific training of mentalizing capacity or other processes fostered by psychotherapy and pharmacology. Overall, rehabilitating social abilities is of great relevance to social functioning and thereby to the general well-being of a person.

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Conflicts of interest

None.

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Table 1.

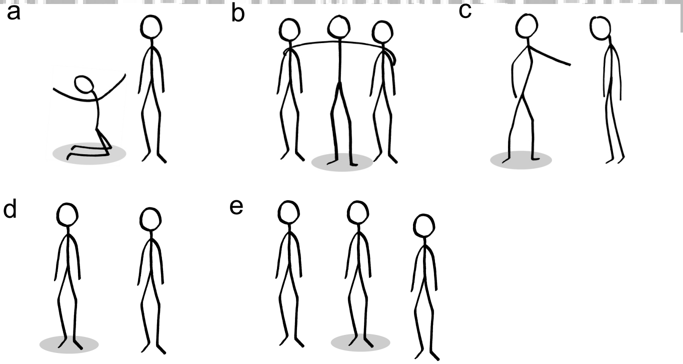
Sociodemographic characteristics of the sample.

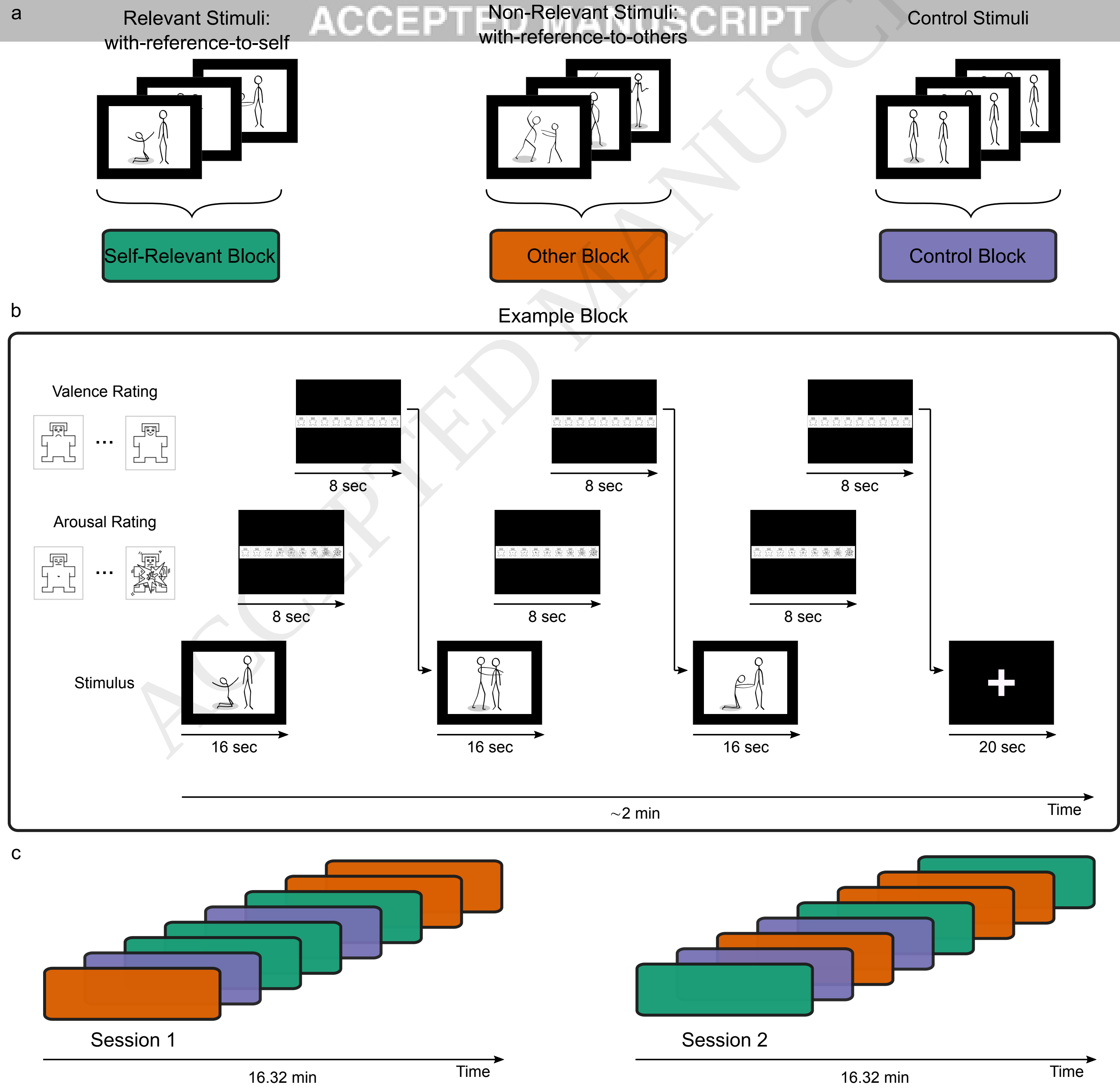
Variables	Total Sample
Age (n = 35)	M = 33.85 (SD = 12.65)
Gender (n = 35)	n
Female	27
Male	8
Years of education (n = 31)	M = 13.71 (SD = 3.31)
Family status (n = 34)	n (%)
Single	15 (42.9 %)
In romantic relationship, living together	3 (8.6%)
In romantic relation, not living together	13 (37.1%)
Married, living together	3 (8.6%)
No information	1 (2.9%)
Mini-DIPS (n = 35)	n (%)
Mental disorder	0 (0%)

