

The impact of rhythm complexity on brain activation during simple singing: An event-related fMRI study

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Abstract. Purpose: Since rhythmical aspects of singing have been neglected up to now our objective was to investigate if it was possible to specify areas concerned with rhythm processing during simple singing.

Methods: In an event-related fMRI experiment we tested 30 healthy non-musicians with rhythm sequences, which had to be repeated as monotonously sung vowel changes with (1) regular groupings, (2) regular groupings and rests, and (3) irregular groupings.

Results: Common activations for all conditions were found in bilateral supplementary motor area, premotor cortex more distinct in the left hemisphere, left cingulate gyrus, and right basal ganglia. Only irregular groupings making the highest demands on attention, working memory, and sequencing capabilities resulted in additional activation of pars orbitalis and insula more distinct in the left hemisphere, as well as bilateral cingulate gyrus, and parietal lobes. Our analyses demonstrated that bilateral pars orbitalis (BA 47), insula, and left cingulate gyrus are core areas whose activity correlates with rhythm complexity.

Conclusions: Rhythm structure is a decisive factor concerning lateralization as well as activation of specific areas during simple singing. This finding suggests a directed use of the singing voice e.g., in order to support language rehabilitation in patients.

Keywords: BA 47, fMRI, insula, cingulate gyrus, rhythm, singing

1. Introduction

Singing is a unique human ability, which combines language as well as musical capabilities. However,

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singing is a many-faceted process because linguistic components as well as acoustic components can be used in very different ways. During conventional singing (e.g., songs or arias) the focus is on melody and intonation and verbal material consists of more or less meaningful lyrics. On the other hand, solo singers or those who study voice are accustomed to train their voice by vocal exercises using single vowels, vowel

changes or syllables. The more runs, coloraturas or ornaments are practiced the more important becomes precise rhythmical articulation.

Furthermore, a rudimentary or simple form of singing is chanting, e.g., as a commonly used spiritual practice in many cultures, which represents rhythmic singing of words or sounds, often primarily on one or two pitches called reciting tones. The spectrum of chanting reaches from Gregorian chant up to reggae and rap music, which also uses elements of chanting.

Over the last nearly two decades singing has been investigated increasingly also by new techniques from the field of neuroimaging.

The basic PET-study of Perry et al., (1999) who investigated chanting or simple singing of a single vowel and pitch in contrast to a pitch perception baseline yielded activations in many of the same regions as does speech, however, with a rightward asymmetry in motor (right ventral precentral gyrus) and auditory regions (right primary auditory cortex).

The PET-study of Brown et al., (2004) demonstrated bilateral activations in the primary auditory cortex (BA 41) and the mouth region of the primary motor cortex (BA 4) of their monotonic vocalization task contrasted with rest. Furthermore, bilateral activations were observed in the auditory association cortex (BA 42 and posterior BA 22), frontal operculum (inferior parts of BA 44, 45, and 6), as well as supplementary motor area (medial BA 6) with a trend towards greater right hemisphere activations.

Other studies compared singing with speaking, though most of these studies used either well-known tunes (Jeffries et al., 2003; Riecker et al., 2000), covert production of well-known material (sung and spoken) compared with perception (Callan et al., 2006), spontaneous and synchronized singing of well-known material compared with respective speaking (Saito et al., 2006), or intoning or speaking words or phrases commonly used in everyday life compared to vowel production, humming or rest (Özdemir et al., 2006). The MEG-study of Gunji et al., (2007) investigated speaking, singing, humming and imagining of a popular song with changing frequency bands. Kleber et al., (2007) examined overt and imagined singing of an Italian aria with professional singers and differences in functional activation in singing of the same aria in professional singer, vocal students, and laymen (Kleber et al., 2010). Zarate and Zatorre (2008) investigated vocal pitch regulation in simple singing comparing non-musicians with singers.

A further study of Zarate et al., (2010) addressed voluntary and involuntary pitch regulation in experienced singers.

Comparisons between the imaging studies mentioned above are difficult due to methodological differences, not only between conditions, but also between analyses. The use of well-known tunes confounds the results with semantic, lexical or emotional influences, and it is hardly possible to distinguish pitch and rhythm effects anyway. Since in most of the studies tasks were compared to auditory control conditions or rest (see Brown et al., 2009 for review) no statements can be made regarding changes of single acoustic components of singing.

Furthermore, in all cited studies singing is performed in a relatively slow and regular manner, which implies that processing of melodic contour and intonation became the focus of attention. Meanwhile the higher proficiency of the right hemisphere in pitch-based processing is well documented (Zatorre et al., 1992, 1994; Johnsrude et al., 2000; Zatorre, 2003; Peretz and Zatorre, 2005; Zatorre and Gandour, 2008). Singing slowly and regularly requires slower articulation rates. This might also be one reason for the often described right hemisphere asymmetries in motor and auditory regions activated by singing (Brown et al., 2004; Callan et al., 2006; Gunji et al., 2007; Jeffries et al., 2003; Kleber et al., 2010; Özdemir et al., 2006; Perry et al., 1999; Riecker et al., 2000).

However, singing also includes rhythmic and temporal components, which to our knowledge have been neglected up to now.

Our interest in examining this subject results on the one hand from theoretical considerations, on the other hand our research findings might be useful for practical application e.g. directed therapy interventions. As concerns theoretical considerations, research working on processing of temporal organization or rhythm points to a dissociation with the two components meter (a regularly repeating pattern of strong and weak beats) and segmentation of an ongoing sequence into temporal groups of events, phrases, motifs (grouping, phrasing) (Altenmüller, 2001; Clarke, 1999; Gabrielson, 1993; Lehrdahl and Jackendoff, 1983; Povel and Essens, 1995; Todd, 1994). Findings from rhythm discrimination research with brain-damaged patients demonstrated a left hemisphere specialization for temporal grouping (DiPietro et al., 2004; Vignolo, 2003) and a right hemisphere specialization for meter (Fries and Swihart, 1990; Wilson et al., 2002).

