

Review articles

Contributions of neuroimaging in singing voice studies: a systematic review

*Contribuições da neuroimagem no estudo da voz cantada:
revisão sistemática*

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ABSTRACT

It is assumed that singing is a highly complex activity, which requires the activation and interconnection of sensorimotor areas. The aim of the current research was to present the evidence from neuroimaging studies in the performance of the motor and sensory system in the process of singing. Research articles on the characteristics of human singing analyzed by neuroimaging, which were published between 1990 and 2016, and indexed and listed in databases such as PubMed, BIREME, Lilacs, Web of Science, Scopus, and EBSCO were chosen for this systematic review. A total of 9 articles, employing magnetoencephalography, functional magnetic resonance imaging, positron emission tomography, and electrocorticography were chosen. These neuroimaging approaches enabled the identification of a neural network interconnecting the spoken and singing voice, to identify, modulate, and correct pitch. This network changed with the singer's training, variations in melodic structure and harmonized singing, amusia, and the relationship among the brain areas that are responsible for speech, singing, and the persistence of musicality. Since knowledge of the neural networks that control singing is still scarce, the use of neuroimaging methods to elucidate these pathways should be a focus of future research.

Keywords: Voice; Neuroimaging; Music

RESUMO

Admite-se que o canto seja uma atividade de alta complexidade pois requer ativação e interconexão de áreas sensório-motoras. Esta pesquisa teve como objetivo apresentar as evidências originadas por estudos de neuroimagem sobre a atuação do sistema motor e sensitivo na produção do canto. Na construção da revisão sistemática, foram premissas o período de publicação entre 1990 e 2016, artigos publicados em periódicos indexados e constantes nas bases de dados *PubMed*, *BIREME*, *Lilacs*, *Web of Science*, *Scopus* ou *EBSCO*, referentes a estudos sobre características do canto humano analisadas por neuroimagem. Os nove artigos analisados, com emprego de magnetoencefalografia, imagem por ressonância magnética funcional, tomografia por emissão de pósitrons ou eletrocorticografia, possibilitaram comprovar existência de uma rede neuronal interligada entre a modalidade falada e cantada para identificação, modulação e correção de violações de *pitch*, que podem ser alteradas com o treinamento do cantor, bem como alteração da estrutura melódica e harmonização do canto, amusia, relação entre áreas cerebrais responsáveis pela fala, canto e persistência da musicalidade. Assim, o conhecimento das áreas cerebrais e das interconexões necessárias ao canto ainda é escasso e deve ser um tema de pesquisas no futuro, empregando métodos de neuroimagem.

Descritores: Voz; Neuroimagem; Música

INTRODUCTION

Singing is a specialized vocal behavior, which is only present in a very limited range of animals, including man and diverse species of birds. The production of a singing voice is mediated by a specialized cerebral system that is constituted of specific interconnected areas of the brain¹.

Singing animals can be differentiated into the following two groups on the basis of song learning: those that learn only for a period, and those that learn their whole lives¹. By comparing these two groups, along with non-singing birds, song learning has emerged as a new evolutionary characteristic, which depends on the formation of new neural centers of control².

Dissimilarities between the vocal behavior of man and their closest genetic relatives (chimpanzees and baboons) highlight that humans' singing ability might not be derived from an ancestral learning of hominids species. The most likely hypothesis is that the system of human singing is a new neural specialization, which is analogous to the singing system of birds^{1,2}. This specialization derives, among other factors, from man's ability to exercise volitional control of vocal fundamental frequency, especially when singing without words, such as an arpeggio, which is crucially dependent on the movements of the vocal folds³.

Studies referring to the neurological aspects of song production in the literature are scarce, as researchers usually do not investigate the musical ability of non-singing subjects for means of comparison.

Within the last two decades, neuroimaging studies that aimed to identify the activation of brain's sensorimotor areas during repetitive or sustained singing of one note, the emission of a sung word in different rhythms, and pieces of popular music or Italian arias. Harmonized singing, which is defined as the simultaneous production of two or more sounds, has also been studied. These findings add to the understanding of the processes of perception and production in singing, which can help train singers and voice professionals, in addition to people with disorders of speech or song production, as both use the same the neural connections^{2,4}. This context is socially relevant when one considers the function of singing in social cohesion, motivation, and the structuring of group identity.

To contribute to this area of knowledge, the objective of the current study was to present original evidence, based on neuroimaging studies with a focus on the activation of the sensorimotor system in the production of song.

