

# How far are we in understanding neuroscience and voice

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# Introduction

The fluency and the reliability of voice production depends on a mechanism that links motor commands and sensory feedback, as the main signal processing. Studies of the neural organisation of fMRI identifies regions where activity during speech production is modulated and where predicted outcome is regulated.

We have earlier studied phonetograms of young brain damaged people, showing no intensity modulation of frequency in a two octave test.

We have also shown a relationship between measurements of high speed films and pharmacological treatment in dystonia patients.

The focus here is to get on to understand how neuroscience aspects can help us in in treatment documentation.

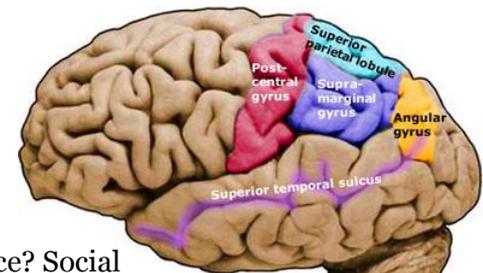
Pedersen MF (1995) Stimmfunktion vor und nach Behandlung von Hirngeschädigten. Mit Stroboskopie,Phonetographie und Luftstrom analyse durchgeführt. Sprache Stimme gehör; 19:84-9

Pedersen M, Eeg M (2012) Does treatment of the laryngeal mucosa reduce dystonia symptoms? A prospective cohort study of mannose binding lectin and other immunological parameters with diagnostic use of phonatory function studies. European Archives of otorhinolaryngology; 260:1477-82

# The origin of voice function.

## Voice evolution and neuroscience

- Voice is one of the most important stimuli to our environment, it carries information that is important for survival and social communication.
- The neuroanatomy of voice and speech is complex. An intricate neural network is responsible for ensuring the main function of the larynx: airway protection, cough and voice. Some examples of diseases that affect laryngeal function are given.
- Studies by using *functional near-infrared spectroscopy (fNIRS)* and *(fMRI)* showed that 7 month olds, but not 4 month olds, demonstrate increased response in right and left superior temporal cortex.  
This suggests that the infant brain becomes tuned to processing specific vocal information between 4 and 7 months age.



# Musicians and music making

## Neuroscience aspects

- It is proven by neuroimaging studies that musicians with extensive music training, and playing experience provide an excellent model for studying plasticity of the human brain, because they have a rich multisensory and motor function.
- There have been many studies that confirm musicians develop better reading, memory, finger tapping, vocabulary skills and increased IQ, than non-musicians. Furthermore musicians show good skills in mathematical performance till now confirming the hypothesis that it is because of shared neural resources involved in the mental manipulation and symbolic representation.
- A study that examined structural differences between musicians and non-musicians reported *larger anterior corpus callosum* in musicians, this finding has since been replicated by different researchers and still it is *not clear* what exactly is the reason behind musicians developing some extra skills.
- By using functional magnetic resonance (fMRI) to compare musicians with non-musicians, differences in activity have been observed across many brain regions. The *left superior temporal gyrus* is identified as the region that is linked with musical training.