Lesion studies from the field of language as well as music demonstrate that patients with left-hemisphere lesions have problems with rhythm and time perception (Efron, 1963; Liégeois-Chauvel et al., 1999; Mangels, 1998; Robin et al., 1990; Schirmer, 2004; von Steinbüchel et al., 1999; Szelag et al., 1997; Tallal et al., 1995). Many studies confirm deficits in aphasia patients with regard to temporal structuring of speech (Baum et al., 1990; Baum and Boyczuk, 1999; Blumstein, 1991; Danly and Shapiro, 1982; Niemi, 1998) but also in apraxia of speech (Kent and Rosenbek, 1982; Wambaugh and Martinez, 2000), a dysfunction of higher-order aspects of speech motor control characterized by deficits in programming or planning of articulatory gestures.

Alcock et al., (2000) who investigated production and perception of pitch and rhythm abilities in adult left-hemisphere-dysphasic and right-hemisphere-damaged subjects reported that singing pitch relations was spared in left-hemisphere patients while oral as well as manual rhythm production was impaired. Right-hemisphere patients, however, had greater difficulty with intonation tasks while rhythm production was less impaired.

The observation that singing capabilities are often spared in patients suffering from aphasia (Olof Dalin cited by Benton and Joynt, 1960; Keith and Aronson, 1975; Ustvedt, 1937; Yamadori et al., 1977) prompted many researchers and therapists to implement singing – although in very different ways – in the treatment of patients suffering from both motor speech disorders as well as aphasia (Albert et al., 1973; Belin et al., 1996; Cohen and Ford, 1995; Keith and Aronson, 1975; Pilon et al., 1998; Schlaug et al., 2008; Sparks et al., 1974; Sparks and Deck, 1994; Van Eeckhout et al., 1983). In doing so singing is performed in a relatively regular manner and the focus is on melody and intonation respectively with the intention to activate homologous language-capable regions in the right hemisphere.

To our opinion an essential and unexplored question is, whether focusing on rhythmic grouping during singing, which includes manipulating sung sounds into segments and requiring differently demanding sequencing performance, might engage specific areas and possibly left hemisphere mechanisms to a greater extent than singing regularly.

Our considerations are also supported by studies investigating timing as well as rhythm perception and production (Benedict et al., 1998; Lewis and Miall, 2003; Macar et al., 2006; Rao et al., 2001), which

report activation of inferior frontal and parietal areas as a result of increasing demands on attention and working memory components. A review of fMRI studies of temporal attention (Coull, 2004) yielded that left parietal cortex activation is associated with motor attention, while left frontal operculum seems to be involved especially in rapid temporal sequencing, irrespective of task demand i.e. linguistic, sensory or motor production.

Since temporal structuring is impaired in patients suffering from aphasia and also apraxia of speech it would appear that an improvement of these capabilities might possibly have positive effects on language performance. Based on our therapeutic experience we expect e.g., that stimulation of phonological and segmental capabilities in connection with simple singing of differently demanding rhythmic groupings may improve sound sequencing.

Some studies emphasize the positive effects of temporal-rhythmic components in therapy (Belin et al., 1996; Boucher et al., 2001). However, as already mentioned singing has not been investigated in connection with potential rhythm or grouping influences, neither with healthy subjects nor with patients.

If it was possible to stimulate remaining language-related areas of the left hemisphere in patients by a directed use of the singing voice, singing might serve as systematically applied training in order to support language rehabilitation.

This fMRI study with healthy subjects is supposed to gain an insight into the involvement of the relevant neuroanatomical structures, which are involved in chanting vowel changes with different rhythm complexity and constitutes the basis for further research with patients suffering from aphasia and apraxia of speech.

These tasks are already approved in therapy (Jungblut, 2005; Jungblut, 2009; Jungblut et al., 2009) and form the basis of further research with patient groups. In order to reduce the influence of melodic components we chose simple singing tasks i.e., vowel changes were repetitively sung on the same pitch. The influence of semantic and lexical components of speech processing was reduced by focusing on phonological processing with a single vowel change. Apart from that we decided for a vowel change with regard to our study with patients because even severely impaired patients are mostly able to cope with this task. Our focus was on production for which the results are presented in this study. Auditory activation in anticipation of repeating

was investigated separately and will not be discussed in this paper.

According to the imaging studies concerned with singing mentioned above we assume that simple singing of rhythm sequences will activate bilateral premotor and prefrontal areas. Furthermore, we hypothesize that common brain areas will be activated in the three rhythms tasks, possibly at different levels depending on rhythm structure, thus testifying to the fact that these areas are concerned with rhythm processing. Based on the studies investigating timing, rhythm and temporal attention mentioned above, we also assume that the more complex the rhythmic structure the more left-hemisphere activation will occur. Furthermore, we expect additional activation of inferior frontal and parietal areas correlating with rhythm complexity as a result of increasing demands on attention and working memory components.

2. Methods

2.1. Participants

A total of 30 healthy German non-musicians (17 male, 13 female, mean age: 26.3, range 21–41) participated in the present study.

In order to avoid the reported sex differences at the level of phonological processing (Shaywitz et al., 1995) and vocal and verbal production (Hough et al., 1994; Weis et al., 2008) only women who used contraceptive devices (birth control pill) were included. All subjects were right-handed as determined by means of the Edinburgh Handedness Scale. Inclusion criterion was a lateralization index >70%. None of the participants had a history of neurologic, psychiatric or medical diseases or any signs of hearing disorders.