METHODS

A systematic review was performed, separately, by three trained researchers (GOA, HJS, and PMMB). The inclusion criteria for articles were as follows: containing one or more of the chosen descriptors (i.e., <neuroimaging>, <voice>, <vocal training>, or <singers>); published in Portuguese, English, or Spanish, between 1990 and 2016, in indexed journals and present in one of the following databases: PubMed, BIREME, Lilacs, *Web of Science*, *Scopus*, or EBSCO.

The exclusion criteria were as follows: conference abstracts, book chapters, master's theses, doctoral dissertations, or articles that involved research relating solely to the spoken voice.

In total, 21 articles were found from the reference databases and analyzed according to the above-mentioned criteria. During the beginning of the analysis, two articles were excluded; one article was excluded because the research subjects were dove-like birds⁴, while the other referred exclusively to issues relating to aspects concerning the spoken voice⁵. After reading the abstracts, two more articles were excluded, since one presented a unique approach regarding the spoken voice⁶ and the other referred to the dopaminergic activation of bird song⁷. When the original version of the remaining articles were read in their entirety, the researchers independently excluded five more articles because of the following reasons: a focus on the auditory-motor mapping of pitch⁸ control, an analysis of the performance of the cerebral cortex after transcranial stimulation while reading and performing musical pieces⁹, a focus on the use of melodic intonation therapy to improve severe cases of non-fluent aphasia¹⁰, as well as two other studies because these were systematic reviews^{11,12}. During the stages of research, study evaluations, and data analyses, the researchers located opposing viewpoints in the respective analyses, compared the results, and settled disagreements by consensus (Figure 1).

