



Case History Study

Self processing in the brain: A paradigmatic fMRI case study with a professional singer



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ABSTRACT

Understanding the mechanisms involved in perception and conception of oneself is a fundamental psychological topic with high relevance for psychiatric and neurological issues, and it is one of the great challenges in neuroscientific research. The paradigmatic single-case study presented here aimed to investigate different components of self- and other-processes and to elucidate corresponding neurobiological underpinnings. An eminent professional opera singer with profound performance experience has undergone functional magnetic resonance imaging and was exposed to excerpts of Mozart arias, sung by herself or another singer. The results indicate a distinction between self- and other conditions in cortical midline structures, differentially involved in self-related and self-referential processing. This lends further support to the assumption of cortical midline structures being involved in the neural processing of self-specific stimuli and also confirms the power of single case studies as a research tool.

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1. Introduction

Theoretical discourse and experimental studies on the *self* in contrast to *others* have a long tradition in scientific debate (for review see: Stich & Warfield, 1994), but no generally accepted understanding exists on what the self is or might be. Neuroscientific research deepened the understanding of the self by using neuroimaging methods which identified the midline of the brain as an area crucially involved in self processing. Differential involvement of cortical midline structures has been proposed by Northhoff and Bermpohl (2004) where the areas of the brain carry out specific processes associated with the self, notably, the orbito-medial prefrontal cortex (OMPFC) referred to as representation and labeling of stimuli as self-referential/self-related. Dorsomedial prefrontal cortex (DMPFC) serves as a function of evaluation or judgment of self-specific stimuli. Anterior cingulate cortex (ACC) is associated with monitoring and control function of the self stimuli, specifically paying attention to error detection and performance monitoring.

Eventually, posterior cingulate cortex (PCC) and precuneus provide integration or linkage of the stimuli with the personal context (see Northhoff & Bermpohl, 2004). However, the proposed model doesn't specify the interaction between four sub-processes, although they might represent a hierarchical structure of the self.

Ordinarily, self-referential processes that constitute the model are studied separately and are considered from various perspectives. Based on empirical findings, two different subtypes of the self have been suggested. On the one hand, self is referred to as "mental self" (James, 1957), "narrative self" (Gallagher, 2000), or "autonoetic consciousness" (Keenan, Wheeler, Gallup, & Pascual-Leone, 2000), which involves higher-order cognitive mechanisms linking them to consciousness. Experimentally, this "self-referential self" is usually analyzed by presenting stimuli such as words or faces that the subjects are asked to evaluate according to their degree of self-referentiality, i.e. being either self- or non-self specific. Thus, they represent predominantly an external point of view to oneself. These studies indicate the involvement of cortical midline structures, specifically medial prefrontal, anterior cingulate, precuneus and posterior cingulate areas of the brain during processing of self-specific stimuli when compared to non-self-specific ones (Han & Northhoff, 2009; Northhoff et al., 2006).

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Alternatively, another concept of the self has been advocated, which focuses not on higher-order cognitive but rather on basic somatic and affective functions, thus, relating more to an internal point of view of oneself. This lower-order concept of self refers to a “corporeal self” (Pribram, 1999), a “proto-self” (Panksepp, 1998), or a “material me” (Craig, 2003), and is associated with “self-related” rather than self-referential processing (Northoff et al., 2006; Northoff, Qin, & Nakao, 2010). Experimentally, this concept is tested while presenting self-specific stimuli like the own name which are distinguished from non-self-related stimuli like the names of others (see for instance Qin et al., 2010). Interestingly, these studies have also indicated that cortical midline structures are activated upon self-specific stimuli presentation (Northoff et al., 2009; Qin et al., 2010). The following concept of the self is also empirically supported by findings demonstrating the division between affective and cognitive components of the self (Moran, Heatherston, & Kelley, 2009; Moran, Macrae, Heatherston, Wyland, & Kelly, 2006) and subcortical areas (Northoff et al., 2009; Schneider et al., 2008) in the processing of self-related stimuli. Thus, sufficient empirical evidence appears to support a conceptual distinction between lower- and higher-order concepts of the self.