Apart from general school education none of the participants had any special musical training. Prior to the experiment all subjects had a pre-training in order to get familiar with the stimuli and to make sure that everybody could manage the tasks. However, stimuli used in the pre-training were comparable but not the same as in the experiment. Only subjects who were able to sing 75% of the repetition samples correctly were included in the study. All participants gave written informed consent in line with the Declaration of Helsinki and the Ethics Committee of the RWTH Aachen. This study was undertaken in compliance with national legislation.

2.2. Stimuli and procedure

Stimuli consisted of quadruple measure groupings with duration of 4 sec. (8 vowel changes, alternately/ a/i/) and differed as follows:

Condition (1): vowel changes with regular groupings

This condition comprises either no vowel change within one beat or the same tone durations and regular changes within one beat. From beat to beat tone durations change in even-numbered ratios.

The rhythmic structure of this condition allows the smoothest (legato) singing.

Condition (2): vowel changes with regular groupings and rests

This condition contains the same tone durations and regular changes within the individual beat. Tone durations change from beat to beat in even-numbered ratios. The implementation of rests brings about higher demands on timing and precise motor execution because legato and staccato vocalization changes from beat to beat.

Condition (3): vowel changes with irregular groupings

This condition consists of varying durations (also odd-numbered within one beat) and irregular changes. Tone durations change from beat to beat in odd-numbered ratios. Legato and staccato vocalization is combined also within individual beats. Syncopations, dotted notes, and rests bring about e.g., accent shifts (off-beats), which make the highest demands on movement timing and precision of motor execution but also on

Figure 1 shows three musical notation examples in bass clef, 4/4 time. Example 1 shows a regular sequence of notes for 'A' and 'I' with consistent durations. Example 2 shows a regular sequence with rests and varying note durations. Example 3 shows an irregular sequence with varying note durations and rests.

Fig. 1. Stimuli examples in musical notation.

Quadruple measure groupings with a duration of 4 sec. (1 beat per sec.) sung at a frequency of 220 Hz (A3) (1) Regular vowel changes (2) Regular vowel changes with rests (3) Irregular vowel changes.

working memory. This assumption is corroborated by studies researching on movement sequence learning (Kennerly et al., 2004; Lewis and Miall, 2003; Macar et al., 2002; Mayville et al., 2002).

Stimuli were sung by a female voice with the vowel change/a/i/ at a frequency of 220 Hz. The length of each stimulus was electronically set to 4 sec. with a max. deviation of 0.05 sec. Male subjects were allowed to transpose the heard stimuli down an octave.

For each condition (1–3) four grouping variations with the same complexity level were available.

Subjects had to listen and to immediately repeat the heard stimuli after the presentation had stopped. Subjects' reactions were recorded in order to assure that tasks were carried out adequately.

We used an event-related design where a total of 25 trials per condition were presented and 25 null-events were randomized included.

The stimuli were presented in a pseudo-randomized order with a mean interstimulus interval of 9 sec (jittered between 8 and 10 sec). The presentation time took 4 sec. and the duration of the repetition period varied according to the estimated jitter time.

The paradigm was implemented in Presentation (Neurobehavioral Systems) and synchronized to the scanner.

As concerns movement artefacts we point out that we compared three conditions utilizing the same response modality i.e., overt chanting. This allows generation of statistical maps that indicate activity more related to cognitive functions than to movement (Barch et al., 1999). Furthermore, we used an event-related design with varying interstimulus intervals and data averaged across a group of participants. Several studies confirm that this is an appropriate way to obtain more clearly interpretable patterns of activation and reduce motion-induced signal changes (Barch et al., 1999; Birn et al., 2004).

A sparse temporal scanning design was not used in this study because it was not our preferential interest to investigate perceptual mechanisms within the auditory cortex. Furthermore, our focus was not on phonetic correctness but on rhythm structure and our stimuli were constantly sung at a frequency of 220 Hz, which is beyond the main frequency peaks of the scanner spectrum.

Additionally we wanted to avoid attention loss and consequently lower functional response caused by relatively long inter-scan-intervals, which are required in sparse temporal schemes (Shah et al., 2000).

Stimuli were presented binaurally through MR-compatible headphones with a sound absorption rate of 30 dBA (Resonance Technology). All conditions were performed with eyes closed.

Participants were instructed to repeat the heard stimuli as exactly as possible and refrain from any motor or cognitive responses such as fingerlifting and silent counting.

2.3. Image acquisition

Functional images were obtained with a whole-body 3 T Siemens Trio MRI-system. Participants were fixated in the head coil using Velcro straps and foam paddings to stabilize head position and minimize motion artefacts. After orienting the axial slices in the anterior-posterior commissure (AC-PC) plane functional images were acquired using a T2*-weighted echo planar imaging (EPI) sequence with a repetition time (TR) of 2200 ms, an echo time (TE) of 30 ms and a flip angle (FA) of 90 degrees. 640 volumes consisting of 41 contiguous transversal slices with a thickness of 3.4 mm were measured. A 64×64 matrix with a field of view (FOV) of 240 mm was used, yielding an effective voxel size of $3.44 \times 3.44 \times 3.74$ mm.

2.4. Image analysis

Functional images were pre-processed and analyzed using SPM8 (Wellcome Department of Cognitive Neurology London UK).