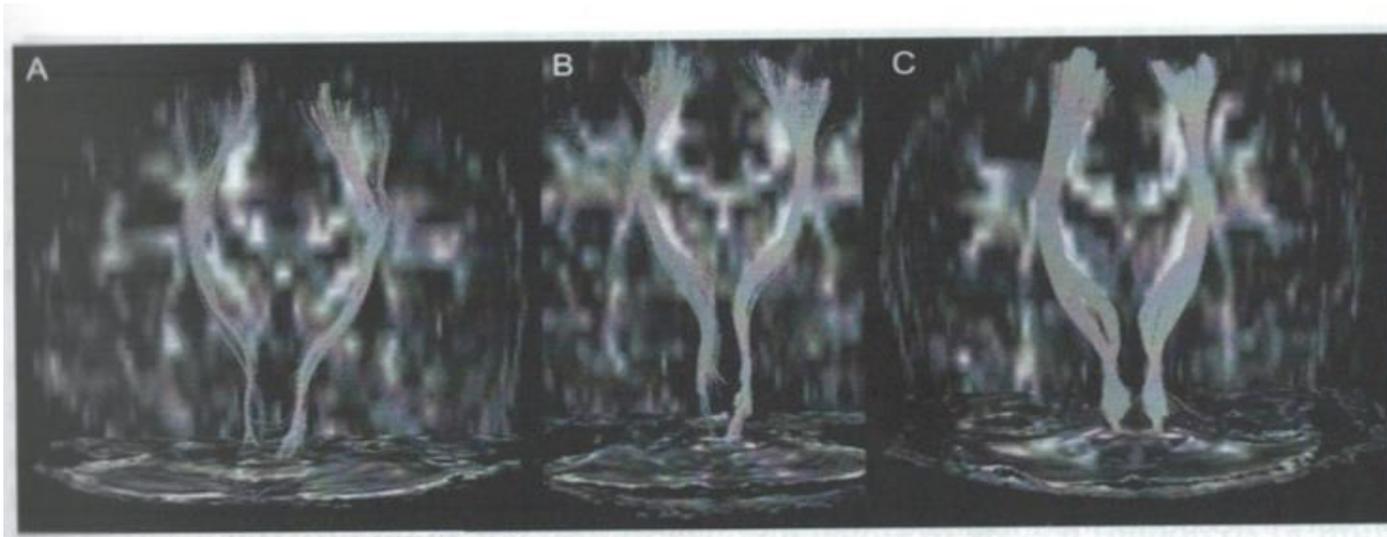
# How fMRI works

for those who do not know

- fMRI is based on the same technology as magnetic resonance imaging (MRI) – a noninvasive test that uses a strong magnetic field and radio waves to create detailed images of the body. But instead of creating images of organs and tissues like MRI, fMRI looks at blood flow in the brain to detect areas of activity. These changes in blood flow, which are captured on a computer, help doctors understand more of how the brain works.
- The first commercial MRI scanner was produced in 1980. Then in the early 1990s the physicist Seiji Ogawa who was working at the Bell Laboratories in New Jersey USA found, that oxygen-poor hemoglobin ( the molecule in blood that carries oxygen) was affected differently by a magnetic field than oxygen-rich hemoglobin- based on the works by Linus Pauling in the 1930s.
- These contrasts could be used in responses of brain activity in normal MRI to determine which parts of the brain are most active.

# Musicians and music making

## Neuroscience aspects



With training musicians get many afferent stimuli to the brain, which results in that the brain adapts - and improves the corticospinal tract which is a descending efferent motor pathway carrying signals from the brain down the spinal cord to the target muscle or organ.

A: Corticospinal tract of a non-musician child.

B : Corticospinal tract of a non-musician adult.

C: Corticospinal tract of an adult musician.

# Music as a driver of brain plasticity

- Music is one of the richest human emotional, sensory-motor and cognitive experience and one of the main drivers of brain plasticity because it involves listening, watching, feelings, moving and coordinating, remembering etc. All these functions are recognized at different places in the brain, which evolve the brain plasticity. It is this multisensory brain representation, which constitutes the typical musical experience.
- The emotional network, including the basis and the *inner surfaces of the two frontal lobes*, the *cingulate gyrus* and brain structures in the evolutionary old parts of the brain such as the *amygdala, hippocampus and the midbrain*, are crucial for the emotional function of music and therefore for an individual's motivation to listen to or for any musical activity.
- The *cerebellum* (little brain) also plays an important role in different cognitive tasks especially when they include demands on timing. Typically the cerebellum is activated in rhythm processing.