Alongside this distinction, recent evidence indicates a substantial structural overlap between neural regions involved in the self processing and those regions which characterize the resting state modes (D’Argembeau et al., 2005; Northoff et al., 2006; Qin et al., 2010; Schneider et al., 2008). However there is a lack of evidence how these internally-oriented stimuli with a high-degree of self-relatedness are linked to external stimuli with different degree of self-relatedness. To date, only few studies specified the interconnection between self and other perception. Thus, Kjaer, Nowak, and Lou (2002) using stimuli in the reflection of the own personality traits and own physical appearance in comparison with reflection of personality and physical appearance of the other reported the connectivity by the synchrony between ACC and precuneus.

In the present study we aim to investigate the neural correlates of the perception of stimuli, which are suspected to be self-related and self-referential without involving an explicit evaluation or judgment. We located a paradigmatic case in the taxonomy of single case studies (Flyvbjerg, 2006), an eminent opera-singer with a prominent professional identity in order to test the following hypotheses: (1) Are cortical midline structures involved in the processing of self-specific stimuli and (2) is there a difference between processing of self-referential and self-related stimuli in the brain? The unique case allowed us to apply both types of stimuli: self-related (listening to the own voice and singing by inner voice) and self-referential (listening of music and listening to the same piece sang by another singer) in fMRI design assuming that cortical midline structures might be differentially recruited in these tasks.

2. Methods

2.1. Participant

A right-handed (Edinburgh Handedness Inventory) person (female, age = 69 years) in good general health and with no history of neurological or psychiatric illness participated in the study. The subject has been professional soprano singer for more than 35 years and currently is a professor of singing. Written informed consent to participate was gained prior to the study, and the subject was informed of her right to discontinue participation at any time. The study was carried out in accordance to the Declaration of Helsinki principles and was approved by the ethics committee of the Medical Faculty of the University of Munich.

2.2. Stimuli and task

Four experimental conditions were used in the study: (1) listening to short excerpts from recordings of the subject’s own singing – *LS*; (2) listening to recordings of the same musical pieces sung by another person – *LO*; (3) listening to instrumental music without vocal part – *LM*; and (4) active inner (not audible) singing accompanied by instrumental music, a task for which professional singers are well trained – *SM*. The stimuli consisted of digitalized music, *coloratura* excerpts of two Mozart arias of 15–20 s duration: (1) *Magic Flute*: “Der Hölle Rache kocht in meinem Herzen” (Königin der Nacht, II); (2) *Don Giovanni*: “Crudele?” – “Non mi dir, bel’ idolo mio” (Donna Anna, II). These excerpts were representative for the repertoire sung by the subject during her professional career. All stimuli were normalized in loudness.

Stimuli were presented under computer control binaurally in pneumatic headphones at a sound level comfortable to the subject. Headphones also served to alleviate the noise of the scanner. The subject was asked to keep her eyes closed during the whole experiment and the light was dimmed to suppress visual stimulation.

The study was conducted in four test sessions (runs). As perception of music requires cognitive integration over time, the experimental paradigm was based on the classical block-design: during each run the four conditions (*LS*, *LO*, *LM*, and *SM*) were presented four times each, in *random order*. At the beginning of each run an additional short (3 s) dummy recording (*coloratura* excerpt from Mozart’s *Die Entführung aus dem Serail*: “Martern aller Arten”, II/3) was presented to avoid startling of the subject and prepare her for the testing period. The subject was instructed to attentively listen to the musical stimuli for the conditions *LS*, *LO* and *LM* or to sing with inner voice (inaudibly) in the condition *SM*. The last task is habitual for professional singers and is typically used to prepare for performances. For the condition *SM* the same instrumental music as in the condition *LM*, preceded by a short recorded instruction (female voice, 3.5 s before each start of the condition *SM*) was used. Between conditions, a silence period was provided for 6, 9, 12 or 15 s – in *random order* (*Baseline*). The functional measurement session lasted approximately 45 min in total.