Image Pre-processing: Images were realigned and unwarped in order to correct for motion and movement-related changes in magnetic susceptibility. Translation and rotation correction did not exceed 1.7 mm and 1.6° respectively for any of the participants. Thereafter, images were spatially normalized into the anatomical space of the MNI brain template (Montreal Neurologic Institute) to allow pixel-by-pixel averaging across subjects with a voxel size of $4 \times 4 \times 4$ mm in the x, y, and z dimensions. Finally, all images were smoothed using a Gaussian filter of $8 \times 8 \times 8$ mm to accommodate intersubject variation in brain anatomy and to increase signal-to-noise ratio in the images.

2.5. Statistical analysis

First, a random effects analysis was performed to search for significantly activated voxels in the individual pre-processed data using the general linear

model approach for time-series-data suggested by Friston and co-workers (Friston et al., 1995a, 1995b, 1995c, 1999) and implemented in SPM8 (<http://www.fil.ion.ucl.ac.uk/spm/spm.html>). Contrast-images were computed after applying the hemodynamic response function. A random effects analysis was performed using a one-sample *t*-test for each condition, where the reported contrasts are inclusively masked by the minuend with $p=0.05$ to eliminate deactivations of the subtrahend becoming significant because of the subtraction. Furthermore, we performed a conjunction analysis using the flexible factorial design to show the common activations of our conditions and a regression analysis to explore the effect of the complexity of the three main conditions. Statistical parametric maps (SPMs) were evaluated and voxels were considered significant if their corresponding linear contrast *t*-values were significant at a voxelwise threshold of $p=0.05$ (FWE-corrected). Only regions comprising at least 10 voxels will be reported. Finally, coordinates of activations were transformed from MNI to Talairach space (Talairach and Tournoux, 1988) using the matlab function `mni2tal.m` implemented by Matthew Brett (<http://www.mrc-cbu.cam.ac.uk/Imaging/mnispac.html>).

Localization of peak neural activity of the cerebellum was classified using the anatomical atlas of Schmahmann et al., (2000).

3. Results

3.1. Behavioral analysis

Recorded data were commonly analyzed by 2 professional musicians (singer and percussionist) post hoc. They assessed each stimulus repetition with either “correct” (score 1) or “incorrect” (score 0). Only unanimous assessments that both matching the pitch and rhythm production had been performed without error were scored 1. Data were only included in the study if

at least 75% of the stimuli were repeated correctly in each condition. 2 participants had to be excluded from the study because they did not fulfill the 75% criteria for all three conditions.

Using the Friedman-test for paired samples of non-normally distributed data no significant difference could be demonstrated concerning performance of the participants in the four grouping variations within each condition.

However, complexity of the condition seems to influence the performance significantly. An additional Wilcoxon-test post-hoc analysis confirmed this result for all three paired comparisons (3-1; 2-1; 3-2) using a Bonferroni-corrected threshold of $p < 0.008$.

3.2. FMRI data

A remark in advance: auditory stimulation was regarded as separately modeled condition in this design, which is not part of this paper. Auditory presentation and reproduction were time-shifted; subjects did not sing along but after the presentation had stopped. Hence the expected activations in the auditory areas caused by the auditory stimulus presentation will not be present in the reported results.

Furthermore, the magnitude of the auditory activation was comparable in each condition, so that the reported subtraction analyses yielded no additional significant activation in auditory areas.

3.3. Basic network for simple singing in rhythm sequences (conjunction)

To determine commonly recruited brain regions during singing for all three conditions a conjunction analysis was performed.

Additional significant activations, which were common for the three singing conditions were determined in bilateral supplementary motor area (BA 6), precentral gyrus (BA 6) and postcentral gyrus (BA 43). Cingulate gyrus (BA 32) was activated in the left

Table 1
Behavioral results: Friedman test

| Friedman test | Complexity levels | Complexity 1 | Complexity 2 | Complexity 3 |
|--------------------|-------------------|--------------|--------------|--------------|
| X^2 | 205.043 | 1.247 | 4.075 | 1.539 |
| df | 2 | 3 | 3 | 3 |
| Exact significance | 0.000* | 0.747 | 0.254 | 0.677 |

*Significant at $p < 0.05$.