Table 2.

Results for the contrast self-relevant > control.

Brain Region	BA	Coordinates


a
b
c
d
e


a
Relevant Stimuli:
with-reference-to-self
Non-Relevant Stimuli:
with-reference-to-others
Control Stimuli
Self-Relevant Block
Other Block
Control Block
b
Example Block
Valence Rating
...
Arousal Rating
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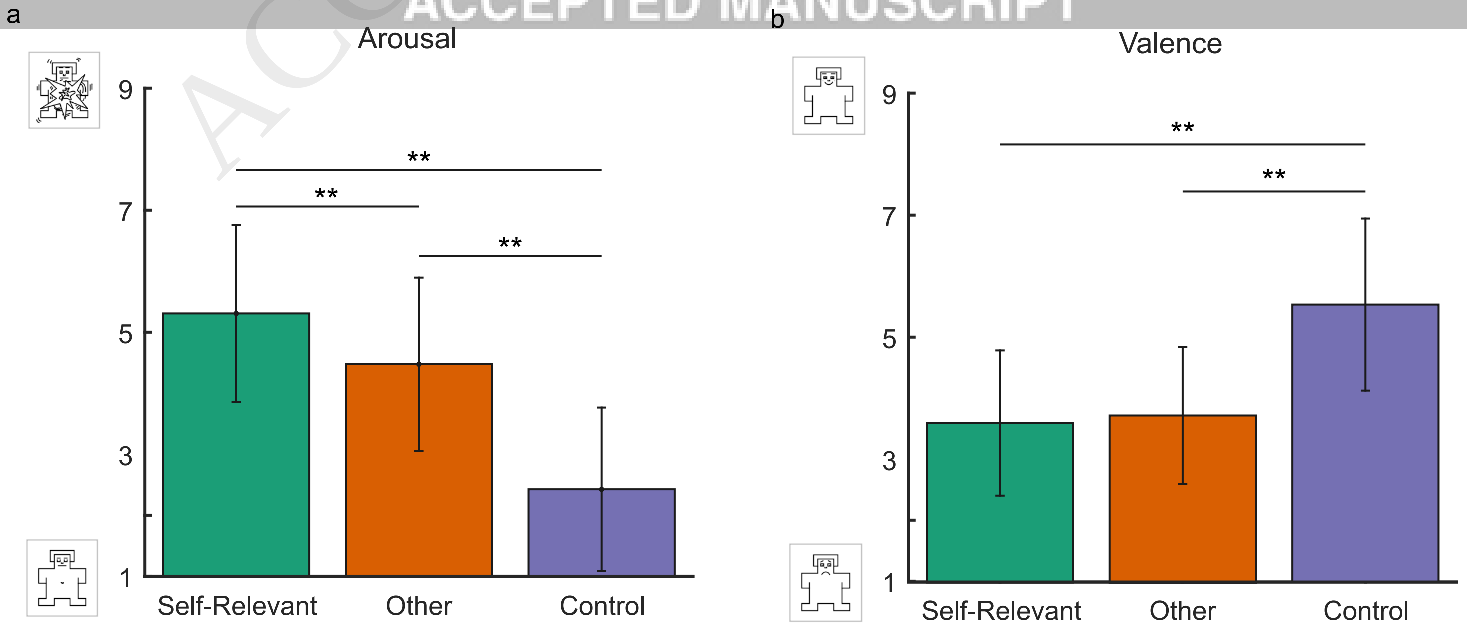
Stimulus
8 sec
8 sec
8 sec
8 sec
8 sec
8 sec
16 sec
16 sec
16 sec
20 sec
~2 min
Time
c
Session 1
16.32 min
Time
Session 2
16.32 min
Time