# Litterature search

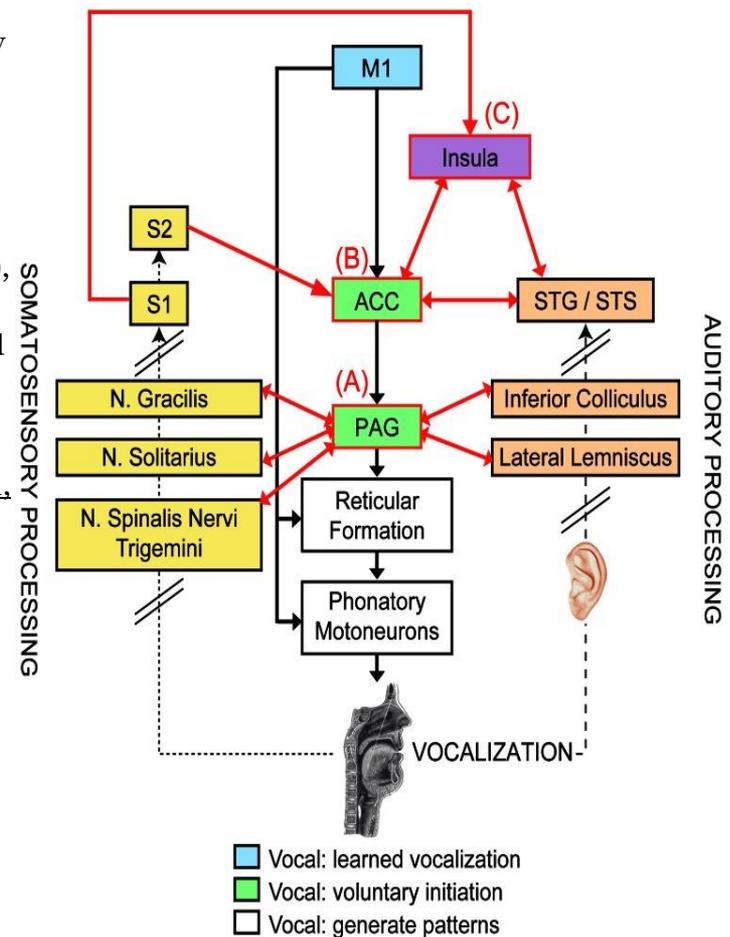
- We have made a research at British Library London and found 845 references with the search words: Neuroscience and voice – for the latest 5 years.
- This shows that the area has some scientific interest.

# Neuroscience of voice - how much do we know

1. Motor and sensory control systems of voice production.
2. Superior temporal and middle temporal gyri activation during voice function
3. Fluency and reliability of voice production examined by fMRI.
4. Structural brain changes related to bilingualism
5. The cortical-subcortical network underlying angry vocalizations.
6. Meta analysis of fMRI studies
  
7. *Combined with nanoscopic measures of voice regulation from the larynx (optical coherence tomography) – hormones and immune systems ?*

# Motor and sensory control systems of voice production

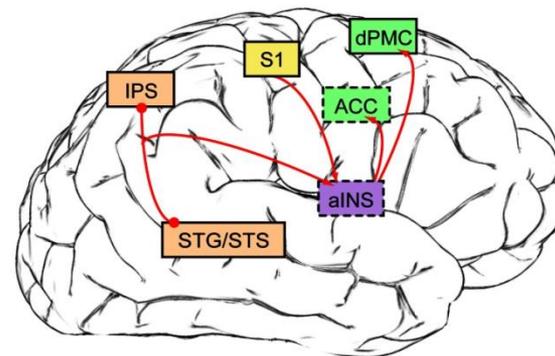
- The vocal motor control hierarchy starts with the generation of complete vocal patterns from the reticular formation and phonatory motor neurons (white boxes)
- the next highest level of control (green boxes) stems from the anterior cingulate cortex (ACC) and periaqueductal gray (PAG), which can initiate and emotionally motivate vocal responses.
- The highest level of vocal control comes from the primary motor cortex (M1, blue box; its modulatory brain regions are not depicted), which is responsible for producing learned vocalizations.
- Somatosensory feedback (arrow) from various receptors distributed throughout the vocal tract is processed in the ascending somatosensory pathway (yellow boxes, left; black slanted lines indicate that only selected regions of this pathway are shown) and transmitted to the primary and secondary somatosensory cortex (S1, S2).
- Auditory feedback (arrow) from the vocalization is processed by the ascending auditory pathway and auditory cortical regions (orange boxes, right).
- Potential neural regions that integrate sensory feedback processing with vocal motor control are indicated with red-outlined boxes, and their shared connections are represented by red arrows: (A) the PAG, (B) ACC, and (C) the insula (in purple, classified as a higher-order associative area).