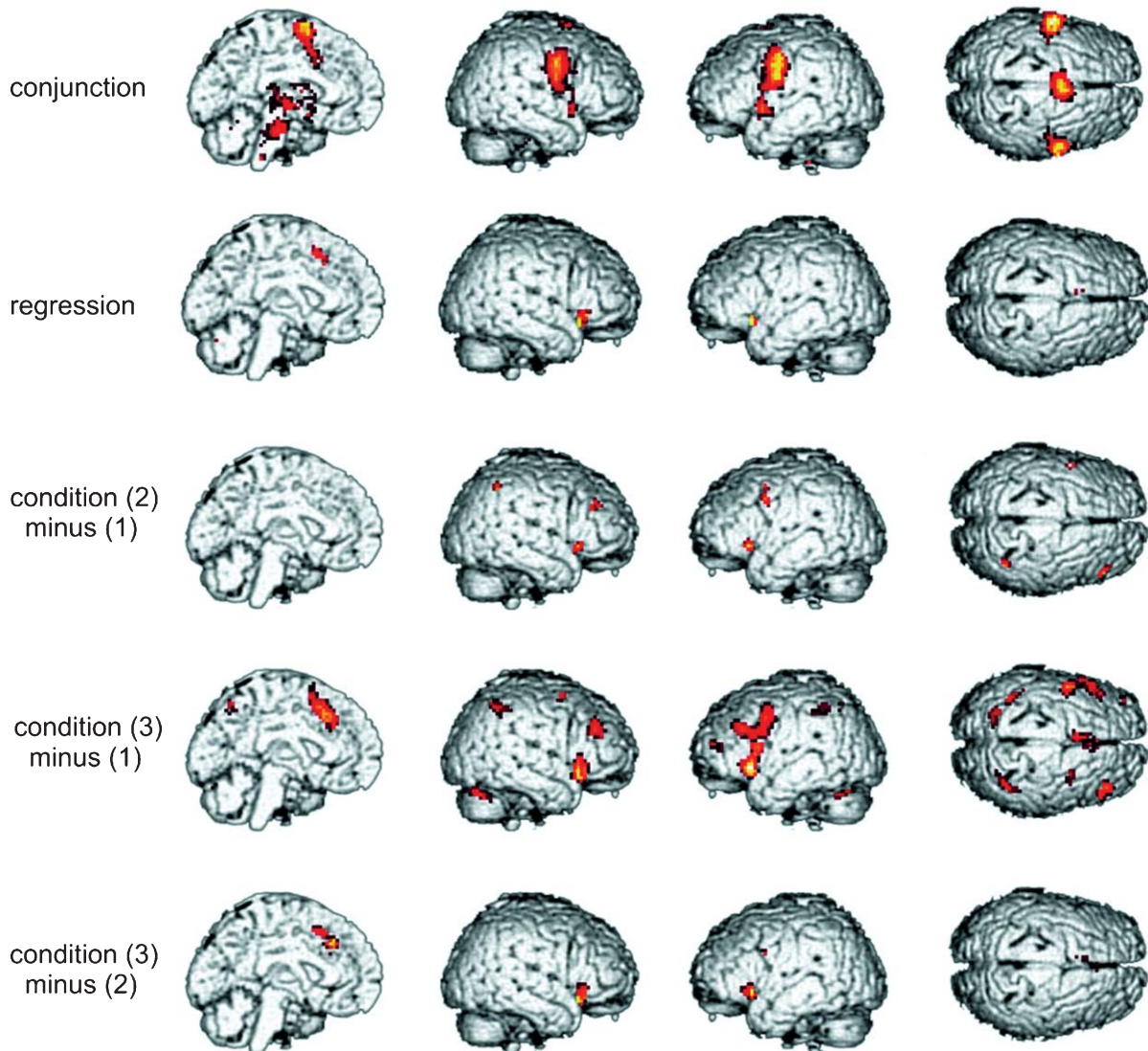


Fig. 2. Areas of significant brain activation derived from group analyses of the conjunction, regression and subtractions of the three singing tasks (FWE-corrected $p = 0.05$, threshold = 10 voxel).

hemisphere, while putamen and thalamus as well as occipital lobe (BA 19) were activated in the right hemisphere.

3.4. Regression

To determine brain regions related to complexity a regression analysis was performed where each complexity level was modeled. This analysis revealed bilateral inferior frontal gyrus (BA 47) and anterior

insula (BA 13) as well as left cingulate gyrus (BA 32) as those areas whose activity correlated with rhythm complexity.

3.5. Subtraction

To determine how neural activity differed between conditions subtractions between conditions were performed. Additional significant activations remained for the singing tasks concerning following subtractions:

3.5.1. *Regions activated in the “regular with rests” condition compared to the “regular” condition*

Subtraction of condition (2) minus (1) yielded significant bilateral activation of inferior frontal gyrus (BA 47). Precentral gyrus (BA 9, 6) was activated in the left hemisphere, while middle frontal gyrus (BA 46) was activated in the right hemisphere. Inferior parietal lobe (BA 40) was activated in the right hemisphere.

3.5.2. *Regions activated in the “irregular” condition compared to the “regular” condition*

Subtraction of condition (3) minus (1) yielded significant bilateral activation of inferior frontal gyrus (BA 47), and anterior insula (BA 13). Precentral gyrus (BA 9, 6) was activated in the left hemisphere. While middle and superior frontal gyrus (BA 6, 9) was activated in the right hemisphere, middle frontal gyrus (BA 10) was activated in the left hemisphere. Cingulate gyrus (BA 32, 24) was activated bilaterally. Bilateral activation was also found in the inferior and superior parietal lobes (BA 40, 7) and posterior cerebellar hemispheres.

3.5.3. *Regions activated in the “irregular” condition compared to the “regular with rests” condition*

Subtraction of condition (3) minus (2) yielded significant bilateral activation of inferior frontal gyrus (BA 47), and anterior insula (BA 13). Precentral gyrus (BA 6) was activated in the left hemisphere. Cingulate gyrus (BA 32) was activated bilaterally.

4. Discussion

Rhythm structure seems to be a decisive factor concerning activation patterns during repetition of monotonously sung vowel changes. We investigated three grouping variations, which were sung as vowel changes with regular groupings, regular groupings with rests, and vowel changes with irregular groupings. To our knowledge comparably demanding tasks using unknown material and requiring differently demanding sequencing performance and working memory capacity while singing a single pitch repetition have not been investigated up to now.

4.1. *Basic network of simple singing in rhythm sequences*

Our conjunction analysis yielded common activations for all three conditions in the following areas: bilateral supplementary motor area and precentral gyrus. Cingulate gyrus was activated in the left hemisphere, while putamen and thalamus as well as occipital lobe were activated in the right hemisphere.

Similar activations have also been reported by other studies concerned with singing (Perry et al., 1999; Riecker et al., 2000; Jeffries et al., 2003; Brown et al., 2004; Callan et al., 2006; Gunji et al., 2007; Kleber et al., 2010; Zarate and Zatorre, 2008), although our results only partially confirm the often described right hemisphere asymmetry in motor regions during singing mentioned in the studies cited above. We would like to emphasize once more that comparisons between these studies and ours can hardly be drawn because of varying designs, the difficulty to distinguish between pitch and rhythm effects, and not at least because of different data analyses.