a
Arousal
9
7
5
3
1
**
**
**
Self-Relevant
Other
Control
b
Valence
9
7
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3
1
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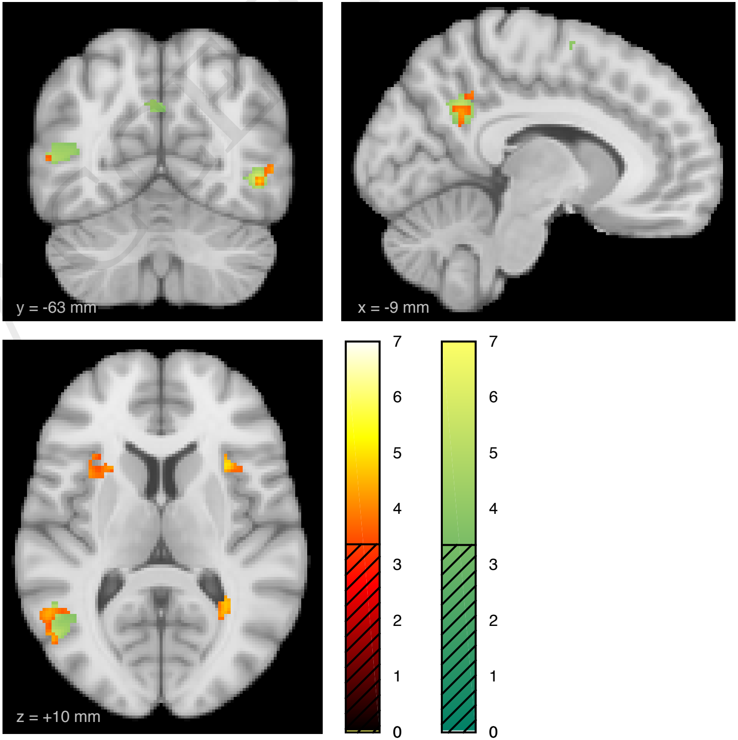
**
Self-Relevant
Other
Control


y = -63 mm
x = -9 mm
z = +10 mm
7
6
5
4
3
2
1
0
7
6
5
4
3
2
1
0

	Hemisphere		*x*	*y*	*z*	Cluster size	Cluster P (FDR-corr)
Parahippocampus	R	30	32	-54	6	252	*0.002
Insula	R	13	32	16	10	108	*0.039
Insula	L	13	-24	16	10	184	*0.006
Precuneus	L	31	-14	-54	30	246	*0.002
Fusiform gyrus	L	37	-54	-68	8	266	*0.002
Fusiform gyrus	R	37	52	-70	0	138	*0.002
Pre-SMA	L	6	-2	2	50	192	*0.001

Note. Pre-SMA = Presupplementary Motor Area, L = left, R = right, BA = Brodmann Area, FDR = False Discovery Rate, * = $p < 0.05$.