# Motor and sensory control systems of voice production

1. Within the functional network, cortical substrates are specific for the sensory-motor control of singing pitch sensitive to the amount of vocal training which have been identified as *IPS for auditory processing and transformation for motor output* (orange box), *S1 for somatosensory processing* (yellow box), *anterior insula* (both for auditory-motor integration and somatosensory feedback gating; purple box), and premotor regions for vocal motor preparation and response initiation (dPMC and ACC; green box)

TRAINING-SENSITIVE  
 SENSORY-MOTOR AREAS FOR SINGING



# Motor and sensory control systems of voice production

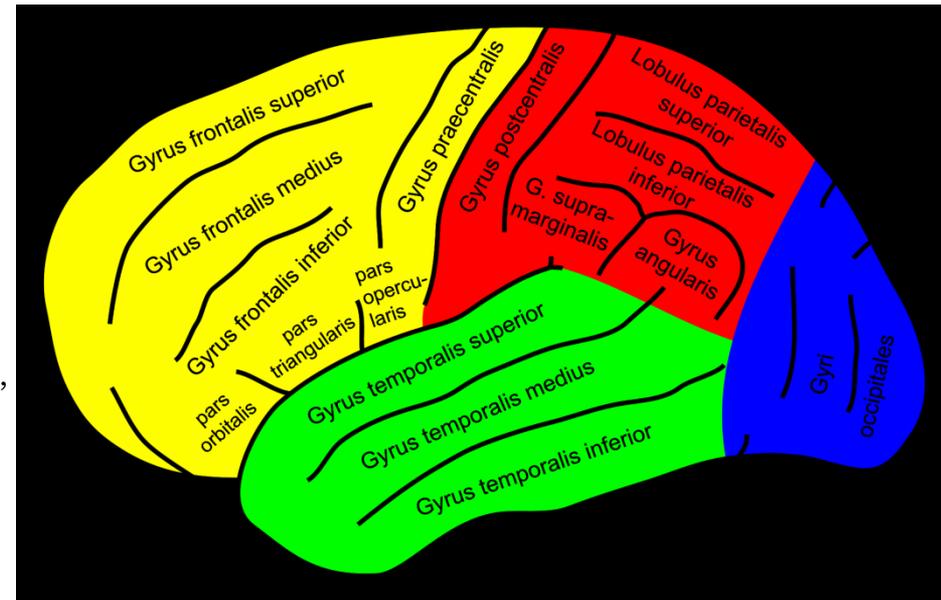
- When the auditory-related findings are placed within a larger framework – a dual pathway (i.e. perception vs. production), sensory model for singing can be made.
- These music findings can be then be linked to broader research interests in auditory cognition, such as auditory spatial localization and speech perception/production, due to the auditory-motor control network's similarity to prevalent dual-stream models of auditory processing as a whole.

# Superior temporal and middle temporal gyri activation during voice function

- The middle temporal gyrus and inferior temporal gyrus serve language and semantic memory processing
- Middle temporal gyrus and inferior temporal gyrus gray matter volumes were measured in 28 healthy male subjects by using high-spatial-resolution MRI.