The PET-study of Perry et al., (1999) yielded that CBF increase during repetitively singing of a single pitch was more robust in the right ventral-most precentral gyrus compared to a perception baseline. The PET-study of Brown et al., (2004) also demonstrated greater right hemisphere frontal operculum (BA 44, 45 and 6) and supplementary motor area (medial BA 6) activation in their monotonic vocalization task contrasted with rest.

If at all these two studies are most likely comparable with our study because they also investigated single pitch repetitions.

All of the above mentioned areas, which were commonly activated in all of our three singing tasks are also reported from speech production related to vocalization (for reviews see Brown et al., 2009; Jürgens, 2002). Precentral gyrus corresponding to the somatotopic orofacial region of the motor and premotor cortices including the large mouth and larynx representations forms one of the essential areas activated by vocalization.

In contrast to the findings of Perry et al., (1999) and Brown et al., (2004) our conjunction analysis yielded activation of precentral gyrus more distinct in the left hemisphere. We assume that tongue movement, which is the essential movement of our vowel change /a/i/ is one of the main reasons (Brown et al., 2009; Schritker, 2008). The fact that our data also yielded activation of

postcentral gyrus, which is reported to represent tongue sensory representation (Guenther et al., 2006) corroborates our assumption. Furthermore, the way in which articulatory movements had to be executed might be an important factor. At least movements of condition (2) and (3) had to be executed precisely, which means exact initiation was needed. We hypothesize that especially the initial phase of vocal preparation became the focus of attention, which is reported to be dominated by the left hemisphere (Jürgens, 2002).

Apart from motor function like initiation control, which we just mentioned attentional and working memory demands are supposed to be the main reasons for additional left hemisphere activation of the cingulate gyrus (Benedict et al., 1998; Macar et al., 2002). While some studies, which investigated singing compared to speaking do not report cingulate gyrus activation during singing (Riecker et al., 2000; Özdemir et al., 2006), others report right cingulate gyrus activation (Jeffries et al., 2003; Saito et al., 2006). Activation of left cingulate gyrus is in accordance with the Perry et al., (1999) and Brown et al., (2004) studies and also with the study of Zarate and Zatorre (2008), though these studies contrasted simple singing either with rest or perception.

As concerns activation of basal ganglia Perry et al., (1999) do not report on that. Brown et al.'s (2004) monotonic vocalization task yielded bilateral putamen activation. The authors attribute this activation to processes supporting the ipsilateral cerebral hemispheres.

Several imaging studies concerned with speech revealed activation of the putamen (Klein et al., 1994; Nota and Honda, 2004; Schnitker, 2008). However, most of the studies concerned with singing do not report basal ganglia activation for their production tasks (Jeffries et al., 2003; Riecker et al., 2000; Saito et al., 2006; Callan et al., 2006; Özdemir, 2006).

Since to our knowledge studies comparable to ours are not available from the field of singing or speech we would like to mention that SMA and premotor activation as well as cerebellar and basal ganglia activation is often reported from studies researching timing, duration perception, rhythm perception and production (Chen et al., 2008; Coull, 2004; Ferrandez et al., 2003; Grahn, 2009; Grahn and Brett, 2007; Halsband et al., 1993; Macar et al., 2006; Rao et al., 2001; Penhune et al., 1998; Thaut, 2003).

Given that all of our conditions required explicit temporal sequencing i.e., generation of an internal beat

(Grahn, 2009; Grahn and Brett, 2007) activation of the basal ganglia, which is reported from the studies mentioned above may be typical for vocal production tasks with corresponding demands as well.

The cortico-subcortical network of supplementary motor areas, premotor cortex, and putamen reflecting analysis of temporal sequences and also internal generation of an underlying beat as suggested by Grahn (2009) can be confirmed by our results also for production of rhythm sequences during simple singing.

4.2. *Main effects of complexity*

The main result of both subtractions (2) minus (1) and (3) minus (1) is the additional significant bilateral activation of inferior frontal gyrus (BA 47), however, subtraction (3) minus (1) yielded a z-score at least twice as high as in subtraction (2) minus (1) (see Table 2).

Since the “easiest” condition is subtracted from the most demanding condition this result is not surprising. Astonishing, however, is the clear distinctness compared to the other subtractions.

It seems as if activation of BA 47 was typical for condition (2) and (3), which implies that regularity with rests as well as irregularity may cause this activation. Although, taking into consideration the enormous increase of activation and the fact that subtraction of condition (3) minus (2) also resulted in significant activation of BA 47 we suppose that irregularity is the most important factor. This applies also for activation of the precentral gyrus, which was additionally activated in the left hemisphere in all of our three subtractions. As already suggested precise and rapid movement execution particularly in the initial phase of vocal preparation is very likely the reason for this additional activation caused by rhythm complexity.

Area 47 activation is reported from studies investigating working memory for pitch (Zatorre et al., 1992, 1994), auditory attention to space and frequency (Zatorre et al., 1999), divided attention for pitch and rhythm (Platel et al., 1997), meter discrimination (Parsons, 2001) or rhythm production to visual inputs (Penhune et al., 1998).