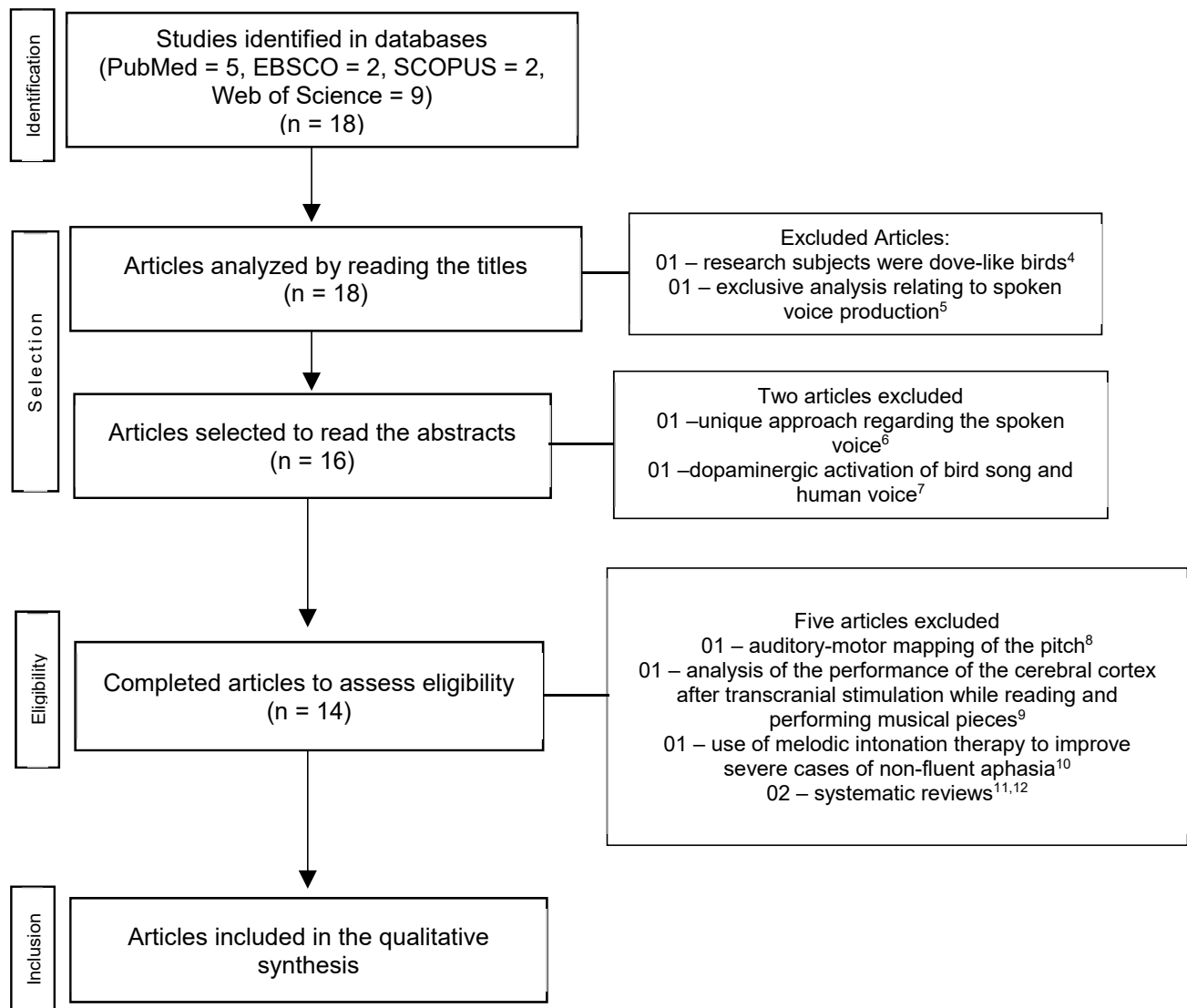


Figure 1. Flowchart outlining the article selection process for the current systematic review

LITERATURE REVIEW

A total of 9 articles were included in this review. The articles were grouped according to the following central themes: alternation of the melodic structure in singing, harmonic singing, amusia, relationship between cerebral areas responsible for speech and song, and the persistence of musicality.

Perry et al.³ published one of the first studies regarding the identification of cerebral regions involved in singing simple songs (where only one note or pitch was maintained, which is known as the fundamental frequency of voice). Brown et al.¹ analyzed the alteration of the melodic structure and harmonization of songs. Terao et al.¹³ performed a study on amusia. The relationship between the areas of the brain responsible for speech and singing was the theme of the studies by

Wilson et al.¹⁴; Zarate, Wood and Zatorre⁴; Rosslau et al.¹⁵; Callan et al.¹⁶; Roux et al.¹⁷; and Jungblut et al.¹⁸, which investigated areas of the brain responsible for the production and perception of rhythm during singing (Figure 2).

Neuroimaging studies demonstrated that the learning and production of song (*song control system*) depend on the action of diverse areas of the brain, acting in a specific neural network, to grant meaning to musicality, conceptualized as the ability to generate meaning through making expressive music¹⁴. Prior research on song production has conducted with a focus on the alteration of its melodic structure, harmonization, amusia, and the persistence of song and musicality in patients with Broca's aphasia¹.

One of the first studies employing neuroimaging was performed by Perry et al.³, who used positron

Author(s)	Year	Objective	Study Design	Findings	Conclusions
Perry et al. ³	1999	To investigate the cerebral blood flow during simple singing when compared to passive listening of complex-tones, using positron emission tomography (PET)	Primary, cross-sectional, observational study	Cerebral blood flow increases in brain areas related to motor control, as during the speech, but the changes in the Heschl's gyrus were related to the perception of fundamental frequency	Singing and the emission of a vowel in a single pitch seem to activate similar brain areas as speech; yet, in some regions an asymmetric activation, which was exclusively linked to singing was observed.
Brown et al. ¹	2004	To investigate the multifactorial vocal system using PET, to assess the listening and response system of non-professional singers, during repeated singing, harmonizing new melodies, or singing monotonically.	Primary, cross-sectional, observational study	In general, there was a greater increase in blood flow to the primary and secondary auditory cortex, primary motor cortex, frontal operculum, insula, posterior cerebellum and posterior Brodmann area 22	The three tasks of listening to a response activated the frontal operculum (Broca's area), which was involved in producing a sequence and motor cognitive imitation, implied in musical imitation and vocal learning
Terao et al. ¹³	2006	To describe psychophysical aspects of vocal amusia in a professional tango singer, following a stroke that affected the upper temporal cortex of the right hemisphere	Case report	Magnetic resonance imaging demonstrated damage in the right parietal cortex, which affected pitch perception	The damage in the cortex of the right brain hemisphere caused perceptive and expressive music loss
Roux et al. ¹⁷	2009	To identify the brain areas involved in singing and speech regions	Case report	Stimulation electrocorticography during surgery for tumor removal demonstrated the dissociation that exists between speech and singing, outside the primary sensorimotor brain area	Identifying the dissociation indicated that these two functions used distinct neural connections
Wilson et al. ¹⁴	2011	To investigate the relationship between musical and speech functions and their interaction with lyric singing tasks	Primary, cross-sectional, observational study	Functional magnetic resonance imaging (fMRI) demonstrated that singing and speech were elicited by contiguous brain areas. The interrelation between these areas was reduced as the singer became more specialized	The specialization of lyrical singers caused less interdependence of the cerebral areas devoted to singing and speech, demonstrating a more refined and less dependent speech process
Zarate, Wood, Zatorre ⁴	2010	To analyze the voluntary and involuntary pitch regulation and its correlation with the neural connections	Primary, cross-sectional, observational study	fMRI proved that lower pitch adjustments are under less voluntary control than the large variations	During pitch corrections, the superior posterior temporal sulcus interacts with the anterior region of the rostral cingulate area and the anterior part of the insula, before the voluntary pitch correction occurs.