## Superior temporal gyrus:

- The superior temporal gyrus contains the primary auditory cortex, which is responsible for processing sounds. Specific sound frequencies map precisely onto the primary auditory cortex.
- This auditory (or tonotopic) map is similar to the homunculus map of the primary motor cortex.
- Specialized for processing combinations of frequencies.
- Specialized for processing changes in amplitude or frequency.
- Essential structure involved in auditory processing as well as in the function of language in individuals.
- Is an important structure in the pathway consisting of the amygdala and prefrontal cortex, which are all involved in social cognition processes.



# Fluency and reliability of voice production examined by fMRI

- fMRI was used to identify regions in which activity during voice production are modulated according to whether auditory feedback matches the predicted outcome or not and by examining the overlap with the network recruited during passive listening to voice sounds.
- Activity along the superior temporal gyrus bilaterally was significantly greater if the auditory stimuli was
  - (a) processed as the auditory concomitant of speaking and
  - (b) did not match the predicted outcome.
- The network exhibiting this Feedback Type: Production/Perception interaction includes a superior temporal gyrus/middle temporal gyrus region that is activated more when listening to speech than to noise.

# Structural brain changes related to bilingualism

- It has been shown that early lifelong bilingualism affects the structure of white matter (WM) of the brain and preserves its integrity in older age. Furthermore similar WM effects were also found in bilingual individuals who learned their second language later in life.

Pliatsikas C. Moschopoulou E. and Saddy JD. (2014) ed. Kuhl PK( 2014) *The effects of bilingualism on the white matter structure of the brain*, Proceedings of the National Academy of Science: 1334-37

- Bilingualism places demands on the integration of motor and sensory discharges not encountered when articulating in the voice of the most fluent language.
- This involves re-tuning the neural circuits in the motor control of articulation to enable rapid unfamiliar sequences of movements to be performed.
- Changes in motor networks is experience-dependent plasticity in auditory and somatosensory cortices - to integrate auditory memories of the target sounds, copies of feed forward commands from premotor and primary motor cortex and post-articulatory auditory and somatosensory feedback.

# The cortical-subcortical network underlying angry vocalisations

- Participants were asked both to repeat and express high- rousing angry vocalizations to command to study fMRI.
- First repeated expressions elicited activity in the left middle superior temporal gyrus (STG) pointing to a short auditory memory trace for the repetition of vocal expressions. Evoked expressions activated the left hippocampus suggesting the retrieval of long term stored scripts.
- Secondly angry compared with neutral expressions elicited activity in the inferior frontal cortex (IFC) and the dorsal basal ganglia (BG). Angry expressions also activated the amygdalae and anterior cingulate cortex (ACC).
- Finally different acoustic measures of angry expressions were associated with activity in the left STG, bilateral inferior frontal gyrus and dorsal BG

Frühholz D, Klaas HS, Patel S, Grandjean D (2015). Talking in Fury: The cortical-subcortical network underlying angry vocalizations. *Cereb Cortex*;25 (9) : 2752-62

Earlier: Ethofer T, Brettecher J, Gschwind M, Kreifelts B, Wildgruber D, Vuilleumier (2012) Emotional voice areas: anatomic location, functional properties, and structural connections revealed by combined fMRI and DTI. *Cereb Cortex*; 22:191-200

# Meta-analyses of fMRI studies

- Reliability in cognitive neuroscience.
- The provocative book challenges the bulk of fMRI research aiming to find a mapping of cognitive function onto brain regions that is consistent and stable across individuals, the aspect is that neuroimaging continues to develop
- (quote Ed Vul, Dept. of Psychology, Univ. of California San Diego).

# Pathology

- A: Dementia
- B: Stroke
- C: Autism
  
- Specific training of motor control
  
- Endoscopic visualisation of the larynx using a dynamic voice assessment is a crucial part of the evaluation

# Dementia

- There are some aspects of therapeutic effects of singing (Melodic intonation therapy) in neurological disorders. Music listening and music making activities are powerful tools to engage multisensory and motor networks.
- The underlying neurological mechanisms are not only the plasticity of the fMRI documented changes of corpus callosum and other areas that are stimulated – also neurochemical measures of dopamine and serotonin changed as documented with PET scans

# Stroke

- White matter changes were shown in patients with non fluent aphasia after intensive intonation-based therapy.
- Reduction in fractional anisotropy was seen in the right inferior frontal gyrus and posterior superior gyrus.
- Improvements in speech fluency were associated with reduction in fractional anisotropy in right inferior frontal gyrus.
- Changes were not seen in a control group of patients scanned twice without any particular therapy between two time points.