Language studies have shown the role of BA 47 especially in semantic processing (Bookheimer, 2002; Klein et al., 1997; Poldrack et al., 1999; Zahn et al., 2004), which has also been confirmed by studies searching for the parallels between music and language

Table 2

Regions of peak activity. Coordinates are reported in Talairach space (Talairach and Tournoux, 1988). BA = Brodmann area; Inf = infinite; SMA = supplementary motor area

| | BA | Left hemisphere | | | | | Right hemisphere | | | | |
|---|-------|-----------------|-----|-----|----------------|----------|------------------|-----|-----|----------------|----------|
| | | x | y | z | Cluster size K | z-scores | x | y | z | Cluster size k | z-scores |
| Conjunction | | | | | | | | | | | |
| Common activations for all three conditions | | | | | | | | | | | |
| Frontal lobe | | | | | | | | | | | |
| SMA | 6 | -2 | 6 | 61 | 343 | Inf | 4 | 6 | 61 | 343 | Inf |
| Precentral gyrus | 6 | -56 | -2 | 26 | 941 | Inf | 50 | -5 | 30 | 463 | Inf |
| Postcentral gyrus | 43 | -54 | -7 | 21 | 941 | Inf | 56 | -7 | 20 | 463 | Inf |
| Cingulate gyrus | 32 | -6 | 10 | 39 | 343 | 6.26 | | | | | |
| Occipital lobe | | | | | | | | | | | |
| Fusiform gyrus | 19 | | | | | | 12 | -36 | -11 | 78 | 7.16 |
| Subcortical | | | | | | | | | | | |
| Putamen | | | | | | | 21 | 5 | -4 | 147 | Inf |
| Thalamus | | | | | | | 12 | -6 | 15 | 147 | 5.68 |
| Regression | | | | | | | | | | | |
| Frontal lobe | | | | | | | | | | | |
| Inferior frontal gyrus | 47 | -45 | 16 | -8 | 15 | 5.61 | 30 | 22 | -8 | 53 | 6.39 |
| Insula | 13 | -31 | 24 | 0 | 15 | 5.61 | 29 | 19 | -8 | 53 | 6.39 |
| Cingulate gyrus | 32 | -9 | 16 | 44 | 22 | 6.05 | | | | | |
| Subtraction (2)-(1) | | | | | | | | | | | |
| Frontal lobe | | | | | | | | | | | |
| Inferior frontal gyrus | 47 | -33 | 19 | -3 | 30 | 5.99 | 33 | 19 | -5 | 22 | 5.58 |
| Precentral gyrus | 9/6 | -44 | 6 | 37 | 20 | 5.33 | | | | | |
| Middle frontal gyrus | 46 | | | | | | 48 | 35 | 27 | 13 | 5.26 |
| Parietal lobe | | | | | | | | | | | |
| | 40 | | | | | | 39 | -48 | 45 | 13 | 5.32 |
| Subtraction (3)-(1) | | | | | | | | | | | |
| Frontal lobe | | | | | | | | | | | |
| Inferior frontal | 47 | -30 | 22 | -5 | 579 | Inf | 33 | 22 | -8 | 214 | Inf |
| Insula | 13 | -28 | 20 | -5 | 579 | Inf | 30 | 19 | -6 | 214 | Inf |
| Precentral gyrus | 6/9 | -42 | 6 | 31 | | 7.39 | | | | | |
| Superior frontal gyrus | 9 | | | | | | 45 | 36 | 32 | 77 | 6.56 |
| Middle frontal gyrus | 6 | | | | | | 27 | 8 | 56 | 19 | 5.71 |
| Middle frontal gyrus | 10 | -36 | 52 | 12 | 25 | 5.43 | | | | | |
| Cingulate gyrus | 32/24 | -4 | 16 | 42 | 276 | 7.07 | 6 | 26 | 24 | 276 | 6.14 |
| Parietal lobe | | | | | | | | | | | |
| Inferior | 40 | -36 | -45 | 42 | 151 | 6.13 | 36 | -51 | 48 | 79 | 6.75 |
| Superior | 7 | -24 | -57 | 45 | 151 | 5.8 | 24 | -54 | 40 | 79 | 5.09 |
| Cerebellum | | | | | | | | | | | |
| Lobule VI | | -36 | -63 | -21 | 27 | 5.45 | 42 | -69 | -21 | 74 | 5.92 |
| Subtraction (3)-(2) | | | | | | | | | | | |
| Frontal lobe | | | | | | | | | | | |
| Inferior frontal | 47 | -33 | 22 | -5 | 48 | 5.71 | 30 | 22 | -8 | 30 | 6.52 |
| Insula | 13 | -29 | 19 | -5 | 48 | 5.71 | 23 | 20 | -6 | 80 | 6.52 |
| Precentral gyrus | 6 | -39 | 3 | 26 | 12 | 5.67 | | | | | |
| Cingulate gyrus | 32 | -9 | 16 | 44 | 26 | 6.11 | 6 | 27 | 33 | 46 | 5.91 |

(Brown et al., 2006; Levitin, 2009; Levitin and Menon, 2003; Steinbeis and Koelsch, 2008). As regards our focus it is important to note that these studies have in common the description of BA 47 involvement in temporal perceptual organization. BA 47 seems to be involved when temporal expectancies and temporal coherence are involved (Brown et al., 2006; Levitin, 2009). According to our analyses pars orbitalis seems

to be one of those areas whose activity correlates with rhythm complexity during simple singing. To the best of our knowledge task-dependent activation of inferior frontal gyrus (BA 47) has not been reported up to now in connection with singing tasks and singing of vowel changes, respectively.

While subtraction of condition (2) minus condition (1) resulted in additional significant activation of (BA

47), only subtraction of condition (3) minus (2) and (3) minus (1) yielded additional activation of inferior frontal gyrus (BA 47) as well as insula (BA 13). The fact that only subtractions from the most demanding condition (3) additionally activated the insula seems to indicate that irregularity is the main reason for this activation.