Author(s)	Year	Objective	Study Design	Findings	Conclusions
Rosslau et al. ¹⁵	2016	To compare the activation of brain regions in singers and actors, who are professionally trained for singing or speech, using magnetoencephalography	Primary, cross-sectional, observational study	Magnetoencephalography proved that there was an interconnected neural network between speech and singing to identify and correct pitch variations	Pitch changes in speech activated the left temporal region. In contrast, singing activated the right temporal region.
Callan et al. ¹⁶	2006	To investigate brain regions that were similarly or differently involved in listening and singing, when compared to speech	Primary, cross-sectional, observational study	fMRI showed that regions of the left temporal plane and superior parietal-temporal areas, bilateral pre-motor cortex, lateral region of the sixth cerebellum lobule, superior anterior temporal gyrus and the planum polare were involved in listening, speech and singing.	There was a differential pattern between speech and singing. Speech activated the left temporal lobe, compared to singing, both in listening and production. However, activation of the right temporal lobe primarily occurred with singing
Jungblut et al. ¹⁸	2012	To investigate the brain areas responsible for music rhythm perception	Primary, cross-sectional, observational study	fMRI showed that activation of the bilateral supplementary motor area and pre-motor cortex in the left hemisphere were common to both singing and speech. Activation of other areas was greater in more complex rhythmical expressions	The rhythmic structure is a decisive factor for the lateralization and activation of specific areas while singing

Figure 2. Characteristics of the articles included in the systematic review

emission tomography (PET) to determine the blood flow of 13 volunteers who repetitively vocalized one pitch or listened to complex tones of varying frequency such as singing, with the aim of comparing areas of the brain that were activated during both tasks. The authors based their study on the results of direct electric brain stimulation that were characterized by the production of sounds. They demonstrated that sound production was associated with an increased blood flow to cortical regions such as the pre-central gyrus, supplementary motor region, and anterior cingulate cortex.

The localization of the supplementary motor region in repetitive singing was fundamentally identical with that of speech in the cingulate sulcus and cerebellum, yet with a peak corresponding to the lowest level of vocal motor control. The authors also identified interactions between the anterior cingulate and auditory cortices, which indicated that auditory cortical areas can perform decoding functions to offer *feedback* for desired vocalizations. This occurred to such an extent that the participants could ignore acoustic events when

concentrating attention on the song itself, which is defined as figure-background⁹.

These findings consequently led to other studies with a focus on the cerebral areas involved in singing. Brown et al.¹, performed a cross-sectional, observational, interventional study, on song harmonization involving male and female participants who were all amateur singers. The study was conducted using PET, while the participants performed complete repetition of melodies, harmonic singing, vocalizing isochronic and monotonic sequences, or rested with closed eyes.

The authors identified that harmonized singing, where the individual produces two or more sounds simultaneously, resembled monophonic singing, in that the melody of the voice is lacking any accompaniment, such as the Gregorian chants. Both involve the creation of a single melody line, making it difficult to parse the predominant cerebral areas involved in one task or the other. However, there was greater bilaterality in areas of high electrical levels (Brodmann's Area [BA] 22 and 38) in harmonization, compared to monophonic singing. Nonetheless, this bilaterality cannot be exclusively

attributed to singing harmonization. The authors attributed their finding to a specialization for harmony in the auditory area of the left hemisphere. Alternatively, an acoustic effect due to the presence of a greater number of notes and musical texture under harmonic conditions was also considered¹.