2.3. Data acquisition

Experiments were conducted on a 3 T whole body system (Magnetom VERIO, Siemens, Erlangen, Germany), equipped with a standard head coil. The subject’s head was securely but comfortably fastened by foam cushioning in order to minimize head movements. For blood oxygen level dependent (BOLD) functional imaging, an T2*-weighted Echo-Planar Imaging (EPI) sequence was used with the following parameters: repetition time (TR) = 3000 ms, echo time (TE) = 30 ms, flip angle (FA) = 90°, number of slices = 28, slice thickness = 4 mm, inter-slice gap = 0.4 mm, interleaved acquisition, field of view (FoV) = 192 × 192 mm, matrix = 64 × 64, in-plane resolution = 3 × 3 mm. Functional images were acquired in axial orientation, covering the whole cerebrum and dorsal cerebellum.

2.4. Data analysis

Data was analyzed with SPM8 (Statistical Parametric Mapping; <http://www.fil.ion.ucl.ac.uk/spm>). The first five volumes were discarded due to T1 saturation effects. All functional images were realigned, spatially normalized into standard stereotaxic space (EPI template; Montreal Neurologic Institute, MNI), resliced to 2 × 2 × 2 mm voxels, and smoothed with an 8 mm full-width at half maximum (FWHM) Gaussian kernel. Statistical parametric maps were thresholded at $p < .001$ (cluster-level FWE corrected at $p < .001$, cluster size threshold = 400 voxels). Anatomical

description was done referring to the AAL atlas (Automated Anatomical Labelling of Activations; Tzourio-Mazoyer et al., 2002) from the MRICroN (<http://www.sph.sc.edu/comd/rorden/mricron>). Internal reliability of the results was confirmed by conducting independent analysis for each music excerpt.

3. Results

The initial comparisons of task-related conditions and baseline were performed sequentially for passive conditions of listening (*LS*, *LO*) and active singing of music (*SM*). Several areas, specifically bilateral temporal cortex and anterior temporal gyrus, sensorimotor, premotor areas exhibited significant increase of BOLD signal during listening to self and other conditions in comparison to the baseline. In active condition (*SM*) versus baseline there has been an increase of BOLD signal in sensorimotor, premotor, prefrontal areas and cerebellum, and to the lesser extends in right and left temporal regions.

To define brain areas particularly involved in the processing of *self* versus *others*, we have conducted several pair-wise comparisons between experimental conditions (Table 1). *LM* served as a control condition in order to show specific neural activations occurring in both *LS* and *LO* conditions. The comparison between listening self and listening music (*LS* > *LM*) revealed bilateral activation in the dorsolateral and medial prefrontal cortex, anterior cingulate cortex, which constitute the biggest cluster of activation in the brain, as well as angular and middle occipital gyri. We also observed activation of the left orbitofrontal cortex with extension into superior frontal gyrus. Similar activation of MPFC and ACC was obtained in comparison of listening to others and listening music conditions (*LO* > *LM*).

The cerebral areas which share common activation in processing of *LS* and *LO* were chosen for conjunction analysis between the following contrasts: *LS* vs *LM* and *LO* vs *LM*. Mutual activation was detected in bilateral dorsomedial prefrontal cortex (DMPFC) and right anterior cingulate (ACC) (Fig. 1A). In the direct comparison of listening to *self* vs *others* (*LS* > *LO*), we observed a relative increase of the BOLD signal in – left thalamus, cerebellum, right-lateralized cuneus and precuneus (Fig. 1B).

Comparison between active singing and listening showed no difference in activation singing music vs. listening self (*SM* > *LS*), as well as singing music vs. listening music (*SM* > *LM*) conditions (Table 1). No activations were obtained between singing music and listening to other condition (*SM* > *LO*). Conjunction analysis

between listening to self/singing self vs. listening to the other contrasts (*SM* vs *LO*) and (*LS* vs *LO*) showed common activation in bilateral precuneus and superior temporal gyri.

4. Discussion

In the present study we aimed to identify the brain structures involved in self-referential and self-related reflective activity being aware of the difficulties interpreting such observations (Bao & Pöppel, 2012). By applying a single case design we elude inter-subject heterogeneity of group studies and focus on complexities arising from the distinctive history and epigenetic influences specific to that individual. The sound of the own voice shapes social identity of a professional opera singer; in this particular case her personal identity is influenced by her professional specialization. We consider an eminent singer who possesses strong long-lasting professional experience and social identity to be a good example how to demonstrate interconnections of self-oriented processes.

