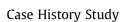
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Self processing in the brain: A paradigmatic fMRI case study with a professional singer



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1. Introduction

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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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 Northoff 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.

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Eventually, posterior cingulate cortex (PCC) and precuneus provide integration or linkage of the stimuli with the personal context (see Northoff & 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 & Northoff, 2009; Northoff 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, Heatherton, & Kelley, 2009; Moran, Macrae, Heatherton, 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 selfrelatedness 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' idol 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, inplane 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 $2 \times 2 \times 2$ 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

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