Extending their study, Brown et al.¹ also confirmed that the human singing system involved in imitation, repetition, and the adaptation of pitch depended on cerebral areas that can be hierarchically grouped into primary and secondary vocal and auditory cortex regions and high-level cognitive areas. The primary auditory cortex (BA 41) and motor cortex, which controls the mouth region (BA 4), were activated in all the study's tasks. The tasks also activated BA 42 in the auditory cortex, BA 22 in the motor region (i.e., BA 6), the frontal operculum (BA 44/6), and the left insula. Thus, the researchers hypothesized that the upper part of the bilateral temporal lobe could comprise a third specialized auditory level for the processing of melodies with high-level pitch.

Amusia has been another focus of studies on studying, based on neuroimaging findings. Amusia is the partial or total difficulty in perceiving melodic sounds or rhythms, due to a dysfunction in the neural processing of music¹⁴. Terao et al.⁹ related a case of amusia in a professional tango singer following a cerebrovascular event. Magnetic resonance imaging (MRI) was used to identify a lesion in the upper part of the temporal cortex of the right hemisphere, which they concluded caused the alterations in the patient's musical perception and recognition, related to pitch, timbre, and musicality. The singer's perception of tempo and rhythm, however, were preserved because the left hemisphere was not affected. As the lesion was present in the right posterior portion of the insula, the authors realized that the deficits in the patient's singing ability were related more to the motor performance of vocalization than to the auditory feedback. This confirmed the possibility that amusia was a result of the impairment of pitch processing involving specific connections between the motor and auditory cortical areas, which destabilized the effective transformation of the auditory mechanism or the memory of intentional vocal emission¹⁹.

Analogous to the study by Terao et al.¹³ five clinical cases based on amateur singers who underwent brain tumor removal surgery, in addition to speaking and singing tests, supported the hypothesis that there are common connections between the brain

regions associated with speech and singing. Electrocortical data generated by cerebral stimulation during the brain surgery to remove the tumors demonstrated that singing was always affected when the pre-central gyrus was stimulated, independent of the handedness of the patient. The stimulation of facial areas, the tongue, and vocal folds also altered the singing, since this function requires bilaterality. However, the stimulation of the medial frontal gyrus and right inferior gyrus only provided interference in the patient's singing. The authors concluded that the different alterations in singing and speech indicated that these functions activate different areas of the brain, at least at some stage, enabling better comprehension in cases of amusia in patients without speech impairments.

Wilson et al.¹⁴ further investigated the hypothesis that distinct areas are used in the processing of speech and singing, such that secondary and tertiary auditory areas are linked to pitch, musicality, monophonic singing, melodic vocalization, and harmonic singing, which is different from speech¹. However, to do this, they subjected high-performing opera singers to functional MRI (fMRI).

Wilson et al.¹⁴ demonstrated that non-high-performance singers used more cerebral areas of speech for singing, since there is an interconnecting neural network between these two areas. This behavior differentiated singers according to the complexity of their performance, in such a way that high-performance singers employed BA 6 with less intensity. Therefore, this study demonstrated that the professional singers' training did not solely include high-performance vocals and pitch adjustments, but rather changed areas of the brain required for this process, making the acts of singing and speaking more independent from one another. Briefly, training processes directed toward the development of singing ability are required to work on activities that explore various neural mechanisms.

Callan et al.¹⁶ also analyzed cerebral regions involved in the perception and production of speech and singing through fMRI. The authors accepted the premise that to sing, one needs to use the auditory-motor system and memory mechanics more intensely, thus accepting that this activity is more complex than speech. The study included 16 subjects (5 of whom were women), aged 19-47 years, who were right-handed and without any previous musical experience or training. The stimulus consisted of listening to six Japanese songs with the simultaneous presentation of the lyrics. Next, each

participant had to read and sing the song presented on a screen, while their brain activity was recorded using fMRI. Among the most important findings was the observation that there was an overlap in the cerebral regions involved in the perception and production of song and speech, denoting the existence of an essential identity between lyrical song and speech. This suggested a mirrored neuronal system, capable of being activated by silently listening to music and producing a song. According to the authors, the most important finding was the increased activity in the right planum temporale during singing, compared to speaking, both for passive auditory perception and for production of songs, indicating that this brain region responded through the representative transformation between the auditory and motor domains. Another important finding of this study was regarding laterality, and statistical analysis of active voxels gave the conclusion more credibility. The authors identified more activity in the left temporal lobe during speech than during singing, which was comparable during listening or production of singing. Further, there was greater activity in the right lobe during singing than during speech.