As our main finding, the direct comparison between listening to *self* and *others* has showed a relative activation of precuneus, visual cortex, posterolateral thalamus, and cerebellum in the perception of *self*. In addition, tasks that involve the *self* processing showed common activation of the precuneus indicating its specific role in self-related processing (Whitfield-Gabrieli et al., 2011). Subcortical structures have been previously considered as crucial subcomponents of functional systems for sensory integration (Tyll, Budinger, & Noesselt, 2011). The metabolic activity in subcortical brain areas and cerebellum has been also shown to be increased in mental processing (Decety, Sjöholm, Ryding, Stenberg, & Ingvar, 1990) and it could be involved in the regulation of the affective reactions and in forming the association between sensory stimuli and their emotional values (Strata, Scelfo, & Sacchetti, 2011). Visual cortex activation may indicate visual imagery (D'Esposito et al., 1997) and/or retrieval from autobiographic memory (Svoboda, McKinnon, & Levine, 2006). Overall, the findings might be an indication for the existence of a more basic, lower-order processing of self in terms of bodily functions and their sensory integration in the constituting of self-relatedness and identity. The derived clusters of neural activations might be a key distinction between the processing of *self* and *others*. One can also assume that self-related conditions might just elicit more memories resulting in more brain activations, therefore capturing also a quantitative (more memories = more effort/more processes) difference between self-related and self-referential processing.

Table 1
Neurofunctional correlates.

	Cluster	kE	Peaks				Z-value	Brain area
			x	y	z			
<i>Passive conditions comparisons</i>								
<i>LS</i> > <i>LM</i>	1	3637	–28	58	2	6.41	L. superior frontal g., middle frontal g., inferior frontal g., cingulate g., R. superior frontal g., middle frontal g., inferior frontal g., cingulate g.	
<i>LO</i> > <i>LM</i>	2	184	–36	–62	36	5.07	L. angular g., middle occipital g.	
<i>(LS</i> > <i>LM</i>) ∩ (<i>LO</i> > <i>LM</i>)	1	1145	8	46	20	5.23	L. superior frontal g., R. superior frontal g., cingulate g.	
<i>(LS</i> > <i>LO</i>) ∩ (<i>SM</i> > <i>LO</i>)	1	1141	6	46	22	5.11	L. superior frontal g., R. superior frontal g., cingulate g.	
	1	514	–16	–56	–22	4.29	L. cerebellum, R. cerebellum	
	2	449	–12	–76	60	4.23	L. precuneus, cuneus, R. precuneus	
<i>LS</i> > <i>LO</i>	1	589	0	–64	–24	5.23	L. cerebellum, R. cerebellum	
	2	184	–24	–16	26	4.48	L. thalamus	
	3	329	–2	–84	36	4.37	L. precuneus, cuneus	
<i>Active conditions comparison</i>								
<i>SM</i> > <i>LO</i>	1	389	–14	–72	64	5.51	L. precuneus, superior parietal g., R. precuneus, superior parietal g.	

LS = listening to self, *LM* = listening to the music, *LO* = listening to the other, *SM* = singing music, ∩ = conjunction. R. = right, L. = left, g. = gyrus. The x, y and z coordinates are in the MNI space.

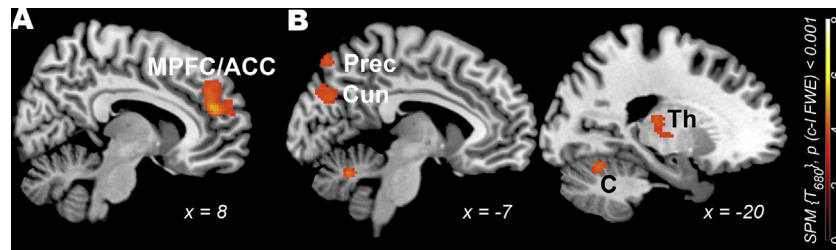


Fig. 1. Neurofunctional correlates of Self and Other processing. (A) Conjunction of *self* vs *music* and other vs *Music* processing: *DMPFC* = dorsomedial prefrontal cortex, *ACC* = anterior cingulate cortex; (B) *Self* versus *Other* processing: *P* = precuneus; *Th* = thalamus; *C* = cerebellum. Statistical parametric maps ($p < .001$, FWE cluster-level corrected). *X* coordinates are MNI coordinates.