The data of the Brown et al., study (2004) yielded activation of the left insula for their monotonic vocalization task, although the authors do not discuss this result. Perry et al., (1999) report bilateral insula activation. The authors attribute left anterior insula activation to its importance in volitional vocalization, and right anterior insula activation to pitch monitoring aspects of singing. Zarate and Zatorre (2008) who investigated vocal pitch regulation revealed for both non-musicians and experienced singers right insula activation during simple singing. They hypothesize that the insula plays an important role in audio-vocal integration. It is important to emphasize, though, that in all three studies simple singing was contrasted either with rest or perception.

Left insula activation is reported from studies concerned with musical rhythm discrimination and attention to changes in rhythm respectively (Platel et al., 1997). Bamiou et al., (2003, see for review) emphasize the role of both insulae for many aspects of auditory temporal processing e.g., sequencing of sounds and detection of a moving sound. As a result of their fMRI study Nota and Honda (2003) conclude that the insula is involved when different syllables have to be sequenced in a special order in contrast to repetitive production of the same syllable. According to our results sequencing in a special order per se does not seem to be the decisive factor but irregular sequencing. In all of our three tasks subjects had to sequence vowel changes in a special order. However, only subtraction from the most demanding i.e., irregular condition yielded additional activation of the insula.

Riecker et al., (2000) conclude in their study, which compared singing and speaking of a well-known non-lyrical tune that left insula supports coordination of speech articulation while right insula mediates temporo-spatial control of vocal tract musculature during singing. In accordance with the “double filtering by frequency theory” (Ivry and Roberston, 1998) Ackermann and Riecker (2004) emphasize the role of the insular cortex operating across different time domains with a left hemisphere specialization for segmental

information and a right hemisphere specialization for suprasegmental information i.e., intonation contours and musical melodies.

Our tasks consisted of segmental material (vowel changes), which had to be sung on a single pitch. While pitch information and number of vowel changes were kept constant temporal information changed requiring differently demanding sequencing performance, working memory capacity and articulatory movements on the one hand but also more pitch monitoring capacities for the most difficult task. We hypothesize that this is the explanation for bilateral activation of BA 47 and insula as two areas whose activity correlates with rhythm complexity.

Likewise only subtractions from the most demanding condition (3) yielded additional activation of bilateral cingulate gyrus. To our opinion this activation can be explained by the fact that especially irregularity of condition (3) requires a complex cognitive process, which includes that response generation and respective action planning have to be coordinated (Macar et al., 2002). Our regression analysis corroborates that activation of left cingulate gyrus correlates with rhythm complexity.

Several studies concerned with temporal processing mention activation of ventrolateral prefrontal cortex (Ferrandez et al., 2003; for review see Lewis and Miall, 2003; Rao et al., 2001). Some of these studies also report premotor cortex activation (Ferrandez et al., 2003; Rao et al., 2001), which is in accordance with our results. We agree with Ferrandez et al., (2003) that activation of ventrolateral prefrontal cortex together with left premotor cortex regions is probably related to sustaining attention in order to maintain temporal information in working memory. A new finding is that these activations increase depending on rhythm complexity during simple singing.

5. Conclusion

To the best of our knowledge singing has not been investigated in connection with potential rhythm or grouping influences, neither with healthy subjects nor with patients.

Our results demonstrate that rhythm structure influences activation patterns and intensity of activation during simple singing. According to our findings the basic network of simple singing in rhythm sequences comprises bilateral supplementary motor area, premo-

tor cortex more distinct in the left hemisphere, left cingulate gyrus, and right basal ganglia.

This activation pattern largely confirms our assumption of bilateral premotor and prefrontal activation. Furthermore, our subtraction analyses yielded that depending on rhythm complexity intensity of activation increased in a core area consisting of bilateral pars orbitalis (BA 47), and left precentral gyrus. Only irregular groupings making the highest demands on attention, working memory and movement timing resulted in additional activation of pars orbitalis and insula more distinct in the left hemisphere as well as bilateral cingulate gyrus, and parietal lobes. According to our results bilateral pars orbitalis, insula, and left cingulate gyrus are those areas whose activity correlated with rhythm complexity.

These findings also substantiate our hypotheses and possibly support our considerations mentioned in the introduction: comparatively slow tempo and regularity are typical for the singing studies cited above, regardless whether monotonous pitch repetitions, well-known tunes or arias were investigated. We suggest that this is one of the main reasons for right hemisphere asymmetries in motor regions reported from most of these studies. Our results are a first evidence for the fact that simple singing of irregular vowel changes, which requires greater processing load i.e. sequencing and working memory performance, engages left hemisphere mechanisms to a greater extent than simple singing of regular vowel changes and regular vowel changes with rests.

As regards our further research, it is important to note that the reported activations comprise also those areas that are affected in patients suffering from aphasia and apraxia of speech (Dronkers, 1996; Ogar et al., 2005). However, the greater bihemispheric organization for singing compared to speech might offer a chance for those patient groups. As we already stated in our introduction right hemisphere abilities like pitch and intonation processing are normally spared in these patients, while left hemisphere processing of temporal-rhythmic structures is often impaired. Since our results point out that activation patterns during simple singing can be influenced by rhythm complexity at least in healthy subjects, we assume that a directed use of the voice might serve as a systematically applied training in order to support language rehabilitation in patients.

If it was possible to improve the impaired capabilities of temporal structuring in patients suffering from aphasia and also apraxia of speech that way e.g. by

activating peri-lesional areas this would be a new and promising approach.

Our current therapy study with patients suffering from aphasia and apraxia of speech will demonstrate if and how improvements in language and speech motor performance will correlate with changes in brain activation.

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