Zarate, Wood, and Zatorre⁴ proceeded with a study employing fMRI to study professional opera singers, with the intention of identifying brain regions used for voluntary and involuntary correction of the pitch by means of vocal motor integration. Initially the authors emphasized the importance of considering the constellation of neural structures involved in adjusting the *pitch* while singing. This complex network included motor/pre-motor cortical networks (including the primary motor cortex, supplementary motor area, and anterior cingulate cortex), subcortical regions (such as the basal ganglia and thalamus), as well as structures in the brain stem, including the periaqueductal gray matter, substantia nigra, the reticular formation, and the band of motor neurons. This entire network of structures and their interconnections were involved in the production of correct pitch, as seen in loud environments where the interlocutors augmented or reduced the intensity of their speech to facilitate communication without losing the emotion of the message. The authors⁴ compared 11 healthy subjects with no hearing problems and no history of singing with 13 professional singers, who were also healthy, with no hearing problems. The participants listened to their vocalizations with altered pitch and corrected their pitch if required. They were asked to maintain the pitch if no correction was needed. The fMRI results demonstrated that activation

of the anterior portion of the rostral cingulate zone was required for the discrete correction of pitch. For tasks where no pitch correction was needed, activation of the posterior superior temporal sulcus was observed. However, this correction was not present in the opera singers. This suggested that large pitch corrections are voluntary, while smaller corrections are involuntary and occur due to an interaction between two cerebral areas, preceding the voluntary correction mechanism. These data revealed the extent of the complexity of the process of frequency modulation and the diversity in the areas of the brain that are involved in this complex vocal activity.

Zarate et al.^{2,4} demonstrated the existence of an organization of neural networks for the perception of music and speech, which suggested the modulation of musical and speaking abilities. The basis of their study was the assumption that professional singers and actors have intensively trained voices, which they use in different semantic, syntactic, and emotional processing contexts. Rosslau et al.¹⁵ was also a pioneer in analyzing the neural modifications required for singing and speech processing, induced by training. They used magnetoencephalography to evaluate brain activity, due to its high sensitivity in the evaluation of tempos and medium-to-high accuracy in determining the sources of brain activity during tasks. The researchers evaluated 15 singers (of whom 8 were women) and 15 actors (9 of whom were women), with a mean age of 29.2 years and 32.4 years, respectively. All the participants had more than 4 years of professional experience and practiced for at least 4 h daily.

Each participant had to judge the accuracy of the semantic congruity and the pitch of the last word of a song or spoken stimulus, and press a button to indicate the correctness or incorrectness of the stimulus. The participants underwent magnetoencephalography while completing the tasks. At the end of the experiment, each participant responded to a semi-structured interview to evaluate how fatigued they became when judging words and pitch. The authors identified the existence of a global syntactic system, which governed melodic and prosodic aspects. The right hemisphere was dominant if the factors involved violation of pitch. Comparatively, the right temporal area were dominant in the presence of musical alterations that required concentrated attention to analyze the frequency. Although these findings pertained to both singers and actors, more activity in the left parietal and right temporal areas were identified exclusively in singers.

This was attributed to more intense mental machinery and a strong command of musical cognition, which could be attributed to extensive training or is a mere prerequisite for this professional activity.

In addition to studies on pitch and harmony, a study on the neural basis of rhythm was also conducted by Jungblut et al.¹⁸. A total of 30 non-musical and healthy subjects were analyzed in the study and they underwent fMRI while rhythmically repeating vowels sung in monotone. The results demonstrated that the same areas involved in speech (i.e., the bilateral supplementary motor area, cingulate gyrus, and pre-motor cortex in the left hemisphere) were activated in the rhythmic emission of vowels. However, the bilateral pars orbitalis and left cingulate gyrus were also responsible for rhythmic complexity.

Some studies have also attempted to functionally investigate aspects, and the respective cerebral areas, which are related to emotions in the voice, to access intentions and feelings that are imprinted in the dynamics of communication,^{20,21} which can differ from the emotion elicited through song. However, further research is required on this topic.

CONCLUSION

Following a variable rhythm, harmonizing voices, and controlling fundamental frequency makes singing a unique human ability. It is a complex cerebral activity that combines the emission of speech and musicality, since it blends linguistic and acoustic components in a variety of ways.

Analyzing the areas of the brain involved in singing is challenging given the interconnection of cerebral areas and superimposition required to elicit speech and singing. Thus, the use of neuroimaging is of fundamental importance in enabling the identification of the brain areas and hemispheric lateralization that is activated by singing. Although there has been an advancement in this field over the past two decades, there is still a large knowledge gap, which still needs to be filled.

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