In listening to *self* versus listening to *music* contrast, higher activation in predominantly dorsomedial PFC/ACC and orbitofrontal cortex (OFC) was detected. These regions are associated with the “first person” perspective and mental state’s attributions (Vogeley et al., 2004) as well as its generally implicated in planning cognitive behavior, personality expression, decision making and error monitoring (Carter et al., 1998; Miller, Freedman, & Wallis, 2002). Moreover, the increased activity of angular gyrus, which was also reported, has been seen in experienced singers and which has also attributed to the action awareness and referred to the processing and comparison of action intentions and action consequences (Farrer et al., 2008). At the same time, listening to *others* versus listening to *music* has similarly shown the involvement of MPFC/ACC. Our results are consistent with the notion that above mentioned higher-order cognitive functions might facilitate the discrimination of self-referential stimuli from the context.

In summary, our findings corroborate the hypothesis of the specific modulation of the neural activity in cortical midline structures (CMS) during *self* processing (Northoff & Bermppohl, 2004, Qin & Northoff, 2011). Nevertheless, there has been a differentiation in activation with regard to self-related (lower-level) and self-referential (higher-level) processing. Firstly, activation in precuneus and subcortical structures proving the distinction between *self* and *others*, might sustain the sensory integration of the stimuli to the personally related context i.e. emotional and autobiographical and hence, comply with the lower-order functions. Secondly, perception of *self* and perception of *others* in reference to self produce common pattern of activation of MPFC and ACC with additional activation of OFC in perception of the *self*. Regarding the specific role of each of the region, one can argue that OFC seems to elucidate continuous representation of self-referential stimuli, it also explains why OFC is not activated in listening to other’s condition. Once the self-referential stimulus is represented it appears to be evaluated in the MPFC and monitored for the performance in the ACC. In a word, the actual self-referential processes are obviously embodied by higher-order cognitive functions. Experimentally, the lower- and higher-order concepts of the *self* can also be distinguished with respect to its active or passive involvement. The higher-order *self* is conceived of as an “active *self*” in a sense that it requires evaluation and judgment and hence explicit conscious awareness. The lower-order *self* is considered as more passive as it does not require active involvement or an explicit representation of selfness and is therefore presumably related to sensory and motor functions or in general to more bodily functions rather than to cognitive processes and considered as internally-oriented self-relatedness (see for instance Grimm et al., 2009; Northoff et al., 2009; Schneider et al., 2008). A further distinction has to be made with respect to the time domain of the different *self* concepts (Pöppel, 2009, 2010; Pöppel & Bao, 2014). Whereas the higher-order *self* possibly represents a long-term perspective as reference is made to stable features of the *self*, the lower-order *self* is characterized by experiential references which are typically

embedded in a shorter time window. This notion might be an interesting target for future research on the *self*.

Our study also showed that activation patterns in active *singing* with inner voice vs listening to *music* as well as active singing vs listening to *self* didn’t differ that is probably due to involuntary silent singing even without an explicit instruction).

5. Conclusions

The present case study is a demonstration of the interconnection and interplay of corresponding neural modules involved in self-related and self-referential processing. These components of *self* should not be understood as independent identities but rather as the elements and working of complex networks. Higher-order cognitive concepts of oneself, connected to personal memories, feelings, and specific mental states which allow a re-experiencing of one’s individual history (Gallagher, 2000) and location of oneself in subjective time (Pöppel, 2009; Pöppel & Bao, 2014), are presumably complemented by lower-order implicit states of a phenomenological pre-reflective self-awareness (Zahavi, 2007), which lack for instance subjective time extension (Strawson, 2002).

In most studies on the neural representation of the *self*, verbal stimuli are used and they trigger an explicit representation with semantic connotations. Our results provide an argument for representation of another sensory channel resulting in a more implicit neuronal information processing and knowledge representation (Pöppel & Bao, 2011) similarly allow uncovering various aspects of the *self* on a neural level. We found differences in neural activity for *self* and *other* perception in the cortical midline structures and subcortical regions. The fact that such differences were indeed observed suggests that musical stimuli can also represent specific aspects of self-relevant sensory inputs.

Conflict of Interest

The authors declare that they have no conflict of interest regarding this study.

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