# Autism

- The purpose was to examine the development of outcomes of children 7 years after their initial diagnosis at 2 years of age.
- Early characteristics that predicted outcome status were age of diagnosis, age 2 cognitive and language scores and total hours of voice speech language therapy between 2-3 years of age.
- At the follow up 32% were able to engage in conversational exchanges

# Specific training of motor control

- Patients were encouraged to play melodies with a paretic hand on a piano or to tap with a paretic arm on eight electronic drum pads that emitted piano tones –
- It was demonstrated that these patients regained faster their motor abilities of timing, precision and smoothness of fine motor skills.
- Along with fine motor recovery an increase in neuronal connectivity between sensor –motor auditory regions was demonstrated by means of EEG-coherence measures.

# Music rehabilitation systems

- **Rhythmic auditory stimulation (RAS)**
  - The key element of RAS is the phenomenon of auditory entrainment, that is, the body's ability to synchronize its movements rhythmically. External auditory activity is mediated by internal unconscious perceptual shaping at the subcortical level, and can arouse and raise the excitability of spinal motor neurons mediated by auditory-motor circuitry at the reticulospinal level.
  - Kwak, E. (2007). Effect of Rhythmic auditory stimulation on gait performance in children with spastic cerebral palsy. *J. of Music Therapy*. 198-216. (Gait means walking patterns).
  - Stahl, B., Kotz, S.A., Henseler, I., Turner, R., Geyer, S. (2011). Rhythm in disguise: why singing may not hold the key to recovery from aphasia. *Brain*; 134, 3083-3093. (Disguise means hidden).
- **Patterned sensory enhancement (PSE)**
  - Regulates functional movement by translating the temporal, spatial and force-dynamic components of movement kinematics into sound patterns, similar to sonification patterns in high performance athletic training, and then plays them back to provide feedback and feedforward regulation for enhanced motor control.
  - Studies based on PSE for home-bound stroke patients by measuring the level of upper extremity function, depression, and interpersonal relationship prove that the PSE upper extremity exercise program for home-bound stroke patients was an effective strategy for enhancing upper extremity function, decreasing the depression level, and improving interpersonal relationships.
  - Hong, M. (2011). The development and effect of an upper extremity exercise program based on patterned sensory enhancement for home-bound stroke patients. *Journal of Korean academy of community health nursing*; vol.22:192-203.
- **Melodic intonation therapy (MIT) and neurological music therapy (NMT)**
  - Is a therapeutic process used by music therapists and speech pathologists to help patients with communication disorders caused by brain damage. This method uses a style of singing called melodic intonation to stimulate activity in the right hemisphere of the brain in order to assist in speech production.
  - Carroll, D. (1996). A study of the effectiveness of an adaptation of melodic intonation therapy in increasing the communicative speech of young children with down syndrome. A thesis, McGill University, Montreal, Canada.
  - Thaut, M. H., Hoemberg, V. Eds. (2014). *Oxford Handbook of Neurologic Music Therapy*. Oxford University Press, Oxford, UK.

# In a clinical situation of neuroscience and voice - accept research results

- Yes the understanding of the vocal folds is still important
- Yes the understanding of voice physiology is important
- Yes the understanding of brain regulation is important
  
- But gene understanding and pharmacological support might be more important
- But hormonal regulation might be more important as in development of voice
- But the immune system might be more important since remembrance seems to be depended hereon

Find the slides on: <http://www.mpedersen.org>

Thank you for your attention!